Pergamon

Tetrahedron Letters 42 (2001) 1957–1959

TETRAHEDRON
LETTERS

# Indium mediated allylation and propargylation reactions of dimethyl acetals and ketals

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Received 11 December 2000; accepted 10 January 2001

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**Abstract**—Indium mediated allylation and propargylation reactions of acetals and ketals with various allyl or propargyl bromides in aqueous media successfully provided the corresponding homoallylic or homopropargylic (and allenylic) alcohol, respectively, in moderate to good yields. Highly chemoselective allylation is also described. The ketal and aryl acetal could be selectively allylated over the aliphatic one in 80–84% yields. © 2001 Published by Elsevier Science Ltd.

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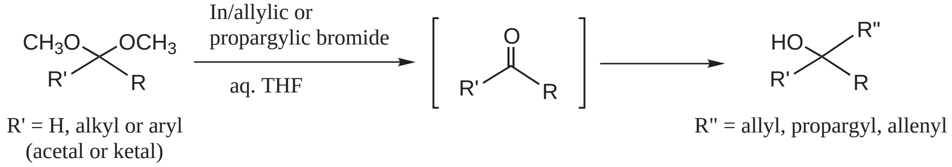
Indium mediated Barbier type reaction of carbonyl compounds has attracted considerable interest since Butsugan and Araki first reported the reaction in 1988.[1] Early this year, we reported deketalization and chemoselective deacetalization reactions with allyl bromide in aqueous media.[2] As an extension of the research, we performed the indium mediated allylation and propargylation reactions of acetals and ketals in aqueous media. The overall reaction is a one-pot deprotection–allylation/propargylation process (Scheme 1).[3]

Firstly, the allylation and propargylation reactions of dimethyl acetals of benzaldehyde (**1**), 4-methoxybenzaldehyde (**2**) and *trans*-cinnamaldehyde (**3**) with nine bromides were examined (Table 1). With the exception of propargylic bromides (Entries 8 and 9), every bromide seemed to have reacted in a γ-addition manner. Propargyl bromide gave mixed products resulting from α- and γ-addition, and 1-bromo-2-butyne provided only the α-addition product. Compared with benzaldehyde itself, benzaldehyde dimethyl acetal (**1**) required a longer reaction time, and gave the corresponding product in somewhat lower yields. In the cases of dimethyl acetals of 4-methoxybenzaldehyde (**2**) and *trans*-cinnamaldehyde (**3**), allylation and propargylation reactions proceeded more efficiently than benzaldehyde dimethyl acetal (**1**).

Allylation and propargylation reactions of cyclohexanone dimethyl ketal were also investigated (Table 2). All reactions were carried out under the same reaction conditions mentioned above.[3] The reaction of 2,3-dibromopropene (Entry 4) and methyl 4-bromocrotonate (Entry 6), which showed low yields with acetals in Table 1, did not proceed at all. These results imply that aliphatic ketals are less reactive than aryl as well as conjugated acetals.

From our previous work,[2] we knew that ketals and aromatic acetals can be selectively deprotected in the presence of aliphatic acetals by the action of allyl bromide in aqueous media. Based on this information, we carried out a chemoselective allylation reaction. Scheme 2 illustrates the chemoselective allylation of [4-(2,2-dimethoxyethyl)phenyl]dimethoxymethane (**4**) and 1,1,5,5-tetramethoxy hexane (**6**). The diacetal of



**Scheme 1.**

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PII: S0040-4039(01)00042-9

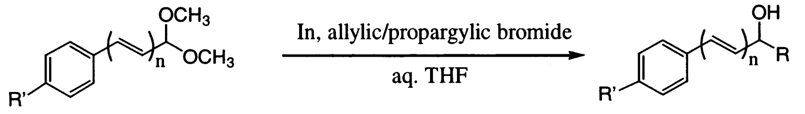
aromatic aldehyde **4** and aliphatic acetal ketal **6** reacted preferentially with aromatic acetal and ketal under the same reaction conditions to provide the selective allylation products **5** and **7** in 84 and 80% yields, respectively.

In conclusion, indium mediated allylation and propargylation reactions of acetals and ketals successfully provided the corresponding alcohol in the presence of various allyl or propargyl bromides in aqueous THF in moderate to good yields, except in a few cases. Furthermore, chemoselective allylations were accomplished in good yields while keeping the aliphatic acetal intact. This method will provide a useful tool for allylation and propargylation of acetals and ketals without deprotection steps in aqueous media.

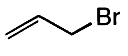
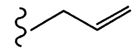
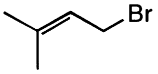
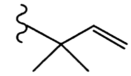
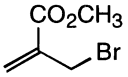
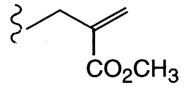
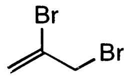
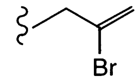
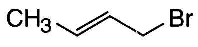
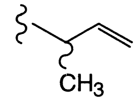
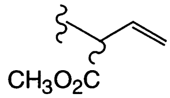
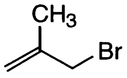
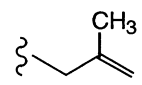
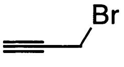
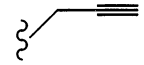
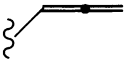
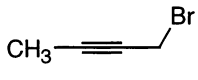
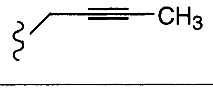
## Acknowledgements

The authors are grateful to the Korea Ministry of Science and Technology for financial support.

**Table 1.** Indium mediated allylation and propargylation of acetals of conjugated aldehydes[a]

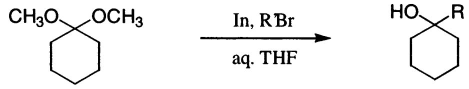


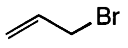
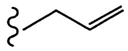
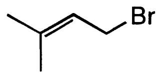
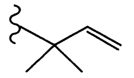
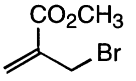
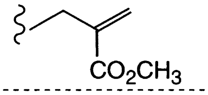
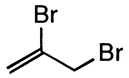
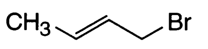
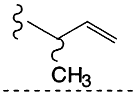
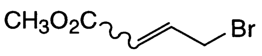
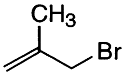
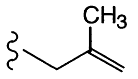
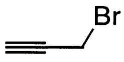
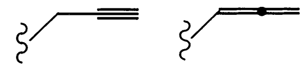
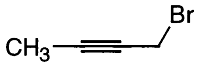
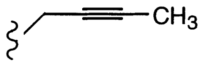
**1** R' = H; n = 0
**2** R' = OCH$_3$; n = 0
**3** R' = H; n = 1

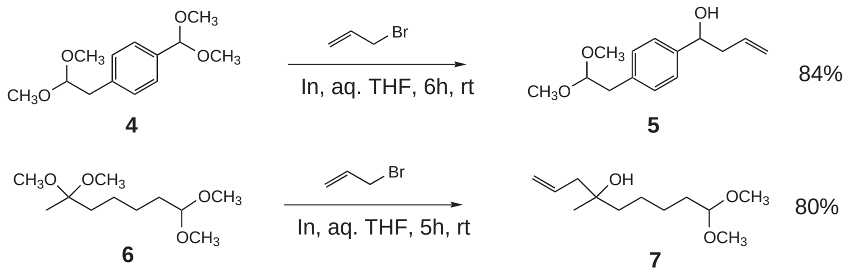
| Entry | Allylic/propargylic bromide | Acetal | Time (h) | Isolated yield (%) | R |
|---|---|---|---|---|---|
| 1 |  | **1** | 7.5 (2.5)[b] | 87 (90)[b] |  |
| | | **2** | 4 | 97 | |
| | | **3** | 5 | 84 | |
| 2 |  | **1** | 21 (6.5)[b] | 44 (49)[b] |  |
| | | **2** | 40 | 59 | |
| | | **3** | 9 | 20 | |
| 3 |  | **1** | 10 (3.5)[b] | 95 (97)[b] |  |
| | | **2** | 3 | 96 | |
| | | **3** | 5 | 88 | |
| 4 |  | **1** | 60 (4)[b] | 40 (74)[b] |  |
| | | **2** | 32 | 46 | |
| | | **3** | 32 | 45 | |
| 5 |  | **1** | 5.5 (4.5)[b] | 87 (70)[b] |  |
| | | **2** | 10 | 97(5:4)[c] | |
| | | **3** | 6 | 84 | |
| 6 |  | **1** | 46 (20)[b] | 41 (59)[b] |  |
| | | **2** | 32 | 40(1:1)[c] | |
| | | **3** | 28 | 81 | |
| 7 |  | **1** | 52 (10)[b] | 86 (88)[b] |  |
| | | **2** | 23 | 95 | |
| | | **3** | 48 | 84 | |
| 8 |  | **1** | 11 (10)[b] | 55[d] (78)[b,e] | <br> |
| | | **2** | 5 | 94 (2:1)[f] | |
| | | **3** | 6 | 94 (5:2)[f] | |
| 9 |  | **1** | 17 (10)[b] | 56 (75)[b] |  |
| | | **2** | 5 | 87 | |
| | | **3** | 6 | 74 | |

[a] All reactions were carried out on a 0.2–0.4 mmol scale at rt. [b] Results for benzaldehyde. [c] Diastereomeric ratio was determined by $^1$H NMR. [d,e] Propargyl:allenyl = 1:2. [f] Propargyl:allenyl.

**Table 2.** Indium mediated allylation and propargylation of cyclohexanone dimethyl ketal[a]



| Entry | Bromide (R'Br) | Time(hr) | Isolated yield % | R |
|---|---|---|---|---|
| 1 |  | 5 | 89 |  |
| 2 |  | 7 days | 28 |  |
| 3 |  | 6 | 98 |  |
| 4 |  | - | nr[b] | - |
| 5 |  | 9 | 85 (1:1)[c] |  |
| 6 |  | - | nr[b] | - |
| 7 |  | 47 | 81 |  |
| 8 |  | 46 | 50 (3:2)[d] |  |
| 9 |  | 28 | 58 |  |



**Scheme 2.**

## References

1. (a) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831–1833; (b) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017; (c) Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181; (d) Paquette, L. A.; Bennett, G. D.; Isaac, M. B.; Chhatriwalla, A. *J. Org. Chem.* **1998**, *63*, 1836; (e) Cho, Y. S.; Lee, J. E.; Pae, A. N.; Choi, K. I.; Koh, H. Y. *Tetrahedron Lett.* **1999**, *40*, 1725.
2. Kwon, J. S.; Lee, J. G.; Pae, A. N.; Choi, K. I.; Koh, H. Y.; Kim, Y.; Cho, Y. S. *Bull. Korean Chem. Soc.* **2000**, *21*, 453.
3. Typical reaction procedure is as follows: An acetal or ketal (0.33 mmol) was dissolved in aqueous THF ($H_2O$/THF = 3/1, *v*/*v*) followed by the addition of allyl or propargyl bromide (0.66 mmol) and indium metal (0.39 mmol) at rt. After an appropriate reaction time (see Tables 1 and 2), the reaction mixture was filtered through Celite and washed with ethyl acetate. The filtrate was treated following a usual aqueous work-up procedure and purified by column chromatography on silica gel to furnish the final products.