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Reduction of Benzaldehydes with Raney Alloys in an Alkaline Solution

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The reduction of benzaldehyde (**1a**) with Raney alloys in a 10% aq NaOH solution afforded benzyl alcohol (**2a**) in various yields (17—81%). In this reaction benzoic acid was also obtained as a by-product at the same time. This suggests that a Cannizzaro reaction competes with the reduction. In a 10% aq Na_2CO_3 solution the reduction of **1a** with Raney alloys proceeded under ultrasonic irradiation to give almost exclusively **2a**. In addition, we almost could not observe a Cannizzaro reaction in these experiments based on a comparison with a reduction in a 10% aq NaOH solution. A crossed Cannizzaro reaction between formaldehyde and benzaldehyde did not occur in a 10% aq NaOH solution/THF/MeOH, but afforded the reductive coupling compound hydrobenzoin.

It was previously reported that the reduction of halogenated acetophenones[1] and benzonitriles[2] with Raney alloys in an alkaline solution afforded 1-phenylethanol and benzylamine, respectively, a dehalogenation and the reduction of the substituent occurring at the same time. Deuterated 1-phenylethanols have been prepared by reduction in a NaOD–D_2O solution under the same conditions.[3]

In the present study, in order to determine the most suitable conditions for this reductive method using Raney alloys, as preliminary work for preparing benzyl-α-d_1 alcohols, the reduction of benzaldehydes with Raney alloys in an alkaline solution was investigated.

Results and Discussion

The reduction of benzaldehydes (**1a**—**c**) with Raney alloys in an alkaline solution was carried out under various conditions. The results are summarized in Table 1.

In a 10% aq NaOH Solution. In the reduction of **1a** it was noted that there was a different distribution of products for every type of Raney alloy used (Scheme 1). For example, in the case of a Raney Ni–Al alloy, although **1a** was not recovered, the yield of the expected benzyl alcohol was low (20%, Run 1). On the other hand, with a Raney Co–Al alloy, the yield was remarkedly improved (81%, Run 7). With a Raney Cu–Al alloy, hydrobenzoin (**3a**) and benzoic acid (**4a**) were obtained as well as **2a** (Run 10). With a Raney Fe–Al alloy, **2a**, **3a**, and **4a** were obtained as in the case of the Raney Cu–Al alloy (Run 16). The formation of **4a** is interesting, since it is formed in spite of the reductive conditions. This probably suggests that a Cannizzaro reaction competes with the reduction. It is apparent that the Raney Cu–Al alloy considerably favors a Cannizzaro reaction, compared to other Raney alloys. The reduction of **1b** with the Raney Ni–Al or Co–Al alloy afforded **2b** in good yields, but with the Raney Cu–Al alloy, the reaction almost did not proceed, and with the Raney Fe–Al alloy, only **1b** was recovered (Runs 18—20, 22). On the other hand, **1c** was not reduced by the Raney Ni–Al alloy, which is usually the strongest reducing agent, compared with other Raney alloys.

In a 10% aq Na_2CO_3 Solution. In the case of preparing monodeuterated benzyl alcohol, we would expect that with the Raney Ni–Al or Co–Al alloy, some deuterium would also be introduced to the aromatic ring as well as the benzylic position.[4,5] With the Raney Cu–Al alloy, the desired monodeuteration of the benzylic position would be impeded by a Cannizzaro reaction. We therefore investigated the reduction of **1a** with Raney alloys under weak alkaline conditions in which the H–D exchange reactions and the Cannizzaro reaction would not occur.

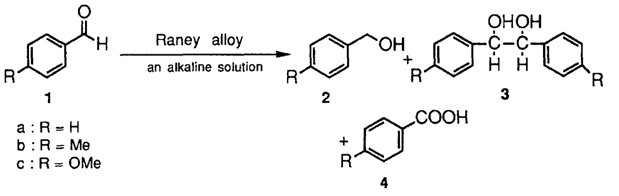
In the reduction of **1a** with the Raney Ni–Al alloy in a 10% aq Na_2CO_3 solution, the starting material was recovered in spite of the higher reaction temperatures, compared to the experiment with a 10% aq NaOH solution (Run 4). Under ultrasonic irradiation, however the reduction of **1a** afforded **2a** in a high yield (96%) within the same reaction time (100 min), compared with the reduction of **1a** in a 10% aq NaOH solution (Run 6). We found that ultrasonification accelerated the reduction with Raney alloys. We also investigated the reduction of **1a** with other Raney alloys in 10% aq Na_2CO_3 solutions under the same reaction conditions. With the Raney Co–Al alloy, the reduction of **1a** proceeded at about the same rate as with the Raney Ni–Al alloy, with the Raney Cu–Al alloy the reduction of **1a** proceeded, but slower than with the Raney Ni–Al or Co–Al alloy (Runs 9, 15). In 10% aq Na_2CO_3 solution systems we almost did not observe any Cannizzaro reaction competing with the reduction, as in the case in 10% aq NaOH solution systems.

Cannizzaro Reaction. We investigated the reduction of benzaldehydes with the Raney Cu–Al alloy in a 10% aq NaOH solution in order to obtain more

Table 1. Reduction of Benzaldehydes with Raney Alloys in an Alkaline Solutiona)

Run	Substrate	Raney alloy	Developing	Reaction	Temp	Solvent	Product yield/%			Recovery of **1**
		g	solution/ml	time/min	°C		**2**	**3**	**4**	Yield/%
1	**1a**	Ni–Al (5)	10% aq NaOH (40)	150	r.t.	—	20	—	4	—
2	**1a**	Ni–Al (2.5)	10% aq NaOH (20)	100	r.t.	THF	34b)	—	7	51b)
3	**1a**	Ni–Al (2.5)	10% aq Na_2CO_3 (40)	40	60	THF	34b)	—	1	45b)
4	**1a**	Ni–Al (2.5)	10% aq Na_2CO_3 (40)	100	60	THF	80b)	—	1	12b)
5d)	**1a**	Ni–Al (2.5)	10% aq Na_2CO_3 (40)	40	60	THF	74b)	—	1	7b)
6d)	**1a**	Ni–Al (2.5)	10% aq Na_2CO_3 (40)	100	60	THF	96	—	2	—
7	**1a**	Co–Al (5)	10% aq NaOH (40)	150	r.t.	—	81	—	6	—
8	**1a**	Co–Al (2.5)	10% aq NaOH (20)	100	r.t.	THF	12b)	—	2	36b)
9d)	**1a**	Co–Al (2.5)	10% aq Na_2CO_3 (40)	100	60	THF	78	—	—	—
10	**1a**	Cu–Al (5)	10% aq NaOH (40)	150	r.t.	—	17	32	20	—
11	**1a**	Cu–Al (2.5)	10% aq NaOH (20)	100	r.t.	—	21	29	34	—
12	**1a**	Cu–Al (2.5)	10% aq NaOH (20)	100	r.t.	THF	44	5	44	—
13e)	**1a**	Cu–Al (2.5)	10% aq NaOH (20)	100	r.t.	THF	41	9	41	—
14d)	**1a**	Cu–Al (2.5)	10% aq Na_2CO_3 (40)	100	60	THF	59b)	17	4	10b)
15d)	**1a**	Cu–Al (2.5)	10% aq Na_2CO_3 (40)	130	60	THF	68b)	8	3	8b)
16	**1a**	Fe–Al (5)	10% aq NaOH (40)	150	r.t.	—	32	30	2	—
17	**1a**	Fe–Al (2.5)	10% aq NaOH (20)	100	r.t.	THF	10b)	7	1	72b)
18	**1b**	Ni–Al (5)	10% aq NaOH (40)	150	r.t.	—	66	—	2	—
19	**1b**	Co–Al (5)	10% aq NaOH (40)	150	r.t.	—	83c)	—	4	17c)
20	**1b**	Cu–Al (5)	10% aq NaOH (40)	150	r.t.	—	11c)	—	—	89c)
21	**1b**	Cu–Al (2.5)	10% aq NaOH (20)	100	60	THF	41b)	—	42	3b)
22	**1b**	Fe–Al (5)	10% aq NaOH (40)	150	r.t.	—	—	—	—	100c)
23	**1c**	Ni–Al (5)	10% aq NaOH (40)	150	r.t.	—	—	—	—	100c)
24	**1c**	Cu–Al (2.5)	10% aq NaOH (20)	100	60	THF	48b)	—	26	—

a) Substrate: 50 mmol; THF: 10 ml; MeOH: 35 ml; Reaction time: In Runs 1, 7, 10, 16, 18, 19, 20, 22, and 23 respectively the time (50 min) of adding the Raney alloy to the reaction solution is included in the mentioned reaction time. In other Runs respectively the time (10 min) of adding the an alkaline solution to the reaction solution is included in the mentioned reaction time. b) Determined by V.P.C. c) Relative yield was determined by V.P.C. d) Under ultrasonic irradiation. e) 10% aq NaOH solution and benzaldehyde were respectively added dropwise with dropping funnel for 10 min.



Scheme 1.

Table 2. Investigation of the Factor of the Cannizzaro Reaction in a 10% aq NaOH–N_2O Solutiona)

Metal	Product yield/%			Recovery of **1a**
	2a	**3a**	**4a**	Yield/%
—	0	0	0	90
Cu	0	0	0	92
Al	3	30	3	50
Cu+Al	45	41	1	0

a) Benzaldehyde; 5.33 g (50 mmol), Metal; 2.5 g, THF; 10 ml, reaction time; 90 min.

detailed information about how the Cannizzaro reaction competes with the reduction of the benzaldehydes under these conditions.

At first, the reduction of **1a** with the Raney Cu–Al alloy in a 10% aq NaOH solution was carried out using either THF as a solvent or no solvent at all (Runs 11—13). In the case of using THF, the Cannizzaro reaction proceeded faster than in the case of no solvent. We almost did not observe a reduction of **1a** with any of the Raney alloys, except for the Raney Cu–Al alloy in a 10% aq NaOH solution/THF (Runs 2, 8, and 17). Almost no Cannizzaro reaction products could be observed in the system using the Raney Ni–Al, Co–Al, and Fe–Al alloys, and we recovered most of the starting material.

The reaction was then run under different conditions, using only Cu powder, only Al powder, both Cu and Al powder and not using any metal (Table 2). In the case of using no metal or only Cu powder, we recovered only the starting material. On the other hand, in the case of using Al powder or both Cu and Al powder, we did not observe any Cannizzaro reaction products, while obtaining a coupling compound of **1a**. This result means that only the alloy made from Cu and Al causes the Cannizzaro reaction in the reduction of **1a** with the Raney Cu–Al alloy in a 10% aq NaOH solution/THF.

Furthermore we investigated the reduction of *p*-tolualdehyde (**1b**) and *p*-anisaldehyde (**1c**) with the Raney Cu–Al alloy (Runs 21 and 24). We observed a more remarkably Cannizzaro reaction product in the reduction of **1b** than in the reduction of **1c** with the Raney Cu–Al alloy in a 10% aq NaOH solution/THF.

Crossed Cannizzaro Reaction. We can expect that benzyl alcohol is obtained in good yield from benzaldehyde by taking a Crossed Cannizzaro reaction. We thus investigated the possibility of a crossed Cannizzaro reaction with the Raney Cu–Al alloy in a 10% aq NaOH solution/THF (Table 3). However, no crossed Cannizzaro reaction was observed, though hydrobenzoin, which is the reductive coupling compound of **1a**, was obtained (Scheme 2). Furthermore, the addition of MeOH to the 10% aq NaOH solution/THF accelerated the formation of hydrobenzoin. This is quite interesting, since the formation of hydrobenzoin takes place in the presence of water. Usually, reductive coupling reactions, in which hydrobenzoin is obtained, proceed only under anhydrous conditions.[6—10)]

In conclusion, reduction with Raney alloys in 10% aq Na_2CO_3 solutions under ultrasonic irradiation is a convenient method for preparing benzyl alcohol from benzaldehyde. The preparation of monodeuterated benzyl alcohol using this method and the reductive coupling reaction of aromatic aldehydes and ketones under aqueous conditions are now in progress and will be reported elsewhere.

Experimental

General. Vapor-phase chromatography was performed on a Yanagimoto Gas Chromatograph G-2800 instrument equipped with a fused-silica capillary column (Quadrex corporation, 007-1-25-0.25F, 0.25 mm i.d. ×25 m, liquid phase: methyl silicone). V.P.C. yields were obtained using *o*-xylene as an internal standard. Product identification was carried out based on the retention time of standard materials (**1a**, **2a**, **1b**, **2b**, **1c**, and **2c**). An ultrasonic clearner (Elma Transsonic T 460) was used for sonication during reduction.

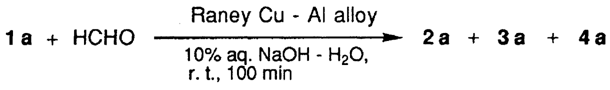
Materials. Benzaldehydes **1a**—**1c** are commercially available. Commercially available Raney alloys were used for the reactions (Kishida Chemical Co.).

Reduction of Benzaldehyde (1a) in a 10% aq NaOH Solution. To a stirred mixture of **1a** (5.33 g, 50 mmol) in a 10% aq NaOH solution (40 ml) at room temperature was added Raney 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 $MgSO_4$, and evaporated in vacuo to afford 1.08 g (20%) of benzyl alcohol (**2a**). The aqueous phase was acidified with concd hydrochloric acid and extracted with Et_2O. The extract was dried over $MgSO_4$, and evaporated in vacuo to afford 0.25 g (4%) benzoic acid (**4a**).

Table 3. Crossed Cannizzaro Reaction in a 10% aq NaOH–H_2O Solution[a)]

Solvent	Reaction temp	Product yield/%		
	°C	**2a**	**3a**	**4a**
THF	r.t.	15	17	3
THF, MeOH	r.t.	10	43	2
THF, MeOH	60	12	56	6

a) Benzaldehyde; 5.33 g (50 mmol), formaldehyde (37%); 5 ml, Raney Cu–Al alloy; 2.5 g, THF; 10 ml, MeOH; 35 ml.



$$\mathbf{1a} + HCHO \xrightarrow[\text{10\% aq. NaOH - H}_2\text{O, r. t., 100 min}]{\text{Raney Cu - Al alloy}} \mathbf{2a} + \mathbf{3a} + \mathbf{4a}$$

Scheme 2.

Reduction of 1a in a 10% aq Na_2CO_3 Solution under Ultrasonic Irradiation. To a stirred mixture of **1a** (5.33 g, 50 mmol), the Raney Ni–Al alloy (2.5 g) and THF (10 ml) at room temperature was gradually added 40 ml of a 10% aq Na_2CO_3 solution for 10 min under ultrasonic irradiation. After the reaction mixture was stirred for 90 min under the same reaction conditions, the formed Ni powder 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 **2a** (5.25 g, 96%). The aqueous phase was acidified with concd hydrochloric acid and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$, and evaporated in vacuo to afford 0.12 g (2%) of **4a**.

Crossed Cannizzaro Reaction Using the Raney Cu–Al Alloy. To a stirred mixture of **1a** (5.33 g, 50 mmol), the Raney Cu–Al alloy (2.5 g), MeOH (35 ml), THF (10 ml), and 37% aq HCHO (5 ml) at room temperature was gradually added 20 ml of a 10% aq NaOH–H_2O solution for 10 min. After the reaction mixture was stirred for 90 min, the Cu powder formed was filtered and the filtrate was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, and evaporated in vacuo to leave a residue which, after being analyzed by V.P.C., was distilled under reduced pressure to give 547 mg (10%) of **2a** and 2.32 g (43%) of hydrobenzoin (**3a**). The aqueous phase was acidified with concd hydrochloric acid and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$, evaporated in vacuo, and afforded 122 mg (2%) of **4a**.

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