(w), 1140 (w), 1125 (m), 1080 (s), 1060 (s), 1020 (w), 1010 (w), and 935 cm.$^{-1}$ (s).

A wax consisting mostly of the *threo* isomer was obtained after concentration of the ethanol–petroleum ether supernatant from the crystallization of compound V; yield 255 mg.; ninhydrin re action, positive.

**Analysis of Aldehydes.**—Vapor phase chromatography[9] of the aldehydes obtained after periodate oxidation of N-methylsphingosine showed two peaks, the first at 10.25 min., hexadecanal (13% of the total aldehydes), and the second at 18.75 min., hexadecenal; the former peak arises from the presence of dihydrosphingosine in the original base preparation. N-Methyldihydrosphingosine under the same conditions gave one peak at 10.25 min. Only 1 major peak at 7.0 min., pentadecanal, was obtained from compound V; the wax from this preparation yielded a similar peak along with a minor one at 10.25 min.

The 2,4-dinitrophenylhydrazone of the aldehyde obtained from the periodate oxidation of compound V melted at 104–106°; this is in agreement with the melting point of the same derivative reported for pentadecanal.[8]

*Anal.* Calcd. for $C_{21}H_{34}N_4O_4$ (406.3): C, 62.03; H, 8.44. Found: C, 62.00; H, 8.30.

**Acknowledgment.**—The author is grateful to both Dr. Warren M. Sperry, in whose laboratory this work was done, and Dr. David Rittenberg for reading this manuscript. Thanks are due, also, to Mr. Richard L. Stiller for his competent technical assistance.

[9] B. Weiss, *J. Biol. Chem.*, **238**, 1953 (1963).

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# Low-Pressure Hydrogenation of Alkoxyanilines with Noble Metal Catalysts

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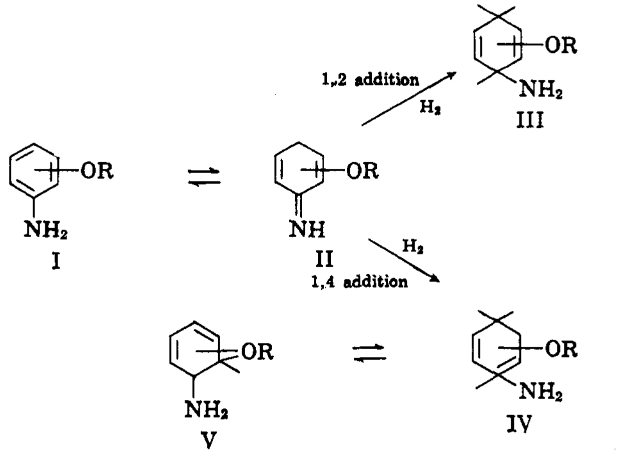
A study of the hydrogenation of nuclear-substituted anilines with ruthenium catalyst included work with some alkoxyanilines.[1] It was found that hydrogenolysis which occurred during conversion of the isomeric methoxyanilines decreased as the alkoxy group became larger. Smith and Thompson, investigating the reduction of mono-, di-, and trimethoxybenzenes, reported that temperature as well as catalyst was a factor in cleavage of the ether groups.[2]

We were interested in studying the effect of other noble metal catalysts under milder conditions than those used with ruthenium (90–100°, 70 atm.); we were particularly interested to see whether the methoxy- and ethoxycyclohexylamines could be produced in good yield.

From the results, rhodium appears to be the catalyst of choice for use under low-pressure conditions. Respectable yields of alkoxycyclohexylamines are obtained, hydrogenolysis is not extensive, and secondary amine formation, in most instances, is at a low level. Reaction time in neutral solvent is sometimes long, but when the reduction is run in the presence of an equivalent of acetic acid hydrogen uptake proceeds much more rapidly.[3] Steric effects, which are likely the cause of the longer reaction period for 2-alkoxyanilines, may also contribute to the lesser amounts of cyclohexylamine found in these reductions than in the conversion of the 4-substituted compounds. It is of interest that less cleavage is also noted when the 3-alkoxyanilines are hydrogenated.

Chart I



Hydrogenolysis probably occurs during an intermediate reduction stage.[1,2] We suggest that allyl-type ethers, which are susceptible to cleavage,[4] are formed as shown in Chart I. 1,2 addition of hydrogen to II (forming III) would yield an allyl ether only if the substituent is in the 4-position. On the other hand, 1,4 addition (forming IV) would yield an allyl ether for 3- and 4-substituted anilines, but not for 2-substituted compounds. Rearrangement of IV to V would make an allyl ether possible for even 2-substituted anilines. Since allyl-type intermediates are statistically favored with 4-alkoxy derivatives, more hydrogenolysis should result with such compounds if the proposed mechanism is correct. This is in accord with experimental findings when rhodium catalyst is used.

Palladium on carbon has some utility but also many drawbacks. No uptake of hydrogen took place in neutral solution or in alcohol containing acetic acid. Hydrogenation, however, did proceed in acetic acid solution, although considerable amounts of secondary amine were obtained and the reaction period was rather long unless a high catalyst ratio was used. Reduction with platinum oxide not only gave cyclohexylamine, but dicyclohexylamine as well as mono- and dialkoxydicyclohexylamines. The large amounts of secondary amine formation with these catalysts made it difficult to assess whether the position of the substituents had any effect on hydrogenolysis (see Table I).

## Experimental[5]

The following is an example of reduction with 5% rhodium on alumina.[6]

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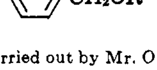
[1] M. Freifelder and G. R. Stone, *J. Org. Chem.*, **27**, 3568 (1962).

[2] H. A. Smith and R. G. Thompson, *Advan. Catalysis*, **9**, 727 (1957).

[3] M. Freifelder [*J. Org. Chem.*, **26**, 1835 (1961)] has reported on the promoter effect of certain acids on rhodium reductions where the end product is a strong base.

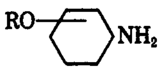
[4] Benzyl ethers, readily hydrogenolyzed catalytically to toluene and alcohols, can be viewed as allyl-type ethers.



[5] Microanalyses were carried out by Mr. O. F. Kolsto and his associates; infrared determinations were by Messrs. A. Kammer and W. Washburn.

TABLE I

ALKOXYCYCLOHEXYLAMINES



| R | Catalyst[a] | Time, hr. | Products, %[b] D | E | F | G | H |
|---|---|---|---|---|---|---|---|
| $2\text{-}CH_3$ | A | 31 | 7.5 | 57.0 | 33.0 | | 2.5 |
| $2\text{-}CH_3$[c] | A | 4.5 | 10.25 | 77.25 | 10.0 | | 2 |
| $3\text{-}CH_3$[c] | A | 3 | 5.5 | 70.0 | 24.5 | | |
| $4\text{-}CH_3$[c] | A | 24 | 24.25 | 74.75 | 1.0 | | |
| $2\text{-}C_2H_5$ | A | 14 | 8 | 70[d] | 9 | | 10 |
| $3\text{-}C_2H_5$ | A | 20 | 9 | 66[e] | 25 | | |
| $4\text{-}C_2H_5$ | A | 8 | 30 | 56.5[f] | 12 | | |
| $2\text{-}C_3H_7$ | A | 24 | 3 | 75–80 | 16 | | |
| $3\text{-}C_3H_7$ | A | 10 | 4 | 80[g] | 15 | | |
| $4\text{-}C_3H_7$ | A | 6–7 | 16 | 79[h] | 4.5 | | |
| $2\text{-}C_4H_9$ | A | 12 | 3.5 | 65 | 9 | | 20 |
| $2\text{-}C_4H_9$[c] | A | 4 | | [i] | | | |
| $4\text{-}C_4H_9$ | A | 4 | 13.5 | 80 | 6.0 | | |
| $2\text{-}CH_3$ | B | 5.5 | 35.5 | 41.5 | 23.0 | | |
| $3\text{-}CH_3$ | B | 6–10 | 9.4 | 27.5 | 8.0 | 26.5 | 25.0 |
| $4\text{-}CH_3$ | B | 6–10 | 19 | 54 | | 9.0 | 17.0 |
| $2\text{-}C_2H_5$ | B | 7 | 6 | 44 | | 11.0 | 38.5 |
| $3\text{-}C_2H_5$ | B | 3.5 | 26.5 | 20.5 | 6 | 37.0 | 10.0 |
| $4\text{-}C_2H_5$ | B | 9 | 20 | 24 | 1.5 | 22.5 | 30.0 |
| $2\text{-}CH_3$ | C | 48 | 3.5 | 60.0 | | 4 | 33 |
| $3\text{-}CH_3$ | C | 3.5 | 35.5 | 3 | | 50 | 7 |
| $4\text{-}CH_3$ | C | 8 | 2 | 61 | | | 37.0 |
| $2\text{-}C_2H_5$ | C | 30 | 2 | 71 | | | 24.0 |
| $4\text{-}C_2H_5$ | C | 15 | 7 | 46.5 | 25 | | 20.5 |

[a] A = 5% rhodium on alumina in a 40% weight ratio of catalyst to alkoxyaniline, solvent was ethyl alcohol unless indicated; B = platinum oxide, 5% weight ratio; C = 5% palladium on carbon, 50% weight ratio. [b] Unless otherwise indicated, per cent composition was determined by g.l.c. D = cyclohexylamine, E = alkoxycyclohexylamine, F = alkoxyaniline, G = dicyclohexylamine, H = high boilers. The high-boiling components as seen from infrared examination were free of aromatic material and showed strong broad ether bands at 9.05 μ. They were assumed to be mixtures of mono- and dialkoxydicyclohexylamines with the latter in far greater amounts. [c] Reduction carried out in alcohol containing 1 equiv. of acetic acid. [d] A 59% yield was obtained on distillation, b.p. 180° (750 mm.), $n^{25}D$ 1.4529; see ref. 1. [e] A 58% yield on distillation, b.p. 194–197° (755 mm.); see ref. 1. [f] A 50% yield on distillation; same constants as in ref. 1. [g] A 60% yield on distillation, b.p. 105–110° (21 mm.), $n^{25}D$ 1.4608; see ref. 1. [h] A 68% yield on distillation, b.p. 115° (40 mm.), $n^{22}D$ 1.4588; see ref. 1. [i] Distilled yield, 61.5%.

**4-Butoxycyclohexylamine.**—A solution of 24.75 g. (0.15 mole) of 4-butoxyaniline in 150 ml. of absolute ethyl alcohol was hydrogenated in the presence of 10.0 g. of 5% rhodium on alumina under 3.5-atm. pressure at 60°. When uptake was complete, the solution was filtered from the catalyst and a sample was subjected to gas–liquid chromatography.[7] The catalyst was washed thoroughly with more alcohol. The solution was then concentrated and the residue was distilled, b.p. 128–130° (32 mm.), $n^{25}D$ 1.4576, 70% yield.

*Anal.* Calcd. for $C_{10}H_{21}NO$: C, 70.14; H,12.36; N, 8.18. Found: C, 70.28; H, 12.19; N, 8.28.

2-Propoxycyclohexylamine was similarly prepared in 62% yield, b.p. 205–208° (758 mm.), $n^{25}D$ 1.4541.

*Anal.* Calcd. for $C_9H_{19}NO$: C, 68.73; H, 12.22; N, 8.90. Found: C, 68.74; H, 12.17; N, 9.13.

When 1 equiv. of acetic acid was used in the reductions the solution, after removal of catalyst, was treated with an equivalent amount of 40% aqueous sodium hydroxide before submitting a sample for chromatography.

Hydrogenation in acetic acid was carried out in a few instances with little or no change in the amounts of the products of reduction, or any improvement in the reaction rate over that in alcohol and acetic acid. The work-up is as described in the next paragraph.

**Reductions with Platinum Oxide or 5% Palladium on Carbon.**—These were carried out at 60° in acetic acid (150 ml.) and 0.15 mole of compound. After removal of catalyst the solutions were concentrated in the presence of water to prevent acetylation. The residues were dissolved in water and kept cold while basified with excess sodium hydroxide solution to prevent loss of cyclohexylamine. The solutions were extracted with ether. After drying the extract over anhydrous magnesium sulfate and removal of drying agent, the ether solution was submitted for chromatography.

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(6) Since there did not appear to be any difference in activity between rhodium on alumina and rhodium on carbon in several comparative runs, the former was chosen because it was less of a fire hazard. All the noble metal catalysts used in this study were purchased from Engelhard Industries, Newark, N. J.

(7) The following conditions for g.l.c. analysis (by one of us, P.F.H.) were used: instrument, Burkell unit, Model K-2; column, 2-m. silicone L-46, 20% on acid-washed Chromosorb W, 80–100 mesh; carrier, helium 60 cc./min.; programmed (nonlinear) temperature at 170–230°. Known standards were used except for high-boiling materials.

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## Synthesis of Monoacyl Hydrazides

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*Received December 24, 1964*

The hydrazides of carboxylic acids are usually prepared[1] by treating hydrazine hydrate with an anhydride, chloride,[2] amide,[3] or ester[4] of the corresponding acid or by heating its hydrazonium salt.[5] A common disadvantage of these reactions in addition to the necessity of preparing and frequently separating the abovementioned carboxylic acid derivatives, consists in the formation of polyacyl hydrazides and tetrazines as by-products, which makes laborious purifications and low yields often inevitable. While looking for a way to obtain only the monoacyl hydrazides by direct reaction between the acid and hydrazine hydrate, avoiding even the isolation of the hydrazonium salt, we observed that complete transformation of the starting reagents requires considerable time and high temperatures and we have noticed that both of these conditions cause formation of by-products.

We have found, however, that activated alumina shows a remarkable catalytic activity, promoting the formation of the monoacyl hydrazides exclusively. Further, the catalyst permits the lowering of the reaction temperatures to the point that by-products are no longer formed. The water produced during the reaction must be continuously drawn off, *e.g.*, by azeotropic distillation.

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(1) A. W. Johnson, C. E. Dalgliesh, and J. Walker, "Chemistry of Carbon Compounds," Vol. I, E. H. Rodd, Ed., Elsevier Publishing Co., New York, N. Y., 1951, p. 600.

(2) C. Naegeli and G. Stefanovitsch, *Helv. Chim. Acta*, **11**, 636 (1928).

(3) H. M. Stanley, British Patent 785,346 (1957).

(4) L. F. Fieser and M. Fieser, "Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1956, pp. 179, 213; H. Henecka and P. Kurtz, "Methoden der Organischen Chemie" (Houben-Weyl), Vol. VIII, Georg Thieme Verlag, Stuttgart, 1952, p. 676; Th. Curtius, *J. prakt. Chem.*, [2] **50**, 275 (1894); Th. Curtius, G. Schöfer, and N. Schwan, *ibid.*, [2] **51**, 185 (1895); Th. Curtius and E. Boetzelen, *ibid.*, [2] **64**, 314 (1901); R. Stollé, *ibid.*, [2] **69**, 145, 154, 486, 497 (1904); Th. Curtius and Melsbach, *ibid.*, [2] **81**, 548 (1910).

(5) Th. Curtius and H. Franzen, *Ber.*, **35**, 3239 (1902).