Hydrogenation and Hydrogenolysis. X. The Hydrogenation of Methoxy- and Ethoxyanilines with Rhodium Catalysts[1)]

Shigeo NISHIMURA, Hiroshi UCHINO and Hisashi YOSHINO

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

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The catalytic hydrogenation of alkoxyanilines is usually accompanied by the hydrogenolysis of the alkoxyl group, which lowers the yields of corresponding alkoxycyclohexylamines.[2,3)] Hydrogenolysis occurs most extensively in hydrogenation of methoxy- and ethoxyanilines. Freifelder and Stone hydrogenated various alkoxyanilines in methanol or ethanol at elevated temperature and pressure, using ruthenium dioxide, a catalyst that has proved useful in reduction of aromatic amines.[4)] However, the yields of methoxy- and ethoxycyclohexylamines were rather low except in the case of *o*-ethoxyaniline where 2-ethoxycyclohexylamine was obtained in 78.7% yield. A low-pressure hydrogenation of alkoxyanilines over 5% rhodium-on-alumina in ethanol in the presence or absence of an equivalent of acetic acid was also reported.[3)] Although hydrogenolysis occurred to a somewhat less extent under these conditions, it appears that, in most instances, rates of hydrogenation were small and considerable amounts of starting materials remained unchanged, even after a long reaction period with a 40% weight ratio of catalyst to alkoxyaniline. Thus, no satisfactory method for hydrogenation of alkoxyanilines, especially for methoxy- and ethoxyanilines, seems to have ever been described in the literature.

As reported in a previous paper,[5)] decrease in the rate during the rhodium-catalyzed hydrogenation of aniline was considerably improved by the presence of a small amount of alkali which was added to or contained in the catalyst. Presence of alkali also depressed formation of secondary amine almost completely. Subsequently, we have studied the hydrogenation of alkoxyanilines with the alkali-promoted rhodium catalysts and found that the rhodium oxide prepared by fusion of rhodium chloride with lithium nitrate affords excellent yields of methoxy- and ethoxycyclohexylamines in hydrogenation of the corresponding methoxy- and ethoxyanilines. Over this catalyst, hydrogenolysis occurred only to a small extent (3.1—5.9%) and hydrogenation was completed within a few hours at 80—90°C under a high pressure of hydrogen with use of less than 2% weight ratio of catalyst to the substrate. Formation of secondary amines was also completely suppressed or only at a very low level over this catalyst. The results of the hydrogenation of isomeric methoxy- and ethoxyanilines are summarized in Table 1. The hydrogenation of ortho isomers was rather difficult to be completed at 80°C, but this difficulty was overcome at a higher reaction temperature. Approximate relative rates of hydrogenolysis, obtained on the basis of the amounts of cyclohexylamine formed during half-hydrogenation time, are also shown in the last column of Table 1, taking the rate for *o*-ethoxyaniline as unity. It will be seen that generally methoxyanilines hydrogenolyze more rapidly than do the corresponding ethoxyanilines, and that the rate of hydrogenolysis is in the order of ortho$<$meta$<$para isomers in both methoxy- and ethoxyanilines, although the proportion of hydrogenolysis is not always in the same order.[6)]

Hydrogenation with the usual rhodium oxide, prepared by sodium nitrate fusion, was often inhibited at a later stage of reaction, although this oxide was as effective in hydrogenation of *p*-methoxyaniline as that by lithium nitrate fusion.[7)] With rhodium hydroxide and lithium hydroxide, which was shown to be an effective catalyst system for hydrogenation of aniline,[5)] *p*-methoxyaniline hydrogenated with a much smaller rate and gave a larger amount of hydrogenolysis product than with the rhodium oxide catalysts. The hydrogenation was strongly inhibited by the addition of sodium hydroxide. From these results, it will be probable that the hydrogenation of an alkoxyaniline is more easily inhibited by presence of a stronger alkali than in the case of aniline, and that the alkali contained in the oxide catalysts works as a weaker base than the corresponding alkali hydroxides. A similar difference in the action of alkali has also been observed in the rhodium-catalyzed hydrogenation of nitriles, where the reaction was retarded by addition of alkali in the order: LiOH$<$NaOH$<$KOH.[8)]

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1) Part IX: S. Nishimura and M. Hama, This Bulletin, **39**, 2467 (1966).

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

3) M. Freifelder, Y. H. Ng and P. F. Helgren, *ibid.*, **30**, 2485 (1965).

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

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

6) *Cf.* Refs. 2 and 3.

7) The rhodium oxide by potassium nitrate fusion was much less active for this hydrogenation (unpublished results).

8) Y. Takagi, S. Nishimura, K. Taya and K. Hirota *Sci. Papers Inst. Phys. Chem. Research* (*Tokyo*), **61**, 114 (1967).

TABLE 1. HYDROGENATION OF METHOXY- AND ETHOXYANILINES WITH RHODIUM CATALYSTS[a]

RO in $RO-C_6H_4NH_2$	Catalyst[b]	Amount of the catalyst (g)	Reac. temp. (°C)	Reac. time (hr)	Mol% composition of products[c]				Yield of I by distillation (%)	Relative rate of hydrogenolysis
					I	II	III[d]	IV		
o-CH_3O	Rh oxide(Li)	0.2	80	8.5	59.1	3.7	7.2	30.0		1.47
o-CH_3O	Rh oxide(Li)	0.2	90	2.5	91.4	4.6	3.7	0.3	77[e]	
o-CH_3O	Rh oxide(Na)	0.2	90	2.5	73.6	5.8	7.3	13.3		
m-CH_3O	Rh oxide(Li)	0.2	80	2.5	94.9	5.1	0.0	0.0	84[f]	3.10
p-CH_3O	Rh oxide(Li)	0.1	80	1.8	94.3	5.3	0.4	0.0	85[g]	3.39
p-CH_3O	Rh oxide(Na)	0.1	80	2.3	95.1	4.9	0.0	0.0		
p-CH_3O	Rh hydroxide[h]	0.1	80	5.0	24.5	5.2	0.9	69.4		
o-C_2H_5O	Rh oxide(Li)	0.2	80	2.7	89.9	4.1	1.6	4.4	81[i]	1.00
o-C_2H_5O[j]	Rh oxide(Li)	0.15	90	2.3	94.1	5.9	0.0	0.0	88	
o-C_2H_5O[j]	Rh oxide(Na)	0.15	90	4.0	92.7	3.1	trace	4.2		
m-C_2H_5O	Rh oxide(Li)	0.2	80	1.7	96.9	3.1	0.0	0.0	86[k]	2.20
p-C_2H_5O	Rh oxide(Li)	0.2	80	1.5	96.8	3.2	0.0	0.0	86[l]	2.28

a) Unless otherwise noted, 0.1 mol of alkoxyaniline was hydrogenated in 30 m*l* of anhydrous *t*-butyl alcohol at 80 or 90°C under 80—100 kg/cm² of hydrogen pressure. b) Li or Na in parentheses indicates the oxide prepared by lithium nitrate fusion or by sodium nitrate fusion, respectively. c) I: Alkoxycyclohexylamine. II: Cyclohexylamine. III: Secondary products. Gas-chromatographic analysis shows that these are not saturated secondary amines, but cyclohexylidenecyclohexylamine derivatives which probably resulted from the products of insufficient hydrogenation. IV: Alkoxyaniline. d) Based on the moles of starting alkoxyaniline. e) Bp 70—71.5°C/20 mmHg; n_D^{25} 1.4592. f) Bp 80.5—83°C/23 mmHg; n_D^{25} 1.4620. g) Bp 93.5—95.5°C/42 mmHg; n_D^{25} 1.4638. h) $LiOH \cdot H_2O$ (10 mg) was added. i) Bp 73.5—74.5°C/16.5 mmHg; n_D^{25} 1.4532. j) Anhydrous isopropyl alcohol was used as solvent. k) Bp 89.5—90.5°C/25 mmHg; n_D^{25} 1.4581. l) Bp 81—82.5°C/17.5 mmHg; n_D^{25} 1.4595.

Experimental

Catalysts. *The Rhodium Oxide Prepared by Lithium Nitrate Fusion.* A mixture of 3 g of rhodium chloride trihydrate and 45 g of lithium nitrate was fused in the same way as in the preparation of Adams platinum oxide.[9] After violent evolution of the oxides of nitrogen, the temperature was raised and kept at 420—460°C for about 15 min. After cooling, the solidified mass was rinsed in distilled water. The solid was collected, washed with 1—2% aqueous solution of lithium nitrate, and then dried over soda lime.

The Rhodium Oxide Prepared by Sodium Nitrate Fusion. This oxide was prepared according to the procedure described previously.[10]

Rhodium hydroxide. This was prepared from aqueous solutions of rhodium chloride and lithium hydroxide as described previously.[1]

Hydrogenation. The hydrogenation was carried out in a 200-m*l* autoclave of an electromagnetically-stirring type under the conditions described in Table 1. Isopropyl and *t*-butyl alcohols used as solvent were carefully dehydrated over calcium oxide, otherwise the hydrolysis products, alkoxycyclohexanols, were often produced during hydrogenation.

Analysis of Products. Products were analyzed by gas chromatography using a column of 10% PEG 6000-10% KOH on Chromosorb W (60—80 mesh). The gas chromatograms of alkoxycyclohexylamines were separated into two peaks except in the case of 2-methoxycyclohexylamine, where only one peak was obtained probably because of incomplete separation. The areas of the larger peaks, which probably correspond to the cis isomers, were 80.7, 69.2, 91.8, 85.3 and 74.1% for 3-methoxy, 4-methoxy-, 2-ethoxy-, 3-ethoxy- and 4-ethoxycyclohexylamine, respectively, in the experiments carried out at 80°C. Methoxy- and ethoxycyclohexylamines were further isolated by distillation at reduced pressure, after most of solvent had been distilled off at atmospheric pressure, with equipment of soda lime tubes.

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[9] R. Adams, V. Voorhees and R. L. Shriner, "Organic Syntheses," Coll. Vol. I, 2nd Ed., p. 463 (1961).

[10] S. Nishimura, This Bulletin, **34**, 1544 (1961).