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NOTE

PREPARATION OF BENZYL-α-D_1-ALCOHOL BY THE REDUCTION OF BENZALDEHYDE WITH RANEY ALLOYS IN AN ALKALINE DEUTERIUM OXIDE SOLUTION

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SUMMARY

Benzyl-α-d_1-alcohol was prepared in high isotopic purity by the reduction of benzaldehyde with Raney Cu-Al alloy in 10% Na_2CO_3-D_2O solution using ultrasonic irradiation.

Key Words: Deuterium Labelling, Synthesis, Raney Cu-Al Alloy, NaOD-D_2O, Na_2CO_3-D_2O

INTRODUCTION

The preparation of benzyl-α-d_1-alcohol has been reported using *n* - BuLi / THF / D_2O,[1)] $LiAlD_4$,[2)] and hv / D_2O.[3)] However, these experiments should be carried out under conditions of low temperature (-70 °C) and / or an inert atmosphere and need a controlled pH. The experimental conditions need therefore to be chosen very carefully.

Recently we have reported that deuteriated aromatic compounds, which possess deuterium atom(s) at specific position(s) of the aromatic ring can be obtained by treating the corresponding halogenated aromatic compounds with Raney Cu-Al alloy in an alkaline deuterium oxide solution.[4)] For example, the deuteriation of halogenated acetophenones affords 1-phenyl ethanol by using this method, dehalogenation and the reduction of the substituent occuring at the same time.[5)] In order to determine the limitation of this method

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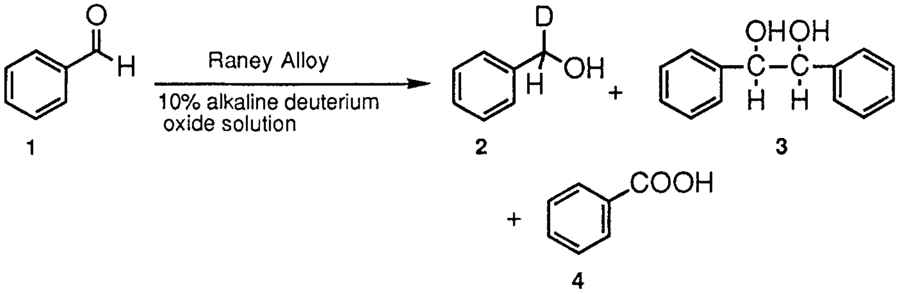
using Raney alloys in an alkaline solution, the preparation of the titled monodeuteriated compound from benzaldehyde was carried out .

RESULTS AND DISCUSSION



Scheme 1

Table 1. Reduction of benzaldehyde with Raney Alloys in an Alkaline Deuterium Oxide Solution.[1]

Raney Alloy	Alkaline	Temp. (°C)	Solvent	Product (Yield %)			Composition of **2** (%)[2]					
				2	3	4	D_0	D_1	D_2	D_3	D_4	D_5
Ni - Al	10% NaOD-D_2O	r. t.	—	25	0	3	2	22	63	9	3	1
Co - Al	10% NaOD-D_2O	r. t.	—	53	0	5	15	38	44	2	1	0
Cu - Al	10% NaOD-D_2O	r. t.	—	5	36	10	79	19	3	1	0	0
Fe - Al	10% NaOD-D_2O	r. t.	—	11	30	1	12	82	5	1	0	0
Ni - Al[3]	10% Na_2CO_3-D_2O	60	THF	67	0	1	21	51	27	1	0	0
Co - Al[3]	10% Na_2CO_3-D_2O	60	THF	83	0	2	19	51	29	1	0	0
Cu - Al[3]	10% Na_2CO_3-D_2O	60	THF	13	51	1	6	91	3	0	0	0

1) Benzaldehyde : 5.33 g (50 mmol), Raney alloy : 5.0 g

2) Compositions were obtained from mass spectral data.

3) Under ultrasonic irradiation, Raney alloy : 2.5 g

At first we investigated the deuteration by reduction of benzaldehyde (**1**) with Raney alloys in 10% NaOD-D_2O, which is our customary method.[4] The reduction of benzaldehyde with Raney Ni-Al or Co-Al alloy in 10% NaOD-D_2O solution did not give the corresponding benzyl-α-d_1 alcohol (**2**) , but higher deuterated benzylalcohols, where more deuteriums were introduced into the aromatic ring and the benzylic position because of H-D exchange. On the other hand, with Raney Cu-Al alloy, **2** was obtained in low isotopic purity (d_1=19 %). This suggests that when using a Raney Cu-Al alloy, a Cannizzaro reaction competes with the reduction.

The results in Table 1 show that we did not obtain the expected deuterated benzyl alcohol in high isotopic purity by the reduction of **1** using any of the Raney alloys in 10% NaOD-D_2O solution because of H-D exchange and / or a competing Cannizzaro reaction.

Next we investigated the reduction of **1** in 10% Na_2CO_3-D_2O solution. It had been found previously that ultrasonic irradiation accelerates the reduction of **1** with Raney alloys in 10% aqueous Na_2CO_3 solution and THF.6) However, when **1** was treated with Ni-Al or Co-Al alloy in 10% Na_2CO_3-D_2O solution and THF under ultrasonic irradiation, H-D exchange occurred just as in the reaction using a 10% NaOD-D_2O solution. Therefore, the isotopic purity of **2** was low. But when we treated **1** with Raney Cu-Al alloy under the same reaction conditions, we obtained **2** in low yield but in high isotopic purity .

In conclusion, we obtained the expected benzyl-α-d_1 alcohol in high isotopic purity by the reduction with Raney Cu-Al alloy in 10% Na_2CO_3-D_2O solution using ultrasonic irradiation. The study of the isotope effect on the oxidation of benzyl-α-d_1 alcohol which we obtained by this method, is now in progress and will be reported elsewhere.

EXPERIMENTAL

The ^1H N.M.R. (internal $SiMe_4$) spectra were taken on a Nippon Denshi JEOL EX 270 n.m.r. spectrometer. The Mass spectra were recorded on a Nippon Denshi JMS-O1SG-2 mass spectrometer at 75 eV using a direct-inlet system. Ultrasonic cleaner of Elma Transsonic T 460 was used for ultrasonication during reduction.

Materials.

We used commercially available benzaldehyde (**1**) after distillation . Commercially available Raney alloys were used for reaction (Kishida Chemical Co.).

Preparation of benzyl-α-d_1 alcohol (**2**) Two typical procedures are given below.

Reduction of benzaldehyde (**1**) in 10% NaOD-D_2O solution

To a stirred mixture of **1** (5.33 g, 50 mmol) in 10% NaOD-D_2O solution (40 ml) at room temperature was added Raney Ni-Al alloy (1.0 g) in 5 portions over 50 min (total amount of the alloy was 5.0 g). After the reaction mixture was stirred at room temperature for 100 min, the Ni powder formed was filtered and the filtrate was extracted with Et_2O. The extract was washed with water, dried over $MgSO_4$, evaporated *in vacuo* to afford 1.30g (25 %) of **2**. The aqueous phase was acidified with conc. hydrochloric acid and extracted with Et_2O. The extract was dried over $MgSO_4$, evaporated *in vacuo*, to afford 0.20 g (3 %) of benzoic acid **4**.

Reduction of benzaldehyde (1) in 10% Na_2CO_3-D_2O solution

To a stirred mixture of **1** (5.33 g, 50 mmol), Raney Ni-Al alloy (2.5 g), and dry THF (10 ml) at room temperature was added gradually dropwise 10% Na_2CO_3-D_2O solution in a period of 10 min under ultrasonic irradiation. After the reaction mixture was stirred for 90 min under the same reaction conditions, the Ni powder formed was filtered and the filtrate was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, evaporated *in vacuo* to leave a residue , which, after being analyzed by V.P.C., was distilled under reduced pressure to give **2** (3.64 g, 67%). The aqueous phase was acidified with conc. hydrochloric acid and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$, evaporated *in vacuo*, to afford 50 mg (1%) of **4**.

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