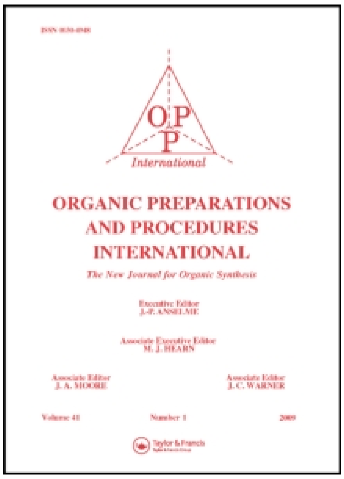

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REDUCTIVE DEHALOGENATION OF HALOACETOPHENONES WITH RANEY ALLOYS IN ALKALINE SOLUTION

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tion of solvent under reduced pressure afforded a yellow solid which was recrystallized from acetic acid:water (1:1) to yield 3.92 g (58%). IR ($CHCl_3$): 1723, 1504, 1436, 1341, 1303, 1052 cm^{-1}. UV (EtOH): $\lambda_{max}(\varepsilon)$ 299 (2116), 289 (2272), 260 (9298), 228 (27,133)nm. ^1H NMR (DMSO-d_6): δ 8.3-7.3 (m,6H, aromatic and amide), 5.57 (d,1H, methine), 4.12 (q,2H, methylene of ester), 1.23 (t,3H, methyl of ester). MS: m/e 279 (M+), 261, 233, 206, 188, 160 (100), 135.

Anal. Calcd. for $C_{13}H_{13}NO_4S$: C,55.90; H,4.69; N,5.01

Found: C,56.20; H,4.48; N,4.91

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4. Omission of the concentration operation resulted in reduced yields of IV.
5. The authors thank Dr. Paul Pranc, Lilly Research Laboratories, for preparation of R,S-2-(2-benzo[b]thienyl)glycine (R,S-V).

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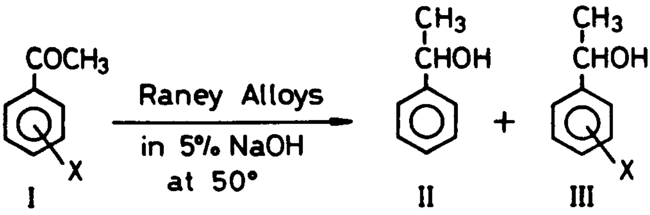
Halophenols and halobenzoic acids are reduced with Raney alloys in an alkaline solution to give phenol and benzoic acid, in good yield, respectively.[1,2] We now report reduction of haloacetophenones (Ia-Ih) with Raney alloys in 5% NaOH solution under various conditions (Table 1).



a: 3-Cl
b: 4-F
c: 4-Cl
d: 4-Br

e: 2,4-Cl_2
f: 2,5-Cl_2
g: 3,4-Cl_2
h: 3,5-Br_2

a: 3-Cl
b: 4-Cl
c: 2-Cl

Papa et al.[3] reported that reduction of both acetophenone and Id with Raney Ni-Al alloy in 10% NaOH-ethanol solution at 90° afforded ethylbenzene (IV). However, as shown in Table 1, the reduction of Ia-Ih with Raney alloys under milder conditions (5% NaOH solution at 50°) did not give IV but 1-phenylethanol (II) was obtained.

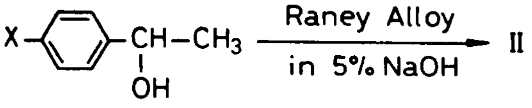
TABLE 1. Raney Alloys Reduction of Haloacetophenones (Ia-Ih)^{a}

Run	Substrate	Alloy(g)	Product(%)^{b}
1	Ia	Ni-Al(2)	II(80)
2	Ia	Cu-Al(2)	II(42)^{c}, IIIa(58)^{c}
3	Ib	Ni-Al(2)	II(86)
4	Ib	Cu-Al(2)	II(93)
5	Ic	Ni-Al(2)	II(88)
6	Ic	Cu-Al(2)	II(44)^{c}, IIIb(56)^{c}
7^{d}	Ic	Cu-Al(2)	II(85)
8	Id	Ni-Al(2)	II(71)
9	Id	Cu-Al(2)	II(91)
10^{e}	Id	Cu-Al(2)	II(89)
11^{f}	Id	Fe-Al(2)	II(18)
12	Ie	Cu-Al(4)	II(86)
13	If	Ni-Al(4)	II(52)
14	If	Cu-Al(4)	II(46)^{c}, IIIa+IIIc(54)^{c}
15	Ig	Ni-Al(4)	II(84)
16	Ig	Cu-Al(4)	II(53)^{c}, IIIa+IIIb(47)^{c}
17	Ih	Cu-Al(4)	II(92)

a) 10% NaOH solution was used at 50°. b) Isolated yields are shown unless otherwise indicated. c) Relative yields obtained by glc analysis are shown. d) This reaction was carried out under irradiation of ultrasound. e) In place of 5% NaOH solution, 10% Na_2CO_3 solution was used. f) Id was recovered.

It should be noted that compounds of type I bearing chlorine, fluorine and bromine atoms were reduced with Raney Cu-Al alloy which is known to be inactive for the reductive dehalogenation of chloro- and fluorophenols[1,2] and of chloro- and fluorobenzoic acids.[3] However, the reduction of Ic, If and Ig with this alloy afforded a low yield of II; ultrasound accelerated the reduction of Ia. Compound II was also obtained from Id with Raney Cu-Al alloy in 10% Na_2CO_3 solution. Table 1 shows that Raney Ni-Al alloy is the most powerful reagent for the reduction of I. Similar reduction of IIIb and IIId with Raney alloys was carried out and the results are summarized in Table 2.

TABLE 2. Reduction of (4-Chloro)- and (4-Bromophenyl)methylcarbinols (IIIb, IIId) with Raney alloys in 5% NaOH

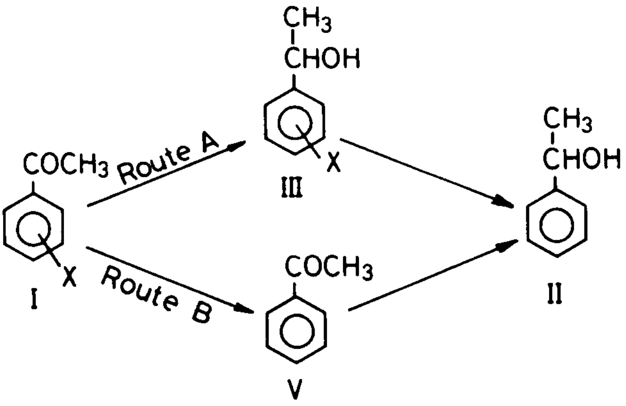


III

Substrate	Alloy	II[b](%)
IIIb	Ni-Al	76
IIIb	Cu-Al	N.R.
IIId	Cu-Al	92

a) Conditions were same as described in Table 1.
b) Isolated yields are shown.

Although the detailed reaction pathway of formation of II from I is still obscure, the data of Table 2 suggests that route B shown below should predominate over that shown in A, at least for the reduction of Ib with Raney Cu-Al alloy.



EXPERIMENTAL SECTION

Materials.- Halogenoacetophenones such as Ib, Ic and Ie were commercially available. Friedel-Crafts acetylations of bromobenzene, p-dichlorobenzene and o-dichlorobenzene were carried out according to the reported methods to give the corresponding Id,[4] If[5] and Ig,[6] respectively. Compound Ia was prepared from m-aminoacetophenone (VI)[7] according to the reported method. Compound Ih was obtained from p-aminoacetophenone (VII) by bromination followed by diazotization and reduction. Raney alloys were purchased from Kansai Shokubai Co. Ltd.

Preparation of 3,5-Dibromo-4-Aminoacetophenone (VII)[8].- To a solution of 6.03 g (45 mmol) of p-aminoacetophenone[9] in 90 ml of 4% HCl solution (4%) at 50° was added gradually 5.5 ml (110 mmol) of bromine. After the reaction mixture was stirred for 30 min, the precipitate was filtered and the filtrate was washed with sodium thiosulfate solution and water, dried over Na_2SO_4. Evaporation *in vacuo* left a residue which was dried in a desiccator under reduced pressure to give 8.9 g (68%) of VII as yellow crystalline powder (EtOAc), mp. 179.5-180.5°. ^{1}H-NMR ($CDCl_3$): δ 2.47 (3H, s), 5.15 (2H, broad s), 8.03 (2H, s); Mass spectrum: m/e 291, 293, 295 (M^+).

Anal. Calcd. for $C_8H_7Br_2NO$: C, 32.80; H, 2.41; N, 4.78

Found: C, 32.82; H, 2.51; N, 4.95

Preparation of 3,5-Dibromoacetophenone (Ih).- To a solution of 8.78 g (30 mmol) of VII in a mixture of benzene (15 ml) and ethanol (100 ml) was added gradually at 50°, 7.3 ml of conc. H_2SO_4. The mixture was refluxed for 3 hrs and then about 20 ml of the solvent was distilled from the mixture. To the mixture cooled in ice-water, was added $NaNO_2$ (4.3 g) in water (5 ml) below 10°. After addition of $NaNO_2$, the reaction mixture was allowed to stand at room temperature for 5 hrs. To the mixture was added 0.25 g of Cu powder and it was stirred for 1 hr. The suspension was filtered and the filtrate was extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to leave a residue which was chromatographed on silica gel using benzene as eluent to give an 8.2 g (98%) of Ih as pale yellow needles, mp. 61-61.5°, lit.[9]

mp. 68°.

Typical Reduction Procedure.- To a suspension of 10 mmol of I and 40 ml of 5% NaOH solution was added gradually with vigorous stirring at 50°, 2.0 g of Raney alloy in eight 0.25 g portions at 10 min. intervals. After addition of all the Raney alloy, the reaction mixture was stirred for 30 min. The solid materials were filtered by suction from the reaction mixture and the filtrate was extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to leave a residue which was analyzed by glc and then distilled under reduced pressure to give the products shown in the Table 1. Reduction products II, IIIa-IIId were identical with commercially available samples (Aldrich Chem. Co.). The reduction of IIIb and IIId was carried out and treated as above.

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