UDC 547.574 : 547.298.1

155. **Minoru Sekiya and Akira Hara** : Reaction of Amide Homologs. IX. Catalytic Hydrogenation of Azomethines in the Presence of Amide and its Mechanism.

(*Shizuoka College of Pharmacy*[*1])

Sekiya previously described a new process for the hydrogenation of nitriles,[1] aldehyde oximes,[2] and aldehyde-ammonia mixtures,[3] which involves the hydrogenation in the presence of formamide under high pressure of hydrogen, resulting in the formation of formamidomethyl derivatives in excellent yield. This method, which will hereafter be called "reductive formylamination" for short, appeared to be a favorable way for the preparation of primary amines, into which the formamidomethyl derivatives were hydrolysed, inhibiting the formation of secondary amines, which are usually formed in a considerable amount by the usual hydrogenation process.

$$\mathrm{RCN + 2H_2 + HCONH_2 \longrightarrow RCH_2NHCHO + NH_3}$$

$$\mathrm{RCH{=}NOH + H_2 + HCONH_2 \longrightarrow RCH_2NHCHO + NH_3 + H_2O}$$

$$\mathrm{RCHO + H_2 + HCONH_2 + NH_3 \longrightarrow RCH_2NHCHO + NH_3 + H_2O}$$

Later, in discussing the mechanism of how the formation of secondary amine is prevented in reductive formylamination, it was proposed by Sekiya, *et al.*[4] that it may be through a reaction of azomethine, regarded as the most likely intermediate in the formation of secondary amine, by hydrogenation in conjunction with formamide as represented by the following equation.

$$\mathrm{RCH{=}NCH_2R' + 2HCONH_2 + H_2 \longrightarrow RCH_2NHCHO + R'CH_2NHCHO + NH_3}$$

This essential reaction has already been shown[4] to occur with some azomethines, but its mechanism has not yet been explained. The present paper reports some extension of the reaction and comment on its mechanism.

1. Catalytic Hydrogenation of Azomethines in the Presence of Amides

It was shown[4] that catalytic hydrogenation of some azomethines in the presence of formamide resulted in the conversion represented by the following general equation.

$$\mathrm{ArCH{=}NR + 2HCONH_2 + H_2 \longrightarrow ArCH_2NHCHO + RNHCHO + NH_3} \qquad (1)$$

In continuation of this study, this hydrogenation reaction was more generalized to some azomethines such as N-benzylideneaniline (I), N-benzylidenebenzylamine (II), and N-(4-methoxybenzylidene)phenethylamine (III). Catalytic hydrogenation of these azomethines in the presence of amide was carried out at 130～140° at approximately 80 kg./cm^2 (at ordinary temperature) initial H_2 pressure, with Raney nickel catalyst. Formamide as well as acetamide was used as the amide, employing three moles to one of the azomethine reactant. The results were summarized in Table I. In comparing formamide

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[*1] Oshika, Shizuoka (関屋 実, 原 明).

1) M. Sekiya : Yakugaku Zasshi, **70**, 524 (1950).

2) *Idem* : *Ibid.*, **70**, 545 (1950).

3) *Idem* : *Ibid.*, **70**, 548 (1950).

4) M. Sekiya, T. Fujita : *Ibid.*, **71**, 941 (1951).

and acetamide, formamide was much more effective than acetamide for the reaction. When the amine residue of the azomethine was aliphatic, yield of the reaction with formamide was nearly theoretical, as shown in the case of II and III.

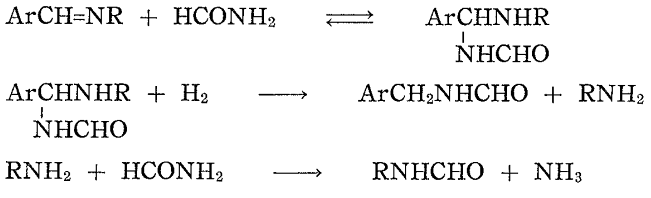
Table I. Hydrogenation of a Mixture of Azomethine and Amide

Azomethine	Amide	Hydrogenation temp. (°C)	Conversion rate (%)
N-Benzylideneaniline	Formamide	136~140	76[a]
N-Benzylidenebenzylamine	〃	132~135	94
N-(4-Methoxybenzylidene)phenethylamine	〃	131~138	91
N-Benzylideneaniline	Acetamide	132~138	16.5
N-Benzylidenebenzylamine	〃	131~136	0
N-(4-Methoxybenzylidene)phenethylamine	〃	130~133	2

a) N,N-Dibenzylformamide and tribenzylamine were simultaneously produced.

2. Suggestion for the Reaction Mechanism

Considering the overall reaction of the hydrogenation of azomethines represented by (1), the following scheme might be considered as a probable reaction path.



$$\mathrm{ArCH{=}NR + HCONH_2 \rightleftarrows \underset{\displaystyle NHCHO}{ArCHNHR}}$$

$$\mathrm{\underset{\displaystyle NHCHO}{ArCHNHR} + H_2 \longrightarrow ArCH_2NHCHO + RNH_2}$$

$$\mathrm{RNH_2 + HCONH_2 \longrightarrow RNHCHO + NH_3}$$

Chart 1.

If, starting from an addition reaction between azomethine and formamide, the addition product should undergo hydrogenolysis followed by formylation, the overall reaction could be satisfactorily explained. But, whether hydrogenolysis can take place in such a way or not is questionable. Investigation on hydrogenolysis of alkylidenediamine derivatives has already been made in this laboratory.[5~7]

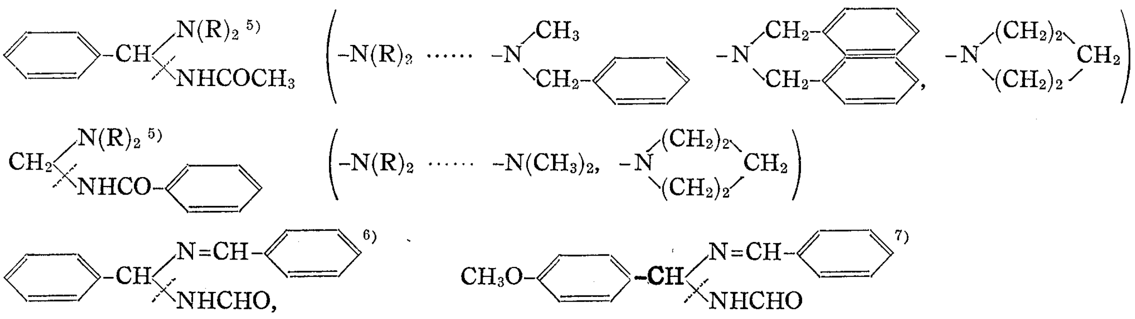


Chart 2.

Hydrogenolysis of N-(α-dialkylaminobenzyl)acetamide and N-(dialkylaminomethyl)-benzamide was carried out in ethanol under high hydrogen pressure using Raney-nickel catalyst and that of N-arylmethylene-1-acylamino-1-arylmethylamine in ethanol under ordinary hydrogen pressure using palladium-charcoal catalyst. Hydrogenolysis of these alkylidenediamine derivatives did not sever the carbon bond connecting to dialkylamino group, but that connecting to amide group. Dotted lines in Chart 2 represent the bonds in which hydrogenolysis occurred.

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5) M. Sekiya, K. Ito: This Bulletin, **11**, 892 (1963).
6) M. Sekiya, T. Oishi: *Ibid.*, **7**, 468 (1959).
7) *Idem*: *Ibid.*, **7**, 857 (1959).

In view of these facts, it seems safe to say that, in the case of the intermediate described in Chart 1, hydrogenolysis would take place at the carbon bond connecting to the formamide group. This does not follow the proposed reaction path shown in Chart 1 and therefore the proposed mechanism cannot be supported.

It was shown in the preceding paper[8] that azomethine can generally react with ammonia as illustrated by the following equilibrium.

$$\mathrm{ArCH{=}NR} + \mathrm{NH_3} \rightleftarrows \mathrm{ArCH{=}NH} + \mathrm{RNH_2} \qquad (2)$$

It is also known[9] that primary amine reacts with formamide affording N-alyklformamide, and particularly in the case of aliphatic amine, exothermic reaction takes place rapidly only by mixing. The reaction is generally represented by the following.

$$\mathrm{RNH_2} + \mathrm{HCONH_2} \longrightarrow \mathrm{RNHCHO} + \mathrm{NH_3} \qquad (3)$$

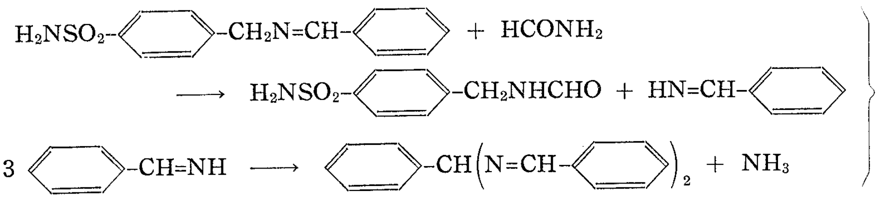
By summation of equations (2) and (3), the following equation may be written.

$$\mathrm{ArCH{=}NR} + \mathrm{HCONH_2} \longrightarrow \mathrm{ArCH{=}NH} + \mathrm{RNHCHO} \qquad (4)$$

Considering the nature of the reaction (2) and (3), the occurrence of the reaction (4) may be assumed with great possibility, *i.e.*, azomethine may react with formamide by the catalytic action of ammonia to give arylmethyleneimine and N-alkylformamide. This reaction was expected to account for the initial stage of hydrogenation of azomethine in the presence of formamide.

Besides, as shown in a previous paper of this series,[6] reaction between azomethine and amide is complex, *i.e.*, it results in the formation of N-arylmethylene-1-acylamino-1-arylmethylamine at boiling water bath temperature, though this reaction is also expected to be initiated by the stage (4). This fact seems to make it difficult to demonstrate the reaction (4).

Nevertheless, the stage (4) was demonstrated by the use of N-benzylidene-4-sulfonamidobenzylamine (IV) as the azomethine. In this case, benzylideneimine, which would be produced by the stage (4), is expected to undergo intermolecular condensation to form hydrobenzamide and the reaction can be represented by the following formulae.



(5)

In order to make it possible to separate hydrobenzamide from other materials, toluene could be used as the solvent. In this experiment, a solution of IV in formamide was vigorously stirred with an immiscible toluene layer on a boiling water bath. In this way, hydrobenzamide would be kept out of further reaction with formamide, which would lead to the formation of N-benzylidene-α-formamidobenzylamine (V), by being extracted with toluene as soon as it is produced. Thus, hydrobenzamide was separated by concentration of the toluene layer accompanying a certain amount of V. Consequently, the occurance of stage (4) could be illustrated by this demonstration.

When considering equation (4) as the initial stage of the hydrogenation of azomethine in the presence of formamide, the reaction path may be explained as in the following:

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8) M. Sekiya, A. Hara, T. Masui : This Bulletin, **11**, 277 (1963).

9) S. Sugasawa, H. Shigehara : Yakugaku Zasshi, **62**, 531 (1942); M. Sekiya : *Ibid.*, **70**, 23 (1950).

$$ArCH{=}NR + HCONH_2 \longrightarrow ArCH{=}NH + RNHCHO \qquad (4)$$

$$ArCH{=}NH + H_2 \longrightarrow ArCH_2NH_2 \qquad (6)$$

$$ArCH_2NH_2 + HCONH_2 \longrightarrow ArCH_2NHCHO + NH_3 \qquad (3')$$

Chart 3.

In stage (3′) the larger the amount of ammonia as the reaction goes on, the more the initiating stage (4) would be accelerated, because reaction (4) is catalyzed by ammonia. Then, the reaction path represented by Chart 3 would be sufficiently comprehensive to account for the hydrogenation of azomethine in the presence of formamide.

In the case of using acetamide instead of formamide, the result of hydrogenation showed poor yield as shown in Table I. As is known,⁹⁾ acetamide has considerably less reactivity than formamide for acylation of amine, which is the type of reaction (3). So, it is safe to consider that the overall reaction with acetamide is not expected to proceed so much.

3. Related Consideration

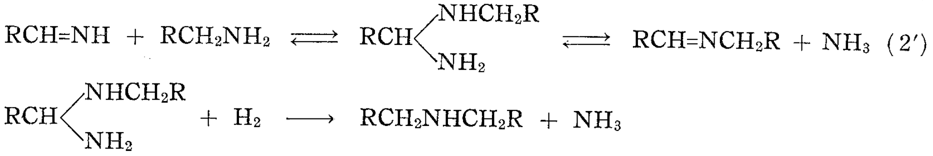
As described above, the reaction path of catalytic hydrogenation of azomethine in the presence of formamide has led to a reasonable one represented by Chart 3.

Based on the occurence of the reaction (4), reaction path of the formation of N-arylmethylene-1-acylamino-1-arylmethylamine by the reaction between azomethine and amide can also be clarified reasonably. The detailed work will be published in the succeeding paper of this series.

In consequence of the above solution, the mechanism inhibiting the formation of secondary amine in the reductive formylamination of nitriles or aldehyde oximes and aldehyde-ammonia mixtures also appears to be solved. When such compounds are hydrogenated in the absence of formamide, it was known⁸⁾,¹⁰⁾ that the formation of secondary amine occurs through an intermediate azomethine or alkylidenediamine, formed in reaction between intermediate alkylideneimine and primary amine. The reaction path can be written in the case of nitriles as follows.

$$RCN + H_2 \longrightarrow RCH{=}NH$$

$$RCH{=}NH + H_2 \longrightarrow RCH_2NH_2 \qquad (6)$$



$$RCH{=}NH + RCH_2NH_2 \rightleftarrows RCH\begin{cases}NHCH_2R\\NH_2\end{cases} \rightleftarrows RCH{=}NCH_2R + NH_3 \qquad (2')$$

$$RCH\begin{cases}NHCH_2R\\NH_2\end{cases} + H_2 \longrightarrow RCH_2NHCH_2R + NH_3$$

or

$$RCH{=}NCH_2R + H_2 \longrightarrow RCH_2NHCH_2R$$

Why the presence of formamide causes the reduction of the secondary amine formation in reductive formylamination may be interpreted as follows.

As mentioned in the preceding, reverse reaction (2′) and reaction (3) can be integrated into reaction (4) and this reaction can be accelerated by the influence of ammonia. Azomethine, if it is formed in reaction (2′), will undergo reaction (4) followed by reaction (6) and (3′), in the presence of formamide, and ammonia, which is formed as reaction (3′) goes on, will accelerate reaction (4). In other words, (i) reaction (2′) is forced to proceed in reverse direction and (ii) the formation of N-formylated primary amine is favored through reaction (3) which proceeds with considerable rate.

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10) J. Braun, G. Blessing, F. Zobel : Ber., **56**,, 1988 (1923); C. F. Windaus, H. Adkins : J. Chem. Soc., **54**, 306 (1932).

Although the work on the mechanism inhibiting secondary amine formation in the reductive formylamination has already been reported,[11] it dealt exclusively with (ii). Conjunction between (i) and (ii) has been recognized in the present paper and the mechanism appearrs to have been clarified.

Experimental

Catalytic Hydrogenation of Azomethines in the Presence of Amides

1. Hydrogenation of N-Benzylideneaniline (I). a) In the Presence of Formamaide——A mixture of 20 g. of I, 15 g. of formamide, 22cc. of EtOH, and Raney Ni catalyst (4 g. as 50% alloy) was heated in an autoclave at 80 kg./cm^2 (25°) of initial H_2 pressure and constantly shaken at 136～140°. The absorption of the calculated amount of H_2 was nearly completed in about 10 min. After filtration, NH_3 and EtOH were evaporated. The residue was fractionated under reduced pressure giving three kinds of distillates.

The first distillate of b.p$_5$ 72～75° was found to be formamide containing some aniline, which was separated by treatment with dil. HCl and KOH solutions, weighing 4.3 g., and was identified as 1,3-diphenylthiourea.

The second distillate of b.p$_3$ 95～140° was found to be a mixture of N-benzylformamide and N-phenylbenzylamine. To separate the components, the mixture was refluxed with 10% HCl, neutralized, and further saturated with KOH. The resultant oily amine layer was extracted with Et_2O, the extract, to which H_2O was added, was saturated with CO_2, and the Et_2O and aqueous layers were separately treated. After drying the Et_2O layer over K_2CO_3, removal of the solvent and distillation of the residue gave two kinds of distillates. The distillate of b.p$_{25}$ 80～86°, weighing 3.5 g., was found to be aniline. Total yield of aniline, 7.8 g. (76%). The subsequent solid distillate, b.p$_{25}$ 183～186° and m.p. 34～36°, weighing 3.5 g. (17% yield), was found to be identical with N-phenylbenzylamine by its failure to depress melting point of an authentic sample.

The foregoing aqueous layer was acidified with dil. HCl and evaporated to dryness, giving benzylamine hydrochloride, weighing 8.1 g. (51% yield), m.p. 255～256°, undepressed on admixture with an authentic sample.

The third distillate, b.p$_3$ 170～180°, was found to be N,N-dibenzylformamide mixed with tribenzylamine. This was treated with 10% HCl and then KOH as usual. Distillation of the liberated amines gave two kinds of distillates. The distillate of b.p$_{18}$ 170～175°, weighing 2.5 g. (23% yield) was found to be dibenzylamine, which was identified as its hydrochloride by mixed melting point test.

Another distillate of b.p$_3$ 150～155°, weighing 0.6 g. (0.5% yield) was identical with tribenzylamine, showing no depression of melting point on admixture with an authentic sample. *Anal.* Calcd. for $C_{21}H_{21}N$: C, 87.76; H, 7.37; N, 4.87. Found : C, 87.70; H, 7.33; N, 5.04.

b) In the Presence of Acetamide——According to the procedure described in a), a mixture of 20 g. of I, 19.5 g. of acetamide, 22 cc. of EtOH, and Raney-Ni catalyst (4 g. as 50% alloy) was hydorgenated at 132～138°. The absorption was nearly completed in about 15 min. After filtration, NH_3 and EtOH were removed and the residue was distilled under reduced pressure. The first distillate of unchanged acetamide was found to contain aniline (1.7 g., 16.5% yield), which was separated by usual treatment with dil. HCl and KOH. The second distillate, b.p$_{18}$ 160～174°, was found to be a mixture of N-phenylbenzylamine and N-benzylacetamide. This was treated with 10% HCl and KOH. To the Et_2O extract of the liberated amines, H_2O was added and CO_2 was passed through the mixture until saturation. By the usual treatment of the Et_2O layer, N-phenylbenzylamine, b.p$_{18}$ 175～178° and m.p. 35～36°, was obtained, weighing 15.6 g. (77.5% yield), which showed no depression of melting point on admixture with an authentic sample.

The above aqueous layer was acidified with HCl and evaporated giving benzylamine hydrochloride, m.p. 253～255°, weighing 1.6 g. (10% yield), which was identified by mixed melting point test.

2. Hydrogenation of N-Benzylidenebenzylamine (II). a) In the Presence of Formamide——A mixture of 20 g. of II, 13.5 g. of formamide, 20 cc. of EtOH, and Raney-Ni catalyst (4 g. as 50% alloy) was hydrogenated at 132～135° in the same manner as in 1a). The absorption was nearly completed in about 15 min. After filtration and removal of NH_3, EtOH, and formamide, the residue was fractionated under reduced pressure. A distillate of b.p$_{15}$ 123～124°, weighing 25.4 g. (94% yield), was identical with N-benzylformamide, needles (from Et_2O), m.p. 60°, undepressed on admixture with an anthentic sample. *Anal.* Calcd. for C_8H_9ON : C, 71.09; H, 6.71; N, 10.39. Found : C, 71.08; H, 6,71; N, 10.33.

A subsequent distillate of b.p$_1$ 137～138°, weighing 0.9 g. (4% yield), was identical with N,N-dibenzylformamide. Dibenzylamine hydrochloride, m.p. 259°, and 1-phenyl-3,3-dibenzylthiourea, m.p. 146°, showed no depression of melting point on admixture with an authentic sample.

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[11] M. Sekiya : Yakugaku Zasshi, **70**, 555 (1950).

b) In the Presence of Acetamide——A mixture of 20 g. of II, 17.7 g. of acetamide, 20 cc. of EtOH and Raney-Ni catalyst (4 g. as 50% alloy) was hydrogenated at 131∼136° in the same manner as in 1a). The absorption was nearly completed in about 15 min. After filtration and removal of the solvent, distillation of the residue gave unchanged acetamide and dibenzylamine. The latter weighed 17.8 g. (89% yield) and was identified as its hydrochloride.

3. Hydrogenation of N-(4-methoxybenzylidene)phenethylamine (III). a) In the Presence of Formamide——A mixture of 24 g. of III, 14.5 g. of formamide, 30 cc. of EtOH, and Raney-Ni catalyst (5 g. as 50% alloy) was hydrogenated at 131∼138° in the same manner as in 1a). The absorption was nearly completed in about 10 min. After filtration and removal of NH_3, EtOH, and formamide, the residue was fractionated under reduced pressure giving the following distillates.

The first distillate of b.p$_2$ 137∼141°, weighing 16 g. (91% yield), was identical with N-phenethylformamide. This was hydrolyzed by the usual procedure to phenethylamine, b.p. 195∼201°. Hydrochloride : Needles (from AcOEt-AcOH), m.p. 217∼218°. *Anal.* Calcd. for $C_8H_{12}NCl$: C, 60.95; H, 7.67; N, 8.88. Found : C, 60.53; H, 7.61; N, 8.88. 1-Phenethyl-3-phenylthiourea : Prisms (from EtOH), m.p. 109∼110°. *Anal.* Calcd. for $C_{15}H_{16}N_2S$: C, 70.29; H, 6.29; N, 10.93. Found : C, 70.29; H, 6.24; N, 10.66.

Another solid distillate, b.p$_2$ 153∼154°, weighing 13.5 g. (82% yield), was identical with N-(4-methoxybenzyl)formamide. Recrystallization from Et_2O gave needles, m.p. 80∼81°. *Anal.* Calcd. for $C_9H_{11}O_2N$: C, 65.44; H, 6.71; N, 8.48. Found : C, 65.16; H, 6.70; N, 8.45. This was hydrolyzed to 4-methoxybenzylamine hydrochloride, needles (from 10% HCl), m.p. 236∼237°. *Anal.* Calcd. for $C_8H_{12}ONCl$: C, 55.33; H, 6.96; N, 8.06. Found : C, 55.36; H, 7.07; N, 8.24. 1-(4-Methoxybenzyl)-3-phenylthiourea : Prisms (from EtOH), m.p. 107°. *Anal.* Calcd. for $C_{15}H_{16}ON_2S$: C, 66.16; H, 5.92; N, 10.29. Found : C, 65.91; H, 6.00; N, 10.25.

b) In the Presence of Acetamide——A mixture of 12 g. of III, 8.9 g. of acetamide, 10 cc. of EtOH and Raney-Ni catalyst (2.4 g. as 50% alloy) was hydrogenated at 130∼133° in the same manner as in 1a). The absorption was nearly completed in about 10 min. After filtration, NH_3, EtOH, and an excess of acetamide were removed and the residue was distilled under reduced pressure. The main distillate of b.p$_2$ 167∼170°, weighing 10.4 g. (86% yield), was identical with N-(4-methoxybenzyl)phenethylamine. Hydrochloride : Needles (from H_2O), m.p. 264∼265°, undepressed on admixture with an authentic sample. A small amount of the distillate of b.p$_2$ 175∼180° was hydrolyzed with 10% HCl giving phenethylamine hydrochloride, m.p. 216∼217°, weighing 0.14 g. (2% yield). No depression in the melting point was observed on admixture with an authentic sample. A small amount of the residue was also hydrolyzed to 4-methoxybenzylamine hydrochloride, m,p, 239—240°, weighing 0.15 g. (2%yield), undepressed on admixture with an authentic sample.

Reaction between N-Benzylidene-4-sulfonamidobenzylamine (IV) and Formamide

To a solution of 6.8 g. of IV in 60 cc. of formamide, 200 cc. of toluene was added. The immiscible mixture was vigorously stirred on a boiling water bath for 3 hr., while a certain amount of NH_3 evolved. After cooling, the toluene layer was separated and concentrated under reduced pressure. The residual crystalline substance was fractionally recrystallized from EtOH to hydrobenzamide, m.p. 99∼101°, weighing 0.6 g., and N-benzylidene-α-formamidobenzylamine, m.p. 124°, weighing 0.65 g. The latter was more soluble in EtOH than the former. No depression in melting points of both compounds was observed on admixture with each of authentic samples.

The foregoing formamide layer was evaporated under reduced pressure giving crystalline residue, which was recrystallized from MeOH to needles, m.p. 150∼151°, weighing 4.6 g. This compound was identical with N-(4-sulfonamidobenzyl)formamide.12) *Anal.* Calcd. for $C_8H_{10}O_3N_2S$: C, 44.86; H, 4.71; N, 13.08. Found : C, 44.98; H, 4.95; N, 12.95.

The authors are grateful to Prof. Emeritus M. Ishidate of the Tokyo University for his kind encouragement during the course of this work. The authors are also indebted to Miss Y. Saito for the elementary analyses.

Summary

Catalytic hydrogenation of some azomethines, such as N-benzylideneaniline, N-benzylidenebenzylamine, and N-(4-methoxybenzylidene)phenethylamine in the presence of amide was examined under high pressure of hydrogen. The reaction resulted in conversion, $ArCH{=}NR+2R'CONH_2+H_2 \longrightarrow ArCHNHCOR'+RNHCOR'+NH_3$, particularly in excellent yields with formamide. With regard to this reaction path, it was recognized

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12) M. Sekiya : Yakugaku Zasshi, **70**, 73 (1950).

that the initiating essential reaction between azomethine and formamide would be the reaction, $\mathrm{ArCH{=}NR+HCONH_2 \longrightarrow ArCH{=}NH+RNHCHO}$ ($\mathrm{NH_3}$ acts as a catalyst), which was demonstrated by using N-benzylidene-4-sulfonamidobenzylamine as azomethine. Based on this reaction, the whole pathway for the above hydrogenation reaction was proposed. Mechanism for hydrogenation reaction of nitriles, oximes, and ammonia-aldehyde mixtures in the presence of formamide was also suggested.

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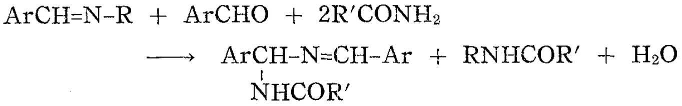
156. **Minoru Sekiya and Akira Hara**: Reaction of Amide Homologs. X. Mechanism of the Formation of N-Arylmethylene-1-acylamino-1-arylmethylamine.

(*Shizuoka College of Pharmacy*[*1])

In a previous paper of this series,[1] it has been shown with several examples that azomethines react with amides resulting in the formation of N-arylmethylene-1-acylamino-1-arylmethylamines, when heated together at a boiling water bath temperature.

$$\mathrm{2ArCH{=}N{-}R + 3R'CONH_2 \longrightarrow \underset{\displaystyle NHCOR'}{ArCH}{-}N{=}CH{-}Ar + 2RNHCOR' + NH_3} \qquad (1)$$

Later,[2] this formation was found to occur when aromatic aldehyde is used as a reactant instead of a part of the azomethine in reaction (1). In this case, only formamide was used as an amide.



$$\mathrm{ArCH{=}N{-}R + ArCHO + 2R'CONH_2 \longrightarrow \underset{\displaystyle NHCOR'}{ArCH}{-}N{=}CH{-}Ar + RNHCOR' + H_2O} \qquad (2)$$

However, the mechanisms of the above reactions have as yet remained unsolved.

In some cases, N-arylmethylene-1-acylamino-1-arylmethylamine was formed when hydroamide or aromatic aldehyde-ammonia mixture was allowed to react with amides. In the light of this fact the mechanism comprehensive for the formation of N-arylmethylene-1-acylamino-1-arylmethylamine is proposed in the present paper.

Benzaldehyde-ammonia and anisaldehyde-ammonia as well as hydrobenzamide was employed for the reaction with amide, for which formamide and acetamide were used. In some experiments, ammonia was passed through a mixture of aldehyde and amide with heating, and in other case, a mixture of hydrobenzamide and amide was heated. All these reactions brought about the formation of corresponding N-arylmethylene-1-acylamino-1-arylmethylamine in a considerable yield. These methods appear to be most practicable for the preparation of the compound. The reaction formula when benzaldehyde-ammonia and hydrobenzamide were used can be represented as follows :

[*1] Oshika, Shizuoka (関屋 実, 原 明).

1) M. Sekiya, T. Oishi : This Bulletin, **7**, 468 (1959).

2) *Idem* : *Ibid.*, **7**, 855 (1959).