The Employment of Indium Nanoparticles in Barbier-type Reaction of Allylic Chloride in Water

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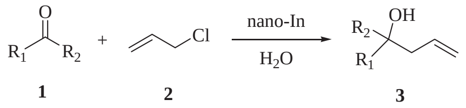
(Received January 30, 2006; CL-060130; E-mail: zwang3@ustc.edu.cn)

Indium nanoparticles have been employed in the reactions of various carbonyl compounds with allyl (crotyl) chloride in water, affording the corresponding alcohols with high yields. The crotylation gave exclusive γ-adducts with a dominant *syn*-isomer.

Organic reactions in aqueous media have been attracting much attention with the time going, and have become one of the important branches in green chemistry.[1,2] Of them, the allylations in aqueous media are investigated widely because the allylations are one of the most important methods to form carbon–carbon bond and to give the corresponding homoallylic alcohols.[3] However, the scope of allylic substrates has usually been limited in the active allyl bromide or iodide.[4] On the other hand, metal nanoparticles have been attracting more and more attention in material chemistry because of the remarkable electronic, magnetic, optical, biological, mechanical, and catalytic properties over the last decade.[5] The smaller the cluster of atoms, the higher the percentages of atoms are on the surface, particularly rendering nanoparticles specially active in catalysis and mediator.[6] Our previous work revealed that nano-sized metal particles, such as nano-Sn and nano-Bi, exhibited promoting activity in allylation reaction of active allyl bromide with carbonyl compounds.[7] However, nano-Sn or nano-Bi did not work well to mediate the allylation of allyl chloride or crotyl chloride with benzaldehyde in water. The indium-mediated allylation is also sluggish with the chloride, and acyclic ketones are usually not sufficiently reactive and thus require longer reaction time.[8] We report herein the successful allylations of various carbonyl compounds with allyl/crotyl chloride promoted by indium nanoparticles in water.

Initially, the allylation of benzaldehyde with allyl chloride was carried out in the mediation of granular indium, affording the corresponding adduct in the yield of 22%. It was assumed that this low yield resulted from the small surface area of the granular indium. Therefore, 200 mesh of indium powder was employed to mediate this reaction. As expected, the reaction yield was improved to 47%. This encouraged us to investigate this reaction further. About 100 nm of indium nanoparticle[9] was employed in this allylation. As a result, the allylation product was obtained with 85% yield while the reaction time was decreased to 10 h. To extend the scope of the reaction substrates, different aldehydes were tested in this allylation. It was found that not only aromatic aldehydes (Table 1, entries 1–9) but also aliphatic ones (Table 1, entries 10 and 11) were allylated smoothly under this condition, giving the corresponding adducts in good to excellent yields. In comparison with 200 mesh of indium, indium nanoparticles are more effective in mediation of the allylations regardless of the difference of the aldehydes. Subsequently, crotylation was investigated under the same condition in order to extend the scope of the allylic chloride. The corresponding results are summarized in Table 2. From Table 2, it was found that crotylations of both aldehyde and ketone were carried out smoothly in the mediation of indium nanoparticles, affording the corresponding alcohols with high yields while the reaction mediated by 200 mesh of indium gave the corresponding product with moderate or poor yields (Table 2, entries 1–18). Also, the corresponding reaction rate was increased remarkably. More importantly, the crotylation of the ketones was improved largely in comparison with that mediated by 200 mesh of indium (Table 2, entries 13–18), which indicated that indium nanoparticles is more effective to ketones than to aldehydes in the mediation of this crotlytion. Also, it was noted that hydroxy group, which contained active proton, need not to be protected and survived during the crotylation (Table 2, entries 4, 12, and 16).

Table 1. The allylation of carbonyl compounds mediated by indium nanoparticles and 200 mesh In in water



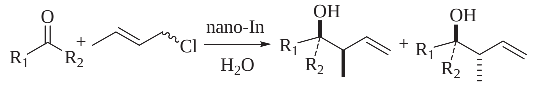
Entry	R_1	R_2	Yield[a]/%/Time/h Nano-In	200 mesh In
1	C_6H_5	H	85/10	47/24
2	2-ClC_6H_5	H	95/10	71/20
3	4-ClC_6H_5	H	78/10	55/20
4	2-HOC_6H_5	H	99/10	56/20
5	4-$CH_3OC_6H_5$	H	96/10	47/20
6	2-$CH_3OC_6H_5$	H	75/10	38/20
7	4-$CH_3C_6H_5$	H	95/10	53/20
8	2-furanyl	H	99/9	72/20
9	Piperonyl	H	97/10	75/20
10	$C_6H_5CH_2$	H	80/12	49/24
11	*n*-C_6H_{13}	H	79/10	56/24

[a]Determined by HPLC and ^{1}H NMR.

In addition, the diastereoselectivity of the crotylation with crotyl chloride is different from crotyl bromide. The crotylation of crotyl chloride mediated by indium nanoparticles exclusively gave γ-adduct with dominant *syn*-isomer except entry 3 (Table 2, entries 1–18). The *anti*-isomer was dominant product in the crotylation of crotyl bromide.[3b] Compared to the 200 mesh of indium, indium nanoparticles can enhance both the yield and the stereoselectivity of the crotylations.

Based on the experimental facts, we proposed a possible reaction mechanism (illustration in Supporting Information). At first, both allylic chloride **2** and carbonyl compound **1** were ab-

Table 2. The crotylations of carbonyl compounds mediated by indium nanoparticles and 200 mesh In in water



1 **2** *syn* **4** *anti*

Entry	R_1	R_2	Yield^a/% (*syn*:*anti*)/Time/h Nano-In	200 mesh In
1	C_6H_5	H	99(61:39)/8	86(58:42)/8
2	4-ClC_6H_5	H	99(61:39)/8	82(60:40)/9
3	2-ClC_6H_5	H	95(36:64)/8	85(35:65)/8
4	2-HOC_6H_5	H	99(67:33)/8	40(51:49)/10
5	4-$CH_3OC_6H_5$	H	98(65:35)/8	69(55:45)/10
6	2-$CH_3OC_6H_5$	H	97(70:30)/8	48(65:35)/10
7	4-$CH_3C_6H_5$	H	94(62:38)/8	60(60:40)/8
8	2-furanyl	H	97(58:42)/10	68(56:44)/10
9	Piperonyl	H	97(64:36)/10	52(60:40)/10
10	$C_6H_5CH_2$	H	89(60:40)/8	40(59:41)/8
11	*n*-C_6H_{13}	H	94(50:50)/15	46(50:50)/15
12^b	1,2-dihydroxyethyl	H	95/12	90/12
13	C_6H_5	CH_3	91(82:18)/14	10(74:26)/14
14	4-ClC_6H_5	CH_3	90(79:21)/10	5(76:24)/10
15	4-$CH_3OC_6H_5$	CH_3	80(68:32)/10	26(64:34)/10
16^b	1-hydroxyethyl	CH_3	98/12	31/12
17	2-cyclohexen-1-one		89(60:40)/14	18(54:46)/14
18	Cyclohexanone		92/15	43/15

[a] The ratio of *syn* and *anti* isomer was determined by ^{1}H NMR and ^{13}C NMR. [b] The diastereoselectivity was not confirmed.

sorbed on the surface of indium nanoparticles, which shortened the distance between these reactant molecules, and activated the carbonyl group. Then, the indium inserted into the C–Cl bond to form the allylindium sesquichloride **5**. In the case mediated by 200 mesh of indium, the formation of **5** is a rate-determining step.[10] Here, this step was accelerated via surface absorption and high reactivity of indium nanoparticles. Once **5** was formed, it reacted immediately with the adjacent carbonyl compound through a six-membered cyclic transition state **6**, giving the adduct **3** ($R_3 = H$) or **4** ($R_3 = CH_3$) with dominant *syn*-isomer. This mechanism can explain that the yield of the crotylation is higher than that of the allylation (Tables 1 and 2) since quantum chemical calculations show that the energy of the intermediate **5** ($R_3 = CH_3$) are lower than that of intermediate **5** ($R_3 = H$). On the other hand, it is possible that *syn*-isomer is a dynamically-controlled product. The enhacement of the reaction rate should favor the formation of *syn*-isomer. Therefore, crotylation mediated by indium nanoparticle had better diastereoselectivities.

In conclusion, Barbier-type allylation of various carbonyl compounds with allyl (crotyl) chloride in water were realized by employing indium nanoparticles as a mediator, giving the corresponding alcohols in good to excellent yields. Especially, the crotylaiton of ketone afforded the corresponding adduct with much better yield than that of crotylation mediated by indium granules or 200 mesh of indium. The experimental results demonstrated the dimension of metal particles has a great influence not only on the yield but also on the stereochemistry of the allylations. The proposed mechanism is consistent with the experimental results and the quantum chemical calculation. The further research is in progress in details in our laboratory.

We are grateful to National Nature Science Foundation of China (Nos. 2047078 and 30572234) for their support.

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Published on the web (Advance View) April 8, 2006; DOI: 10.1246/cl.2006.498