A Facile Method for Synthesis of 5-Hydroxypentene via Sonochemical Barbier Reaction

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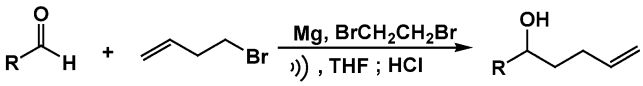
A series of 5-hydroxypentenes was synthesized from the reaction mixture of Mg powder, 1,2-dibromoethane, 4-bromobutene and aldehydes in THF under ultrasound. This sonochemical Barbier reaction provides a simple and alternative method for preparation of 5-hydroxypentene instead of the allylating reagent with epoxide.

Keywords: 5-Hydroxypentene; Sonochemical Barbier reaction; Cannizzaro-type reaction.

INTRODUCTION

5-Hydroxypentenes have received much attention as synthetic intermediates for synthesis of biologically active tetrahydrofuran derivatives.[1-11] 5-Hydroxypentenes have been prepared by the reactions of allylic organometallics of indium,[12] magnesium,[13] and tin,[13] with epoxide or cyclopropylmethylmagnesium bromide[14] with aldehyde. A mixture of regioisomeric alcohols was generally produced. High regioselectivity is usually manipulated by the tedious reaction conditions or by limiting functionalized epoxide. Only a few direct reactions of Grignard reagent of 4-bromobutene with aldehydes or ketones to produce 5-hydroxypentenes have been reported in the literature.[15-17] Our previous studies showed that Barbier-type allylation reactions of allylic bromide to aldehydes were successfully achieved by introducing ultrasound or Lewis acid.[18-20] Thus, we introduced and investigated the addition reaction of 4-bromobutene with aldehyde under Barbier reaction conditions. Herewith, we wish to report a simple sonochemical Barbier reaction condition for the synthesis of 5-hydroxypentene (Scheme I).

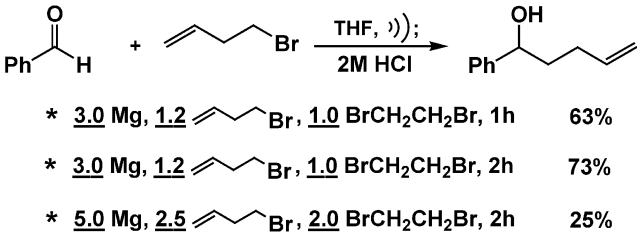
Scheme I



RESULTS AND DISCUSSION

To a reaction mixture of magnesium powder, 1,2-dibromoethane and 4-bromobutene was added dropwise a solution of benzaldehyde (0.2 M, THF) under ultrasound, and the reaction mixture was continuously sonicated at room temperature for 1-2 hours. The highest yield was obtained when 3 equivalents of Mg, 1 equivalent of 1,2-dibromoethane and 1.2 equivalents of 4-bromobutene were introduced and sonicated for 2 hours (Scheme II). Increments of Mg, 1,2-dibromoethane and 4-bromobutene produced a 25% yield of 5-hydroxypentene with a mixture of unidentified compounds.

Scheme II Aldehyde in THF (0.2 M) was added dropwise



We further investigated the substituent effect of substrate under the reaction conditions. *para*-Methoxy- and *para*-fluorobenzaldehydes were firstly chosen and investigated. The much lower yield of 5-hydroxypentene and a

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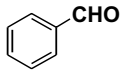
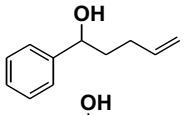
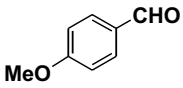
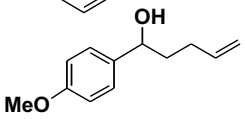
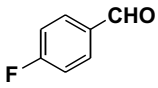
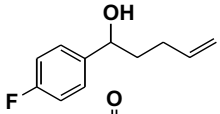
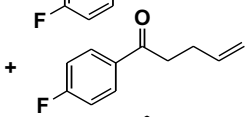
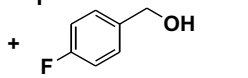
Table 1. The sonochemical reaction of 4-bromobutene with aldehyde

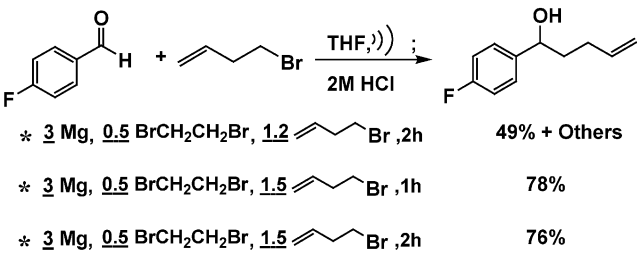
Entry	Aldehyde	Product	Yield[a]
1			73%
2			20%[b]
3			40%
			12%
			27%

[a] The yields were determined after chromatographic purification.
[b] Many unidentified compounds were not separated.

mixture of unidentified compounds were obtained when the electron-donating group (-OMe) was introduced to the substrate and investigated under the reaction conditions (Table 1, Entry 2). It should be noted that a Cannizzaro-type reaction[21-23] and direct reduced products were obtained when the electron-withdrawing group (-F) was attached on the aldehyde. A mixture of 5-hydroxypentene (40%), pentenone (12%) and phenylmethanol (27%) was obtained under this sonochemical Barbier reaction condition (Table 1, Entry 3).

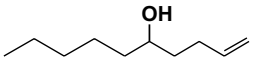
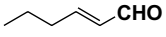
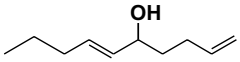
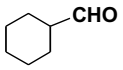
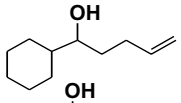
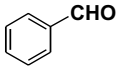
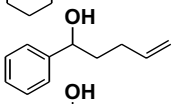
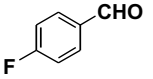
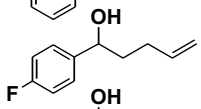
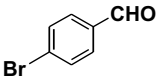
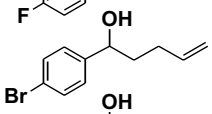
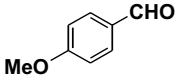
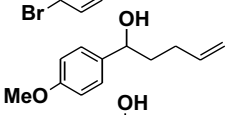
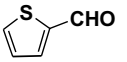
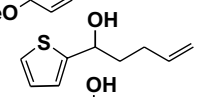
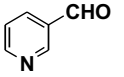
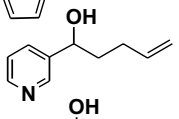
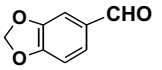
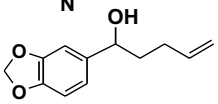
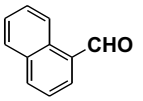
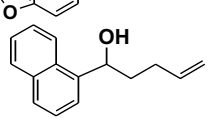
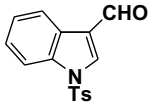
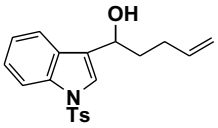
The experimental results showed that this reaction condition also presents a direct reduction process by magnesium metal and a competitive Cannizzaro-type reaction process. The addition of 1,2-dibromoethane was used for the activation of metal, and it reacted with Mg powder *in situ* to generate Lewis acid $MgBr_2$ and ethene.[24] The presence of $MgBr_2$ accelerates additional reaction, competitive direct reduction[25] and a Cannizzaro-type reaction.[26] Thus, decreasing the amount of 1,2-dibromoethane may retard the undesirable process of direct reduction or Cannizzaro-type reaction. A lower amount of 1,2-dibromoethane was used and investigated under the reaction conditions. A mixture of 3 equivalents of Mg, 0.5 equivalent of 1,2-dibromoethane, 1.2 equivalents of 4-bromobutene and *para*-fluorobenzaldehyde was sonicated at room temperature for two hours and a mixture of expected 5-hydroxypentene (49%), unexpected petenone (13%) and phenylmethanol (12%) were obtained (Scheme III). Increasing the amount of 4-bromobutene to 1.5 equivalents and shortening the sonication time improved the formation of expected 5-hydroxypentene dramatically to 78%. The longer sonication did not improve the formation yield of 5-hydroxypentene.

Scheme III Aldehyde in THF was added dropwise



A series of aldehydes was investigated under this sonochemical Barbier reaction condition, and the results are shown in Table 2. The experimental results showed that an electron-withdrawing group attached to an aldehyde usually gives a lower yield of 5-hydroxypentene because the presence of competitive processes of direct reduction and Cannizzaro-type reaction (Table 2, Entries 5, 6). The 1,2-addition reaction is the major reaction pathway for

Table 2. Synthesis of 5-hydroxypentenes

Entry	Aldehyde	Product	Yield[a]
1			52%[b]
2			77%[b]
3			92%
4			91%
5			78%
6			77%[c]
7			86%
8			57%
9			96%
10			88%
11			70%[d]
12			89%

[a] The yields were determined after chromatographic purification.
[b] The yield is low because the product is highly volatile.
[c] 18% of *p*-bromophenylmethanol was also produced.
[d] 18% of naphthylmethanol was also produced.

α,β-unsaturated aldehyde under this reaction condition (Table 2, Entry 2). Decomposition was observed when thiophenylaldehyde was treated under the reaction condition (Table 2, Entry 8). The heterocyclic aldehydes were reacted and gave good yields under the reaction conditions (Table 2, Entries 9, 12).

In conclusion, this reaction condition provides a simple method for the preparation of 5-hydroxypentene which is an important synthetic intermediate for synthesis of tetrahydrofuran compounds.

EXPERIMENTAL SECTION

All reagents were purchased from Aldrich and RiedeldeHaen, and all were used directly without further purification. 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.

General Procedure for Synthesis of 5-Hydroxypentene

A solution of aldehyde (1.0 mmol in 1 mL THF) was

added dropwise to a reaction mixture of Mg powder (3.0 mmol), 1,2-dibromoethane (0.5 mmol), and 4-bromobutene (1.5 mmol) in anhydrous THF (5.0 mL) under ultrasound and the reaction mixture was sonicated for an hour in a commercial ultrasonic cleaning bath[28] (Elma-T490DH, 50 kHz). After the sonication, a 2 M HCl solution 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.

Dec-1-en-5-ol (Table 2, Entry 1)

^{1}H-NMR: δ 0.85 (3H, t, *J* = 6.7 Hz), 1.26-1.53 (11H, m), 2.03-2.15 (2H, m), 3.55 (1H, m), 4.88-5.02 (2H, m), 5.78 (1H, m). ^{13}C-NMR: δ 13.8, 22.5, 25.2, 29.9, 31.8, 36.5, 37.4, 71.3, 114.4, 138.6. IR (neat): 3343, 2929, 2859, 1641, 1455 cm^{-1}. HRMS: 156.1520 (calcd. for $C_{10}H_{20}O$, 156.1514). MS: *m/z* 156 (1, M), 154 (13), 117 (72), 113 (11), 100 (11), 99 (base), 97 (15), 84 (40), 83 (40), 71 (36), 69 (26), 56 (26), 55 (61).

(E)-Deca-1,6-dien-5-ol (Table 2, Entry 2)

^{1}H-NMR: δ 0.88 (3H, t, *J* = 7.3 Hz), 1.36-1.44 (2H, m), 1.56-1.65 (3H, m), 1.99-2.02 (2H, m), 2.10-2.14 (2H, m), 4.07 (1H, m), 4.94-5.06 (2H, m), 5.46 (1H, m), 5.65 (1H, m), 5.84 (1H, m). ^{13}C-NMR: δ 13.4, 22.2, 29.6, 34.1, 36.4, 72.3, 114.4, 131.7, 133.1, 138.3. IR (neat): 3356, 2959, 2928, 2873, 1641, 1454 cm^{-1}. HRMS: 154.1348 (calcd. for $C_{10}H_{18}O$, 154.1348).

1-Cyclohexylpent-4-en-1-ol (Table 2, Entry 3)

^{1}H-NMR: δ 1.01-1.78 (14H, m), 2.09-2.30 (2H, m), 3.34-3.39 (1H, m), 4.94-5.07 (2H, m), 5.84 (1H, m). ^{13}C-NMR: δ 26.2, 26.3, 26.5, 27.7, 29.2, 30.3, 33.2, 43.7, 75.6, 114.6, 138.8. IR (neat): 3357, 2923, 2852, 1641, 1449 cm^{-1}. HRMS: 168.1510 (calcd. for $C_{11}H_{20}O$, 168.1514). MS: *m/z* 168 (M, 9), 151 (12), 135 (11), 126 (26), 121 (12), 113 (30), 111 (19), 95 (base), 86 (53), 85 (33), 84 (84), 67 (21), 55 (16).

1-Phenylpent-4-en-1-ol (Table 2, Entry 4)

^{1}H-NMR: δ 1.77-1.95 (3H, m), 2.10-2.20 (2H, m), 4.71 (1H, m), 4.97-5.07 (2H, m), 5.85 (1H, m), 7.27-7.36 (5H, m). ^{13}C-NMR: δ 29.6, 37.7, 73.3, 114.4, 125.7, 126.9, 127.9, 137.9, 144.4. IR (neat): 3348, 3030, 2937, 1641, 1494, 1453 cm^{-1}. HRMS: 162.1041 (calcd. for $C_{11}H_{14}O$, 162.1045). MS: *m/z* 162 (M, 9), 145 (98), 144 (26), 120 (84), 107 (98), 104 (38), 79 (base), 77 (89), 51 (22), 50 (6).

1-(4-Fluorophenyl)pent-4-en-1-ol (Table 2, Entry 5)

^{1}H-NMR: δ 1.69-1.85 (2H, m), 2.01-2.11 (2H, m), 2.89 (1H, s), 4.59 (1H, m), 4.95-5.05 (2H, m), 5.74 (1H, m), 6.95-7.02 (2H, m), 7.21-7.27 (2H, m). ^{13}C-NMR: δ 29.9, 38.1, 73.3, 115.0, 115.3, 127.4, 127.5, 138.0, 140.3, 160.5, 163.8. IR (neat): 3355, 3078, 2937, 1641, 1605, 1509 cm^{-1}. HRMS: 180.0957 (calcd. for $C_{11}H_{13}FO$, 189.0950). MS: *m/z* 180 (M, 14), 163 (70), 162 (48), 151 (14), 138 (49), 125 (base), 123 (13), 97 (20), 95 (5), 28 (75), 18 (9).

1-(4-Bromophenyl)pent-4-en-1-ol (Table 2, Entry 6)

^{1}H-NMR: δ 1.70-1.85 (2H, m), 2.03-2.12 (2H, m), 2.51 (1H, s), 4.59 (1H, m), 4.97-5.05 (2H, m), 5.81 (1H, m), 7.15-7.18 (2H, m), 7.42-7.46 (2H, m). ^{13}C-NMR: δ 29.8, 37.9, 73.2, 115.1, 121.1, 127.6, 131.4, 137.8, 143.5. IR (neat): 3342, 3078, 2936, 1640, 1593, 1487 cm^{-1}. HRMS: 240.0141 (calcd. for $C_{11}H_{13}BrO$, 240.0150). MS: *m/z* 240 (M, 2), 200 (25), 198 (26), 187 (93), 185 (base), 157 (13), 78 (34), 77 (76), 51 (12), 50 (7), 28 (49).

1-(4-Methoxyphenyl)pent-4-en-1-ol (Table 2, Entry 7)

^{1}H-NMR: δ 1.76-1.92 (2H, m), 2.04-2.14 (2H, m), 3.80 (3H, s), 4.65 (1H, m), 4.95-5.06 (2H, m), 5.84 (1H, m), 6.87-6.90 (2H, m), 7.25-7.28 (2H, m). ^{13}C-NMR: δ 30.0, 37.8, 55.1, 73.4, 113.7, 114.7, 127.1, 136.7, 138.2, 158. IR (neat): 3380, 2936, 2837, 1640, 1612, 1586, 1512, 1442 cm^{-1}. HRMS: 192.1149 (calcd. for $C_{12}H_{16}O_2$, 192.1150). MS: *m/z* 192 (M, 12), 150 (16), 138 (16), 137 (base), 135 (12), 109 (34), 94 (16), 77 (18), 66 (5), 65 (5).

1-(Thiophen-2-yl)pent-4-en-1-ol (Table 2, Entry 8)

^{1}H-NMR: δ 1.89-2.05 (3H, m), 2.09-2.22 (2H, m), 4.92-5.10 (3H, m), 5.85 (1H, m), 6.95-6.97 (2H, m), 7.24 (1H, m). ^{13}C-NMR: δ 30.0, 38.2, 69.7, 115.2, 123.7, 124.5, 126.6, 137.8, 148.6. IR (neat): 3346, 3075, 2937, 1640, 1440 cm^{-1}. HRMS: 168.0623 (calcd. for $C_9H_{12}OS$, 168.0609).

1-(Pyridin-3-yl)pent-4-en-1-ol (Table 2, Entry 9)

^{1}H-NMR: δ 1.64-1.89 (2H, m), 1.98-2.14 (2H, m),

4.63 (1H, m), 4.90-4.98 (2H, m), 5.75 (1H, m), 7.15-7.20 (1H, m), 7.65 (1H, d, J = 7.7 Hz), 8.25-8.31 (2H, m). ^{13}C-NMR: δ 29.8, 38.0, 71.1, 115.1, 123.5, 133.9, 137.8, 140.5, 140.7, 147.4, 148.2. IR (neat): 3243, 2936, 1641, 1581, 1428 cm^{-1}. HRMS: 163.1013 (calcd. for $C_{10}H_{13}NO$, 163.0997). MS: *m/z* 163 (M, 5), 146 (18), 144 (10), 134 (9), 109 (13), 108 (base), 106 (18), 105 (18), 80 (56), 78 (15), 53 (19), 51 (10).

1-(Benzo[d][1,3]dioxol-6-yl)pent-4-en-1-ol (Table 2, Entry 10)

^{1}H-NMR: δ 1.73-1.93 (3H, m), 2.03-2.15 (2H, m), 4.59 (1H, m), 4.96-5.06 (2H, m), 5.83 (1H, m), 5.94 (2H, s), 6.75-6.83 (2H, m), 6.85 (1H, s). ^{13}C-NMR: δ 29.9, 37.9, 73.7, 100.8, 106.3, 107.9, 114.8, 119.2, 138.1, 138.6, 146.7, 147.6. IR (neat): 3361, 2914, 1640, 1503, 1486, 1441 cm^{-1}. HRMS: 206.0942 (calcd. for $C_{12}H_{14}O_3$, 206.0943). MS: *m/z* 206 (M, 19), 164 (12), 152 (10), 151 (base), 149 (10), 137 (12), 123 (13), 122 (5), 121 (6), 94 (5), 93 (50), 77 (6).

1-(Naphthalen-4-yl)pent-4-en-1-ol (Table 2, Entry 11)

^{1}H-NMR: δ 1.97-2.12 (3H, m), 2.25-2.33 (2H, m), 5.02-5.13 (2H, m), 5.50 (1H, m), 5.91 (1H, m), 7.46-7.55 (3H, m), 7.66 (1H, d, J = 7.1 Hz), 7.79 (1H, d, J = 8.1 Hz), 7.91 (1H, m), 8.12 (1H, d, J = 1.7 Hz). ^{13}C-NMR: δ 30.4, 37.3, 70.6, 115.2, 122.9, 123.1, 125.4, 125.5, 126.0, 127.9, 127.9, 130.4, 133.8, 138.2, 140.3. IR (neat): 3395, 3070, 2925, 1640, 1510 cm^{-1}. HRMS: 212.1201 (calcd. for $C_{15}H_{16}O$, 212.1201). MS: *m/z* 212 (M, 19), 194 (3), 179 (3), 170 (4), 158 (9), 157 (base), 155 (5), 130 (5), 129 (67), 128 (29), 127 (16).

1-(1-Tosyl-1H-indol-3-yl)pent-4-en-1-ol (Table 2, Entry 12)

^{1}H-NMR: δ 1.95-2.02 (3H, m), 2.12-2.18 (2H, m), 2.33 (3H, s), 4.93-5.07 (3H, m), 5.84 (1H, m), 7.19-7.35 (4H, m), 7.50 (1H, s), 7.64 (1H, d, J = 7.8 Hz), 7.74-7.77 (2H, m), 7.99 (1H, d, J = 8.3 Hz). ^{13}C-NMR: δ 21.5, 30.0, 36.0, 67.5, 113.8, 115.2, 120.4, 122.7, 123.1, 124.8, 125.7, 126.8, 128.8, 129.8, 135.2, 135.6, 137.9, 144.9. IR (neat): 3394, 3006, 2989, 2386, 2349, 1640, 1597, 1447 cm^{-1}. HRMS: 355.1262 (calcd. for $C_{20}H_{21}NO_3S$, 355.1242). MS: *m/z* 355 (M, 23), 301 (24), 300 (base), 155 (30), 145 (7), 117 (10), 108 (21), 91 (48), 80 (81), 55 (9).

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