CHEMICAL
&
PHARMACEUTICAL BULLETIN

Vol. 11 No. 3 March 1963

UDC 547.554.07

45. Minoru Sekiya, Akira Hara, and Toshio Masui : Catalytic Hydrogenation of Azomethines in the Presence of Ammonia or Amines.

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

It seems probable that azomethines react with ammonia or primary amines resulting in the replacement of the amine residues of azomethines by those of the ammonia or amine reactants. The reaction may be reversible and represented by the following general equation (1).

$$ArCH{=}NR + R'NH_2 \rightleftarrows ArCH{=}NR' + RNH_2 \qquad (1)$$

(R : alkyl or aryl; R' : H, alkyl or aryl)

Recently, the replacement reactions of the amine residues of some aromatic azomethines (R : aryl) by aromatic amines were reported by Poraǐ-Koshits,[1] *et al.*, however, the authors have not yet had the chance to hear about the details of the work.

As for a method to pursue the possibilities that the reaction between azomethines and ammonia or aliphatic primary amines might also occur, the catalytic hydrogenation of the azomethines in the presence of ammonia or amine reactant was undertaken.

The hydrogenation should take place as in the following equation, arylmethyleneimines or N-arylmethylene alkylamines liberated on reaction (1) being respectively hydrogenated to primary or secondary amines.

$$ArCH{=}NR + R'NH_2 + H_2 \longrightarrow ArCH_2NHR' + RNH_2 \qquad (2)$$

This hydrogenation reaction was found in several examples to proceed more easily in the case of the ammonia or aliphatic amine reactants rather than in the case of the aromatic amine reactants.

While it seems almost reasonable to infer the occurrence of the above mentioned replacement reaction (1) from the result of the hydrogenation reaction, in order to make this more clear, the demonstration of the replacement reaction could actually be carried out in the case of azomethine, N-benzylidene-4-sulfonamidobenzylamine, the 4-sulfonamidobenzylamine residue being replaced by that of ammonia, methylamine or aniline.

1. Catalytic Hydrogenation of Azomethines in the Presence of Ammonia or Amine

As well known, azomethines are catalytically hydrogenated to the corresponding secondary amines. However, it is shown that in the presence of ammonia or amine, some of the azomethines were found to be hydrogenated as shown in reaction (2). The experiments dealt with some typical azomethines such as N-benzylideneaniline (I), N-benzylidenebenzylamine (Ⅱ) and N-(4-methoxybenzylidene)phenethylamine (Ⅲ).

[*1] Oshika, Shizuoka (関屋 実, 原 明, 増井俊夫).

1) B. A. Poraǐ-Koshits, A. L. Remizow : C. A., **49**, 5367 (1955); **50**, 16686 (1956).

These azomethines were submitted to catalytic hydrogenation under high hydrogen pressure in the presence of ammonia or amines. In every case, the hydrogenation was carried out at 130~140° with Raney nickel catalyst under about 80 kg./cm^2 (at ordinary temperature) of initial hydrogen pressure. The ammonia or primary amine reactants were used 3 times of the azomethines in mole as 5*M* alcoholic solution. As the primary amine reactants, the typical aliphatic and aromatic amine such as methylamine and aniline were used. However, in the case of II, butylamine had to be used instead of methylamine, because of the difficulties in isolating the amines formed in the reaction mixture, when methylamine was used.

In most cases, the reactions took place in the way of (2) affording two kinds of amines, accompanied by the secondary amine which was formed by hydrogenation of the azomethine. As shown in experimental part, the separation of these amines was carried out by fractional neutralization utilizing the differences in their basicities or by fractional distillation.

The data given in Table I indicate percentages of the conversions estimated from the amount of the starting azomethines. In all cases with the ammonia or aliphatic amine reactants, the reactions proceeded at rates of more than 71%. However, in the cases with aniline, the reactions proceeded a little or did not, as shown in Table I.

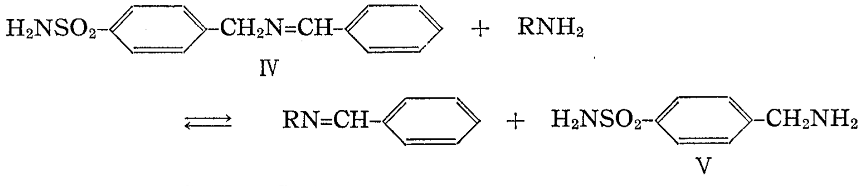
Table I. Hydrogenation of a Mixture of Azomethine and Ammonia or Amine

Azomethine	Ammonia or Amine	Hydrogenation temp. (°C)	Conversion (%)
N-Benzylideneaniline	Ammonia	130~137	85
N-Benzylidenebenzylamine	〃	130~135	85
N-(4-Methoxybenzylidene)phenethylamine	〃	130~134	87
N-Benzylideneaniline	Methylamine	130~136	83
N-Benzylidenebenzylamine	Butylamine	130~135	71
N-(4-Methoxybenzylidene)phenethylamine	Methylamine	130~134	91
N-Benzylidenebenzylamine	Aniline	130~138	7
N-(4-Methoxybenzylidene)phenethylamine	〃	130~138	0

2. Replacement Reaction between N-Benzylidene-4-sulfonamidobenzylamine and Ammonia or Amines

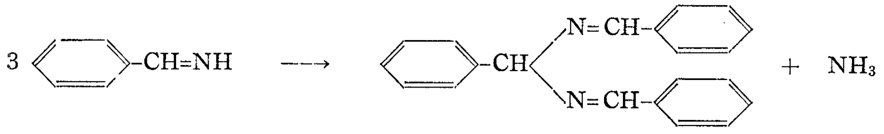
Although the replacement reaction of amine residues of some aromatic azomethines by aromatic amines have been reported by Poraĭ-Koshits *et al.*,[1] the reaction should also be extended to take place with ammonia or aliphatic amines as shown in the reaction (1). These reactions would be the stages preceding hydrogenations in the foregoing catalytic hydrogenations of azomethines in the presence of ammonia or amines. Then, with the purpose of making the scheme of the catalytic hydrogenation clear, the reactions were demonstrated by means of using N-benzylidene-4-sulfonamidobenzylamine (IV) as an azomethine. In general, there are some difficulties in separating the products from the reaction mixture, but, in the case of the application of IV, it was possible to separate one of the products by means of utilizing the differences of the solubilities in none polar solvent.

Ammonia, methylamine and aniline were reacted with IV respectively. The reactions can be represented as in the following.



R : H, CH$_3$ or C$_6$H$_5$

In the case of ammonia, hydrobenzamide was formed instead of benzylideneimine, because, the latter is known to be readily converted into the former.



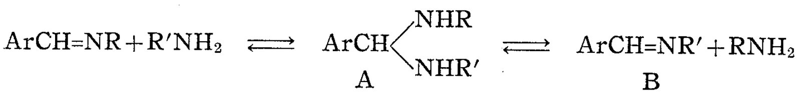
All these reactions may be reversible, so both the reactions from left to right and from right to left were examined.

For carring out the reactions from left to right, in the cases of ammonia and methylamine, a solution of IV dissolved in glycol was vigorously stirred with an immiscible layer of toluene on a boiling water bath, and ammonia or methylamine was passed through until saturation. In this way, only the azomethine, hydrobenzamide or N-benzylidenemethylamine, formed in the reaction was extracted into the toluene layer. In the case of aniline, a mixture of IV and a large amount of aniline was heated to react and then N-benzylideneaniline was extracted with toluene from the resultant solution.

In the reverse reactions, 4-sulfonamidobenzylamine (V) was reacted with hydrobenzamide or N-benzylidenemethylamine in glycol on heating, when ammonia or methylamine evolved, and then IV was obtained almost quantitatively. The reaction with N-benzylideneaniline was carried out without a solvent and only aniline was isolated as a product by extraction with toluene, because of the difficulties of isolating IV.

3. Conclusion and Related Considerations

It was observed that the catalytic hydrogenation of azomethines in the presence of ammonia or amines proceeded as shown in the reaction (2). In this hydrogenation reaction the stage preceding hydrogenation is supposed as in the following.



$$\mathrm{ArCH{=}NR + R'NH_2} \rightleftarrows \underset{\mathrm{A}}{\mathrm{ArCH}\left\langle\begin{matrix}\mathrm{NHR}\\ \mathrm{NHR'}\end{matrix}\right.} \rightleftarrows \underset{\mathrm{B}}{\mathrm{ArCH{=}NR'}} + \mathrm{RNH_2} \qquad (3)$$

And the following hydrogenation would affect arylmethylenediamine (A) or arylmethyleneamine (B). But, it would be difficult to decide uniformly in all cases whether the hydrogenation takes place in the former or the latter or simultaneously the former and the latter.

$$\mathrm{ArCH}\left\langle\begin{matrix}\mathrm{NHR}\\ \mathrm{NHR'}\end{matrix}\right. + \mathrm{H_2} \longrightarrow \mathrm{ArCH_2NHR' + RNH_2} \qquad (4)$$

or

$$\mathrm{ArCH{=}NR' + H_2} \longrightarrow \mathrm{ArCH_2NHR'} \qquad (5)$$

However, this consideration for the reaction path seems to be sufficiently reasonable being supported by the demonstrations of the replacement reactions of IV, which actualized reaction (3) as shown in the preceding. And it can be said that the reversibie replcement reaction of azomethines with ammonia or amines would become generally understandable.

In addition, the above conclusion leads to a suggestion for mechanism of the hydrogenation of nitriles in the presence of ammonia, reported by Schoegler and Adkins,[2] which has been applied as an available method for depressing the formation of secondary amine for the purpose of preparing primary amine.

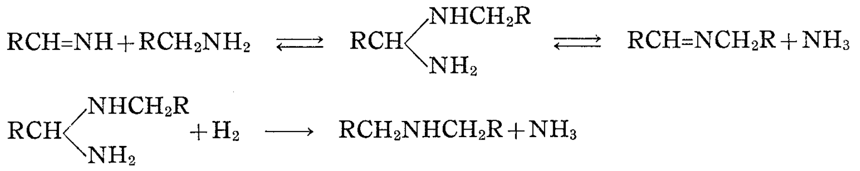
---

[2] E. J. Schoegler, H. Adkins: J. Am. Chem. Soc., **61**, 3499 (1939).

As for the scheme[3] of the formation of secondary amine in hydrogenation of nitrile, it has been supported that the secondary amine is formed by the hydrogenation of an intermediate, alkylidenediamine or azomethine, formed in reaction (8) between intermediate alkylideneimine and primary amine, as shown in the following.

$$\mathrm{RCN+2H \longrightarrow RCH{=}NH} \qquad (6)$$

$$\mathrm{RCH{=}NH+2H \longrightarrow RCH_2NH_2} \qquad (7)$$



$$\mathrm{RCH{=}NH+RCH_2NH_2 \rightleftarrows RCH{<}\genfrac{}{}{0pt}{}{NHCH_2R}{NH_2} \rightleftarrows RCH{=}NCH_2R+NH_3} \qquad (8)$$

$$\mathrm{RCH{<}\genfrac{}{}{0pt}{}{NHCH_2R}{NH_2} + H_2 \longrightarrow RCH_2NHCH_2R+NH_3}$$

or

$$\mathrm{RCH{=}NCHR+H_2 \longrightarrow RCH_2NHCH_2R}$$

This proposal has come to be sufficiently understandable by the realization of the reaction (8) as described in the foregoing conclusion.

As shown in the preceding, azomethines were hydrogenated in the presence of ammonia to two moles of primary amines as explained in the conjunction of the reactions (3), and (4), or (5), in the case of R′=H. This is just the reaction in which azomethines are hydrogenated in a reverse direction of the reaction (8) in the presence of a considerable excess of ammonia. And this is the reason why the formation of secondary amines can be reduced in Schoegler's hydrogenation of nitrile.

Experimental

Hydrogenation of Azomethines in the Presence of the Ammonia or Amine

Hydrogenation of N-Benzylideneaniline (I) 1) **Hydrogenation in the presence of ammonia**——A solution of 20 g. of I in 66 cc. of 5*M* alcoholic NH_3 was mixed with Raney-Ni catalyst (4 g. as 50% alloy) in an autoclave. Under 80 kg./cm^2 (19°) of initial H_2 pressure, the whole was heated and constantly shaken at 130~137°. The absorption was nearly completed in about 15 min. After filtration, the fitrate was evaporated to remove NH_3 and EtOH. The ethereal solution of the residue, to which H_2O was added so as to form two layers, was saturated with CO_2 and both the ethereal and aqueous layers were separately treated as follows.

The ethereal layer was dried over anhyd. K_2CO_3, evaporated to remove Et_2O, and the residue was distilled under reduced pressure giving two kinds of distillates, b.p$_{16}$ 76~80° and b.p$_{16}$ 171~175°. The first distillate, weighing 8.6 g. (84% yield), was identical with aniline. N,N′-Diphenylthiourea, m.p. 152°, showed no depression in the melting point on admixture with an authentic sample. The second distillate, m.p. 35~36°, weighing 2 g. (10% yield), was identical with N-benzylaniline. This and its derivative, N,N′-diphenyl-N-benzylthiourea, prisms (from EtOH), m.p. 103°, failed to depress melting point of authentic sample. *Anal.* Calcd. for $C_{20}H_{18}N_2S$: C, 75.42; H, 5.69; N, 8.79. Found : C, 75.32; H, 5.68; N, 8.90.

The foregoing aqueous layer was acidified with dil. HCl and then evaporated to give benzylamine hydrochloride, weighing 13.5 g. (85% yield). No depression in the melting point was observed on admixture with an authentic sample.

2) **Hydrogenation in the Presence of Methylamine**——According to the procedures described in 1), a solution of 20 g. of I in 66 cc. of 5*M* alcoholic CH_3NH_2 was hydrogenated at 130~136° with Raney-Ni catalyst (4 g. as 50% alloy) under 80 kg./cm^2 (18°) of initial H_2 pressure. The absorption was nearly completed in about 15 min. After filtration, CH_3NH_2 and EtOH were removed and the ethereal solution of the residue, to which H_2O was added, was saturated with CO_2 and both the ethereal and aqueous layers were separately treated as follows.

After drying over anhyd. K_2CO_3, the ethereal solution was evaporated to give the residue, which was distilled under a reduced pressure giving two kinds of distillates b.p$_{17}$ 77~81° and b.p$_{17}$ 173~178°.

---

[3] J. Braun, G. Blessing, F. Zobel : Ber., **56**, 1988 (1923); C.F. Winaus, H. Adkins : J. Am. Chem. Soc., **54**, 306 (1932).

The first distillate weighing 8.5 g. (83% yield) and the second distillate weighing 2.2 g. (11.5% yield) were identified as aniline and benzylaniline respectively, by the same method as described in 1).

The aqueous layer was acidified with dil. HCl and evaporated giving 14.6 g. (84% yieid) of N-methylbenzylamine hydrochloride, m.p. 174～175°, undepressed on admixture with an authentic sample.

Hydrogenation of N-Benzylidenebenzylamine (II)

1) **Hydrogenation in the Presence of Ammonia**——A solution of 19.5 g. of II in 66 cc. of 5*M* alcoholic NH_3 was mixed with Raney-Ni catalyst (4 g. as 50% alloy) in an autoclave. The whole was heated under 80 kg./cm^2 (27°) of initial H_2 pressure and constantly shaken at 130～135°. The absorption was nearly completed in about 15 min. After removal of the catalyst and evaporation, the residue was distilled under a reduced pressure giving two kinds of distillates.

The first distillate of b.p$_{30}$ 87～88°. weighing 18.2 g. (85% yield), was identical with benzylamine. Its hydrochloride and N-phenyl-N′-benzylthiourea failed to depress the melting point of authentic samples on admixture. The subsequent distillate of b.p$_6$ 137～141°, weighing 1.2 g. (6% yield), was identical with dibenzylamine. The m.p.s. of its hydrochloride and N-phenyl-N′,N′-dibenzylthiourea were not depressed on admixture with authentic samples. N-phenyl-N′,N′-dibenzylthiourea, m.p. 145～146°, prisms (from EtOH). *Anal.* Calcd. for $C_{21}H_{20}N_2S$: C, 75.86; H, 6.06; N, 8.45. Found: C, 75.61; H, 5.98; N, 8.50.

2) **Hydrogenation in the Presence of Butylamine**——According to the procedures described in 1), a solution of 19.5 g. of II in 60 cc. of 5*M* alcoholic buthylamine was hydrogenated at 130～135° with Raney-Ni catalyst (4 g. as 50% alloy) under 80 kg./cm^2 (24°) of initial H_2 pressure. The absorption was nearly completed in about 13 min. After filtration, EtOH and an excess of butylamine were removed and the residue was distilled under reduced pressure giving three kinds of distillates. The first distillate, b.p$_{17.5\sim18}$ 82～85°, weighing 7.6 g. (71% yield), was identical with benzylamine. Its hydrochloride and N-phenyl-N′-benzylthiourea failed to depress the m.p.s. of authentic samples on admixture.

The second distillate, b.p$_{17.5\sim18}$ 120～123°, weighing 11.5 g. (70% yield), was identical with N-butylbenzylamine. Hydrochloride: Needles (from EtOAc-HOAc), m.p. 240°. No depression in the melting point was observed on admixture with the sample prepared by hydrogenation of N-benzylidenebutylamine with Pd-C catalyst. *Anal.* Calcd. for $C_{11}H_{18}NCl$: C, 66.29; H, 9.10; N, 7.03, Found: C, 66.30; H, 9.12; N, 7.05.

The third distillate of b.p$_1$ 120～124°, weighing 5.5 g. (25.5% yield) was identified as dibenzylamine. The melting point of its derivative, N-phenyl-N′,N′-dibenzylthiourea, was not depressed on admixture with an authentic sample.

3) **Hydrogenation in the Presence of Aniline**——According to the procedures described in 1), a solution of 19.5 g. of II in 60 cc. of 5*M* alcoholic aniline was hydrogenated at 130～138° with Raney-Ni catalyst (4 g. as 50% alloy) under 80 kg./cm^2 (26°) of initial H_2 pressure. The absorption was nearly completed in about 20 min. After filtration, EtOH was removed and the residue was distilled under a reduced pressure to give two kinds of distillates.

The first distillate, b.p$_{18}$ 78～80°, was added with H_2O, so as to form two layers, and then saturated with CO_2. To the aqueous layer dil. HCl was added and evaporated giving 2.1 g. (7% yield) of benzylamine hydrochloride, which was proved by mixed melting point tests of itself and its derivative, N-benzyl-N′-phenylthiourea. The upper oily layer was shown to be unchanged aniline.

The second distillate, b.p$_2$ 135～139°, was dissolved in dil. HCl and diluted with a large amount of H_2O. The resultant solution was cautiously steam distilled adding 5% NaOH dropwise until the distillate came to be basic to litmus. The distillate was acidified with dil. HCl and then evaporated giving 3.2 g. (7.3% yield) of benzylaniline hydrochloride, m.p. 207～208°. This and N-phenyl-N-benzyl-N′-phenylthiourea failed to depress the melting point of an authentic sample on admixture.

The residual solution of the foregoing steam distillation was concentrated giving 19.2 g. (82% yield) of dibenzylamine hydrochloride, which was proved by mixed melting point tests of itself and N,N-dibenzyl-N′-phenylthiourea, m.p. 143～144°.

Hydrogenation of N-(4-Methoxybenzylidene)phenethylamine (III)

1) **Hydrogenation in the Presence of Ammonia**——A solution of 12 g. of III in 30 cc. of 5*M* alcoholic NH_3 was mixed with Raney-Ni catalyst (2 g. as 50% alloy) in an autoclave. The whole was heated under 80 kg./cm^2 (24°) of initial H_2 pressure and constantly shaken at 130-134°. The absorption was nearly completed in about 10 min. After filtration, NH_3 and EtOH were evaporated and the residue was distilled under a reduced pressure, giving three kinds of distillates.

The first distillate of b.p$_{15}$ 98～104°, weighing 5.3 g. (87% yield), was identified as β-phenethylamine. Hydrochloride: Plates (from AcOEt-AcOH), m.p. 217°. *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. N-phenethyl-N′-phenylthiourea; prisms (from EtOH), m.p. 110°, undepressed on admixture with an authentic sample. *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.

The second distillate of b.p$_{15}$ 114～119°, weighing 6 g. (87.5% yield), was identified as 4-methoxybenzylamine. Hydrochloride, m.p. 243～244°, showed no depression of the melting point on admixture with an authentic sample. N-4-methoxybenzyl-N′-phenylthiourea: Plates (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.

The third distillate of b.p$_2$ 167～170°, weighing 0.3 g. (2.5% yield), was identified as N-(4-methoxybenzyl)-phenethylamine. Hydrochloride, needles (from H_2O-EtOH), m.p. 265～266°, showed no depression of melting point on admixture with an authentic sample. *Anal.* Calcd. for $C_{16}H_{20}ONCl$: C, 69.18; H, 7.25; N, 5.04. Found: C, 69.20; H, 7.32; N, 5.14.

2) **Hydrogenation in the Presence of Methylamine**——According to the procedures described in 1), a solution of 12 g. of Ⅲ in 30 cc. of 5 *M* alcoholic CH_3NH_2 was hydrogenated at 130～134° with Raney-Ni catalyst (2 g. as 50% alloy) under 80 kg./cm^2 (24°) of initial H_2 pressure. The absorption was nearly completed in about 10 min. After filtration, CH_3NH_2 and EtOH were removed and the residue was distilled under reduced pressure giving three kinds of distillates.

The first distillate of b.p$_{15}$ 97～103°, weighing 5.5 g. (91% yield), was identified as phenethylamine. The melting point of its derivative, N-phenethyl-N′-phenylthiourea, was not depressed on admixture with an authentic sample.

The second distillate of b.p$_{15}$ 114～120°, weighing 6.7 g. (89% yield), was identified as N-methyl-4-methoxybenzylamine. Hydrochloride, m.p. 166°, undepressed on admixture with an authentic sample. *Anal.* Calcd. for $C_9H_{14}ONCl$: C, 57.59; H, 7.51; N, 7.41. Found: C, 57.45; H, 7.54; N, 7.71.

The third distillate of b.p$_2$ 168～170°, weighing0.3 g. (2.5% yield), was identified as N-(4-methoxybenzyl)phenethylamine. The melting point of its hydrochloride was not depressed on admixture with an authentic sample.

3) **Hydrogenation in the Presence of Aniline**——According to the procedures described in 1), a solution of 24 g. of Ⅲ in 30 cc. of 5*M* alcoholic $C_6H_5NH_2$ was hydrogenated at 130～138° with Raney-Ni catalyst (4 g. as 50% alloy) under 80 kg./cm^2 (27°) of initial H_2 pressure. The absorption was nearly completed in about 15 min. After filtration, EtOH was removed and then the unreacted aniline (27 g.) was recoveredy distillation. The residue was further distilled under a reduced pressure giving N-(4-methoxybenzyl) phenethylamine, b.p$_6$ 185～188°, weighing 22 g. (92% yield). Hydrochloride, needles (from EtOH), m.p. 265～266°, showed no depression of melting point on admixture with an authentic sample. Picrate, prisms (from EtOH), m.p. 127°. *Anal.* Calcd. for $C_{22}H_{22}O_8N_4$: C, 56.17; H, 4.71; N, 11.9. Found: C, 56.21; H, 4.68; N, 11.98.

Replacement Reaction

Preparation of N-Benzylidene-4-sulfonamidobenzylamine (IV)——To a solution of 20 g. of 4-sulfonamidobenzylamine dissolved in 5% NaOH, 12 g. of benzaldehyde was added and allowed to dissolve with shaking for few minutes. The reaction solution was neutralized by the introduction of CO_2 to give colorless precipitates. Recrystallization from EtOH gave 22 g. of Ⅳ, m.p. 153～154°. *Anal.* Calcd. for $C_{14}H_{14}O_2N_2S$: C, 65.13; H, 5.46; N, 10.85. Found: C, 65.14; H, 5.43; N, 10.87.

1) **Reaction between IV and Ammonia**——To a solution of 6.8 g. of Ⅳ dissolved in 60 cc. of glycol under heating, 200 cc. toluene was added. NH_3 was passed through the immiscible mixture on a boiling water bath under vigorous stirring until saturation. Then, the toluene layer was separated and concentrated to dryness *in vacuo*, The residue was washed with ligroin to yield nearly pure crystals of hydrobenzamide weighing 2.0 g. (81% yield). Prisms (from EtOH), m.p. 100～101°, undepressed on admixture with an authentic sample. *Anal.* Calcd. for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08; N, 9.39. Found: C, 84.19; H, 6.21; N, 9.21.

2) **Reaction between IV and Methylamine**——To a solution of 6.8 g. of Ⅳ dissolved in 60 cc, of glycol, 200 cc. of toluene was added. The mixture was treated with CH_3NH_2 in the same manner as described in 1). The separated toluene solution was concentrated to remove the solvent and the residue was distilled *in vacuo* giving a distillate, b.p$_{25}$ 83～84°, weighing 2.5 g. (84% yield), which was identical with N-benzylidenemethylamine. The IR spectrum of this was entirely identical with that of an authentic sample, and by heating with aq. oxalic acid solution, this was hydrolysed to give benzaldehyde, proved as its phenylhydrazone, and methylamine hydrogenoxalate, m.p. 165～170°.

3) **Reaction between IV and Aniline**——A mixture of 6.8 g. of Ⅳ and 30 cc. of aniline was heated on a boiling water bath for 30 min., when turning into a solution. To the resultant solution, 200 cc. of toluene was added and the precipitates which immediately separated was removed by centrifugation. The toluene solution was washed with dil. NaOH, dried over anhyd. K_2CO_3 and evaporated to remove the solvent. The residue was distilled under a reduced pressure giving a solid distillate, b.p$_{18}$ 163～165°, after removal of a first distillate of aniline. This distillate, weighing 3.9 g. (87% yield) was recrystallized from Et_2O to plates, m.p. 50～51°, which were identical with N-benzylideneaniline. *Anal.* Calcd. for $C_{13}H_{11}N$: C, 86.16; H, 6.12; N, 7.73. Found: C, 85.97; H, 6.15; N, 7.84.

4) **Reaction between 4-Sulfonamidobenzylamine (V) and hydrobenzamide**——A mixture of 4.6 g. of V, 2.5 g. of hydrobenzamide and 20 cc. of glycol was heated on a boiling water bath until no more NH_3 was evolved. The resultant solution was concentrated under reducee pressure to remove the solvent. The solid residue was washed with 60% EtOH and recrystallized from EtOH to prisms. m.p. 152～154°, weighing 6.4 g. (94% yield), undepressed on admixture with Ⅳ.

5) **Reaction between V and N-Benzylidenemethylamine**——A mixture of 4.6 g. of V, 3.0 g. of N-benzylidenemethylamine and 20 cc. of glycol was allowed to react, when evolution of CH_3NH_2 was observed. By the same procedures as described in 1), IV was obtained in yield of 6.3 g. (92% yield).

6) **Reaction between V and N-Benzylideneaniline**——A mixture of 4.6 g. of V, 4.5 g. of N-benzylideneaniline and 20 cc. of glycol was heated on a boiling water bath for 6 hr. After standing overnight, a part of IV deposited was filtered and the filtrate was extracted with toluene. After removal of the toluene, aniline, weighing 12 g. (52% yield), was obtained by distillation of the residue. This was proved as its derivative, N,N′-diphenylthiourea, by mixed melting point test.

The authors are grateful of 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

In the presence of ammonia or amine some azomethines were catalytically hydrogenated under high hydrogen pressure to give two kinds of amines according to the equation:

$$ArCH{=}NR + R'NH_2 + H_2 \longrightarrow ArCH_2NHR' + RNH_2$$
$$(R' : \text{H or alkyl})$$

In the pathway of this hydrogenation reaction, the first stage preceding hydrogenation was proposed to be the replacement reaction of amine residue of azomethine by that of ammonia or amine. This was demonstrated using N-benzylidene-4-sulfonamidobenzylamine as azomethine.

(Received February 13, 1962)

UDC 547.972.2/.3

46. Koichi Nakazawa and Manzo Ito: Syntheses of Ring-substituted Flavonoids and Allied Compounds. X.[*1] Synthesis of Ginkgetin.

(*Gifu College of Pharmacy*[*2])

Ginkgetin, $C_{32}H_{22}O_{10}$, a flavone from the leaves of *Ginkgo biloba*, was isolated first by one of the authors (K. N.) who suggested a biflavonyl structure for it1). Recently, Baker *et al.*2) put forward for ginkgetin the structure of 4′,7-dimethoxy-4‴,5,5″,7″-tetrahydroxy-3′,8″-biflavone (I), which consists of two apigenin (4′,5,7-trihydroxyflavone) moieties linked at the 3′- and 8″-positions. In a previous work,[*1] the coupling position of the two flavone units was confirmed by the synthesis of ginketin dimethyl (II) and tetramethyl ethers (III).

This paper deals with the total synthesis of ginkgetin by the condensation of 3′- and 8-iodinated flavones, (VII or VI) and (XIV or X), in the presence of activated copper powder, without a solvent, followed by removal of the protecting group.

[*1] Part IX. This Bulletin, **10**, 1032 (1962); A preliminary report was published in this Bulletin, **7**, 748 (1959).

[*2] Kokonoe-cho, Gifu (中沢浩一, 伊藤万蔵).

1) K. Nakazawa: Yakugaku Zasshi, **61**, 174, 228 (1941).

2) W. Baker, A. C. M. Finch, W. D. Ollis, K. W. Robinson: Proc. Chem. Soc., 91 (1959).