# Synthesis of 2,5-Dibromobenzaldehyde and Its Reaction with Hexylmagnesium Bromide

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2,5-Dibromobenzaldehyde (**3**) is synthesized by the oxidation of 2,5-dibromotoluene (**1**) via 2,5-dibromobenzylidene diacetate (**2**). Grignard reaction of hexylmagnesium bromide with **2** gives the normal addition product, 2,5-dibromo-α-hexylbenzyl alcohol (**5**) and reduced product, 2,5-dibromobenzyl alcohol (**6**).

Methyl groups directly attached to aromatic or heteroaromatic rings are oxidized to aldehydes by Thiele reagent. The oxidation reaction is carried out with chromium(VI) oxide in a mixture of acetic anhydride and acetic acid at 0–5 °C in the presence of concentrated sulfuric acid. The aldehyde stays in the form of the diacetate, produced by reaction with the acetic anhydride, thereby avoiding further oxidation to the acid. Simple hydrolysis of the diacetate by dilute hydrochloric acid or sulfuric acid re-forms the aldehyde.[1-3]

We have examined the use of this method in the oxidation of 2,5-dibromotoluene (**1**) and further examined the Grignard addition of hexyl bromide to the produced aldehyde. The Grignard reaction of aldehydes and ketones have been widely studied and various pathways have been reported.[4] In the reaction of 2,5-dibromobenzaldehyde (**3**) and hexylmagnesium bromide, 2,5-dibromo-α-hexylbenzyl alcohol (**5**), the normal addition product, and 2,5-dibromobenzyl alcohol (**6**), a two-electron reduction product, were obtained. About 70% of the raw product was primary alcohol **6**.

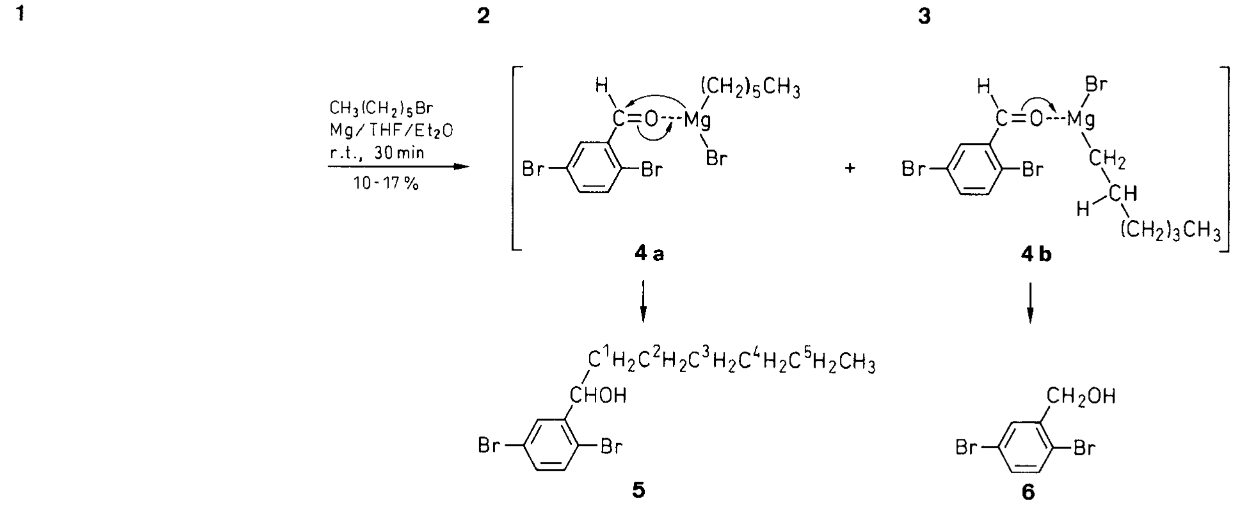
The small yield of normal addition product can be explained by the slowing down of the addition reaction compared with other reactions as the result of steric hindrance by the large groups neighboring the carbonyl and the effect of the solvent surrounding the Grignard reagent.[5] We have examined the ordinary Grignard addition reaction and the reduction of 2,5-dibromobenzaldehyde by hexylmagnesium bromide with regards to solvent [diethyl ether and tetrahydrofuran (THF)] and temperature.

Variation of temperature from 0 to 30 °C in both solutions had no effect on Grignard product yield. THF gave better combined yield (73 %) compared to diethyl ether (61 %), however, more 2,5-dibromo-α-hexylbenzyl alcohol was obtained in diethyl ether (0.5 g from 2.9 g of crude product *cf.* 0.6 g from 3.5 g of crude product in THF). THF is more basic than diethyl ether because of its ring structure and strongly coordinates to the Grignard reagent. Accordingly, reactivity becomes higher in THF, but the rigid ring structure of THF disturbs the addition of Grignard reagent to the carbonyl group and promotes the reduction reaction.

All reagents were of reagent quality and used as supplied. 2,5-Dibromotoluene was purchased from Aldrich Chemical Co. and all other chemicals from Kanto Chemical Co. $Et_2O$ and THF were dried with calcium hydride. Melting points were taken using a Melting Temp apparatus and are uncorrected. Microanalyses were obtained using a Perkin-Elmer 240 element analyser. IR spectra were obtained using Shimadzu IR-460 and Shimadzu FTIR-4300 spectrometers. $^1H$ and $^{13}C$ NMR spectra were obtained using a JEOL GSX 270 MHz FT-spectrometer.

**2,5-Dibromobenzylidene Diacetate (2):**

To a mixture of 2,5-dibromotoluene (18 g, 0.072 mol), AcOH (122 g, 1.2 mol) and $Ac_2O$ (120 g, 2.0 mol) were added conc. $H_2SO_4$ (26.8 g, 0.274 mol) and $CrO_3$ (18 g, 0.18 mol) below 3 °C. After being stirred for 3 h at 3 °C, the mixture was poured into ice–water, filtered, and vigorously stirred in 2 % aqueous $Na_2CO_3$ (100 mL). The product was filtered off, washed thoroughly and dried. Yield after crystallization from hot light petroleum (bp 30–60) was 13–14 g (48–53 %).



Scheme 1

**Table.** Compounds 2, 3, 5, 6 Prepared

| Product | Yield (%) | mp (°C) | Molecular Formula[a] | IR (KBr) $\nu$ (cm$^{-1}$) | $^1$H NMR (CDCl$_3$/TMS) $\delta$, $J$ (Hz) | $^{13}$C NMR (CDCl$_3$) $\delta$ |
|---|---|---|---|---|---|---|
| **2** | 48–53 | 115.5 | $C_{11}H_{10}O_4Br_2$ (366.0) | 3100, 2990, 1780, 1370, 1230, 1190, 970, 840 | 2.16 (s, 6H, $CH_3$), 7.37–7.67 (m, 3H, $C_6H_3$), 7.85 (s, 1H, CH) | 20.69 ($CH_3$), 88.33 (CH), 121.09, 121.57 ($C_{arom}Br$), 131.06, 134.08, 134.57 ($C_{arom}H$), 136.85 ($C_{arom}CH$), 168.25 (CO) |
| **3** | 76–87 | 85.5–86 | $C_7H_4OBr_2$ (263.9) | 3100, 2880, 2750, 1685, 1380, 1190, 1025, 830 | 7.51–8.03 (m, 3H, $C_6H_3$), 10.29 (s, 1H, CHO) | 122.24, 125.43 ($C_{arom}Br$), 132.69, 135.29, 138.05 ($C_{arom}H$), 137.02 ($C_{arom}CHO$), 190.42 (CHO) |
| **5** | 10–17 | 85.5–86 | $C_{13}H_{18}OBr_2$ (350.1) | 3250, 2970, 2960, 2850, 1470, 1450, 1385, 1025, 805 | 0.88 (t, 3H, $J = 6.6$, $CH_3$), 1.29–1.73 (br s, 10H, $CH_2$), 1.96 (d, 1H, $J = 4.0$, OH), 4.97–5.03 (m, 1H, CH), 7.22–7.70 (m, 3H, $C_6H_3$) | 14.09 ($CH_3$), 22.61 (5-$CH_2$), 25.70 (2-$CH_2$), 29.02 (3-$CH_2$), 31.74 (4-$CH_2$), 37.67 (1-$CH_2$), 72.70 (CH), 120.31, 121.83 ($C_{arom}Br$), 130.48, 131.64, 133.96 ($C_{arom}H$), 146.11 ($C_{arom}CH$) |
| **6** | 44–48 | 100.5–101 | $C_7H_6OBr_2$ (265.9) | 3210, 3090, 2900, 2850, 1450, 1430, 1390, 1055, 1020, 810 | 2.11 (t, 1H, $J = 6.1$, OH), 4.71 (d, 2H, $J = 5.9$, $CH_2$), 7.26–7.66 (m, 3H, $C_6H_3$) | 64.26 ($CH_2$), 120.55, 121.63 ($C_{arom}Br$), 131.34, 131.81, 133.77 ($C_{arom}H$), 141.68 ($C_{arom}CH_2OH$) |

[a] Satisfactory microanalyses: C ± 0.07, H ± 0.09.

**2,5-Dibromobenzaldehyde (3):**

2,5-Dibromobenzylidene diacetate (**2**) (8 g, 22 mmol), $H_2O$ (20 mL, 1 mol), EtOH (40 mL) and conc. $H_2SO_4$ (2 mL) were heated for 80 min at 75 °C. The solution was filtered and cooled to crystallize the product, which was then washed with 2% aqueous $Na_2CO_3$ and cool water. Yield: 4.4–5.0 g (76–87%) after crystallization from light petroleum (bp 30–60).

**Reaction with hexylmagnesium bromide:**

Mg ribbon (0.72 g, 0.03 mol) and a catalytic amount of $I_2$ were put in THF (20 mL), and a THF solution (20 mL) of hexyl bromide (3 mL, 22 mmol) was gradually added. Ninety minutes after the initiation of the reaction, 2,5-dibromobenzaldehyde (3.6 g, 14 mmol) in THF (20 mL) was added. The mixture was swirled for 30 min, water (30 mL) was added, and the solvent was evaporated. The product were extracted three times with toluene (15 mL). The extract was cooled to crystallize primary alcohol **6**, which was recrystallized from toluene giving 2,5-dibromobenzyl alcohol (1.8 g). The filtrate was co-evaporated with toluene and the residue was recrystallized from methanol giving 2,5-dibromo-α-hexylbenzyl alcohol (**5**). Yield: 0.5–0.8 g (10–17%).

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