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FACILE HYDROGENATION OF AROMATIC NUCLEI WITH SODIUM BOROHYDRIDE-RHODIUM CHLORIDE IN HYDROXYLIC SOLVENTS

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Sodium borohydride-rhodium chloride in hydroxylic solvent was proved to be very useful for the reduction of aromatic nuclei to the corresponding saturated cycles under mild conditions.

In previous papers[1)-5)], we reported that the combination of sodium borohydride and various kinds of metal salts enhanced the reducing power and made it possible to reduce several functional groups which were inert to sodium borohydride alone. Olefinic esters could be reduced by sodium borohydride and transition metal salts such as nickel chloride, cobaltous chloride and cupric chloride to the corresponding saturated esters in quantitative yields[2)] and 2-cyano-1,1-diphenyl-1-butanol could be easily reduced by sodium borohydride-cobaltous chloride in methanol at room temperature to the corresponding primary amine without any hydrogenolysis of its hydroxy-group[3)]. On the other hand, a sodium borohydride-stannous chloride system showed a very high selectivity for the reduction of aromatic nitro compounds into amines in the presence of keto, nitrile or olefinic functionality in the same molecules[5)].

In the course of the investigation of the hydrogenolysis of aryl ketones with sodium borohydride-noble metal salts, we observed that hydrogenation of the aromatic nuclei readily occurred on treating them with sodium borohydride -rhodium chloride. These findings prompted us to examine the generality of the reducing procedure.

The methods so far reported for the hydrogenation of aromatic nuclei were mainly catalytic ones using several kinds of metal catalysts[6)-9)] under severe reaction conditions. The reduction of benzenoids with the combination of metal-amine was also reported to give a mixture of cyclohexenes and cyclohexanes in moderate yields[10)].

In this paper, we would like to report on a convenient hydrogenation method using sodium borohydride-rhodium chloride in a hydroxylic solvent.

As shown in Fig. 1, in the reduction of β-phenethyl alcohol(I), the yield of β-cyclohexyl alcohol(II) depended largely on the molar ratio of the rhodium chloride used to I.
When rhodium chloride was used in a molar ratio below 1, the yield of II increased almost proportionally to the quantity of rhodium chloride.

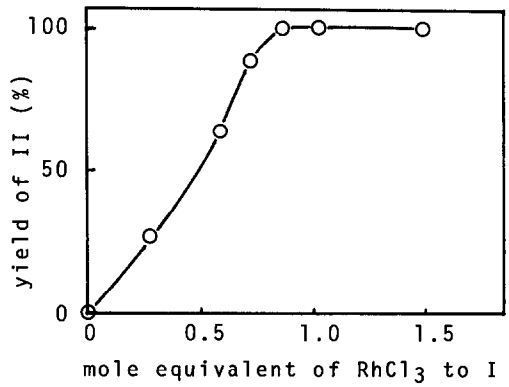
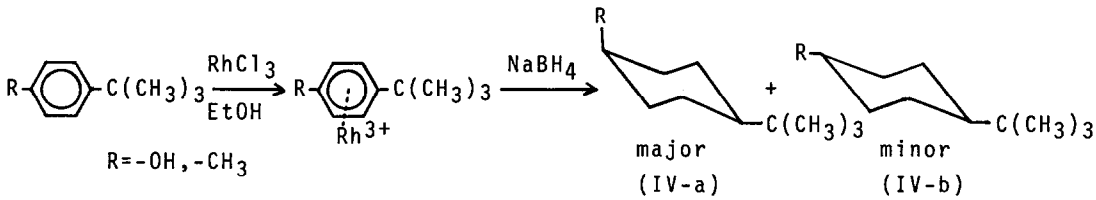


Fig. 1 Dependence of molar ratio of $RhCl_3$ to β-phenethyl alcohol(I) on the yield of β-cyclohexylethyl alcohol(II)
(molar ratio of $NaBH_4$/I=10, solvent:EtOH,30 °C)

It was observed that preincubation of benzenoids with rhodium chloride in a hydroxylic solvent at moderate temperature(0∿30 °C) before the addition of sodium borohydride was essential for the performance of the reduction.

These facts suggest that this reaction proceeds via the formation of complexes between benzenoids and rhodium chloride.

The reduction of p-t-butylphenol was examine in order to clarify the temperature dependence of the reaction on the yield of geometric isomers(IV).



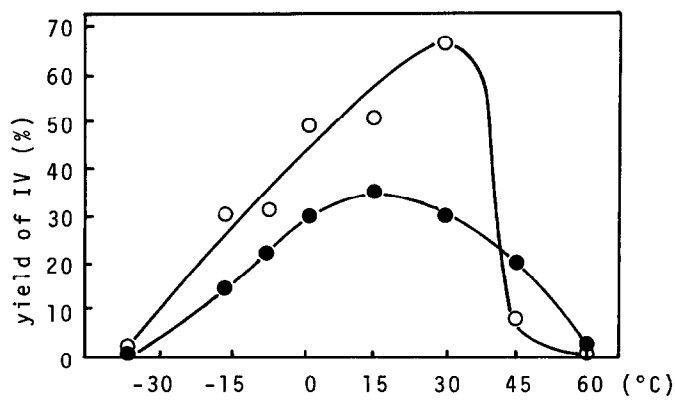


Fig. 2 Reduction of p-t-butylphenol(III)

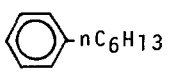
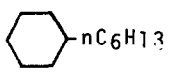
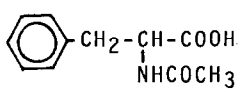
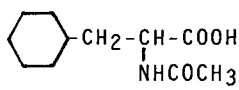
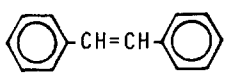
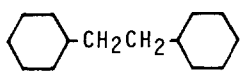
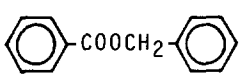
The reaction proceeded in a limited range of reaction temperature(-35∿60 °C) to afford cis- and trans-cyclohexane derivatives. In this reaction, the predominent formation of cis isomers was similar to that in the catalytic reduction of benzenoids[9] and the yields of cis and trans isomers were 66 and 28% respectively at the optimal reaction temperature(30 °C).
No reaction product was obtained at reaction temperature above 60 °C, and the starting material was quantitatively recovered.

A similar tendency was observed in the reduction of p-t-butyltoluene exept for the slight shift of the effective reaction temperature(-30∿40 °C). The yield of 4-t-butyl-1-methylcyclohexane was 70% and the cis-trans ratio was 2:1 at the optimal temperature(0∿10 °C).

Monosubstituted aromatic compounds were reduced very smoothly to give hydrogenated ones in their aromatic nuclei in exellent yields.

The selective reducibility of the sodium borohydride-rhodium chloride system toward aromatic nuclei are considerably high as shown in Table 1.

Table.1 Reduction of Aromatic Compounds with $NaBH_4$-$RhCl_3$ in EtOH

Aromatic Compounds	Temperature(°C)	Products	Yield(%)
	40		quantitative
	30		94
	40		quantitative
	40		75
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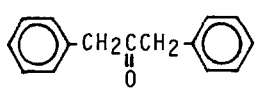
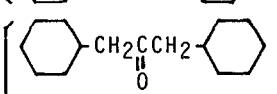
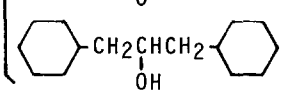
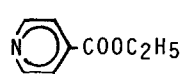
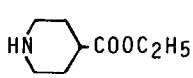
	5		22
			21
	40		60

Not only are carboxylic acids, esters and amides unaffected by the reduction system, but even ketones were only partially reduced, though olefinic bonds were completely reduced simultaneously.

The fact that cyclohexylmethyl benzoate was obtained as a major product by the reduction of benzyl benzoate suggests that selective hydrogenation of an aimed aromatic nuclus is possible when the starting materials have more than two nuclei which are situated in different environments.

The reduction could be conveniently performed in ethanol as described above, but this reaction can be conducted even in water. For example, N-acetyl-L-phenylalanine was reduced in 0.1M phosphate buffer(pH 4) at 30 °C into N-acetyl-L-cyclohexylalanine in 99%.

The following is a typical procedure of the reduction: A solution of N-acetyl-L-phenylalanine(200 mg, 0.966 mmol) and rhodium chloride trihydrate(519 mg, 1.93 mmol) in ethanol(20 ml) was stirred for 2 h at 30 °C. Sodium borohydride(370 mg, 9.74 mmol) in ethanol(20 ml) was added dropwise during 30 min. at 30 °C. A black precipitate appeared in the reaction mixture with the addition of sodium borohydride. The reaction mixture was stirred at 30 °C for 1 h and the black precipitate was filtered and washed with ethanol. The mixture of the filtrate and the washings were evaporated in vacuo and the residue was quenched with cold 1N HCl(50 ml) and the product was extracted with ethyl acetate. The extract was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded N-acetyl-L-cyclohexylalanine as colorless needles in 94% yield[11].

References and Notes

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11) Analytical data of N-acetyl-L-cyclohexylalanine thus obtained is as follows: mp 196-197 °C; IR ν=2920, 1703 cm^{-1}; MS m/e 213(M^+); $[\alpha]_D^{20}$ -4.4(c=2.0,EtOH) Elemental analysis for $C_{11}H_{13}NO_3$; Calcd. C,61.94, H,8.98, N,6.57 Found C,62.01, H,9.23, N,6.38
12) We thank Miss Yoko Taguchi for her helpful cooperation in this work.

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