CHEMICAL & PHARMACEUTICAL BULLETIN

Vol. 17, No. 5 **May 1969**

Regular Articles

Chem. Pharm. Bull. 17(5) 861—865 (1969)

UDC 542.941.7 : 547.574.04

Catalytic Hydrogenation of Hydroamide in the Presence of Ammonia and of Butylamine

KEIICHI ITO and MINORU SEKIYA

Shizuoka College of Pharmacy[1]

(Received April 3, 1968)

Catalytic hydrogenations of hydroamides under high hydrogen pressure in the presence of ammonia and of butylamine were examined to see effects of these bases on the composition of products. The product analyses show the predominant formation of primary amine in the former case and in the latter case the formation of primary and secondary amines possessing butyl residue at 2:1 molar ratio. From these results comments on the course of the hydrogenation are given.

It has previously been reported[2] from this laboratory that catalytic hydrogenation of azomethine under high pressure of hydrogen in the presence of ammonia or amine proceeds according to the following equation 1, the course being inferred to be exchange of amino portion of azomethine with ammonia or amine followed by hydrogenation.

$$\mathrm{ArCH{=}NR} + \mathrm{R'NH_2} + \mathrm{H_2} \longrightarrow \mathrm{ArCH_2NHR'} + \mathrm{RNH_2} \qquad (1)$$

$$(\mathrm{R{=}alkyl},\quad \mathrm{R'{=}H\ or\ alkyl})$$

N,N'-Bis(arylmethylene)-1-arylmethylenediamine (referred to as hydroamide hereinafter) has been known[3] to be capable of conversion with ammonia to aldimine, and its conversion with aniline to azomethine has also been reported.[4] Catalytic hydrogenation of hydroamide in the presence of primary amine[5] led to incomplete hydrogenation to give azomethine as a major product, when ordinary pressure of hydrogen was applied.

The present paper deals with high pressure hydrogenation of hydroamide in the presence of ammonia or aliphatic primary amine at a raised temperature using Raney nickel catalyst in ethanolic medium. As hydroamide are selected hydrobenzamide and its 4,4',4''-trimethoxy- and 3,4:3',4':3'',4''-tris(methylenedioxy)substituted derivatives. It has already been reported[6] that hydrobenzamide or 3,4:3',4':3'',4''-tris(methylenedioxy)hydrobenzamide is hydro-

---

[1] Location: *160, Oshika, Shizuoka.*

[2] M. Sekiya, A. Hara and T. Masui, *Chem. Pharm. Bull.* (Tokyo), **11**, 277 (1963).

[3] H.H. Strain, *J. Am. Chem. Soc.*, **49**, 1558 (1927).

[4] Lachowicz, *Monatsch.*, **9**, 695 (1888); P.I. Petrenko-Kritchenko, *C.A.*, **34**, 7845 (1940).

[5] R. Juday and H. Adkins, *J. Am. Chem. Soc.*, **77**, 4559 (1955).

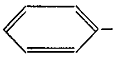
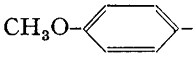
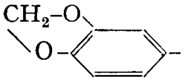
[6] M. Sekiya, A. Hara, K. Ito, J. Suzuki and K. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **15**, 774 (1967).

genated in the above manner in the absence of base to give the primary and secondary amines at approximately 1:1 molar ratio as represented by Eq. 2. It would, therefore, be of interest to examine the effect of ammonia or amine in the above hydrogenation system on the composition of the products. Hydrogenation of hydroamide in ethanolic ammonia (molar ratio of ammonia to hydroamide, 3:1) was carried out under the condition similar to that employed for the hydrogenation of hydroamide reported previously.[6] At hydrogenation temperature of 130—135° very rapid absorption of hydrogen took place, and the absorption ceased after uptake of nearly three molar equivalent of hydrogen. The results are summarized in Table I. Approximately three molar equivalent of primary amine was found to be formed as major product in the hydrogenation. This reaction can be represented by Eq. 3. This appears suggestive of the occurrence of the ammonia reaction [$ArCH(N{=}CHAr)_2 + NH_3 \rightleftarrows 3ArCH{=}NH$] prior to hydrogenation.

$$ArCH(N{=}CHAr)_2 + 3H_2 \longrightarrow ArCH_2NH_2 + ArCH_2NHCH_2Ar \qquad (2)$$

$$ArCH(N{=}CHAr)_2 + NH_3 + 3H_2 \longrightarrow 3ArCH_2NH_2 \qquad (3)$$

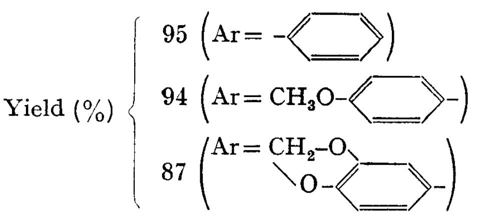
Table I. Catalytic Hydrogenation[a] in the Presence of Ammonia

$ArCH(N{=}CHAr)_2$ Ar-	Hydrogenation time (min)	Yield of products[b] (moles)	
		$ArCH_2NH_2$	$(ArCH_2)_2NH$
	3	2.48	0.14
	4	2.70	0.15
	3	2.46	0.14

a) substrate: 0.05 mole. General procedure is given in Experimental.
b) Yield of products estimated from one mole of substrate.

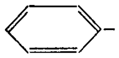
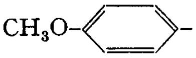
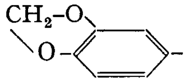
Next, behavior of the hydroamide in catalytic hydrogenation in the presence of primary amine was investigated. Butylamine was chosen as the primary amine reactant. Similarly to the previously reported reaction with aniline,[4] the conversion to azomethine from hydroamide was recognized by the demonstrations, which were carried out by heating the mixtures of the hydroamide and butylamine at 1:4.5 molar ratio in open vessel, resulting in high yield of N-arylmethylenebutylamine with rapid evolution of ammonia.

$$ArCH(N{=}CHAr)_2 + 3C_4H_9NH_2 \longrightarrow 3ArCH{=}NC_4H_9 + 2NH_3 \qquad (4)$$



Taking this result into account, we then conducted high pressure hydrogenation of hydroamide in ethanolic butylamine (molar ratio of butylamine to hydroamide, 9:1) under the condition similar to that in the presence of ammonia. A more variety of products were formed in comparison with those in the foresaid hydrogenation in the presence of ammonia. Careful fractional distillation of the reaction mixture led to fine separation of the products, giving three kinds of products, N,N-bis(arylmethyl)amine (A), N-butylarylmethylamine (B) and arylmethylamine (C). The comparison of the products in each experiments is shown in Table II. The formation of B, which might have been expected according to Eq. 4 followed by hydrogenation, was not predominant. This is undoubtedly due to suppression of the reaction shown by Eq. 4 under the sealed system from which ammonia can not escape.

Table II. Catalytic Hydrogenation[a] in the Presence of Butylamine

$ArCH(N{=}CHAr)_2$ Ar-	Hydrogenation time (min)	Yield of products[b] (moles) (A) $(ArCH_2)_2NH$	(B) $ArCH_2NHC_4H_9$	(C) $ArCH_2NH_2$	(C-A)/B
	60	0.23	0.79	1.78	1.96
	80	0.07	0.76	1.67	2.10
	100	0.15	0.75	1.65	2.00

[a] substrate: 0.05 mole; butylamine: 90 ml of 5M ethanolic soln. General procedure is given in Experimental.

[b] Yield of products estimated from one mole of substrate.

From the results shown in Table II, the effect of butylamine on the composition of the products would be discussed in the following. Hydrogenation of the hydroamide alone under the same condition as above has been provided[6] to give equimolar amounts of both A and C. Product A in the above hydrogenation is considered as a product directly derived from hydroamide by hydrogenation without participation of butylamine. In this case, an equimolar amount of C should be simultaneously formed. Therefore, the amounts of B and C–A are considered to express the quantity of products which were formed by the participation of butylamine. In every run, the molar ratio (C–A)/B was found to be nearly 2. Further, we examined the effect of quantity of butylamine on the composition of the products. The results of the experiments on this respect using hydrobenzamide as substrate are shown in Table III. As can be seen, it was found that the ratio (C–A)/B is not changed even in the cases with decreased amount of butylamine, and the increasing yield of dibenzylamine is reasonably assumed to be due to decrease of participation of butylamine in the system.

Table III. Effect of Butylamine on Catalytic Hydrogenation[a] of Hydrobenzamide

Ratio[b]	Hydrogenation time (min)	Yield of products[c] (moles) (A) $(C_6H_5CH_2)_2NH$	(B) $C_6H_5CH_2NHC_4H_9$	(C) $C_6H_5CH_2NH_2$	(C-A)/B
9	60	0.23	0.79	1.78	1.96
5	60	0.27	0.66	1.64	2.08
3	40	0.35	0.59	1.47	1.90

[a] substrate: 0.05 mole General procedure is given in Experimental.

[b] molar ratio of butylamine to substrate

[c] Yield of products estimated from one mole of substrate.

Overall reaction resulting in the formation of C and B at 2:1 molar ratio can be written by the following equation 5.

$$ArCH(N{=}CHAr)_2 + C_4H_9NH_2 + 3H_2 \longrightarrow 2ArCH_2NH_2 + ArCH_2NHC_4H_9 \qquad (5)$$

It is, therefore, very likely that at a raised temperature the initial equilibrium stage prior to initiation of hydrogenation is the formation of aldimine and azomethine at 2:1 molar ratio by reaction between hydroamide and butylamine as represented by Eq. 6. And then hydrogenation process follows on each of the products.

$$\mathrm{ArCH(N{=}CHAr)_2 + C_4H_9NH_2 \rightleftarrows 2ArCH{=}NH + ArCH{=}NC_4H_9} \qquad (6)$$

$$\mathrm{ArCH{=}NH + H_2 \longrightarrow ArCH_2NH_2}$$

$$\mathrm{ArCH{=}NC_4H_9 + H_2 \longrightarrow ArCH_2NHC_4H_9}$$

The reaction written by Eq. 6 is distinguished from the reaction represented by Eq. 4 carried out in an open vessel. It is probable that in open vessel system the reaction written by Eq. 7 following to Eq. 6 proceeds favorably to attain to Eq. 4 since ammonia thus formed is removed readily from the reaction system.

$$\mathrm{ArCH{=}NH + C_4H_9NH_2 \rightleftarrows ArCH{=}NC_4H_9 + NH_3} \qquad (7)$$

It can be said that the reaction written by Eq. 6 is favored in sealed vessel system, while reaction of Eq. 7 is suppressed. As can be seen from Table III, the reaction of Eq. 7 was not admitted even in the presence of rather larger quantity of butylamine. Sekiya, *et al.*[2] of this laboratory have reported the high pressure hydrogenation of azomethine in the presence of ammonia in a similar manner, which resulted in the predominant formation of two kinds of primary amines, in the interpretation of very inclination of Eq. 7 to the left. This also supports the above proposal.

Experimental

Materials——The following three hydroamides which had been purified were used; Hydrobenzamide, mp 100—101° (lit.[7] mp 102°), 4,4′,4″-trimethoxyhydrobenzamide, mp 125—126° (lit.[8] mp 126—127°), 3,4:3′,4′:3″,4″-tris(methylenedioxy)hydrobenzamide, mp 169—170° (lit.[9] mp 172°).

Catalytic Hydrogenation of Hydroamides

I. In the Presence of Ammonia——General Procedure: A mixture of 0.05 mole of hydroamide, 30 ml of 5M ethanolic NH_3 (0.15 mole as NH_3) and Raney nickel catalyst prepared from 2 g of 50% alloy in the usual manner was placed in an autoclave having a capacity of 175 ml. Under 80 kg/cm² (at room temperature) of initial hydrogen pressure the whole was heated and constant shaking was started at 130—135°. Dropping of hydrogen pressure was almost terminated within 3—4 min and heating and shaking were continued for additional 30 min. Hydrogen uptake was about 0.15 mole equiv. in every run.

The catalyst was removed from the reaction mixture by filtration, and the filtrate was evaporated to remove NH_3 and EtOH. The residue was submitted to fractional distillation under a reduced pressure. The fractions thus obtained were almost pure amines. The identification of the amines was made by comparison of their IR spectra with those of authentic samples, the mixing melting point test of their hydrochlorides obtained by evaporation of the amines with hydrochloric acid, and elementary analyses of their hydrochlorides. The yields of the products are indicated in Table I. The following are the products obtained.

1) Hydrogenation of Hydrobenzamide: Benzylamine: bp 84—87° (30 mmHg); hydrochloride, mp 249—251°. Dibenzylamine: bp 134—140° (4 mmHg); hydrochloride, mp 251—253°.

2) Hydrogenation of 4,4′,4″-Trimethoxyhydrobenzamide: 4-Methoxybenzylamine: bp 126—127° (14 mmHg); hydrochloride, prisms from EtOH, mp 228—230° (lit.[10] mp 230—231°). *Anal.* Calcd. for $C_8H_{12}ONCl$: C, 55.33; H, 6.96; N, 8.07. Found: C, 55.34; H, 6.90; N, 8.27. 4,4′-Dimethoxydibenzylamine: bp 225—230° (10 mmHg); hydrochloride, leaves from EtOH, mp 243° (lit.[11] mp 243°). *Anal.* Calcd. for $C_{16}H_{20}O_2NCl$: C, 65.40; H, 6.86; N, 4.77. Found: C, 65.25; H, 6.91; N, 4.79.

3) Hydrogenation of 3,4:3′,4′:3″,4″-Tris (methylenedioxy)hydrobenzamide: 3,4-Methylenedioxybenzylamine: bp 115—120° (4 mmHg); hydrochloride, prisms from EtOH, mp 226—227° (lit.[12] mp 227°). *Anal.* Calcd. for $C_8H_{10}O_2NCl$: C, 51.25; H, 5.33; N, 7.47. Found: C, 51.15; H, 5.36; N, 7.64. 3,4:3′,4′-Bis (methyl-

---

[7] M.A. Laurent, *Ann.*, **21**, 130 (1837).

[8] L.B. Howard, G.H. Hilbert, W.R. Wiebe and V.L. Gaddy, *J. Am. Chem. Soc.*, **54**, 3637 (1932).

[9] C. Lorenz, *Ber.*, **14**, 785 (1881).

[10] H. Goldschmidt and N. Polonowska, *Ber.*, **20**, 2407 (1887).

[11] O.J. Steinhart, *Ann.*, **241**, 332 (1888).

[12] C. Mannich and R. Kuphal, *Ber.*, **45**, 318 (1912).

enedioxy)dibenzylamine: Obtained as the distillatlon residue, needles from EtOH, mp 112—114° (lit.[13]) mp 114°). *Anal.* Calcd. for $C_{16}H_{15}O_4N$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.61; H, 5.12; N, 4.74. Hydrochloride, mp 254—256° (lit.[14]) mp 257°). *Anal.* Calcd. for $C_{16}H_{16}O_4NCl$: C, 59.72; H, 4.98; N, 4.35. Found: C, 59.61; H, 4.99; N, 4.47.

II. In the Presence of Butylamine——General Procedure: The procedure for hydrogenation in the presence of butylamine was the same as described in part I except that 5M ethanolic butylamine (the amount used are indicated in Table II and III) was used instead of ethanolic NH_3. Hydrogen absorption almost ceased within 40—100 min. The yields of the products are indicated in Table II and III. The following are the products obtained.

1) Hydrogenation of Hydrobenzamide: Benzylamine: bp 80—83° (28 mmHg); hydrochloride, mp 249—251°. N-Butylbenzylamine: bp 99—105° (18 mmHg); hydrochloride, leaves from EtOH, mp 237—238° (lit.[15]) mp 241°). *Anal.* Calcd. for $C_{11}H_{18}NCl$: C, 66.06; H, 9.00; N, 7.07. Found: C, 66.06; H, 9.03; N, 7.10. Dibenzylamine: bp 130—136° (3 mmHg); hydrochloride, mp 245—248°.

2) Hydrogenation of 4,4′,4″-Trimethoxyhydrobenzamide: 4-Methoxybenzylamine: bp 96—101° (5 mmHg); hydrochloride, mp 229—230°. N-Butyl-4-methoxybenzylamine: bp 126—130° (2 mmHg) (lit.[16]) bp 120—125° (0.7 mmHg)); hydrochloride, leaves from EtOH, mp 185—186°. *Anal.* Calcd. for $C_{12}H_{20}ONCl$: C, 62.71; H, 8.77; N, 6.09. Found: C, 62.52; H, 8.65; N, 6.10. 4,4′-Dimethoxydibenzylamine: bp 186—191° (2 mmHg); hydrochloride, mp 242—243°.

3) Hydrogenation of 3,4:3′,4′:3″,4″-Tris (methylenedioxy) hydrobenzamide: 3,4-methylenedioxybenzylamine: bp 113—115° (3 mmHg); hydrochloride, mp 225—227°. N-Butyl-3,4-methylenedioxybenzylamine: bp 126—130° (1 mmHg); hydrochloride, leaves from EtOH, mp 204—205°. *Anal.* Calcd. for $C_{12}H_{18}O_2NCl$: C, 59.12; H, 7.44; N, 5.74. Found: C, 58.93; H, 7.49; N, 5.67. 3,4:3′,4′-Bis (methylenedioxy)-dibenzylamine: Obtained as the distillation residue, mp 110—112°.

Thermal Reaction of Hydroamides with Butylamine——General Procedure: A mixture of 0.025 mole of hydroamide and 0.11 mole (8.2 g) of butylamine was heated with stirring at 50—60° for 1.5 hr on a water bath. The mixture turned a homogeneous liquid and NH_3 evolved during the course of the reaction. After removal of excess of butylamine by evaporation the residual liquid was distilled under a reduced pressure, whereupon N-arylmethylenebutylamine was obtained in high yield in every run.

N-Benzylidenebutylamine: Yield, 11.4 g (95%). bp 91—93° (7 mmHg) (lit.[17]) bp 112—113° (14 mmHg)), n_D^{13} 1.5269. IR cm^{-1}: $\nu_{C=N}$ 1645 (liquid). *Anal.* Calcd. for $C_{11}H_{15}N$: C, 81.93; H, 9.38; N, 8.69. Found: C, 82.18; H, 9.39; N, 8.58.

N-4-Methoxybenzylidenebutylamine: Yield, 15.0 g (94%). bp 120° (3 mmHg) (lit.[15]) bp 108—109° (1 mmHg)), n_D^{13} 1.5531. IR cm^{-1}: $\nu_{C=N}$ 1643 (liquid). *Anal.* Calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.40; H, 8.87; N, 7.30.

N-3,4-Methylenedioxybenzylidenebutylamine: Yield, 13.0 g (87%). bp 134° (4 mmHg) (lit.[18]) bp 160° (10 mmHg)), n_D^{13} 1.5419. IR cm^{-1}: $\nu_{C=N}$ 1644 (liquid). *Anal.* Calcd. for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.27; H, 7.26; N, 6.82.

Acknowledgement We thank Mr. K. Narita, Mrs. H. Suzuki and Mrs. T. Hoshikawa for elementary analyses.

---

13) J. Malan and R. Robinson, *J. Chem. Soc.*, **1927**, 2653.
14) P. Pratesi and G. Castorina, *C.A.*, **49**, 5468 (1955).
15) A. Einhorn and H. Pfeiffer, *Ann.*, **310**, 225 (1900).
16) J.B. Wright and R.C. Elderfield, *J. Org. Chem.*, **11**, 111 (1946).
17) C.W.C. Stein and A.R. Day, *J. Am. Chem. Soc.*, **64**, 2569 (1942).
18) T.I. Crowell and D.W. Peck, *J. Am. Chem. Soc.*, **75**, 1075 (1953).