Zirconyl Chloride (=Dichlorooxozirconium) as an Efficient Catalyst for One-Pot Multicomponent Synthesis of Homoallylic Amines[1])

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Zirconyl chloride ($ZrOCl_2$) catalyzes efficiently the one-pot three component reactions of aldehydes, amines, and allyltributylstannane at room temperature to furnish the corresponding homoallylic amines in short reaction times and in excellent yields.

Introduction. – Homoallylic amines are useful intermediates for the synthesis of various bioactive natural products and related compounds [1]. They are generally prepared by allylation of imines with allyl organometallics in the presence of a catalyst such as $BF_3 \cdot OEt_2$, $[PdCl_2(Ph_3P)_2]$ or $[PtCl_2(Ph_3P)_2]$ [2][3]. The one-pot method involving the *in situ* generation of imines from aldehydes and amines followed by allylation is more convenient for the synthesis of these compounds [4]. However, many of the methods reported for this one-pot conversion suffered from different disadvantages, such as requirement of a surfactant or molecular sieve (along with the catalyst) or an N_2 atmosphere, longer reaction times, and unsatisfactory yields. Hence, it is desirable to develop a suitable efficient method for the one-pot preparation of homoallylic amines.

Results and Discussion. – In recent years, Zr^{IV} compounds have gained much importance in organic synthesis as reagents as well as catalysts. The high abundance of Zr^{IV} compounds in the earth's crust make them less costly and easily available. They also possess low toxicity [5]. $ZrCl_4$ has already been found to be a more effective catalyst in various organic transformations than conventional *Lewis* acids [6]. However, like other metal oxy salt based organic reactions, $ZrOCl_2$-catalyzed chemical transformations are also limited [7].

In continuation of our work [8] on the applications of zirconium compounds for the development of useful synthetic methodologies, we have recently observed that zirconyl chloride (=dichlorooxozirconium; $ZrOCl_2$) can efficiently catalyze the one-pot three-component reactions of aldehydes **1**, amines **2**, and allyltributylstannane (**3**) to form the corresponding homoallylic amines **4** at room temperature (*Scheme*).

Multicomponent one-pot reactions are highly valuable in organic synthesis as the desired products are obtained in a single operation without isolating the intermediates [9]. Thus, the reaction times are reduced, and both energy and raw materials are saved.

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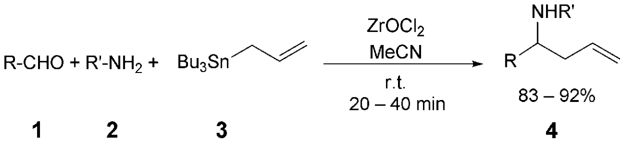
[1]) Part 101 in the series, 'Studies on novel synthetic methodologies'; IICT Communication No. 061214.

Scheme



The present three-component coupling reaction catalyzed by $ZrOCl_2$ is a simple and efficient method for the synthesis of homoallylic amines.

Various aldehydes **1** and amines **2** were treated with allyltributylstannane (**3**) in the presence of $ZrOCl_2$ to produce a series of homoallylic amines **4** (*Table*). The initial reaction of aldehydes and amines formed the corresponding imines which underwent allylation with allyltributylstannane. The products were formed within 20–40 min, and in high yields. Aromatic, heteroaromatic, and aliphatic aldehydes afforded the desired products smoothly. Aldehydes containing both electron-donating and electron-withdrawing groups in the aromatic ring worked well. An acid-sensitive aldehyde, such as furan-2-carboxaldehyde (**1k**) and a sterically hindered aldehyde, such as naphthalene-2-carboxaldehyde (**1j**) also afforded the corresponding homoallylic amines. Additionally, the method was suitable for the conversion of aliphatic aldehydes. Previously, some methods were not useful for such conversion [4]. However, ketones did not yield the products under the present reaction conditions. Homoallylic alcohols (adducts between aldehydes and allyltributylstannane) were also not formed. This is possibly due to the rapid formation and selective activation of imines under the catalytic activity of $ZrOCl_2$. In absence of this catalyst, only a trace amount of the desired products were produced. The structures of the homoallylic amines **4** were established by their IR,^{1}H-NMR, MS, and analytical data.

In conclusion, we developed an efficient one-pot multi-component synthesis of homoallylic amines using $ZrOCl_2$ as a catalyst. The simple experimental procedure, mild reaction conditions, short reaction times, and high yields are the notable advantages of the method.

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Experimental Part

Homoallylic Amines General Procedure. To a mixture of an aldehyde **1** (1 mmol), an amine **2** (1 mmol), and allyltributylstannane (**3**; 1.2 mmol) in MeCN (5 ml), $ZrOCl_2$ (10 mol-%) was added. The mixture was stirred at r.t. and the reaction was monitored by TLC. After completion, the solvent was evaporated and H_2O (10 ml) was added. The mixture was extracted with AcOEt (3 × 10 ml) and the extract concentrated. The residue was subjected to column chromatography (silica gel, hexane): pure homoallylic amine **4**. The IR, ^{1}H-NMR, MS, and anal. data of some representative homoallylic amines are given below.

*4-Methyl-*N*-phenyl-α-prop-2-enylbenzenemethanamine* (**4e**): IR (KBr): 3412, 1603, 1505, 1430. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.21 (*d*, $J = 8.0$, 2 H); 7.08 (*d*, $J = 8.0$, 2 H); 7.01 (*t*, $J = 8.0$, 2 H); 6.55 (*t*, $J = 8.0$, 1 H); 6.41 (*d*, $J = 8.0$, 2 H); 5.74 (*m*, 1 H); 5.21–5.10 (*m*, 2 H); 4.31 (*dd*, $J = 6.5$, 5.5, 1 H); 4.02 (br. *s*, 1 H); 2.61–2.40 (*m*, 2 H); 2.32 (*s*, 3 H). FAB-MS: 238 ($[M+H]^+$). Anal. calc. for $C_{17}H_{19}N$: C 86.08, H 8.02, N 5.91; found: C 86.17, H 8.14, N 5.82.

Table. *Zirconyl Chloride Catalyzed Synthesis of Homoallylic Amines*[a])

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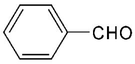
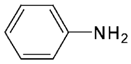
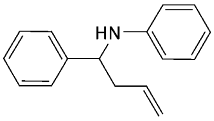
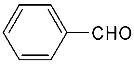
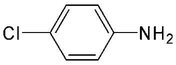
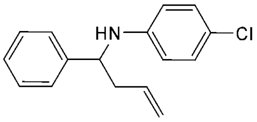
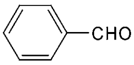
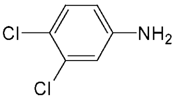
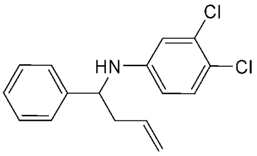
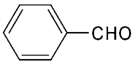
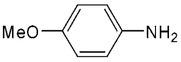
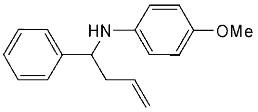
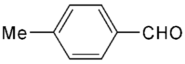
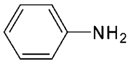
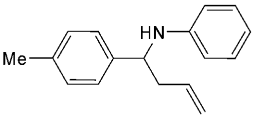
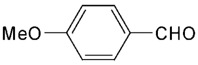
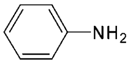
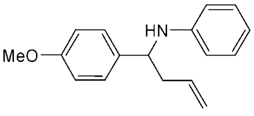
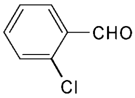
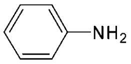
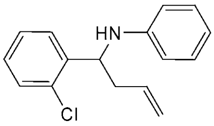
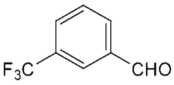
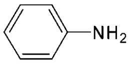
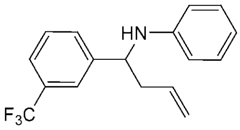
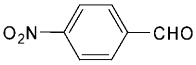
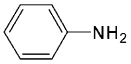
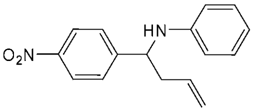
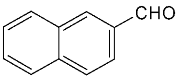
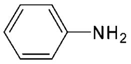
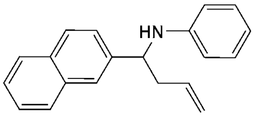
a				20	90
b				20	89
c				30	92
d				25	85
e				25	91
f				20	92
g				25	87
h				30	88
i				30	83
j				35	87

Table (cont.)

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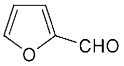
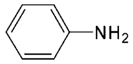
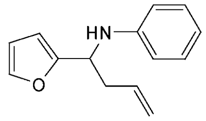
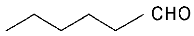
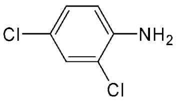
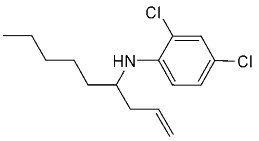
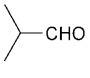
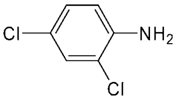
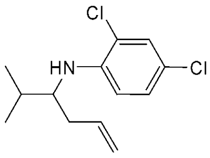
k				30	91
l				40	85
m				40	83

[a]) The structures of the homoallylic amines **4** were established from their spectral (IR, ^{1}H-NMR, and MS) and analytical data. [b]) Yield of isolated material.

N-*Phenyl-α-prop-2-enylnaphtalene-2-methanamine* (**4j**): IR (KBr): 3412, 1602, 1504, 1431. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.82–7.71 (*m*, 4 H); 7.49–7.34 (*m*, 3 H); 6.99 (*t*, $J=8.0$, 2 H); 6.58 (*t*, $J=8.0$, 1 H); 6.48 (*d*, $J=8.0$, 2 H); 5.85–5.71 (*m*, 1 H); 5.24–5.12 (*m*, 2 H); 4.51 (*dd*, $J=6.5$, 5.5, 1 H); 4.12 (br. *s*, 1 H); 2.73–2.48 (*m*, 2 H). FAB-MS: 274 ($[M+H]^+$). Anal. calc. for $C_{20}H_{19}N$: C 87.91, H 6.96, N 5.13; found: C 87.84, H 6.91, N 5.21.

N-*Phenyl-α-prop-2-enylfuran-2-methanamine* (**4k**): IR (KBr): 3412, 1603, 1505, 1429. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.30 (*d*, $J=1.8$, 1 H); 7.06 (*t*, $J=8.0$, 2 H); 6.64 (*t*, $J=8.0$, 1 H); 6.52 (*d*, $J=8.0$, 2 H); 6.23 (*dd*, $J=2.0$, 1.8, 1 H); 6.09 (*d*, $J=2.0$, 1 H); 5.72 (*m*, 1 H); 5.20–5.08 (*m*, 2 H); 4.52 (*t*, $J=5.5$, 1 H); 3.89 (br. *s*, 1 H); 2.64 (*t*, $J=5.5$, 2 H). FAB-MS: 214 ($[M+H]^+$). Anal. calc. for $C_{14}H_{15}NO$: C 78.87, H 7.04, N 6.57; found: C 78.81, H 7.13, N 6.62.

*2,4-Dichloro-*N*-[1-(prop-2-enyl)hexyl]benzenamine* (**4l**): IR (KBr): 3438, 1618, 1505, 1442; ^{1}H-NMR (200 MHz, $CDCl_3$): 7.51 (*d*, $J=2.0$, 1 H); 7.20 (*dd*, $J=8.0$, 2.0, 1 H); 6.42 (*d*, $J=8.0$, 1 H); 5.75 (*m*, 1 H); 5.12–5.04 (*m*, 2 H); 4.17 (*d*, $J=5.0$, 1 H); 3.39 (*m*, 1 H); 2.30 (*t*, $J=5.0$, 2 H); 1.61–1.45 (*m*, 2 H); 1.32–1.23 (*m*, 6 H); 0.88 (*t*, $J=7.0$, 3 H). FAB-MS: 290, 288, 286 ($[M+H]^+$). Anal. calc. for $C_{15}H_{21}Cl_2N$: C 62.94, H 7.34, N 4.90; found: C 62.83, H 7.41, N 4.95.

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