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Synthesis of homopropargyl alcohols via sonochemical Barbier-type reaction

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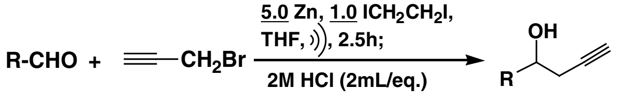
Abstract—A series of homopropargyl alcohols were synthesized from the reaction mixture of zinc powder, 1,2-diiodoethane, 3-bromo-1-propyne and aldehyde or ketone in anhydrous THF under ultrasound. The homopropargyl alcohols were obtained as the only product in all cases when aldehydes were reacted with 3-bromo-1-propyne under this sonochemical Barbier-type reaction condition. The homopropargyl alcohol was produced as the major product and the low contamination of allenyl alcohol was also obtained when ketone was used as substrate under the reaction condition.

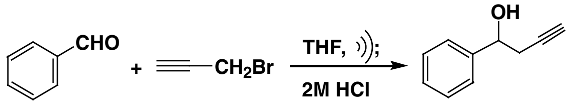
Homopropargyl alcohols have received much attention as synthetic intermediates in organic synthesis and as the structural moiety in a variety of biologically active compounds.[1–6] Homopropargyl alcohols have been prepared by the reactions of propargyl or allenyl organometallics of antimony,[7] borane,[8] cadium,[9] cerium,[10] chromium,[11] galium,[12] germanium,[13] indium,[14,15] lead,[16] magnesium,[1] manganese,[17] silicon,[18,19] tin,[20,21] titanium[22] and zinc[23] with aldehydes or ketones. A mixture of homopropargyl alcohol and allenyl alcohol was generally produced by reactions involving propargylic or allenic anion equivalents. Our previous studies showed that homoallyl alcohols were generated by a sonochemical Barbier-type reaction method.[24,25] Thus, we introduced and investigated the addition reaction of propargyl organometallic with aldehyde or ketone under this sonochemical Barbier-type reaction condition. Herewith, we wish to report a regioselective alkylation method for the synthesis of homopropargyl alcohol as the only or major product (Scheme 1).



Scheme 1.

Based on our previous studies for the ultrasound-induced reactions, firstly we investigated the reaction of propargyl bromide with benzaldehyde under sonochemical Barbier-type reaction condition. A reaction mixture of zinc, 1,2-diiodoethane, propargyl bromide and benzaldehyde in THF was sonicated for 2.5 h and the homopropargyl alcohol was produced with 56% yield and the formation of allenyl alcohol was not detected from ^{1}H NMR spectrum (Scheme 2). The yield of homopropargyl alcohol was improved to 93% when the Zn amount was increased to five equivalent to substrate. It should be noted that an 88% yield of homopropargyl alcohol was also obtained as the major product when the reaction mixture was proceeded under refluxing reaction condition. A series of aldehydes was investigated under the sonochemical Barbier-type reaction condition and the results are shown in Table 1.

Homopropargyl alcohols were produced as the only products and without the formation of allenyl alcohols in all cases (Table 1). The starting material was



* 3.5 Zn, 1.0 ICH_2CH_2I, 2.5h — 56% + 19% S.M.
* 4.5 Zn, 1.0 ICH_2CH_2I, 2.5h — 63% + 3% S.M.
* 5.0 Zn, 1.0 ICH_2CH_2I, 2.5h — 93%
* 5.0 Zn, 1.0 ICH_2CH_2I, reflux, 2.5h — 88%

Scheme 2.

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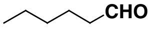
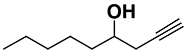
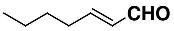
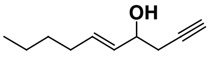
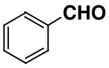
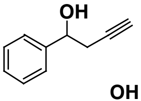
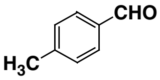
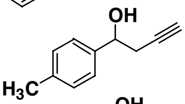
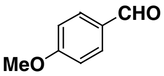
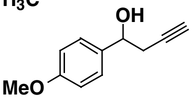
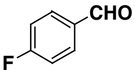
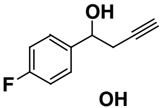
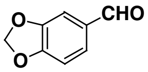
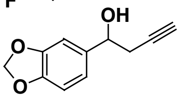
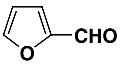
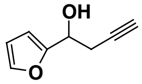
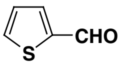
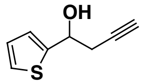
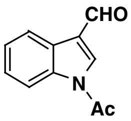
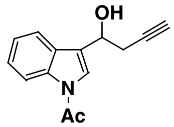
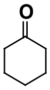
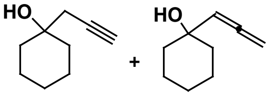
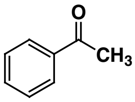
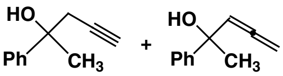
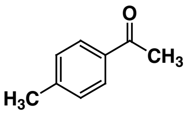
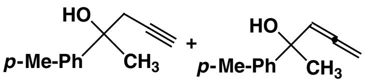
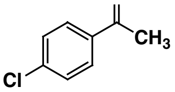
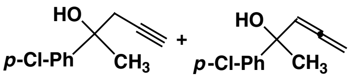
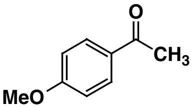
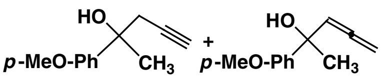
Table 1. Synthesis of homopropargyl alcohols from aldehydes

Entry	Substrate	Product	Yield[a] (%)
1			96
2			96
3			93
4			90
5			88
6			95
7			88
8			85
9			78
10			43+(18)[b]

[a] The yields were determined after chromatographic purification.

[b] The recovery yield of starting material.

Table 2. Synthesis of homopropargyl alcohols from ketones

Entry	Substrate	Products	Yield[a] (%)
1			89+6
2			55+4+(31)[b]
3			32+3+(59)[b]
4			80+10+(7)[b]
5			70+5+(21)[b]

[a] The yields were determined after chromatographic purification.

[b] The recovery yield of ketone.

recovered when the less reactive indole-3-carboxyaldehyde was introduced under the reaction condition (Table 1, entry 10). Thus, we further investigated that ketone as reacting substrate under this sonochemical Barbier-type reaction. A series of ketones was investigated under the reaction conditions and the results are shown in Table 2. Allenyl alcohols were produced as the minor products in all cases (Table 2). The starting material was recovered when the less reactive ketone was reacted under this sonochemical reaction condition.

In conclusion, this sonochemical Barbier-type reaction condition provides a simple and facile method for the synthesis of homopropargyl alcohol with the low contamination of allenyl alcohol. This procedure features in situ activation of metal to generate propargyl metal, which reacted with aldehyde or ketone to form homopropargyl alcohol after acidic quenching. These results lead us to apply and expand these homopropargyl alcohols to synthesize some biologically active compounds.

The typical procedure[26] for synthesis of a homopropargyl alcohol is as follows: A reaction mixture of zinc powder (5.0 mmol) and 1,2-diiodoethane[27] (1.0 mmol), aldehyde (1.0 mmol) and 3-bromo-1-propyne (1.5 mmol) in anhydrous THF (5.0 mL) was sonicated in a commercial ultrasonic cleaning bath[28] (Elma-T490DH, 50 kHz) for 2.5 h. After the sonication, an aqueous HCl (2 M, 2 mL/1.0 mmol) was added and the filtrate was extracted with ether (20 mL × 3). The combined organic layer was washed with brine (20 mL), dried with $MgSO_4$, filtered and then the organic solvent was removed under reduced pressure. Further purification was achieved on a flash chromatograph with silica gel and ethyl acetate/hexane as eluant.

Acknowledgements

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References and notes

1. Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 5198.
2. Nicolaou, K. C.; Skokotas, G.; Furuya, S.; Suemune, H.; Nicolaou, D. C. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1064.
3. Fryhle, C. B.; Williard, P. G.; Rybak, C. M. *Tetrahedron Lett.* **1992**, *33*, 2327.
4. Hirama, M.; Tokuda, M.; Fujiwara, K. *Synlett* **1991**, 651.
5. Chan, T.-H.; Arya, P. *Tetrahedron Lett.* **1989**, *30*, 406.
6. Frissen, R. W.; Blouin, M. *Tetrahedron Lett.* **1997**, *38*, 443.
7. Zhang, L.-J.; Mo, X.-S.; Huang, Y.-Z. *J. Organomet. Chem.* **1994**, *471*, 77.
8. Araki, S.; Ito, H.; Butsugan, Y. *J. Organomet. Chem.* **1988**, *347*, 5.
9. Brown, H. C.; Khire, U. R.; Narla, G.; Racherla, U. S. *J. Org. Chem.* **1995**, *60*, 544.
10. Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.
11. Hojo, M.; Sakuragi, R.; Okabe, S.; Hosomi, A. *Chem. Commun.* **2001**, 357.
12. Han, Y.; Chi, Z.; Huang, Y.-Z. *Synth. Commun.* **1999**, *29*, 1287.
13. Hasimoto, Y.; Kagoshima, H.; Saigo, K. *Tetrahedron Lett.* **1994**, *35*, 4805.
14. Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1833.
15. Isaac, M. B.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003; Tanaka, H.; Hamatani, T.; Yamashita, S.; Torii, S. *Chem. Lett.* **1986**, 1461.
16. Hojo, M.; Harada, H.; Ito, H.; Hosomi, A. *Chem. Commun.* **1997**, 2077.
17. Iseki, K.; Kuroki, Y.; Kobayashi, Y. *Tetrahedron: Asymmetry* **1998**, *9*, 2889.
18. Pornet, J. *Tetrahedron Lett.* **1981**, *22*, 455.
19. Iyoda, M.; Kanao, Y.; Nishizaki, M.; Oda, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3380.
20. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 621.
21. Nakagawa, T.; Kasatkin, A.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 3207.
22. Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Org. Chem.* **1982**, *47*, 2225.
23. Lee, A.S.-Y.; Chang, Y.-T.; Wang, S.-H.; Chu, S.-F. *Tetrahedron Lett.* **2002**, *43*, 8489.
24. Lee, A. S.-Y.; Wu, C.-W. *Tetrahedron* **1999**, *55*, 12531.
25. Lee, A. S.-Y.; Cheng, R.-Y.; Pan, O.-G. *Tetrahedron Lett.* **1997**, *38*, 443.
26. All reagents were purchased from Aldrich and Riedel-deHaen and all were used directly without further purification.
27. The ZnI_2 and ethene were generated from Zn powder and 1,2-diiodoethane under sonication.
28. The bath should be filled with water containing some 3–5% detergent. In our laboratory, we used Decon 90, which permits much more even cavitation in bath water.