

Zinc Catalyzed Claisen Rearrangement of Allyl Aryl Ethers to *o*-Allylated Phenols in Liquid Phase

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Abstract: A simple and efficient method is developed for the zinc catalyzed Claisen rearrangement of allyl aryl ethers to *o*-allyl phenols by stirring in an oil-bath at 55 °C in liquid phase. Moreover, zinc powder is re-cyclable up to six times use without much loss of significant activity. In addition to it, the products are obtained in good to excellent yields and are in a state of high purity. The structures of the products are confirmed by ¹H NMR, ¹³CNMR, IR and mass spectral data and comparison with authentic samples prepared according to the literature methods.

Keywords: Allyl aryl ethers, *o*-allyl phenols, zinc powder, THF, recyclable.

INTRODUCTION

Claisen rearrangement [1-3] finds numerous applications in the biosynthesis of natural products [4], such as fatty acids and polyketides. It occupies a unique place in the biomimetic total synthesis of desoxymorellin [5], and forbesione [6] which proceeds in a regioselective manner and produces desired scaffold exclusively like hanburin [7], morellin [8] and bractatins [9].

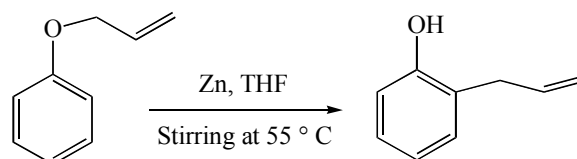
Ethers are very routinely used as protecting groups for hydroxyl functions during organic synthesis and besides a large number of ethers are known as good blocking groups [10], the role of aliphatic, benzylic and allylic ethers are particularly noteworthy. The conversion of ethers to phenols can be performed in numerous ways, although the success of the transformation largely depends on the judicious choice [11] of the deblocking agent that is compatible with other functional groups present in the ether molecule. Numerous reagents are available for the rearrangement of ethers to corresponding phenols such as bismuth triflate [12,13], chiral lewis acid [14,15], orthometallated complex(R,R)-di- μ -chlorobis{9-[(1-dimethylamino)ethyl]-10-phenanthrenyl-C,N} dipalladium [16], chiral aluminium reagent [17] and KHMDS [18]. But most of the reported reagents are associated with certain drawbacks such as expensiveness, toxic nature and tedious work-up procedure. Thus, there remains a need to find a new environmentally benign procedure, which should be simple, safe and economic for Claisen rearrangement of allyl aryl ethers.

Since zinc powder is non-toxic and inexpensive. It has been used for selective α -haloacylation and gem-bisacylation of alkyl aldehydes [19], synthesis of *o*-arylene dizinc compounds [20], synthesis of benzhydrols [21], transesterification of β -ketoesters [22], acylation and sulfonation of pyrrole [23], Fries rearrangement [24] and in Williamson synthesis of ethers [25]. Moreover, zinc oxide, a versatile reagent for benzylic oxidations has also been reported [26].

Keeping in view the importance of Claisen rearrangement of allyl aryl ethers in organic synthesis and our continued interest in devising environmentally benign methodologies, we have successfully developed a zinc catalyzed synthesis of *o*-allylated phenols in liquid phase. This method is superior to already existing methods as there is no need of toxic and expensive reagents, work-up being simply reduced to filtration followed by treatment with crushed ice.

RESULTS AND DISCUSSION

The experimental conditions were optimized to proceed the reaction safely and in milder conditions. The amount of catalyst used was found to be crucial to proceed the reaction faster and in environment-friendly way. After carrying out the reaction under different set of conditions, the optimum conditions selected were: for 10 mmole of allyl aryl ether, 2.5 mmole of zinc powder was required. In a test reaction, to allyl phenyl ether (10 mmol) and zinc powder (2.5 mmol), THF (5 mL) was added and stirred at 55°C, product was isolated in 80 % yield in 40 min. (Scheme 1).



Scheme 1.

To the best of our knowledge, this type of Claisen rearrangement of allyl aryl ethers in the presence of zinc powder is unprecedented. This prompted us to investigate this unusual Zn catalyzed synthesis of *o*-allylated phenols. It was found that zinc has not yet been used for such rearrangement under milder conditions. This rearrangement was also compared with the reported reagent such as orthometallated complex(R,R)-di- μ -chlorobis{9-[(1-dimethylamino)ethyl]-10-phenanthrenyl-C,N} dipalladium in case of allyl aryl ether and found that the reaction took more time, lesser yield, work-up procedure was tedious and moreover, the expensive nature of the reagent made the

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Table 1. Results of Zinc Powder Catalyzed Claisen Rearrangement of Allyl Aryl Ethers to *o*-Allylated Phenols in THF

Entry	Reactant	Product ^a	Time (min.)	Yield ^b (%)
1.	Allyl phenyl ether	2-Allyl phenol	40	80
2.	Allyl (4-chlorophenyl)ether	2-Allyl4-chlorophenol	45	92
3.	Allyl(4-methylphenyl) ether	2-Allyl4-methylphenol	75	93
4.	Allyl(4-formylphenyl) ether	2-Allyl4-formylphenol	60	85
5.	Allyl(4-acetylphenyl) ether	2-Allyl4-acetylphenol	30	79
6.	Allyl(4-formyl-2-methoxyphenyl)ether	6-Allyl2-methoxy-4-formyl phenol	120	78
7.	Allyl(4-nitrophenyl)ether	2-Allyl4-nitrophenol	25	83
8.	Allyl(4-bromophenyl)ether	2-Allyl4-bromophenol	50	78
9.	Allyl(4-methoxy phenyl) ether	2-Allyl4-methoxy phenol	70	70
10.	Allyl(4-ethoxyphenyl)ether	2-Allyl4-ethoxy phenol	65	87

^aAll the products are liquids and purified by passing through a column of silica gel and elution with ethylacetate and petroleum ether (1:2). These products were characterized by ¹H NMR, ¹³CNMR, IR and mass spectral data.

^bYields refer to the isolated yields.

process highly expensive while the reaction with easily available zinc powder can be carried out under mild reaction conditions. Moreover, work-up procedure is simple and recyclability of the catalyst makes the process cost-effective.

To demonstrate the versatility of reagent, a series of allyl aryl ethers substituted with electron-releasing and electron-withdrawing groups were subjected to Claisen rearrangement under the similar reaction conditions, products were obtained in good to excellent yields as shown in Table 1.

The plausible mechanism involved is the ionic mechanism and it is expected that lone pair of electrons from oxygen atom gets interacted with zinc generating a polar transition state. Then pi electrons of allyl shifted giving positive charge on the end terminal carbon providing the driving force to balance the partial +ve charge on oxygen atom. O-Zn bond cannot stay for longer time. It gets broken with the result C=O is formed shifting the pi electrons of the ring towards positive centre of allyl group and finally the aromaticity of the ring is maintained by shifting the H atom thereby converting C=O to C-OH.

Another important feature of zinc powder lies in the fact that after carrying out the reaction using optimum conditions, product was isolated after the separation of zinc powder. This much amount of zinc powder, which is left after first use, can be re-used up to six times after simple washing with diethyl ether and dilute HCL without much loss of activity, thus rendering the process still more economic (Table 2). Catalytic activity goes on decreasing after every use which can be shown in Table 2 but the zinc cannot be regenerated for re-use.

CONCLUSIONS

In conclusion, we have developed a Zn catalyzed procedure for very simple and efficient Claisen rearrangement of allyl aryl ethers to corresponding *o*-allylated phenols by stirring in an oil-bath at 55° C and the products are isolated in excellent yields and are in a state of high purity. Moreover, zinc powder can be re-cycled up to six times without much loss of significant activity that makes the process cost-effective.

Table 2. Results of Re-Use Studies of Claisen Rearrangement in the Case of Entry 1 Using Zinc Powder by Stirring at 55°C

Entry ^a	No. of Uses	Time (min.)	Yield ^b (%)
1.	1	40	80
1.	2	55	79
1.	3	72	76
1.	4	80	72
1.	5	85	70
1.	6	92	66

^aIn case of entry 1, reaction optimum conditions are: for allyl phenyl ether (10 mmol) and zinc powder (2.5 mmol), THF (5 mL) was required. The reaction mixture was stirred at 55 ° C. The reaction was completed in 40 min., then product was isolated in 80 % yield by distilled off the solvent.

^bYields refer to the isolated yields.

EXPERIMENTAL SECTION

General

All the melting points were determined on a Perfit melting point apparatus and are uncorrected. ¹H NMR and ¹³CNMR spectra were recorded on a Bruker DPX-200 NMR spectrometer (200 MHz) in CDCl₃ using tetramethyl silane as internal standard and IR spectra was recorded using KBr disc on a Perkin Elmer FTIR spectrometer. The mass spectral data was obtained on Bruker Esquires 3000 (ESI). The reactions were monitored qualitatively by TLC.

General Procedure for the Zinc Powder Catalyzed Claisen Rearrangement of Allyl Aryl Ethers to *o*-Allyl Phenols

Allyl aryl ether (10 mmol), zinc powder (2.5 mmol) and THF (5 mL) were taken in a round bottomed flask (25 mL) The reaction mixture was stirred in an oil-bath at 55°C for the required time. After completion of the reaction (monitored by TLC, visualization in iodine vapours), filtered off the reaction mixture so as to remove the zinc powder.

Now, the solvent was distilled off and the product was isolated in good to excellent yields. The products were purified by crystallization through a column of silica gel and elution with ethyl acetate and petroleum ether (1:2).

The structures of the products were confirmed by IR, ^1H NMR, ^{13}C NMR and mass spectral data.

Spectral Data of the Synthesized Compounds (1-10)

Entry 1. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1000; ^1H NMR (CDCl_3): δ 3.22(d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.60-6.70 (m, 2H, Harom), 6.80-6.90 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 137.5(-CH), 136.4(C-1), 134.2 (C-4), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 134

Entry 2. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1000, 728; ^1H NMR (CDCl_3): δ 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.55-6.60 (m, 1H, Harom), 6.85-6.95 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 150 (C-4), 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 168.5

Entry 3. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1000; ^1H NMR(CDCl_3): δ 2.35 (s, 3H, CH_3), 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.45-6.52 (m, 1H, Harom), 6.65-6.70 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 127(C-4), 29.1(- CH_2); Mass: m/z (M^+): 148

Entry 4. IR (ν_{max} in cm^{-1} , KBr): 3600, 3020, 2925, 1690, 1000; ^1H NMR (CDCl_3): δ 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.75-6.80 (m, 1H, Harom), 7.38-7.45 (m, 2H, Harom), 9.87 (s, 1H, CHO); ^{13}C NMR (CDCl_3): δ 137.5(-CH), 136.4(C-1), 132(C-4), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 163.

Entry 5. IR (ν_{max} in cm^{-1} , KBr): 3600, 3020, 2925, 1715, 1000; ^1H NMR (CDCl_3): δ 2.55 (s, 3H, COCH_3), 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.70-6.75 (m, 1H, Harom), 7.45-7.55 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 197.6(CO), 137.5(-CH), 136.4(C-1), 132(C-4), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2), 26.3(- CH_3); Mass: m/z (M^+): 176.

Entry 6. IR (ν_{max} in cm^{-1} , KBr): 3600, 3020, 2925, 1690, 1060, 1000; ^1H NMR (CDCl_3): 3.22 (d, 2H, CH_2), 3.92 (s, 3H, OCH_3), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.75-6.80, 6.95-7.00 (m, 1H, Harom), 7.38-7.45, 9.87 (s, 1H, CHO); (m, 2H, Harom), 9.87 (s, 1H, CHO); ^{13}C NMR:(CDCl_3): δ 137.5(-CH), 136.4(C-1), 132(C-4), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 55 (OCH_3), 29.1(- CH_2); Mass: m/z (M^+): 191.

Entry 7. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1440, 1000; ^1H NMR(CDCl_3): δ 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00(s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.45-6.52 (m, 1H, Harom), 6.65-6.70 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 138.3 (C-4), 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 180

Entry 8. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1000, 838; ^1H NMR(CDCl_3): δ 2.35 (s, 3H, CH_3), 3.22 (d, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.45-6.52 (m, 1H, Harom), 6.65-6.70 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 140 (C-4), 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 212

Entry 9. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 1275, 1000; ^1H NMR(CDCl_3): δ 3.22 (d, 2H, CH_2), 4.12 (s, 3H, CH_3), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.45-6.52 (m, 1H, Harom), 6.65-6.70 (m, 2H, Harom); ^{13}C NMR (CDCl_3): δ 160 (C-4), 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 29.1(- CH_2); Mass: m/z (M^+): 164

Entry 10. IR (ν_{max} in cm^{-1} , KBr): 3500, 3020, 2925, 2800, 1275, 1000; ^1H NMR(CDCl_3): δ 2.28 (t, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.22 (d, 2H, CH_2), 4.12 (q, 2H, CH_2), 4.93-4.96 (m, 2H, $=\text{CH}_2$), 5.00 (s, 1H, OH), 6.30 (d, 1H, $=\text{CH}$), 6.45-6.52 (m, 1H, Harom), 6.65-6.70 (m, 2H, Harom); ^{13}C NMR(CDCl_3): δ 160 (C-4), 137.5(-CH), 136.4(C-1), 129.5(C-2), 128.5 (C-5,6), 128.4($=\text{CH}_2$), 128(C-3), 60 (OCH_2), 29.1(- CH_2), 13.8(OCH_2CH_3); Mass: m/z (M^+): 178

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