BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 499—501 (1969)

Hydrogenation and Hydrogenolysis. XI.[1] The Hydrogenation of Methoxy- and Ethoxyanilines with a Ruthenium Catalyst[*1]

Shigeo NISHIMURA and Hisashi YOSHINO

Department of Industrial Chemistry, Tokyo University of Agriculture and Technology, Koganei, Tokyo

(Received June 10, 1968)

Hydrogenation of methoxy- and ethoxyanilines with a ruthenium catalyst was investigated at 80°C under the hydrogen pressure of 80—100 kg/cm^2. The amount of hydrogenolysis which occurred during hydrogenation varied with solvent from 35.1% in methanol to 8.5% in *t*-butyl alcohol in the hydrogenation of *p*-methoxyaniline. With use of *t*-butyl alcohol as solvent, good yields of methoxy- and ethoxycyclohexylamines were obtained from corresponding alkoxyanilines. It was shown that the rate of formation of cyclohexylamine increases with increasing polarity of solvent. *m*-Alkoxyanilines were found to hydrogenolyze more readily than the corresponding ortho or para isomers. For the greater tendency of meta isomers toward hydrogenolysis, an explanation based on the ionic cleavage of the carbon-oxygen bond was suggested.

In the preceding paper,[1] we have reported an effective method of the hydrogenation of methoxy- and ethoxyanilines, the alkoxyl group of which is rather labile to hydrogenolysis, with the rhodium oxide catalyst prepared by the lithium nitrate fusion of rhodium chloride. Over this catalyst, hydrogenolysis occurred only to slight extent and methoxy- and ethoxycyclohexylamines were obtained in excellent yields.

The hydrogenation of alkoxyanilines with ruthenium catalysts is usually accompanied by more extensive hydrogenolysis than with rhodium, although ruthenium has proved to be a useful metal in the catalytic hydrogenation of aromatic amines.[2] Freifelder and Stone[3] hydrogenated various alkoxyanilines with a ruthenium dioxide as catalyst in methyl or ethyl alcohol at elevated temperature and pressure. However, hydrogenation of methoxy- and ethoxyanilines gave only rather low yields of the corresponding alkoxycyclohexylamines under these conditions, except in the case of *o*-ethoxyaniline where 2-ethoxycyclohexylamine was obtained in 78.7% yield.

In this paper, we have investigated the ruthenium-catalyzed hydrogenation of methoxy- and ethoxyanilines, especially with reference to the effect of solvents on accompanying hydrogenolysis. It has been shown that the nature of the solvent used has a profound effect on the extent of hydrogenolysis and that the rate of formation of cyclohexylamine increases with increasing polarity of the solvent.

Experimental

Catalyst. The ruthenium hydroxide, prepared from aqueous solutions of ruthenium chloride and lithium hydroxide according to the procedure described previously,[4] was used as the catalyst throughout the experiments.

Hydrogenation and Analysis of Products. These were carried out in the same way as described in the preceding paper.[1] On direct gas chromatography of the reaction mixture, *n*-butyl alcohol could not be separated from cyclohexylamine and the analysis in this case was done after separation of produced amines from the solvent through their hydrochlorides. Alkoxycyclohexylamines gave two peaks on gas chromatogram, except in the case of 2-methoxy isomer where only one peak was obtained probably because of insufficient separation. The areas of the larger peaks, which probably corresponded to the cis isomers, were 84.3, 67.6, 93.1, 82.3 and 66.7% for 3-methoxy-, 4-methoxy-, 2-ethoxy-, 3-ethoxy- and 4-ethoxycyclohexylamines, respectively.

Solvents. All solvents used in hydrogenations were carefully dehydrated according to the methods recommended in the literature,[5] otherwise small amounts of hydrolysis products, alkoxycyclohexanols, were often formed during hydrogenation.

---

[1] Part X: S. Nishimura, H. Uchino and H. Yoshino, This Bulletin, **41**, 2194 (1968).

[*1] Presented at the 21st Annual Meeting of the Chemical Society of Japan, Osaka, April, 1968.

[2] P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York (1967), p. 352.

[3] M. Freifelder and G. R. Stone, *J. Org. Chem.*, **27**, 3568 (1962).

[4] Y. Takagi, T. Naito and S. Nishimura, This Bulletin, **38**, 2119 (1965).

[5] "Organic Solvents," 2nd Ed. ("Technique of Organic Chemistry," Vol. VII ed. by A. Weissberger), Interscience Publishers, New York (1955).

TABLE 1. THE EFFECT OF SOLVENTS ON THE RUTHENIUM-CATALYZED HYDROGENATION AND HYDROGENOLYSIS OF *p*-METHOXYANILINE[a]

Solvent	ε[b] at 80°C	Reac. time (hr)	Hydrogenolysis (mol %)	Half-hydrogenation time (min)	Rate of formation of cyclohexylamine ($\text{mol}\cdot\text{min}^{-1}\cdot\text{g}\cdot\text{cat}^{-1}\times 10^3$)
MeOH	23.9	5.8	35.1	40	4.4
EtOH	16.8	2.5	30.1	50	3.0
PrOH	13.1	2.0	26.2	50	2.6
i-PrOH	12.2	2.3	16.5	50	1.65
BuOH	11.3	2.5	21.7	60	1.8
s-BuOH	9.4	3.0	13.1	60	1.1
t-BuOH	6.1	2.5	8.5	50	0.85
THF	6.7	5.0	11.3	90	0.63
i-Pr_2O	3.3[c]	6.5	15.6	170	0.46
MCH[d]	1.9	5.5	13.1	110	0.60

a) *p*-Methoxyaniline (0.1 mol) was hydrogenated in 30 m*l* of solvent at 80°C under 80—100 kg/cm^2 in the presence of 0.1 g of ruthenium hydroxide and 0.01 g of $LiOH\cdot H_2O$.

b) Dielectric constants were obtained by extrapolating the values taken from "Landolt-Börnstein Tabellen," 6 Aufl. II Band, 6 Teil, Springer-Verlag (1959), p. 613.

c) The temperature dependence was approximated by that of ethyl isoamyl ether.

d) Methylcyclohexane.

Results and Discussion

The effect of various solvents was investigated in the hydrogenation of *p*-methoxyaniline at 80°C under the hydrogen pressure of 80—100 kg/cm^2 in the presence of ruthenium hydroxide and a small amount of lithium hydroxide, which has been shown to be an effective catalyst system for hydrogenation of aniline.[6] The results are summarized in Table 1. It is seen that hydrogenolysis occurred most extensively in methanol and ethanol, and varied considerably with the kind of solvent from 35.1% in methanol to 8.5% in *t*-butyl alcohol. It is noteworthy that hydrogenolysis took place to greater extent in less polar non-alcoholic solvents (isopropyl ether and methylcyclohexane) than in *t*-butyl alcohol. The amount of hydrogenolysis was thus found to be the smallest in *t*-butyl alcohol of the solvents investigated.[7] In Fig. 1 the rate of formation of cyclohexylamine, obtained on the basis of the amount of cyclohexylamine formed during half-hydrogenation time, is plotted *versus* the reciprocal of the dielectric constant of the solvent in which hydrogenation was carried out. It will be seen that the rate of formation of cyclohexylamine is a function of polarity of solvent: the greater the dielectric constant of a solvent is, the larger is the rate of formation of cyclohexylamine in the solvent. As noted above, the extent of hydrogenolysis is not always in the order of polarity of solvent. Generally, hydrogenation proceeded more slowly in non-alcoholic solvents than in alcoholic solvents (see Table 1) and probably this is the reason of rather large amounts of hydrogenolysis obtained in the former solvents notwithstanding their small dielectric constants. If we assume that the effect of solvent on the rate of hydrogenation is similar for alkoxyaniline and for the intermediate allyl-type ethers which probably undergo hydrogenolysis when further hydrogenated,[8] it may be considered that the change in the rate of formation of cyclohexylamine in various solvents represents the effect of solvents on the rate of hydrogenolysis of the alkoxyl group. Thus, the effect of solvents indicated in Fig. 1 can be interpreted as showing the effect of polarity of solvent on the rate of hydrogenolysis of the carbon-oxygen linkage. The observed effect thus suggests that more polarized transition states are involved in hydrogenolysis of the intermediates leading to the formation of cyclohexylamine. This is also in line with the currently accepted mechanism of catalytic hydrogenolysis in which an ionic cleavage of the carbon-oxygen bond is involved.[9]

Since it has been found that hydrogenolysis occurs only to a small extent in *t*-butyl alcohol, isomeric methoxy- and ethoxyanilines have been hydrogenated in this solvent, the results being summarized in Table 2. It is seen that hydrogenolysis is generally at low level and methoxy- and

---

[6] S. Nishimura, T. Shu, T. Hara and Y. Takagi, This Bulletin, **39**, 329 (1966).

[7] A similar effect of solvents was reported in hydrogenation of some benzyl alcohols with platinum oxide catalyst, where the amount of hydrogenolysis decreased with solvent in the order : primary>secondary>tertiary alcohol [Y. Ichinohe and H. Ito, This Bulletin, **37**, 887 (1964)].

[8] This may be presumed by considering that the hydrogenolysis probably occurs by the S_N type mechanism (see Ref. 9) and such reaction will occur more easily in the allyl-type ether than in the corresponding aryl ether, because the formation of the transition state of carbonium ion character will be much favored in the allyl-type ether.

[9] a) W. A. Bonner and J. A. Zderic, *J. Am. Chem. Soc.*, **78**, 3218 (1956). b) S. Mitsui and Y. Nagahisa, *Chem. Ind.* (*London*), **1965**, 1975 and references cited therein.

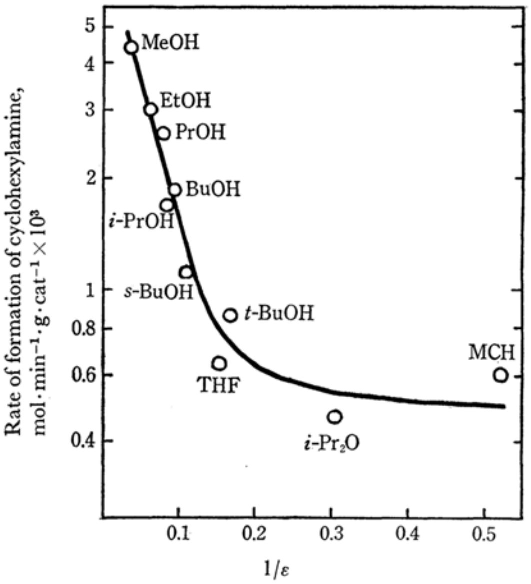
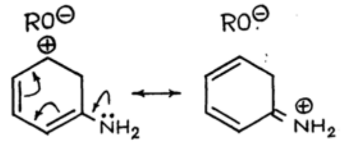


Fig. 1. Effect of solvents on the rate of formation of cyclohexylamine as a function of the reciprocal of dielectric constant in hydrogenation of *p*-methoxyaniline with Ru catalyst.

ethoxycyclohexylamines were obtained in more than 80% yields by distillation of products. Thus, the hydrogenation of alkoxyanilines with ruthenium hydroxide catalyst in *t*-butyl alcohol affords an excellent alternative method for the synthesis of alkoxycyclohexylamines.[10] The relative rates of formation of cyclohexylamine are also listed in the last column of Table 2, taking the rate for *o*-ethoxyaniline as unity. A noteworthy feature of the results is the fact that the meta isomers hydrogenolyze more easily than the corresponding ortho and para isomers. These results are in contrast with those obtained previously with rhodium catalyst in which the rate of formation of cyclohexylamine increased in the order: ortho<meta<para isomer, although differences between meta and para isomers were rather small.[1] The greater tendency of the meta isomer toward hydrogenolysis has been observed also in other hydrogenations.[11] It appears difficult to explain this phenomenon only either by the steric factor or by the probability of the formation of allyl-type ethers.[12] On the basis of an ionic cleavage of the carbon-oxygen bond, it may be suggested that the electron-releasing ability of the amino group at the meta position will stabilize the transition states of carbonium ion character when the allyl-type ethers undergo hydrogenolysis, as shown below in one example of dihydro intermediates. Such an effect will not be expected in the allyl-type intermediates resulting from the hydrogenation of *o*- or *p*-alkoxyaniline.[13]



This work was supported by the Mitsubishi Chemical Industries Co., Ltd., to which our thanks are due.

TABLE 2. HYDROGENATION OF METHOXY- AND ETHOXYANILINE WITH RUTHENIUM CATALYST[a]

RO in RO–$C_6H_4NH_2$	Reac. temp. (°C)	Reac. time (hr)	Mol% composition of products[b]				Alkoxycyclohexylamine			Relative rate of formation of cyclohexylamine
			I	II	III	IV	Yield by dist. (%)	Bp (°C/mmHg)	n_D^{25}	
o-CH_3O	80	6.3	83.3	12.7	1.3	2.7				0.739
o-CH_3O	90	2.5	89.2	10.6	0.2	0.0	81.1	67.5—68.5/18	1.4599	
m-CH_3O	80	2.3	86.4	13.6	0.0	0.0	80.9	81—82.5/21	1.4620	1.58
p-CH_3O	80	1.5	93.9	6.1	0.0	0.0	84.8	75—76.2/18.5	1.4630	0.724
o-C_2H_5O	80	1.5	93.1	6.9	0.0	0.0	82.3	78.5—79.5/23	1.4531	1.00
m-C_2H_5O	80	1.3	90.4	8.9	0.7	0.0	81.2	87.5—89.4/24	1.4585	1.13
p-C_2H_5O	80	1.4	95.6	4.4	0.0	0.0	84.7	83—86.5/20	1.4597	0.616

a) Methoxy- or ethoxyaniline (0.1 mol) was hydrogenated in 30 m*l* of anhydrous *t*-butyl alcohol under 80—100 kg/cm² in the presence of 0.2 g of ruthenium hydroxide and 0.02 g of LiOH·H_2O.

b) I: Alkoxycyclohexylamine. II: Cyclohexylamine. III: Secondary products. IV: Alkoxyaniline

---

[10] Although hydrogenolysis occurred more extensively with the ruthenium catalyst than with rhodium oxide catalyst (see Ref. 1), use of the ruthenium catalyst will be advantageous in hydrogenations at a larger ratio of substrate to catalyst because of lesser decrease in the rate during hydrogenation.

[11] More extensive hydrogenolysis in meta isomer than in ortho or para isomer has been observed, *e. g.*, in hydrogenation of isomeric dimethoxybenzenes with platinum metal catalysts (Y. Takagi and S. Nishimura, unpublished results). *Cf.* also H. A. Smith and R. G. Thompson, "Advances in Catalysis," Vol. 9, p. 727 (1957).

[12] M. Freifelder, Y. H. Ng and P. F. Helgren, *J. Org. Chem.*, **30**, 2485 (1965).

[13] *p*-Methoxyaniline was reported to hydrogenolyze to a much greater extent than the meta isomer in hydrogenation with rhodium-on-alumina in the presence of one equivalent of acetic acid.[12] This fact may support the explanation suggested above, but similar results were also obtained in ethanol with ethoxy- and propoxyanilines. For further discussion, a detailed study will be necessary.