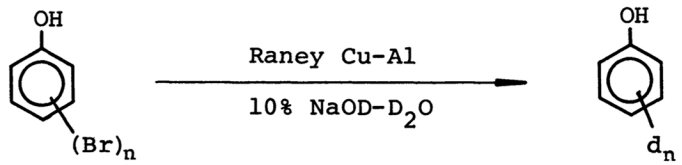
CHEMISTRY LETTERS, pp. 359-362, 1981.

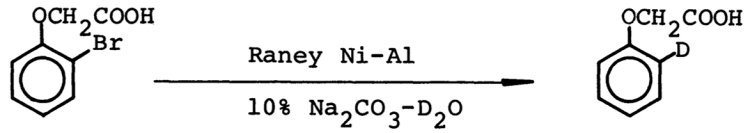
REDUCTION OF HALOBENZOIC ACIDS TO DEUTERATED BENZOIC ACIDS[1] WITH RANEY ALLOYS IN NaOD-D_2O SOLUTION

Masashi TASHIRO*, Kouji NAKAYAMA, and Gouki FUKATA
Research Institute of Industrial Science, Kyushu University 86,
Hakozaki, Higashi-ku, Fukuoka 812

Reduction of bromobenzoic acids with Raney Cu-Al alloy in 10% NaOD-D_2O solution afforded the corresponding deuterated benzoic acids in high yields and in high isotopic purities. However, use of Raney Ni-Al alloy instead of Cu-Al alloy leads to the introduction of more than the expected number of deuterium atoms. It was also found that treatment of benzoic acid with Raney Ni-Al alloy in 10% NaOD-D_2O solution gave a mixture of the deuterated benzoic acids.

It has been previously reported that[2] reduction of bromophenols with Raney Cu-Al alloy in 10% NaOD-D_2O solution afforded the corresponding deuterated phenols in high yields and in high isotopic purities, and that the treatment of 2-bromophenoxyacetic acid with Raney Ni-Al alloy in 10% Na_2CO_3-D_2O solution gave phenoxyacetic-2-d acid in good yield.

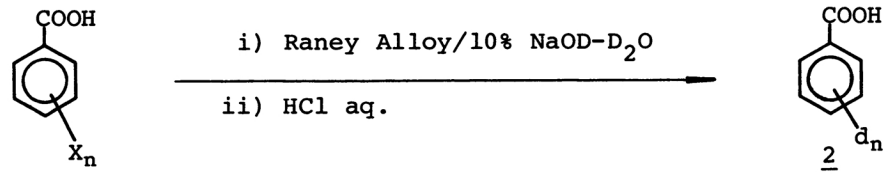




The latter result suggests that this reductive method for the introduction of deuterium atoms on the desired position of aromatic ring might be applied to carboxylic compounds such as benzoic acid.

Reduction of 2-chloro-(1a), 2-bromo-(1b), 3-bromo-(1c), 4-bromo-(1d), and

2,4,6-tribromobenzoic acid (1e) with Raney Cu-Al and Ni-Al alloys in 10% NaOD-D_2O solution was carried out under various conditions and the results are summarized in Table 1.



1

a: 2-Cl d: 4-Br
b: 2-Br e: 2,4,6-Br_3
c: 3-Br

2

a: 2-d
b: 3-d
c: 4-d
d: 2,4,6-d_3

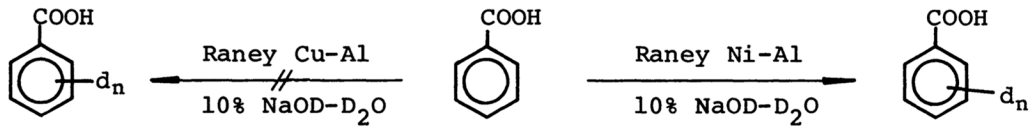
Table 1. Reduction of Halobenzoic Acids with Raney Alloys in 10% NaOD-D_2O Solution.[a)]

Run	Substrate (mmol, mg)	Raney Alloy (mg)	10% NaOD-D_2O (ml)	Temp.[b)] (°C)	Time (min.)	Yield[c)] (%)	Composition of 2[d)] d_0	d_1	d_2	d_3	d_4	d_5
1	1a (2.5, 390)	Ni-Al (250)	10	40	60	84	13.0	51.7	19.7	9.0	5.3	1.3
2	1a (2.5, 390)	Cu-Al (210)	10	50	60	no reaction						
3	1b (1.5, 300)	Cu-Al (150)	12	50	60	84	3.7	93.1	2.5	0.7	0	0
4	1c (1.5, 300)	Cu-Al (150)	12	50	60	82	2.1	96.6	0.7	0.6	0	0
5	1d (1.5, 300)	Cu-Al (150)	15	50	60	81	5.7	94.3	0	0	0	0
6	1d (1.0, 200)	Ni-Al (100)	8	80	40	80	3.7	29.7	34.7	28.2	3.3	0.4
7	1e (2.5, 890)	Cu-Al (500)	12	50	60	83	0.1	0.5	6.2	89.2	2.5	1.5

a) To a solution of 1 in 10% NaOD-D_2O was added slowly Raney alloy and the mixture was stirred for the specified time shown in this table.
b) Temperature of the oil bath.
c) Isolated yield. The yields determined by gas chromatographic analyses were almost quantitative.
d) The compositions were obtained by mass spectroscopic method.

The data of Table 1 show that the expected deuterated benzoic acid 2 were obtained in good yields. Although, with Raney Cu-Al alloy, the desired deuterated benzoic acids such as 2a-2d were formed in high isotopic purities from the corresponding bromobenzoic acids 1b-1e, the reduction with Raney Ni-Al alloy afforded the deuterated benzoic acids in low purities. It should be noted that 2-chlorobenzoic

acid 1a could hardly be reduced with Raney Cu-Al alloy (Run 2). It was also found that treatment of benzoic acid 3 itself with Raney Ni-Al alloy in 10% NaOD-D_2O solution afforded the deuterated benzoic acids 2 (Composition; d_0:36.4, d_1:23.0, d_2:19.5 %). On the contrary, the Raney Cu-Al alloy did not give the deuterated benzoic acid but the starting compound 3 was recovered in almost quantitative yield.



2 3 2

This result means that in the reduction of halobenzoic acids in NaOD-D_2O solution, use of Raney Ni-Al alloy should be avoided since more than the expected number of deuterium atoms may be introduced in the aromatic rings.

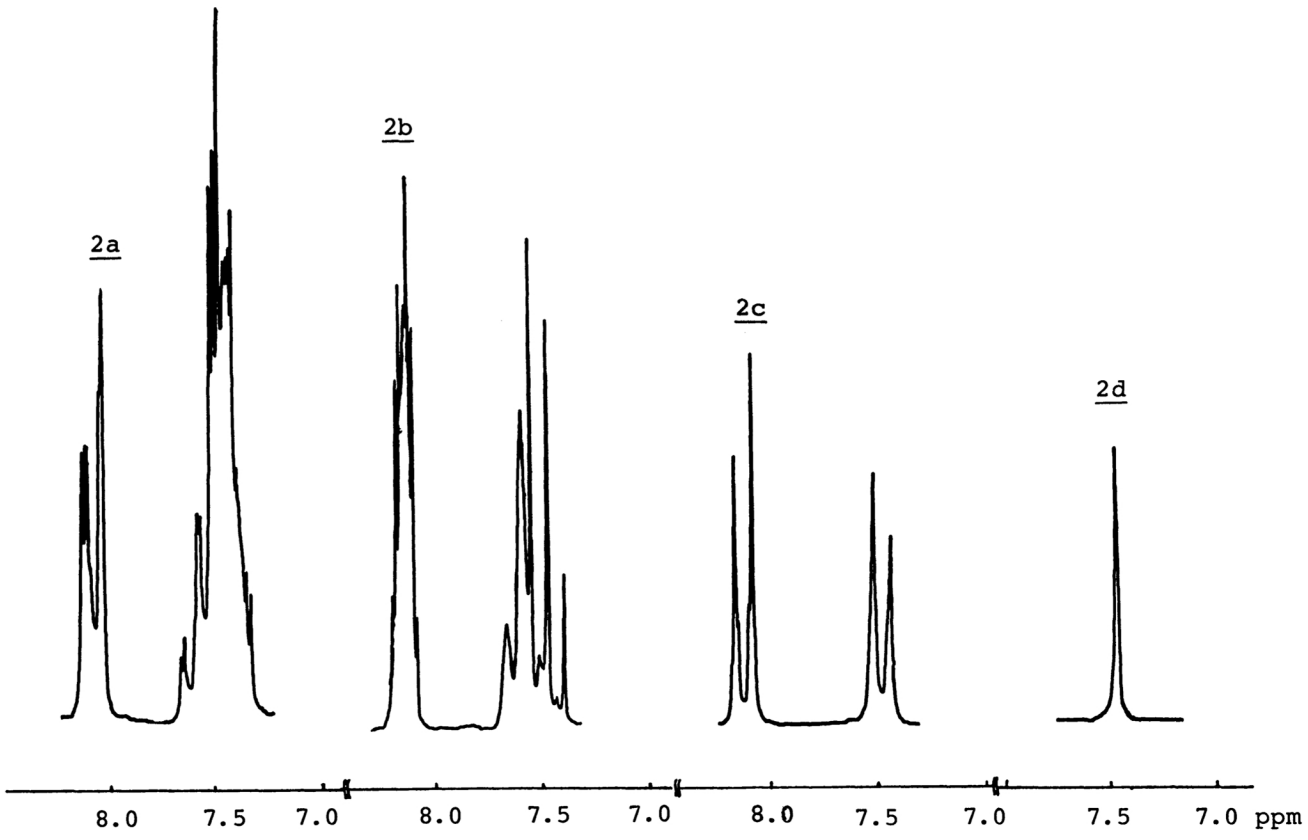


Fig. 1. The ^{1}H-NMR spectra of 2a-2d (Solvent $CDCl_3$)

The ^{1}H-NMR spectra of 2a-2e shown in Figure 1 indicate that the desired number of deuterium atoms were introduced on the desired positions of the ring of 2 in the reductive system of Cu-Al alloy and bromobenzoic acids.

Based on the results described above, it might be concluded that the reduction of bromobenzoic acids with Raney Cu-Al alloy in 10% NaOD-D_2O solution is a more convenient method for the introduction of a desired number of deuterium atoms on the specified position of aromatic rings than the previously reported methods.[3-7] Preparation of the other possible deuterated benzoic acids will be published in near future.

REFERENCES

1. Selective Preparation; 34. Part 33. M. Tashiro, G. Fukata, and T. Itoh, submitted in Synthesis.
2. M. Tashiro, A. Iwasaki, and G. Fukata, J. Org. Chem., 43, 196 (1978).
3. F. N. Jones, M. F. Zinn, and C. R. Hauser, J. Org. Chem., 28, 663 (1963).
4. B. H. Kwant, J. Labelled Compounds, 14, 393 (1978).
5. H. Erlenmeyer, H. Lobeck, H. Gärtner, and A. Epprecht, Helv. Chim. Acta, 19, 336 (1936).
6. L. H. P. Weldon and C. L. Wilson, J. Chem. Soc., 1964, 235.
7. R. S. P. Hsi, J. Labelled Compounds, 12, 601 (1976).

(Received December 25, 1980)