Journal of Organometallic Chemistry, 369 (1989) 291–296
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands
JOM 09928

A Barbier allylation and a Reformatsky reaction of carbonyl compounds mediated by indium(I) iodide

Shuki Araki, Hirokazu Ito, Nobuhito Katsumura, and Yasuo Butsugan *

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466 (Japan)

(Received January 11th, 1989)

Abstract

Indium(I) iodide was found to mediate in the Barbier allylation and in the Reformatsky reaction of aldehydes and ketones to give homoallylic alcohols and β-hydroxy esters, respectively, presumably via allylindium(III) diiodide.

Introduction

Despite a growing interest in the use of heteroatom elements in synthetic chemistry, indium still remains an unfamiliar element to organic chemists. We recently described that metallic indium is effective in Barbier allylation [1] and Reformatsky reaction [2] of aldehydes and ketones to give homoallylic alcohols and β-hydroxy esters, respectively, in high yields. In these reactions, indium sesquihalide ($R_3In_2X_3$) is suggested to be the key intermediate and only two of the three R groups are transferred to carbonyl compounds, the remaining R group is unused. From a synthetic standpoint, this is a serious disadvantage to be overcome. We have now found that when indium(I) iodide is used in place of metallic indium in such coupling reactions, the organic halides are quantitatively utilized in the nucleophilic addition to carbonyl compounds.

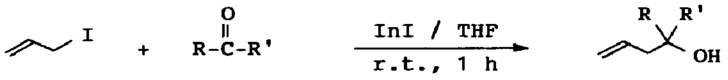
Results and discussion

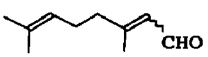
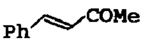
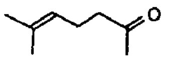
Barbier allylation. A mixture of a carbonyl compound (1.0 mmol), allyl iodide (1.2 mmol), and indium(I) iodide (1.2 mmol) in tetrahydrofuran (THF) was stirred at room temperature for 1 h. After an aqueous work-up, the product was purified by column chromatography to give a homoallylic alcohol. Results for various aldehydes and ketones are listed in Table 1. Although an equimolar amount of allyl iodide gave satisfactory yields, a slight excess (1.2 equiv.) of allyl iodide gave the best

0022-328X/89/$03.50

Table 1

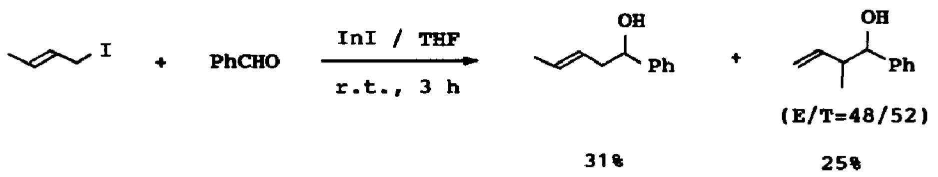
Indium(I) iodide-mediated allylation of carbonyl compounds [a]



Carbonyl compound	Yield (%)
$Me(CH_2)_6CHO$	83
PhCHO	74
$4\text{-}ClC_6H_4CHO$	68
$4\text{-}MeOC_6H_4CHO$	93
$2\text{-}HOC_6H_4CHO$	96
	91[b]
	88[b]
$Me(CH_2)_5COMe$	69
	80[c]
	83[b]
PhCOMe	69
$MeCOCH_2CO_2Et$	84
	73

[a] All the reactions were carried out using allyl iodide (1.2 mmol), carbonyl compound (1.0 mmol), and indium(I) iodide (1.2 mmol) in THF (1 ml). [b] 1,2-Addition only. [c] Axial/equatorial alcohol 81/19.

results. As shown in Table 1, the yields are generally high even for substrates having an active hydrogen such as ethyl acetoacetate and salicylaldehyde. This suggests that the basicity of the intermediate organoindium species is lower than that of organolithium and -magnesium reagents. α,β-Unsaturated carbonyl compounds gave exclusively 1,2-addition products. 4-t-Butylcyclohexanone gave an 81 : 19 mixture of the axial and equatorial alcohols. These properties of indium(I) iodide are similar to those of metallic indium [1], but the regioselectivity of the coupling of allylic halides is better for indium(I) metal than for indium iodide. Indium(I) iodide-mediated reaction of crotyl iodide (1-iodo-2-butene) with benzaldehyde yielded both the α- and γ-coupling products in a 55 : 45 ratio (eq. 1). With metallic indium, only γ-coupling occurred [1]. Crotyl bromide and cinnamyl bromide (3-bromo-1-phenyl-1-propene) also gave α- and γ-coupling mixtures (eq. 2 and 3), though the reactions



(1)

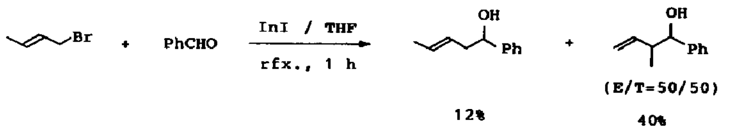
of these bromides were slower than with allylic iodides and in addition required refluxing in THF. THF is the solvent of choice for indium(I) iodide, *N*,*N*-dimethylformamide (DMF) gave the products in less satisfactory yields.

The intermediate species of our indium(I) iodide-mediated Barbier coupling is probably allylindium(III) diiodide which is formed by the oxidative addition of indium(I) iodide to allyl halide (eq. 4) [3]. Allylindium(III) diiodide has been

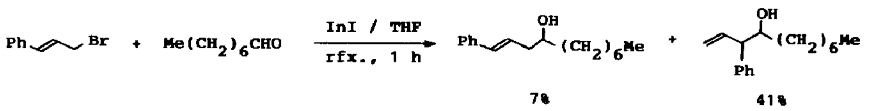
(4)

prepared from allyl iodide and indium(I) iodide by Gynane et al. [4], but no spectral data were reported. We treated allyl iodide with indium(I) iodide in THF-d_8 in the absence of carbonyl compounds. The 200 MHz ^{1}H NMR spectrum (Fig. 1) of the product revealed signals at δ 2.14 (2H, d, J 8 Hz, CH_2In), 4.75 (1H, dd, J 10, 2 Hz, olefin H), 4.92 (1H, dd, J 16, 2 Hz, olefin H), and 5.96 (1H, m, olefin H). Evaporation of the solvent left a white semi-solid which showed absorptions at 455, 204, 188, 147, and 79 cm^{-1} in the far infrared region. These spectral data are consistent with the formulation of allylindium(III) diiodide for this product [5]. The reaction of this semi-solid with cinnamaldehyde in THF (room temperature, 4 h) gave 1-phenyl-1,5-hexadien-3-ol in 59% yield.

Reformatsky reaction. Indium(I) iodide was also found to be effective for Reformatsky-type reaction. As summarized in Table 2, various types of aldehydes and ketones gave the corresponding β-hydroxy esters by the reaction of ethyl iodoacetate-indium(I) iodide in THF. The Reformatsky reaction is slower than the above Barbier allylation, thus requiring longer reaction time (3–44 h at room temperature). The characteristics of this reaction are: (1) α, β-unsaturated carbonyl



(2)



(3)

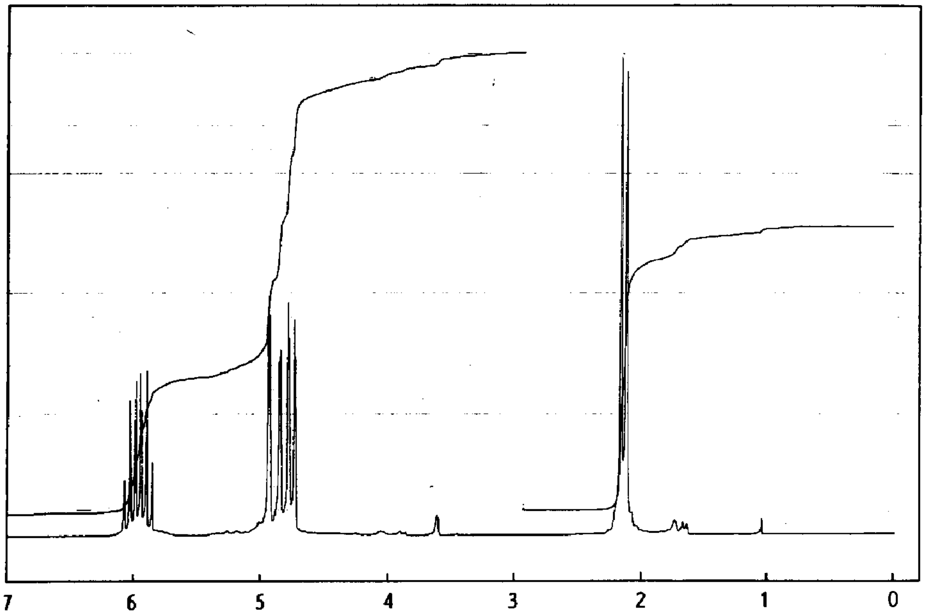
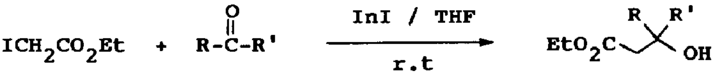
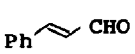
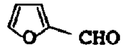
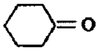
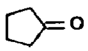


Fig. 1. ^{1}H NMR spectrum (200 MHz, in THF-d_8 at −9 °C) of $CH_2{=}CHCH_2InI_2$ prepared from allyl iodide and indium(I) iodide.

Table 2

Indium(I) iodide-mediated Reformatsky reaction of carbonyl compounds [a]



Carbonyl compound	Reaction time (h)	Yield (%)
$Me(CH_2)_6CHO$	22	69
$Me(CH_2)_2CHO$	21	58
PhCHO	3	75
$2\text{-}HOC_6H_4CHO$	21	50
	17	100[b]
	21	93
	44	79
	41	52
PhCOMe	26	66
$4\text{-}O_2NC_6H_4COMe$	23	37
$4\text{-}MeC_6H_4COMe$	44	69

---

[a] All the reactions were carried out using ethyl iodoacetate (1.2 mmol), carbonyl compound (1.0 mmol), and indium(I) iodide (1.2 mmol) in THF (1 ml). [b] 1,2-Addition only.

compounds undergo exclusively 1,2-addition, (2) hydroxyl groups in the substrate need not be protected, (3) no reaction occurs when ethyl bromoacetate is used in place of the iodide, and (4) the corresponding α,β-unsaturated esters (Wittig-type product) are not formed. These features are very similar to those of the indium-metal-induced Reformatsky reaction [2]; however, only a slight excess (1.2 equiv.) of the iodoacetate is sufficient for obtaining satisfactory yields. Again, the intermediacy of organoindium(III) diiodide is highly probably in this Reformatsky reaction.

Although expensive, indium(I) iodide is commercially available and, if necessary, it can be readily prepared from indium metal and iodine [6]. Our finding that with indium(I) iodide organic halides are quantitatively utilized in the allylation of carbonyl compounds and the synthesis of β-hydroxy ester must enhance the usefulness of organoindium chemistry in organic synthesis.

Experimental

Indium(I) iodide was purchased from Morton Thiokol, Inc., Alfa Products, and used as received. THF was dried with lithium aluminum hydride and distilled immediately before use. All the reactions were conducted under argon.

Indium(I) iodide-mediated Barbier allylation of carbonyl compounds

The following reaction of allyl iodide and cinnamaldehyde represents the general procedure. To a suspension of indium(I) iodide (293 mg, 1.2 mmol) in THF (1 ml) was added a mixture of allyl iodide (202 mg, 1.2 mmol) and cinnamaldehyde (132 mg, 1.0 mmol). An exothermic reaction occurred immediately. The mixture was stirred at room temperature for 1 h and quenched with dilute hydrochloric acid (1 *M*, 3 ml). The product was extracted with ether (20 ml × 3), washed successively with aqueous sodium thiosulfate, water, and brine, and then dried over anhydrous sodium sulfate. After evaporation, the residue was chromatographed on silica gel (eluent: dichloromethane) to give 1-phenyl-1,5-hexadien-3-ol (159 mg, 91% yield). All the other reactions were carried out similarly. All the products obtained in this work are known compounds, so the structures were determined by comparison of their spectral data with those given in the literature [7].

Indium(I) iodide-mediated Reformatsky reaction

The following reaction of ethyl iodoacetate and benzaldehyde represents the general procedure. To a suspension of indium(I) iodide (293 mg, 1.2 mmol) in THF (1 ml) were added ethyl iodoacetate (262 mg, 1.2 mmol) and benzaldehyde (107 mg, 1.0 mmol). The mixture was stirred at room temperature for 3 h. After the addition of hydrochloric acid (1 *M*, 3 ml), the product was extracted with ether (20 ml × 3). The extracts were washed with water and brine, and dried (Na_2SO_4). Column chromatography (SiO_2-CH_2Cl_2) furnished ethyl 3-hydroxy-3-phenylpropionate (145 mg, 75% yield). All the other reactions were carried out similarly and the structures of the products were confirmed from their spectral data or by direct comparison with the authentic samples prepared by standard methods [2,8].

References

1 S. Araki, H. Ito, and Y. Butsugan, J. Org. Chem., 53 (1988) 1831.

2 S. Araki, H. Ito, and Y. Butsugan, Synth. Commun., 18 (1988) 453.

3 J.S. Poland and D.G. Tuck, J. Organomet. Chem., 42 (1972) 315; M.J.S. Gynane, L.G. Waterworth, and I.J. Worrall, ibid., 43 (1972) 257.

4 M.J.S. Gynane, L.G. Waterworth, and I.J. Worrall, Inorg. Nucl. Chem. Lett., 9 (1973) 543.

5 For a review on the structures of organoindium compounds, see: D.G. Tuck, Gallium and Indium in G. Wilkinson (Ed.), Comprehensive Organometallic Chemistry, Chap. 7, 1982, pp. 683–723.

6 L.-C. Chao and R.D. Rieke, J. Organomet. Chem., 67 (1974) C64.

7 S. Araki, H. Ito, and Y. Butsugan, J. Organomet. Chem., 347 (1988) 5, and references cited therein.

8 R.L. Shriner, Org. React., 1 (1942) 1; R.D. Rieke and S.J. Uhm, Synthesis, (1975) 452; T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, and M. Yokoyama, J. Org. Chem., 49 (1984) 3904.