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188. Shiro Ikegami and Shun-ichi Yamada: Chemistry of Sodium Borohydride and Diborane. Ⅱ.*[1] Reduction of Schiff Bases with Diborane in Tetrahydrofuran.

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In a previous paper,*[1] the authors reported that the reaction of 3,4-dihydroisoquinoline derivatives with diborane in tetrahydrofuran afforded the corresponding amine boranes (A) (new type of borane complex), instead of the expected reduced products. The reasons why the reduction did not occur and also why the unexpected amine borane compounds (A) were obtained in these dihydroisoquinoline series, have not been disclosed yet. Accordingly, the present investigation was aimed to find out whether any analogous imine borane compounds (B) would be obtainable in the reaction of diborane with Schiff bases (Ⅲa~e and Ⅵa~f) which are of the open chain type and seem to be much weaker bases than 3,4-dihydroisoquinoline derivatives.

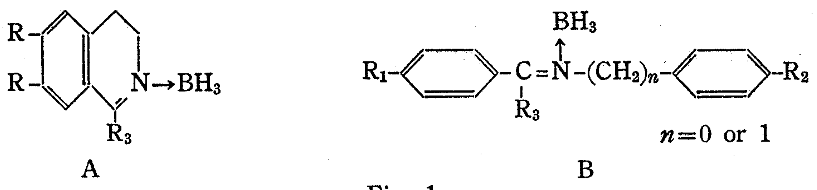


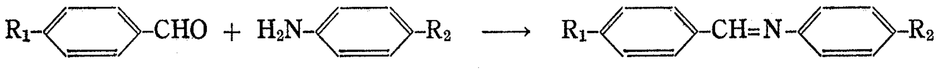
Fig. 1.

Results and Discussion

Reaction of Schiff Bases with Diborane

Various Schiff bases of the three series, the methoxy and nitro derivatives of N-benzylideneaniline (Ⅲa~e), N-benzylidenebenzylamine (Ⅵa~c) and N-(α-methylbenzylidene)benzylamine (Ⅵd~f) as the parent compounds were synthesized from the condensation of either benzaldehyde (I) or acetophenone (Ⅳ) derivatives with *p*-substituted anilines (Ⅱ) or benzylamine (Ⅴ) according to the method described in the

Table I. Properties of N-Benzylideneaniline Derivatives (Ⅲ)



I Ⅱ Ⅲa~e

Compd.	R_1	R_2	Recryst. solvent	Appearance	m.p. (°C) in lit.	m.p. (°C)
a	H	H	EtOH	pale yellow plates	52[a]	51.5~52.5
b	CH_3O	H	EtOH	white plates	57[b], 58~59[c]	58~59
c	NO_2	H	EtOH	yellow needles	90~93[c]	90~92
d	CH_3O	CH_3O	EtOH	white plates	146[b]	147~148
e	NO_2	NO_2	C_6H_6	yellow needles	198~200[c]	200~201

a) "Organic Syntheses," Coll. Vol. I, p. 80 (1956).
b) H.H. Keasling, F.W. Schneler: J. Am. Pharm. Assoc., **39**, 87 (1950).
c) B.A. Poraĭ-Koskits, *et al.*: J. Gen. Chem. (U.S.S.R.), **17**, 1774 (1947) (Chem. Abstr., **42**, 5863h (1948)).

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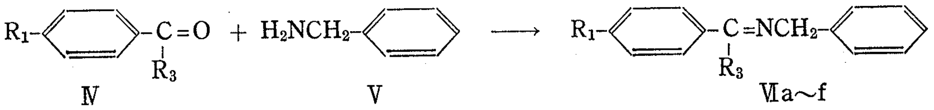
*[1] S. Yamada, S. Ikegami; This Bulletin, **14**, 1382 (1966).
*[2] Hongo, Tokyo (池上四郎, 山田俊一).

Table II. Properties of N-Benzylidenebenzylamine Derivatives (VI)



IV V VIa∼f

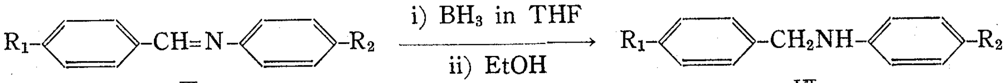
Compd.	R_1	R_3	Recryst. solvent	Appearance	m.p. or b.p. (°C) in lit.	m.p. or b.p. (°C)
a	H	H	(dist.)	colorless oil	116∼117/0.1mm.a)	142∼144/3mm.
b	CH_3O	H	(dist.)	white waxy solid	39.9∼40.8b)	200∼201/3mm., 41∼42
c	NO_2	H	EtOH-hexane	yellow plates	56c)	57.5∼58
d	H	CH_3	EtOH	white prisms	45d)	44.5∼45.5
e	CH_3O	CH_3	EtOH-petr. ether	colorless plates		61∼62
f	NO_2	CH_3	iso-C_3H_7OH	orange needles		68.4∼69

a) R. Juday, H. Adkins: J. Am. Chem. Soc., **77**, 4559 (1955).
b) H.R. Snyder, J.R. Demuth: *Ibid.*, **78**, 1981 (1956).
c) C.K. Ingold, H.A. Piggott: J. Chem. Soc., **121**, 2381 (1922).
d) W. Schlenk, E. Bergmann: Ann., **463**, 294 (1928).

literatures*3 except the syntheses of N-(α-methyl-*p*-methoxybenzylidene)benzylamine (VIe) and N-(α-methyl-*p*-nitrobenzylidene)benzylamine (VIf) as summarized in Tables I and II.*3 The latter two compounds, VIe and VIf, were prepared by the reaction of an equimolar amount of the corresponding ketone with benzylamine in toluene using the water separator.

These Schiff bases were submitted to the reaction with diborane in tetrahydrofuran according to the similar method described in Part I. After removing the solvent, the residues were dissolved in ethanol and it was refluxed gently until the evolution of gas ceased. The reaction products were found to be the amines (VII and VIII) isolated

Table III. Reaction Conditions and Results of the Reaction of N-Benzylideneaniline Derivatives (III) with Diborane in Tetrahydrofuran



III VII

Compd.	III		III		Reaction		Red. prod. VII, gr.	Yield (%)	m.p. of VII (°C)	m.p. of VII (°C) in lit.
	R_1	R_2	5 mmoles (gr.)	THF (ml.)	temp. (°C)	time (hr.)				
a	H	H	0.90	20	3.0∼3.5	3	0.98 (as HCl salt)	90.7	36∼36.5a) 213∼213.5c) 93∼94e)	37∼38a,b) 214∼216c,d) 92e,f)
b	CH_3O	H	1.06	20	2.0∼2.5	4	0.98	91.6	48∼49	46.5∼47b) 63.5∼64g) 64.5,h) 46∼47i)
c	NO_2	H	1.13	20	2.0∼2.5	4	1.05	92.2	70∼71	67∼68b)
d	CH_3O	CH_3O	1.20	25	2.0∼2.5	3	1.15	95.1	97∼98	94.5∼95.5i)
e	NO_2	NO_2	1.36	30	2.0∼2.5	3	1.11	81.1	188∼189	185∼185.5b) 189∼189.5g) 192j)

a) m.p. of free base.
b) J.H. Billman: J. Org. Chem., **22**, 1068 (1957).
c) m.p. (decomp.) of HCl salt.
d) K. Braud: Ber., **42**, 3462 (1909).
e) m.p. of 1,3,5-trinitrobenzene complex.
f) J.J. Sudborough, S.H. Beard: J. Chem. Soc., **97**, 788 (1910).
g) J.H. Billman: J. Org. Chem., **26**, 1437 (1961).
h) O.J. Steingart: Ann.. **241**, 337 (1887).
i) M. Oki, H. Iwamura: Bull. Chem. Soc. Japan, **32**, 955 (1959).
j) C. Paal, C. Bemker: Ber., **32**, 1256 (1899).

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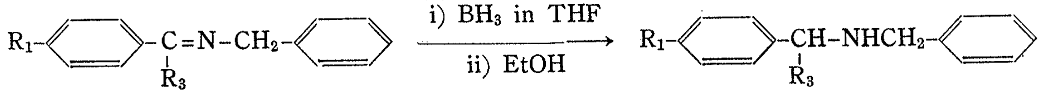
*3 Tables I and II are shown in the experimental part and the literatures are given in them.

Table Ⅳ. Reaction Conditions and Results of the Reaction of N-Benzylidenebenzylamine Derivatives (Ⅵa, c, d) with Diborane in Tetrahydrofuran



Ⅵa, c, d

Ⅷ

Compd.	Ⅵ		Ⅵ		Reaction		Red. prod. Ⅷ-HCl (mg.)	Yield (%)	m.p. (decomp.) of Ⅷ (°C)	m.p. (decomp.) of Ⅷ (°C) in lit.
	R_1	R_3	1 mmole (mg.)	THF (ml.)	temp. (°C)	time (hr.)				
a	H	H	200	25	2.5～3.5	2	230	98.7	257～258	256,[a] 255.5[b]
c	NO_2	H	240	25	2.5～3.0	2	210	75.3	248～249	248[c]
d	H	CH_3	210	25	2.5～3.0	2	200	80.7	179～180	184[d]

[a] H. Limpricht: Ann., **144**, 308 (1867).
[b] T. Curtius: J. prak. Chem., [2] **62**, 99 (1900).
[c] H. R. Snyder, J. R. Demuth: J. Am. Chem. Soc., **78**, 1981 (1956).
[d] K. Parck: J. park. Chem., [2] **86**, 284 (1912).

in a good yield as either free bases or hydrochlorides. The crude products obtained after removing the solvent from the reaction mixtures showed a very weak band assigned to C=N group in the infrared absorption spectra. In every experiment, however, imino borane compounds (B) analogous to dihydroisoquinoline derivatives (A) had not been obtained in spite of the various attempts to isolate them. The reaction conditions and the products are summarized in Tables Ⅲ and Ⅵ.

No convicing interpretation for the different behaviors of these two types of C=N bond has been given. However, it might be assumed that the different reactivity of these two types of C=N bond toward diborane depends on the basicity of each type of the compounds. The determination of basicities of 3,4-dihydroisoquinolines and Schiff bases was undertaken.

Measurements of the Basicity

Measurements of the basicity of Schiff bases by the usual titrimetric method using pH-meter was found to be greatly difficult, because hydrolysis of Schiff bases occurred at the neutralized point. Recently, Ishidate, *et al.*[1~4] have reported the determination of basicity of amines by the dielectrometric titration in non-aqueous solvents. This method was applied to the Schiff bases, however, the results were found to be unsatisfactory.

On the other hand, Weinstein and McIninch[5] have shown the determination method of the dissociation constants for the complex formation through hydrogen between *p*-substituted N-benzylideneanilines and *p*-nitrophenol. The method depends on the fact that the formation of O--H···N bond in the equilibrium between Schiff bases and *p*-nitrophenol decreases the intensity of the free OH infrared absorption band of *p*-nitrophenol. Measurements of our compounds under the reported conditions in carbon tetrachloride exhibited the free OH stretching band of *p*-nitrophenol at 3597 cm^{-1} or 2.78 μ (3610 cm^{-1} or 2.77 μ in the literature[5]) and the dissociation constants, *K*, for the equilibrium either between Schiff bases or 3,4-dihydroisoquinoline derivatives and *p*-nitrophenol were calculated from the absorbance of the free OH band of *p*-nitrophenol. The values of the dissociation constants of various Schiff bases and 3,4-dihydroisoquinoline derivatives are summarized in Tables Ⅴ, Ⅵ and Ⅶ respectively. In each

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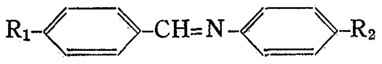
1) M. Ishidate, H. Nishizawa, H. Sano, I. Horikoshi: Yakugaku Zasshi, **81**, 1303 (1961).
2) *Idem*: *Ibid.*, **81**, 1307 (1961).
3) H. Sano: *Ibid.*, **81**, 1310 (1961).
4) *Idem*: *Ibid.*, **81**, 1313 (1961).
5) J. Weinstein, E. McIninch: J. Am. Chem. Soc., **82**, 6064 (1960).

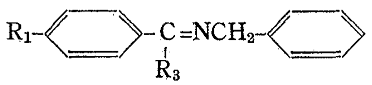
Table V. Values of Dissociation Constant for N-Benzylideneaniline Derivatives (III)



Compd.	R_1	R_2	$K \times 10^{-1}$ a)			
			29°	(27.5°)	45°	(48.0°)
a	H	H	3.3	(3.9)	2.3	(1.9)
b	CH_3O	H	7.6	(8.8)	4.9	(4.5)
c	NO_2	H	1.1	(1.2)	0.9	(0.66)
d	CH_3O	CH_3O	11.5	(1.2)	7.7	(6.4)
e	NO_2	NO_2	insoluble in CCl_4			

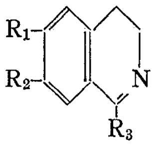
a) The values in the literature (J. Weinstein, E. McIninch: J. Am. Chem. Soc., **82**, 6064 (1960)) are presented in parenthesis.

Table VI. Values of Dissociation Constant for N-Benzylidenebenzylamine (VI)



Compd.	R_1	R_3	$K \times 10^{-1}$, 29°
a	H	H	9.3
b	CH_3O	H	17.1
c	NO_2	H	1.6
d	H	CH_3	16.2
e	CH_3O	CH_3	24.0
f	NO_2	CH_3	2.0

Table VII. Values of Dissociation Constant for 3,4-Dihydroisopuinoline Derivatives



R_1	R_2	R_3	$K \times 10^{-2}$, 29°
H	H	H	9.35
H	H	CH_3	17.6
CH_3O	CH_3O	H	19.4
CH_3O	CH_3O	CH_3	38.9

series of Schiff bases, there is a decrease in hydrogen bonding power in going from methoxy to nitro group. In comparison between the values obtained for Schiff bases and those for 3,4-dihydroisoquinoline derivatives, remarkable differences were observed. It is noteworthy that 3,4-dihydroisoquinoline derivatives have extraordinary stronger basicity than that of Schiff bases. This marked difference of the basicity might participate in the different reactivity between 3,4-dihydroisoquinoline derivatives and Schiff bases toward diborane even though both of them have the similar carbon-nitrogen double bond. Presumably, it might be supposed that when the basicity of the compounds containing carbon-nitrogen double bond is extremely strong, the stable amine borane complexed (A) are formed without further reduction, but in case of weaker bases such as Schiff bases (Ⅲ and Ⅵ), the reduction occurred predominantly regardless of minor variation of basicity among them. It is of interest to investigate the mechanism where the reduction may occur smoothly in case of Schiff bases. For such purpose a somewhat detailed kinetic study of the reduction of Schiff bases with diborane seemed to be necessary.

Rates of the Reaction of Schiff Bases with Diborane

In earlier works,[6] it had been shown that on hydroboration of unhindered *cis*-olefins with diborane, 3 moles of olefins react per mole of borane (BH_3) to form trialkylborane. Ioffe, *et al.*[7] pointed out that the reduction of 3 moles of cyclohexanone oxime with 1 mole of diborane smoothly took place without any evolution of gas. As the similar considerations are adopted to the hydroboration of Schiff bases, this hydroboration process may be considered to involve three stages as shown in Chart 1.

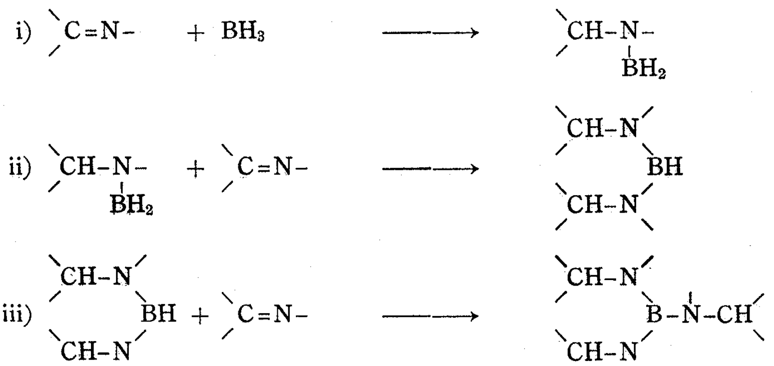


Chart 1.

In Fig. 2 is shown the rate of reduction of N-benzylideneaniline (Ⅲa) with one third molar amount of borane in tetrahydrofuran at different temperatures, 0°, 35° and 66° (refluxing temperature). At each temperature the first step of the reduction was found to be very faster as compared with the following steps. However, when the reduction was performed at 0°C, only one mole of Ⅲa was reduced even after 120 min., but at 35°, one mole of Ⅲa was reduced rapidly and the subsequent reduction occurred gradually. Under the reflux 2 moles of Ⅲa were rapidly reduced and further reduction took place until nearly 3 moles of Ⅲa were reduced. On the assumption that the reduction step proceeds as proposed in Chart 1, the initial step reduction, *i. e.* the reduction at 0°C, might be considered to correspond to equation (i) (Chart 1). In this step, the basicity of Schiff bases discussed above seems to take part in the reaction rate. Therefore, the rate determination was carried out at this initial step at 0°C.

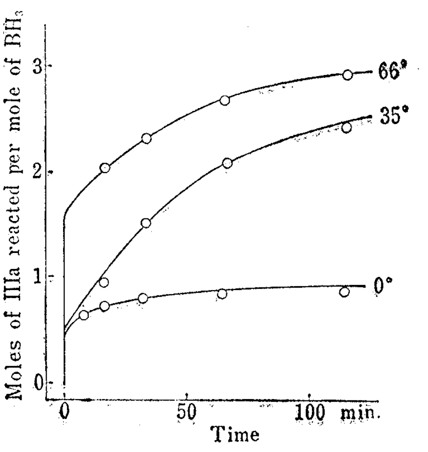


Fig. 2. The Reaction of N-Benzylideneaniline with Borane in Tetrahydrofuran at 0°, 35° and 66°

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[6] H. C. Brown, "Hydroboration," p. 102 (1962), W. A. Benjamin, Inc., Publishers, New York.

[7] S. L. Ioffe, V. A. Tartakovski, A. A. Medvedeva, S. S. Novikov: Izv. Akad. Nauk SSSR, Ser. Khim., **1964**, 1537.

As the results of our experiments, these reactions were considerably fast and accordingly, might include unavoidable errors; *e.g.* in initiating and timing the reaction. An attention was paid to minimize possible errors. The reaction was initiated by adding a BH_3-THF solution of a definite concentration with a fast-draining pipette to each of the solution of Schiff bases in tetrahydrofuran. Each of the reaction mixtures was quenched with triethylamine and a few drops of ethanol was added to this reaction mixture for the cleavage of boron-nitrogen bond of aminoborane which would be formed from the reaction and then the ratio of Schiff bases and their reduced products was determined by gas chromatography.

With respect to quenching reactions, two methods were expected to be utilized; 1) the decomposition of excess diborane by adding hydroxylic reagents, such as ethanol and water, or 2) the consumption of diborane by adding the reagents which seem to be more reactive than Schiff bases toward diborane. In the former case, the further reduction of Schiff bases occurred only by the addition of either ethanol or water and in the latter case, the similar reduction was observed while the reagents such as acetic acid (this reagent also may be regarded as an hydroxylic reagent), acetone and acetonitrile being added. In addition, these reductions occurred even in the mixed solvent of acetone and tetrahydrofuran. Accordingly, it would be suggested that the carbon-nitrogen double bond of these Schiff bases were more reactive than acid, ketone and nitrile toward diborane.

As the results of various experiments, triethylamine which would possess much stronger basicity than Schiff bases was found to be the best reagent to stop the reaction of Schiff bases with diborane. The reaction seemed to be stopped by rapid formation of triethylamine borane which would be almost unreactive under the performed mild condition.

The cleavage of the aminoborane which would be formed by the addition of diborane to the carbon-nitrogen double bond of Schiff bases were achieved only by the treatment with ethanol. Actually the free amines were isolated by the gentle reflux of the crude products in ethanol which were obtained from the reaction of Schiff bases with diborane and an analogous method was already reported by Ioffe, *et al.*,[7] who found that the isolation of hydroxylamines from the crude products prepared by the reduction of oximes with diborane are achieved only by the treatment of methanol.

It has been shown[8,9] that diborane, which exists in the dimeric state in many ethereal solvents, dissociates to form the monomeric borane $C_4H_8O : BH_3$ in tetrahydrofuran. Consequently, in this study the concentration of diborane in tetrahydrofuran will be expressed as the monomer.

On the mechanism of the roaction of diborane with the carbonyl group such as aldehydes and ketones, Brown *et al.*[10] suggesied that the initial stage of the reaction involves an acid-base interaction with borane adding to the oxygen atom, being followed by the transfer of a hydride unit from boron to carbon.

An application of the similar consideration to the reaction in this work will lead to the following reaction equation,

$$\text{Schiff base} + BH_3 \underset{K_{-1}}{\overset{K_1}{\rightleftarrows}} C \xrightarrow{K_2} \text{Aminoborane,}$$

so that the reaction rate is given by

$-d[\text{Schiff bases}]/dt = K_2[C] = \dfrac{K_1K_2}{K_{-1}+K_2}[\text{Schiff bases}][BH_3]$, where C is an active inter-

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8) J.R. Elliott, W.L. Roth, G.F. Roedel, E.M. Boldebuck: J. Am. Chem. Soc., **74**, 5211 (1952).

9) B. Rice, J.A. Livasy, G.W. Schaeffer: *Ibid.*, **77**, 2750 (1955).

10) H.C. Brown, B.C. Subba Rao: *Ibid.*, **82**, 681 (1960).

mediate, which is supposed to be Schiff base borane complex. When $K_{-1} \ll K_2$ or $K_1 \gg K_2$, the following equations, respectively, can be readily obtained from the above equation.

i) $K_{-1} \ll K_2$; $-d[\text{Schiff base}]/dt = K_1[\text{Schiff base}][BH_3]$
ii) $K_{-1} \gg K_2$; $-d[\text{Schiff base}]/dt = K_1K_2/K_{-1}[\text{Schiff base}][BH_3]$

In both cases these equations represent a simpie second-order reaction, first order in Schiff base and first order in borane.

Treatment of the experimental data in the reaction of borane with IIIa as a simple second-order reaction afforded good agreement (Fig. 3).*4

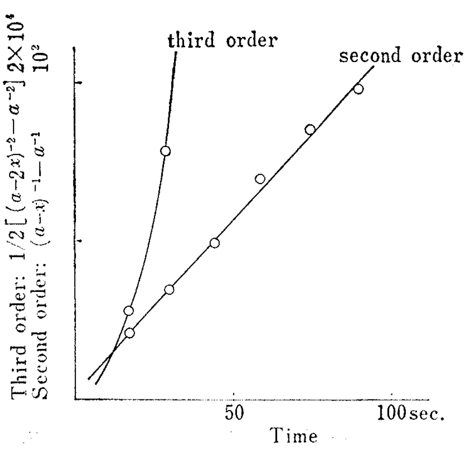

Fig. 3. Second and Third Order Plots of the Reaction N-Benzylideneaniline (IIIa) with Borane in Tetrahydrofuran at 0°

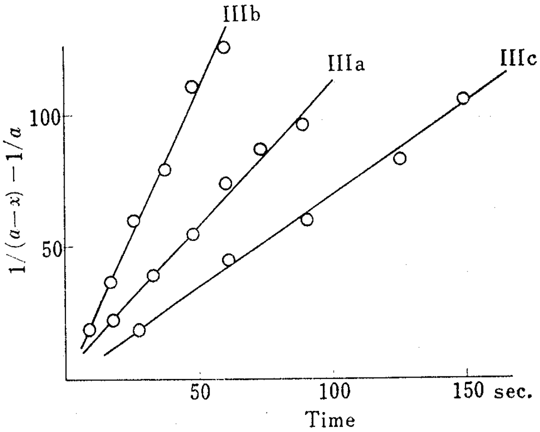

Fig. 4. Second-order Plots of the Reaction of N-Benzylideneaniline (IIIa), N-(*p*-Methoxybenzylidene)aniline (IIIb) and N-(*p*-Nitrobenzylidene)aniline (IIIc) with Borane in Tetrahydrofuran at 0°

Furthermore, the conclusion that the reaction conforms to the second-order kinetics was checked by half life method. In this way, the value of the reaction order was calculated to be approximately 1.8 indicating that the reaction follows the second-order kinetics within an slight error.

The rates of the reactions of N-(*p*-methoxybenzylidene)aniline (IIIb) and N-(*p*-nitrobenzylidene)aniline (IIIc) with diborane were measured by the similar method. Second-order plots of these reactions were shown in Fig. 4, yielding a straight line in each

TABLE VIII. Approximate Rate Constants for the Reaction of N-Benzylideneaniline Derivatives (III a, b, c) with Diborane in Tetrahydrofuran at 0°

Compd.	Rate const. ***k***, L. mole^{-1} sec^{-1}
N-Benzylideneaniline (IIIa)	1.2
N-(*p*-Methoxybenzylidene)aniline (IIIb)	2.1
N-(*p*-Nitrobenzylidene)aniline (IIIc)	0.66

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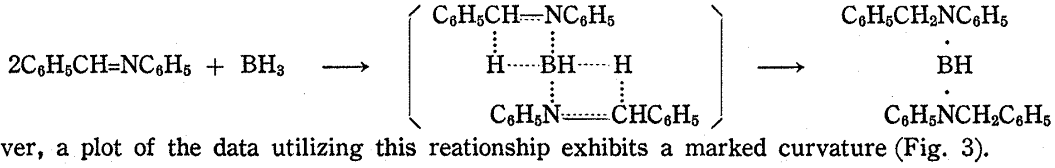
*4 If the following equation represents the reaction mechanism, the reaction should exhibit the third order kinetics, first order in borane and second order in N-benzylideneaniline.



$$2C_6H_5CH{=}NC_6H_5 + BH_3 \longrightarrow \left(\begin{array}{c} C_6H_5CH{=}NC_6H_5 \\ H\cdots BH\cdots H \\ C_6H_5N{=}CHC_6H_5 \end{array} \right) \longrightarrow \begin{array}{c} C_6H_5CH_2NC_6H_5 \\ BH \\ C_6H_5NCH_2C_6H_5 \end{array}$$

However, a plot of the data utilizing this reationship exhibits a marked curvature (Fig. 3).

case. The approximate rate constants established for Ⅲa, Ⅲb and Ⅲc in the reaction with diborane are summarized in Table Ⅷ, in which with increasing of the basicity, it was shown to lead to the increase of the relative reactivity of these three compounds of Schiff base toward diborane.

In case of N-benzylidenebenzylamine (Ⅵa) and N-(α-methylbenzylidene)benzylamine derivatives (Ⅵd~f), plots of the rates in the similar reaction are shown in Fig. 5 and 6 respectively. Since the reactions in the series of Schiff bases were observed to be very fast, the calculation of their rate constants was found to be extremely difficult. However, it is possible to compare their relative reactivities each other. In Fig. 6, because of the exceedingly fast reactions of N-(α-methylbenzylidene)benzylamine (Ⅵd) and N-(α-methyl-*p*-methoxybenzylidene) benzylamine (Ⅵe) with diborane, the unambiguous results of the rate were not obtained. However, the tendency of the relative reactivity toward the basicity would appear to be resemble to those observed in Fig. 4 and Fig. 5. In addition, the reaction of 3,4-dihydroisoquinoline derivatives with diborane described in Part I was likewise carried out, according to the procedure of reacting at 35° and the reaction rates were determined by ultraviolet spectrometer, however no change on ultraviolet spectra was observed even after 2 hours of the reaction.

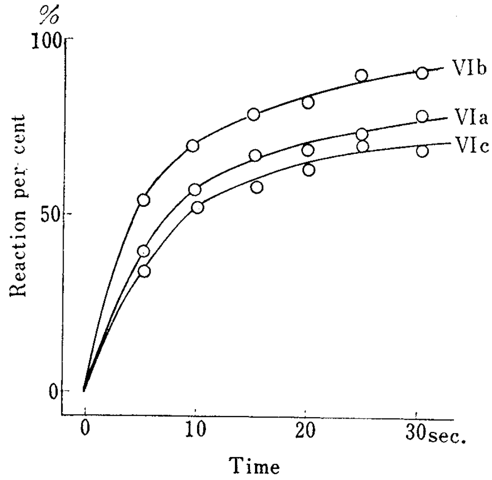


Fig. 5. The Reaction of N-Benzylidenebenzylamine Derivatives (Ⅵa, b, c) with Borane in Tetrahydrofuran at 0°

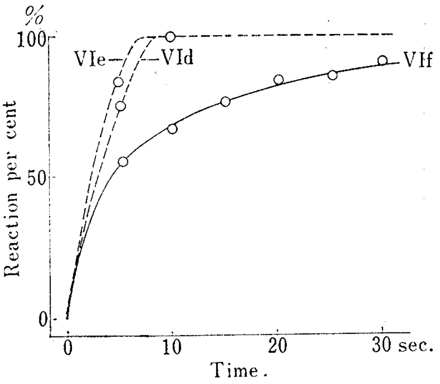


Fig. 6. The Reaction of N-(α-Methylbenzylidene)benzylamine Derivatives (Ⅵd, e, f) with Borane in Tetrahydrofuran at 0°

The ambiguous results in the case of Ⅵd and Ⅵe are showed in a dotted line.

The following conclusions may be drawn from the results mentioned above, that is: 1) In the reaction of 3,4-dihydroisoquinoline derivatives with diborane, whose basicities are as strong as that of usual tertiary amines, the corresponding amine borane complexes are merely formed and after that further reactions did not proceed. 2) In the case of Schiff bases such as Ⅲ and Ⅵ, the rate of the reduction with diborane in the first stage increases with an increase of the strength of the basicity. 3) The reduction of trisubstituted Schiff bases with diborane (Ⅵd~f) is shown to be faster than that of disubstituted Schiff bases (Ⅲa~c and Ⅵa~c), and finally the phenyl group is considered to have an effect for decreasing the reaction.

The plausible mechanisms of the reduction may involve either a coordination of the borane to the nitrogen of Schiff base followed by an intramolecular hydride transfer from boron to carbon such as proposed for reduction of carbonyl with diborane in diglyme or tetrahydrofuran,[10] or otherwise a four-center transition mechanism such as postulated for hydroboration of olefin with diborane.[11,12] As shown in Fig. 7, it would be expected that the transition state in the reaction of both 3,4-dihydroisoquinoline derivatives and Schiff bases with diborane may differ. In the former case the stable imine borane complexes (C) are formed and a hydride transfer does not occur, whereas in the latter case, the possible forms of the transition state may be the complex (D_1) having either a weak coordination bond or four-denter intermediate (D_2), followed by a hydride transfer from boron to carbon. Furthermore, on the basis of the results discussed above and the mechanism such as postulated by Brown[10] for the reduction of carbonyl group with diborane, it would be considered that the stage of the formation of the complex would be rate-determining step in this reduction.

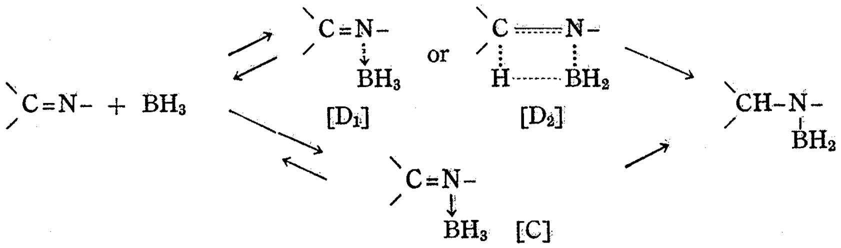


Fig. 7. The Plausible Mechanisms for the Reaction of Schiff Bases and 3,4-Dihydroisoquinoline Derivatives with Borane

Experimental*5

Materials——Tetrahydrofuran (THF), diglyne (DG) and boron trifluoride etherate were purified as previously described.*2 Sodium borohydride from Merck, Co., was used without purification. Carbon tetrachloride (extra pure grade) from Wako Yakuhin, Co., was used without further purification.

Standard solutions of diborane in THF in the range 0.3 to $0.5M$ were prepared according to the method of Brown, *et al.* and stored at ca. 4° in a refrigerator.

Schiff Bases——The properties of various Schiff bases which were used in our work are summarized in Tables I and II.

N-(α-Methyl-*p*-methoxybenzylidene)benzylamine (VIe)——A solution of benzylamine (3.2 g., 0.03 mole), 4′-methoxyacetophenone (3.0 g., 0.02 mole) and a few crystals of *p*-toluenesulfonic acid in dehyd. toluene (30 ml.) was refluxed using water separating apparatus until the calculated volume of water formed. The solvent was evaporated *in vacuo* to leave a colorless viscous oil. On standing, the oil solidified and the resultant solid was recrystallized from EtOH-petr. ether to give colorless plates of m.p. 60~61°. Further recrystallization gave the similar crystalline forms of m.p. 61~62°, which were analytically pure. Yield, 3.17 g. or 66.4%. *Anal.* Calcd. for $C_{16}H_{17}ON$: C, 80.30; H, 7.16; N, 5.85. Found : C, 80.26; H, 7.04; N, 6.12. IR ν_{max}^{KBr} cm^{-1} : 1632 (C=N).

N-(α-Methyl-*p*-nitrobenzylidene)benzylamine (VIf)——The reaction of benzylamine (3.2 g., 0.03 mole) with 4′-nitroacetophenone (3.3 g., 0.02 mole) was carried out according to the similar procedure described above. Evaporation of the solvent left a reddish brown oil, which solidified on standing. EtOH (5 ml.) was added to the solid to remove impure materials and the mixture was filtered to give orange crystals, which were then recrystallized from EtOH-petr. ether to afford orange needles of m.p. 68~69°. Further recrystallization gave the similar crystals of m.p. 68.5~69°, which were analytically pure. Yield, 3.22 g. or 63.3%. *Anal.* Calcd. for $C_{15}H_{14}O_2N_2$: C, 70.85; H, 5.55; N, 11.02. Found : C, 71.17; H, 5.82; N, 10.82. IR ν_{max}^{KBr} cm^{-1} : 1630 (C=N).

General Procedures

Reaction of Schiff Bases (IIIa~e) with Diborane——Diborane generated by treating a solution of $NaBH_4$ (0.18 g., 4.9 mmole) in DG (5 ml.) with $BF_3 \cdot O(C_2H_5)_2$ (1.0 g., 7.3 mmole) was passed through a wash bottle containing a small quantity of $NaBH_4$ in DG (to remove traces of BF_3) into a solution of Schiff base (IIIa~e : 5 mmoles) in THF (20~30 ml.) at 3~5° for 10~20 min. with stirring. After heating diborane generator at 60~70° for 30 min., the reaction mixture was stirred at 2.0~3.5° for additional 2.5~3.5 hr. The solvent was evaporated *in vacuo* to dryness and the residue dissolved in EtOH (10 ml.) was gently refluxed for 10

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*5 All melting points are uncorrected.

11) H. C. Brown, G. Zweifel : J. Am. Chem. Soc., **82**, 4708 (1960).

12) *Idem* : *Ibid.*, **83**, 2544 (1961).

min. to decompose aminoborane which would be formed from this reaction. Removal of the solvent left a solid, which was recrystallized from EtOH except the case of Ⅲa to give the crystals of melting point as shown in Table Ⅲ. In case of Ⅲa, a semi-solid thus obtained was converted to its hydrochloride. The coditions of the reaction of Schiff bases (Ⅲa~e) with diborane, the yields of the reduced products and m.p.s of amines or amine hydrochloride are given in Table Ⅲ.

Reaction of Schiff Base (VIa,c,d) with Diborane——To a solution of Schiff base (Ⅵa, c, d : 1 mmole) in THF (25 ml.), standard diborane solution (0.05*M*, 20 ml.) was added at 2.5~4.0° for 5 min. with stirring and the reaction mixture was stirred at 2.5~3.5° for 2 hr. Evaporation of the solvent left a viscous oil, which was dissolved in EtOH (5 ml.) and then the solution was gently refluxed for 10 min. The residue obtained by removal of the solvent was converted to its hydrochloride. The results are shown in Table Ⅳ.

Infrared Absorbance Measurements—— A Parkin-Elmer Model 221 (Grating & NaCl) spectrophotometer was used. Most of the procedures was carried out according to the method of Weinstein and McIninch.[5] The concentrtion of *p*-nitrophenol in CCl_4 was maintained in $1\times10^{-3}M$. The concentration of the Schiff base (Ⅲa~e and Ⅵa~e) was kept usually in $8\times10^{-3}M$. Solutions of 3,4-dihydroisoquinoline derivatives described in Part I at the same concentration employed for measurement of the Schiff bases showed a significant decrease in the intensity of the 3597 cm^{-1} band of *p*-nitrophenol. Accordingly, the measurement was carried out at the $1.5\times10^{-3}M$ concentration of 3,4-dihydroisoquinoline derivatives. The results obtained for Schiff bases and 3,4-dihydroisoquinoline derivatives are given in Tables Ⅴ, Ⅵ and Ⅶ.

Measurement of the Rate in the Reaction of Schiff Bases with Diborane——Standard solution ($1.5\times10^{-2}M$) of Schiff bases was prepared and transferred 1 ml. to every several reaction vessels and these reaction vessels were cooled to 0° under N_2 atmosphere. The BH_3-THF solution of the $3.0\times10^{-2}M$ concentration was prepared and cooled at 0° under N_2 atmosphere. The determination of diborane was carried out according to the following description. To a solution of an about twofold excess of N-benzylideneanilne to diborane in THF was added the BH_3-THF solution at 0° and then the solution was refluxed for 3 hr. The sample of 1 μl. for the gas chromatographic analysis with a Jintan microsyringe was injected into the Shimadzu GC-1B gas chromatograph (hydrogen flame ionizable detector) containing a 225 cm. of 1.5% NGC (Neopentylglycol succinate) column maintained at 166°. Symmetrical peaks of N-benzylideneaniline and its reduced product were obtained with a relative retention time as shown in Table Ⅸ. Quantity of diborane was calculated from the areas determined by the half-width method. Besides, the value thus obtained was in accordance with that obtained by the determination of the active hydride.

TABLE Ⅸ. Relative Retention Times of Schiff Bases and Amines[a]

Compd.	Column (225 cm. × 4 mm.)	Column temp. (°C)	Retention time (min.)
$C_6H_5CH{=}NC_6H_5$ (Ⅲa)	1.5% NGS	166	5.7
$C_6H_5CH_2NHC_6H_5$ (Ⅶa)	〃	166	9.9
p-$CH_3OC_6H_5CH{=}NC_6H_5$ (Ⅲb)	〃	198	6.1
p-$CH_3OC_6H_5CH_2NHC_6H_5$ (Ⅶb)	〃	198	9.1
p-$NO_2C_6H_5CH{=}NC_6H_5$ (Ⅲc)	1.5% SE-30	192	11.0
p-$NO_2C_6H_5CH_2NHC_6H_5$ (Ⅶc)	〃	192	14.9
$C_6H_5CH{=}NCH_2C_6H_5$ (Ⅵa)	7% QF-1	160	7.9
$C_6H_5CH_2NHCH_2C_6H_5$ (Ⅷa)	〃	160	6.3
p-$CH_3OC_6H_5CH{=}NCH_2C_6H_5$ (Ⅵb)	〃	190	8.6
p-$CH_3OC_6H_5CH_2NHCH_2C_6H_5$ (Ⅷb)	〃	190	6.5
p-$NO_2C_6H_5CH{=}NCH_2C_6H_5$ (Ⅵc)	〃	200	15.7
p-$NO_2C_6H_5CH_2NHCH_2C_6H_5$ (Ⅷc)	〃	200	18.0
$C_6H_5C(CH_3){=}NCH_2C_6H_5$ (Ⅵd)	1.5% NGS	166	11.4
$C_6H_5CH(CH_3)NHCH_2C_6H_5$ (Ⅷd)	〃	166	4.7
p-$CH_3OC_6H_5C(CH_3){=}NCH_2C_6H_5$ (Ⅵe)	〃	200	10.0
p-$CH_3OC_6H_5CH(CH_3)NHCH_2C_6H_5$ (Ⅷe)	〃	200	4.3
p-$NO_2C_6H_5C(CH_3){=}NCH_2C_6H_5$ (Ⅵf)	7% QF-1	200	25.7
p-$NO_2C_6H_5CH(CH_3)NHCH_2C_6H_5$ (Ⅷf)	〃	200	17.3

[a] Shimadzu Gas Chromatograph Model GC-1B equipped with hydrogen flame ionizable detector was used. Nitrogen as carrier gas was employed and its flow rate was controlled in 56~63 ml./min.

The fast-draining pipettes were maintained at 0° before use. In order to minimize the loss of active hydride in the pipette, a small amount of diborane solution was used to rinse the pitette before the pipette was used to transfer the standard diborane solution. The reaction was initiated by injecting 0.5 ml. of the standard diborane solution, containing 15 μg. of borane (BH_3) within 3 sec. Each reaction in the reaction containers was stopped at a definite time after suitable intervals of time by adding 3~5 drops of $(C_2H_5)_3N$

maintained at 0° before use. EtOH (3∼5 drops) was added to each of the quenched solution and then the samples, 2∼10 μl., for the gas chromatographic analysis were injected into the GC apparatus described above being equipped with the column as shown in Table Ⅸ. The areas were determined by graphical integration.

The authors are indebted to Sankyo Co., Ltd. for the measurements of infrared absorption spectra. Thanks are also due to the members of the Central Analysis Room of this Faculty for microanalytical, infrared and ultraviolet spectral data.

Summary

The reduction of the various Schiff bases with diborane in tetrahydrofuran was smoothly proceeded, being followed by the simple treatment with alcohol, to give the corresponding amines. The relative reactivity of the Schiff bases toward diborane increased with an increasing order of their basicities determined by the infrared absorption spectral method.

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189. **Zen-ichi Horii, Koichi Morikawa, Yasumitsu Tamura, and Ichiya Ninomiya**: Studies on Azasteroids and Related Compounds. I. The Reaction of Ethyl 2-Piperidineacetate with 2-Tetralone.

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The reaction of methyl 2-methyl-3-methylaminopropionate with 2-tetralone has been reported to give the rearranged compound (Ⅲ) as a major product.[1] This was explained by the thermal decomposition of the initially formed enamine (V), followed by the recombination of the resulted enamine and methyl acrylate moieties. Therefore, if one can provide the product of type I in good yield by using the thermally stable β-aminoester, the reaction of ketone and β-aminoester can be a useful method for the preparation of the skeleton of 14-azasteroids bearing oxygen function at C_{11} position. Actually, methyl 3-methylaminopropionate, when reacted with cyclohexanone at the boiling point of toluene, yielded the normally acylated product as a major, along with the rearranged product as a minor.[1]

This paper deals with the investigation of the intramolecular cyclization of the enaminoester derived from 2-tetralone and ethyl 2-piperidineacetate,[2] which was found to be stable upon treating it under the reaction condition, suggesting the possible exclusion of the formation of the rearranged product like Ⅲ.

Heating of ethyl 2-piperidineacetate and cyclohexanone in the presence of *p*-toluenesulfonic acid gave the enamine (Ⅵ), which was then refluxed in ethylene glycol to afford the compound (Ⅶ) in 69% yield, and its structural assignment was obtained mainly from its infrared spectrum, showing peaks at 1620 and 1550 cm^{-1} characteristic

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[*1] Toneyama, Toyonaka, Osaka-fu (堀井善一, 森川浩一, 田村恭光, 二宮一弥).

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