

Zn Mediated Regioselective Barbier Reaction of Propargylic Bromides in THF/aq. NH₄Cl Solution

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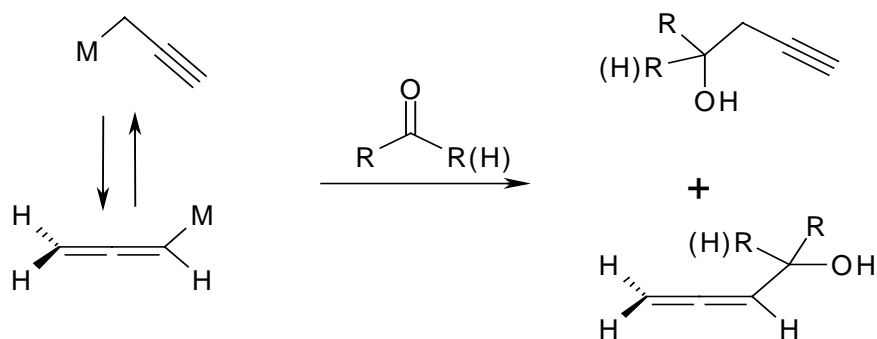
Abstract: The reaction of substituted and unsubstituted propargylic bromides with butanal in presence of zinc powder in THF/saturated aqueous NH₄Cl solution gave corresponding allenic and propargylic alcohols with high selectivity.

Keywords: Allenic alcohol, regiospecific Barbier reaction, propargylic bromides, zinc.

Introduction

The Barbier reaction has been known for more than hundred years and has been well investigated [1]. Barbier type reactions in aqueous solution using tin, zinc, indium and other metals are also described [2]. The Barbier reaction has been successfully applied recently in the preparation of new β -lactam antibiotics [3], in propargylation of cyclic imides [4], in asymmetric allenylation of aliphatic aldehydes catalyzed by a chiral formamide [5] and for the synthesis of propargylic and allenic alcohols [6,7]. A mechanism for the Barbier reaction has also been proposed (Scheme 1)[8]:

Scheme 1

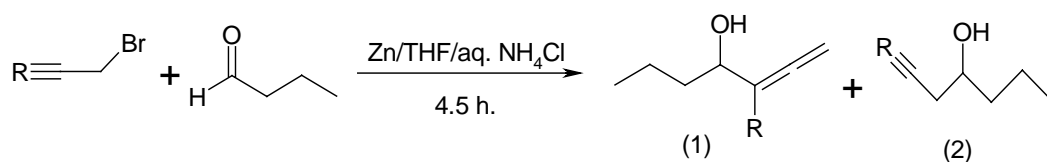


The regioselectivity of this reaction is highly dependent on the nature of the propargyl halide and carbonyl compound, steric hindrances, solvent effects and the metal used. Use of cheap zinc powder in the Barbier reactions of substituted propargylic halides in water gave a mixture of allenic and propargylic alcohols but unsubstituted propargyl halides always gave the corresponding propargylic alcohols with high selectivity [9]. It was reported recently that allenic alcohols were obtained with high selectivity by indium-mediated coupling of propargylic halides with aldehydes in aqueous media [7]. The zinc mediated regioselective synthesis of allenic alcohols in media containing water is not documented. Here we describe the regiospecific Barbier reaction of two representative model compounds giving exclusively the corresponding substituted propargylic or allenic alcohol.

Results and Discussion

In our investigation we chose 1-bromo-2-propyne and 1-bromo-2-nonyne as two model compounds that would react preferentially as the corresponding propargyl or allenyl metal derivatives in Barbier reactions [8]. A mixture of anhydrous THF and saturated aqueous NH_4Cl solution was used as solvent. First zinc powder was stirred with the propargylic bromide in anhydrous THF media, then butanal was added. After 3 hours of stirring saturated aqueous NH_4Cl solution was added. It was confirmed by GLC that the coupling reaction started only after addition of the sat. aq. NH_4Cl solution and was complete within 15 minutes. The coupling of substituted and unsubstituted propargylic bromide with butanal in presence of zinc powder gave the corresponding propargylic and allenic alcohols in modest yield albeit with high selectivity (Scheme 2):

Scheme 2. Zinc-mediated coupling of propargylic bromides with butanal in THF/ aq. NH_4Cl



Propargylic bromide (R)	Yield, %	Allenic (1) : Propargylic (2) alcohol
C ₆ H ₁₃	47	100 : 0
H	25	0 : 100

The purity and structure of the alcohols obtained was proven by GLC, IR, ¹H-NMR and ¹³C-NMR spectroscopy.

Conclusions

We have presented a facile route for the selective synthesis of allenic and propargylic alcohols in THF/aq. NH₄Cl media. This represents the first successful preparation of these allenic and propargylic alcohols in the presence of cheap zinc powder and the first reported synthesis of the allenic alcohol 3-hexyl-1.2-heptadien-4-ol (1).

Acknowledgements

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Experimental

General

¹H- and ¹³C-NMR spectra were recorded at 200 and 50 MHz respectively using a Bruker AC 200P instrument (Spektrospin AG, Switzerland). GLC analysis: Chrom-5 instrument (Laboratori Pastroje, Praha) equipped with a FID and glass column, 2.5 x 3 mm, 20% Carbowax 20M, Chromosorb W/AW-DMCS, 100-120 mesh. Products were purified on a 40-63 mesh silica chromatography column (A/S Tanel, Estonia), using 1:3 ethyl acetate:hexane as the eluting solvent. Reagents and chemicals were obtained from Aldrich Chemical Company (USA) and from REACHIM (USSR). The substituted and unsubstituted propargylic bromide starting materials were prepared according to the published standard procedure [10]: propargyl bromide, bp 82-83 °C, 60-70% yield; 1-bromo-2-nonyne, bp 92-95 °C/4 mmHg, 58% yield.

Typical synthetic procedure

Propargylic bromide (28 mmol) in THF (30 mL) was added to a stirred mixture of zinc (1.84 g, 28 mmol) in THF (60 mL) and after stirring for 1 hour, butanal (2.02 g, 28mmol) in THF (10 mL) was added.

The mixture was stirred 3 hours, then saturated aqueous NH₄Cl solution (100 mL) was added. After 0,5 hour the reaction mixture was filtered to remove the remaining zinc, 10% hydrochloric acid (20 mL) was added and organic layer was separated. The aqueous layer extracted with small portions of ether, the combined organic extracts were dried over MgSO₄ and concentrated in vacuo. The resulting brown liquid was purified by column chromatography. All experiments were performed at room temperature.

Spectral Data

3-hexyl-1,2-heptadien-4-ol (**1**): ¹H-NMR (CDCl₃) δ: 0.85-1.0 (m, 6H), 1.25-1.70 (m, 12H), 1.90-2.05 (m, 3H), 3.98-4.08 (m, 1H), 4.78-4.85 (m, 2H); ¹³C-NMR (CDCl₃) δ: 14.819, 14.871, 19.729, 23.521, 28.624, 28.779, 30.005, 32,639, 38.762, 72.756, 78.932, 108.606, 205.569; IR (thin film) cm⁻¹: 3308 (broad), 3024, 1931, 1036, 999, 845.

1-heptyn-4-ol (**2**) [11]: ¹H-NMR (CDCl₃) δ: 0.9-1.0 (m, 3H), 1.2-1.6 (m, 4H), 2.0-2.1 (m, 1H), 2.32-2.42 (m, 2H), 3.65-3.85 (m, 2H); ¹³C-NMR (CDCl₃) δ: 13.981, 18.845, 27.410, 38.447, 69.780, 70.673, 81.182; IR (thin film) cm⁻¹: 3350 (broad), 3308, 2122, 1017, 665.

References and Notes

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Sample Availability: Samples of compound **1** are available from MDPI.

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