Hydrochlorid : Farblose Prismen vom Schmp. 272~273° aus AcOEt-MeOH. $C_{19}H_{30}O_2N_2 \cdot 2HCl \cdot \frac{1}{4}H_2O$—Ber. : C, 57.64; H, 8.21; N, 7.08. Gef. : C, 57.30; H, 8.27; N, 7.61.

Allo-1-hydroxy-2-(2-amino-5-methoxyphenyl)-8-propylperhydrochinolizin (IV′)—Eine Lösung von 0.32 g (III′) in 50 ccm Tetrahydrofuran wurde in einer Suspension von 0.6 g $LiAlH_4$ in 30 ccm Tetrahydrofuran ganz analog wie oben reduziert und aufgearbeitet. 0.17 g ölige Base vom $Sdp_{0.001}$. 220~230° (Badtemp.). Diazotest : positiv. In ihrem IR-Spektrum ist die Laktam-Bande von (III′) verschwunden.

2-Propyl-9-methoxy-1,3,4,6,7,12b-hexahydro-2*H*,12*H*-indolo[2,3-*a*]chinolizin (V)—(i) 1.0 g getrocknetes (IV) wurde mit 1.35 g Li-*tert*-Butoxyd und 9 g Benzophenon in 3.5 ccm Benzol suspendiert und in einem mit N_2-Strom gesättigten Einschlussrohr 72 Std. lang auf 110~120°(Ölbadtemp.) erhitzt. Nach 8 Std. wurde der Inhalt klar, färbte sich orangerot und nach 48 Std. schied sich eine gelatinartige Masse aus. Nach dem Abkühlen wurde das Reaktionsgemisch mit 10-proz. HCl extrahiert, die dabei in 10-proz. HCl ungelöste Substanz abfiltriert und diese bis zur vollkommenen Entfernung von Benzophenon mit Benzol gewaschen. Die HCl-Schicht wurde auch mit Benzol umgeschüttelt, wobei sich aus der Benzolschicht beim Stehen über Nacht Kristalle ausschieden, die abfiltriert und nochmals mit Benzol gewaschen wurden. Die gesamten kristallinischen Teile wurden mit der 10-proz. HCl-Schicht zusammen durch Ammoniak alkalisch gemacht, mit $CHCl_3$ ausgezogen und die $CHCl_3$-Phase nach dem Trocknen über Na_2SO_4 durch eine Al_2O_3-Säule chromatographisch gereinigt. 0.4 g farblose Nadeln (V) aus Äther vom Schmp. 108°. Diatotest: negativ. $[\alpha]_D^{26}$ +14.94° (EtOH, c=1.37, α=+0.205°). $C_{19}H_{26}ON_2 \cdot \frac{1}{2}H_2O$—Ber. : C, 74.23; H, 8.85; N, 9.11. Gef. : C, 74.18; H, 8.66; N, 8.95. UV λ_{max}^{EtOH} : 281~282 mμ (log ε 3.96). Farbreaktion eines Tetrahydro-β-carbolins nach Kaneko[4] : Blau.

Pikrat : Orangerote Nadeln aus MeOH, Zp. 232°. $C_{19}H_{26}ON_2 \cdot C_6H_3O_7N_3$—Ber. : C, 56.92; H, 5.54; N, 13.28. Gef. : C, 57.21; H, 5.60; N, 12.78.

Hydrochlorid : Nadeln aus Aceton vom Schmp. 219~220°.

(ii) 0.17 g (IV′) wurden ganz analog wie beim Versuch (i) mit 0.27 g Li-*tert*-Butoxyd und 1.8 g Benzophenon oxydiert und aufgearbeitet. Beim Chromatographieren des Reaktionsproduktes wurde der unter einer UV-Lampe fluorescierte Anteil (10 mg) gesammelt. Der letztere liess sich nicht kristallisieren, bildete jedoch ein nadelförmiges Pikrat vom Zp. 229~231°, welches bei einer Mischprobe mit dem beim Versuch (i) erhaltenen Pikrat vom Zp. 232° keine Depression des Auftau- u. Zersetzungspunktes zeigte. Diazotest : negativ. UV : λ_{max}^{EtOH} 281 mμ.

Zusammenfassung

2′-Hydroxydihydronichin (I) wurde durch die in der Tafel 1 angegebenen Reaktionsstufen in die Verbindung (V) mit dem Tetrahydro-β-carbolin-Skelett übergeführt. Die sterische Beziehung der Zwischenprodukte, (II), (II′), (III), und (III′) wurde diskutiert.

(Eingegangen am 29. November, 1958)

UDC 547.856.1 : 546.172

89. Kikuo Adachi : Studies on Condensed Systems of Aromatic Nitrogenous Series. XXI.[1] Mode of Formation of Quinazoline 3-Oxides from Quinazoline and Hydroxylamine.

(*Pharmaceutical Faculty, University of Kanazawa**)

In the preceding papers, a novel method was described for synthesizing quinazoline 3-oxide from corresponding quinazoline,[2] 4-alkoxyquinazoline,[3] and 4-methylquinazoline[1] with the action of hydroxylamine but without use of any oxidizing agent. 4-Aminoquinazoline and 4-methylquinazoline 3-oxides were obtained directly in the reaction with hydroxylamine, but quinazoline 3-oxide was prepared by treating an intermediate product with acetone.

* Tsuchitoribanaga-machi, Kanazawa (足立亀久夫).

1) Part XX : Yakugaku Zasshi, **77**, 514(1957).
2) K. Adachi : *Ibid.*, **77**, 507(1957).
3) *Idem.* : *Ibid.*, **77**, 510(1957).

The subject of the present paper concerns the reaction mechanism and chemical structure of the intermediate product.

The intermediate product, described in the preceding paper[1] as $C_{24}H_{22}O_4N_8$, was synthesized from quinazoline which was produced by the modified Gabriel's method,[4] but a new intermediate, $C_{16}H_{15}O_3N_5$ (I), was obtained from quinazoline by Elderfield's method.[5] Since thorough investigations have shown that both modified Gabriel's and Elderfield's methods yielded identical quinazoline, the formula $C_{24}H_{22}O_4N_8$ adopted formerly must be discarded. Another intermediate, $C_8H_9O_2N_3$ (II), was once obtained under the same reaction conditions, but this reaction was not reproducible. (I) was converted into the same compound (II) on chromatography over alumina in the course of purification. Thus the molecular formula $C_{16}H_{15}O_3N_5$ (I) will hereafter be used for the intermediate instead of the formula $C_{24}H_{22}O_4N_8$ mentioned in the preceding paper.

The chemical structure of the intermediates was determined as (I) and (II) from the following experimental results:

(1) (II) was readily soluble in sodium hydroxide solution and was precipitated out on decreasing the basicity of the solution with gaseous carbon dioxide. When treated with ferric chloride, (II) gave rise to a violet color.

(2) When (II) was treated with 2*N* sodium hydroxide solution at 90~95°, it was decomposed into formic acid, ammonia, and *o*-aminobenzaldehyde oxime. By the action of hydroxylamine and sodium acetate mixture on (II), *o*-formamidobenzaldehyde oxime was produced, and on acetylation with acetic anhydride (II) gave *o*-aminobenzaldehyde oxime O,N-diacetate.

(3) Treated with acetone, (II) gave quinazoline 3-oxide and acetone oxime. On the other hand, formylation of *o*-aminobenzaldehyde oxime with ethyl orthoformate or formic acid produced quinazoline 3-oxide, instead of the anticipated N-formyl derivative and the same oxide was also obtained from *o*-formamidobenzaldehyde oxime with conc. sulfuric acid.

These results indicate that the partial structure (IV) should be present in (II).

As in the case of acetone, it was expected that (II) should give quinazoline 3-oxide and oximes by the action of other carbonyl compounds. On treating (II) with *p*-nitrobenzaldehyde, (III) was obtained as pale yellow crystalline plates melting at 164° and having

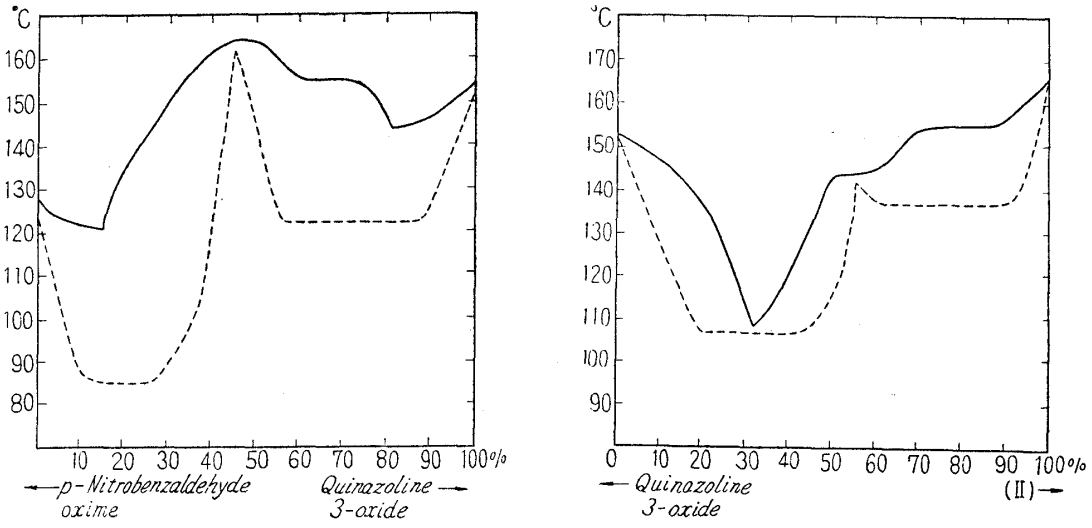

Fig. 1. Thermal Analysis Curve of (I) and (III)

4) K. Adachi: *Ibid.*, **75**, 1423(1955).
5) R.C. Elderfield, T.A. Williamson, W.J. Gensler, C.B. Kremer: J. Org. Chem., **12**, 405(1947).

the molecular formula $C_{15}H_{12}O_4N_4$. When decomposed with conc. sulfuric acid, (III) gave quinazoline 3-oxide and *p*-nitrobenzaldehyde oxime. On the other hand, (III) was obtained from equimolar amounts of quinazoline 3-oxide and *p*-nitrobenzaldehyde oxime in ethanol solution, indicating that (III) was a molecular compound, which was also proved by thermal analysis (Fig. 1).

Since quinazoline 3-oxide was produced from *o*-aminobenzaldehyde oxime, some other oxime not involved in the formation of quinazoline 3-oxide but reacting with the carbonyl compounds must be present in (II).

From the above experimental results, the chemical structure of (II) was deduced as shown in Chart 1 and all other possible structures with the same molecular formula were left out of consideration, as well as the hypothesis that it was a molar compound of quinazoline 3-oxide and hydroxylamine or aminoquinazoline oxide hydrate.

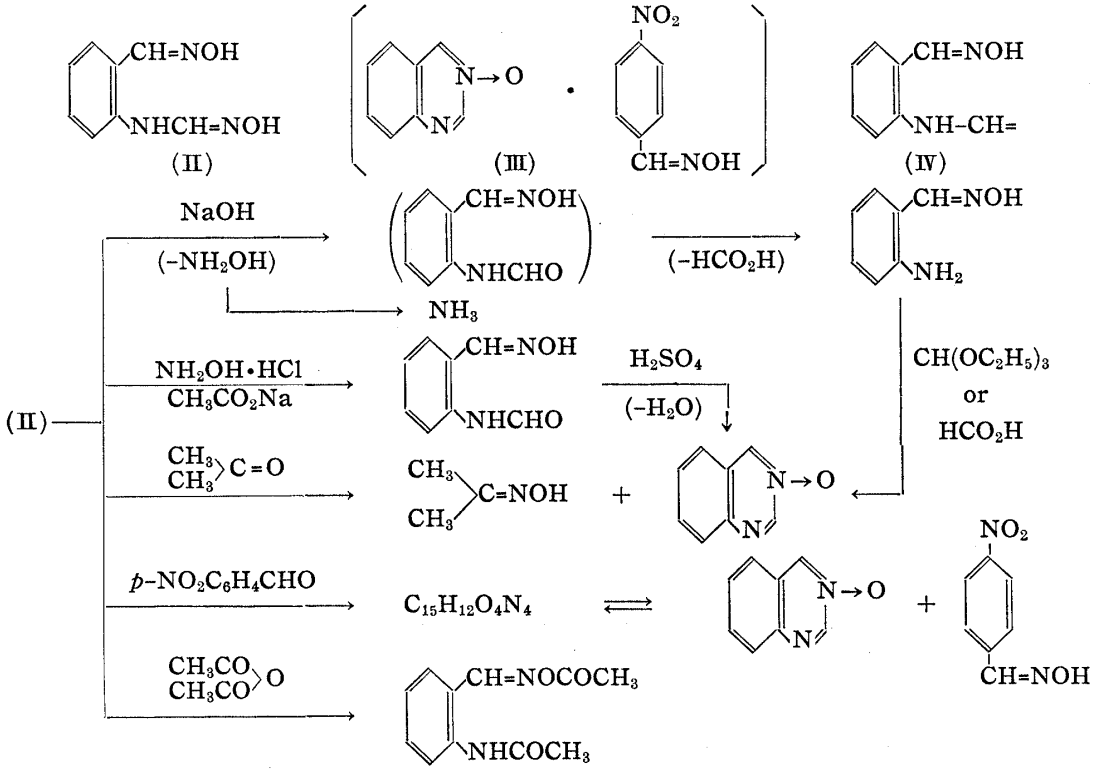

Chart 1.

(4) The other intermediate (I) had the same behavior as (II) toward some of the reagents: (I) gave rise to a brown color with ferric chloride, and quinazoline 3-oxide and acetone oxime were obtained by treating it with acetone. When (I) was treated with *p*-nitrobenzaldehyde, it gave quinazoline 3-oxide and (III), indicating the presence of an

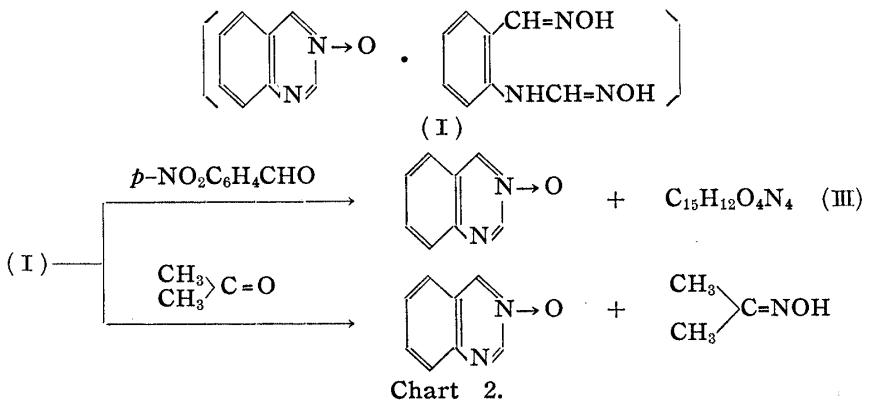

Chart 2.

excess of quinazoline 3-oxide in compound (I).

From (4) and the result of thermal analysis (Fig. 1), it was confirmed that (I) was a molecular compound of quinazoline 3-oxide and (II).

The mechanism of the specific reaction with hydroxylamine, in accordance with the structure of the intermediates as shown above appears to be as shown in Chart 3.

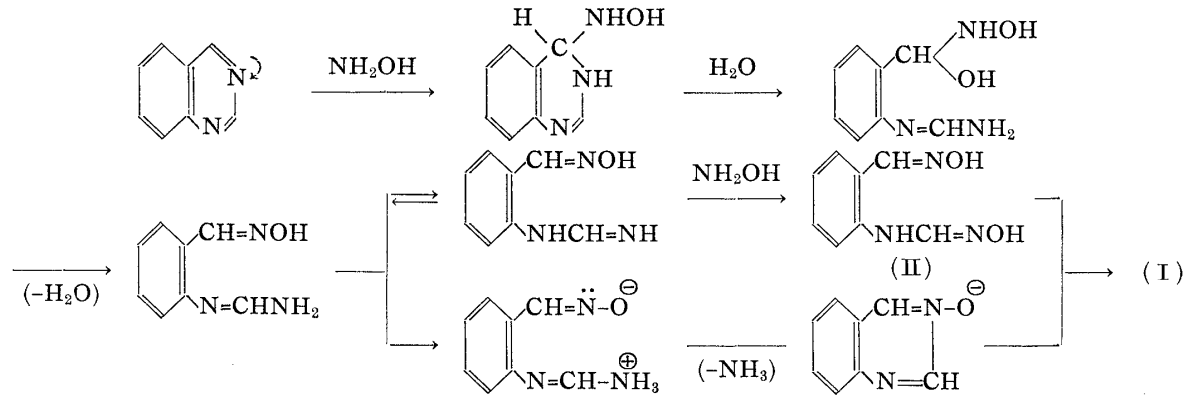

Chart 3.

In the case of 4-alkoxy- and 4-methylquinazoline no intermediate corresponding to (I) or (II) was obtained, but it may be safely concluded that the reaction proceeds in like manner.

The author expresses his deep gratitude to Prof. Eiji Ochiai of the University of Tokyo for his kind guidance throughout the course of this study. Thanks are also due to Prof. Yoshihisa Mizuno of the University of Hokkaido and Prof. Kotaro Takahashi of the University of Kanazawa for their kind advices and suggestions, and to Mr. Yoshitaka Itatani of the University of Kanazawa for the elemental analysis.

Experimental

Quinazoline—It was produced from 4-chloroquinazoline by Elderfield's method. m.p. 45~48°, b.p_{15} 115~118°. *Anal.* Calcd. for $C_8H_6N_2$: C, 73.84; H, 4.61. Found : C. 74.08; H, 5.03. The IR spectrum of this sample showed satisfactory agreement with the authentic spectrum.[6]

Reaction of Quinazoline and Hydroxylamine—(1) Preparation of $C_{16}H_{15}O_3N_5$ (I) : A mixture of 5 g. of quinazoline, 5.5 g. of $NH_2OH \cdot HCl$, and 40 cc. of 2*N*NaOH was shaken till a clear solution was obtained. After 1~2 hr. an oil separated out, which solidified in 2~3 hr., and the reaction mixture was allowed to stand for 12~15 hr. at room temperature. When the product was collected and dried in air, 5.5 g. of pale yellow needles, m.p. 110~120°(decomp.), were obtained. By recrystallization from 50% MeOH, white needles were obtained, m.p. 145°(decomp.); 1.5 g. *Anal.* Calcd. for $C_{16}H_{15}O_3N_5$: C, 59.07; H, 4.61; N, 21,54. Found : C, 58.74; H, 4.28; N, 21.64.

This intermediate is soluble in NaOH solution, MeOH, EtOH, and acetone, and insoluble in Et_2O and benzene, and colored brown with $FeCl_3$.

(2) Preparation of $C_8H_9O_2N_3$ (II) : Acetone solution of (I) was placed on 1.5×10 cm. column of alumina and developed with an acetone-benzene (2:1) mixture. (II) was thereby eluted from the column and white needles were obtained by repeated recrystallization from 50% MeOH, m.p. 167~169° (decomp.). Yield, 0.1 g. from 1 g. of (I). *Anal.* Calcd. for $C_8H_9O_2N_3$: C, 53.68; H, 5.02; N, 23.46; mol. wt., 179. Found : C, 53.74; H, 5.46; N, 23.01; mol. wt. (Barger's method, MeOH and EtOH) 170, 185.

The intermediate (II) is soluble in NaOH solution, MeOH, and EtOH, silghtly soluble in $CHCl_3$ and water, and insoluble in Et_2O, benzene, and Na_2CO_3 solution. The product (II) colored violet with $FeCl_3$.

A pale yellow solution was obtained when 0.1 g. of (II) was dissolved in 10 cc. of 5% NaOH, and on decreasing the basicity of solution with CO_2, white needles precipitated, m.p. 163~165°(decomp.). Yield, 0.07 g. This product was identified with (II) by mixed m.p. test and IR spectra.

Alkaline Cleavage of (II)—An alkaline solution of (II) (20 cc. of 2*N*NaOH and 0.1 g. of (II)) was heated on a steam bath at 90~95° for 2 hr. The color of the solution changed from deep red to yellow and a gas evolved vigorously. The gas was trapped in 50 cc. of *N*HCl solution and was identified

6) H. Culbertson, J.C. Decius, B.E. Christensen : J. Am. Chem. Soc., **74**, 4834(1952).

to be NH_3 by converting it into benzamide (m.p. 125°). After cooling and decreasing the basicity of solution with CO_2, *o*-aminobenzaldehyde oxime was obtained, m.p. 130~132°. Yield, 0.07 g. HCOOH from the filtrate was identified by reaction with chromotropic acid.

Acetylation with Acetic Anhydride—A solution of 0.1 g. of (II) in 1 cc. of Ac_2O was allowed to stand for 12~15 hr. at room temperature. The solution was poured into 5 cc. of ice water, neutralized with $NaHCO_3$, and extracted with $CHCl_3$. After evaporation of $CHCl_3$, the residue was recrystallized from cyclohexane to *o*-aminobenzaldehyde oxime O,N-diacetate, m.p. 129°. Yield, 0.05 g. The product was identified with an authentic sample by mixed m.p. determination. *Anal.* Calcd. for $C_{11}H_{12}O_3N_2$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.21; H, 5.30; N, 12.81.

Decomposition with Hydroxylamine and Sodium Acetate—A mixture of 0.5 g. of (II), 0.6 g. of $NH_2OH \cdot HCl$, 0.7 g. of AcONa, and 10 cc. of water was heated on a steam bath at 90~95° for 2 hr. After cool, the crystals produced were washed with 25 cc. of Et_2O. The Et_2O-insoluble crystals, m.p. 145~149°(decomp.), were recrystallized from water to white prisms, m.p. 157°(decomp.). Yield, 0.1 g. *Anal.* Calcd. for $C_8H_8O_2N_2$: C, 58.54; H, 4.88; N, 17.07. Found: C, 58.53; H, 5.11; N, 16.76.

This substance was readily soluble in NaOH but insoluble in Na_2CO_3 solution, colored brown with $FeCl_3$, and gave quinazoline 3-oxide by dehydration with conc. H_2SO_4, and *o*-aminobenzaldehyde oxime by decomposition with NaOH. The product was presumed to be *o*-formamidobenzaldehyde oxime from its properties and the result of elemental analysis. From Et_2O filtrate, *o*-aminobenzaldehyde oxime was obtained, m.p. 130°. Yield, 0.3 g. Formylation of *o*-aminobezaldehyde oxime with formic acid gave a low melting product (m.p. 80~110°), which could not be purified by recrystallization from either water or any organic solvent, and quinazoline 3-oxide.

Preparation of Quinazoline 3-Oxide—(1) From (I): A mixture of 0.5 g. of (I) and 10 cc. of acetone was heated at 95° for 5 hr. in sealed tube. After the reaction was completed, acetone was removed by distillation and 10 cc. of Et_2O was added to the residue, from which 0.3 g. of acetone-insoluble crystals, m.p. 148~150°, was obtained. The product was recrystallized from acetone, m.p. 153°. Et_2O was evaporated from the filtrate and the residue of m.p. 55~60° was identified as acetone oxime, 0.03 g.

(2) From (II): A mixture of 0.5 g. of (II) and 5 cc. of acetone was treated as in (1), and 0.11 g. of quinazoline 3-oxide and 0.02 g. of acetone oxime were obtained.

(3) From *o*-Aminobenzaldehyde Oxime with Ethyl Orthoformate: A mixture of 0.6 g. of *o*-aminobenzaldehyde oxime and 5 cc. of ethyl orthoformate was heated at 140° in an oil bath for 1 hr. and unchanged ethyl orthoformate was recovered under a reduced pressure. The residue was recrystallized from acetone to 1.1 g. of quinazoline 3-oxide, m.p. 150~152°.

(4) From *o*-Aminobenzaldehyde Oxime with Formic Acid: A mixture of 3 g. of *o*-aminobenzaldehyde oxime and 20 cc. of 100% HCOOH was heated on a steam bath at 90~95° for 2 hr., poured into 50 cc. of cold water, and neutralized with $NaHCO_3$. A low-melting product (m.p. 80~110°), which could not be purified by means of recrystallization, was obtained (1 g.). The filtrate was extracted with $CHCl_3$ and 0.8 g. of white crystals, m.p. 150°, was obtained by recrystallization from acetone.

(5) From *o*-Formamidobenzaldehyde Oxime: A mixture prepared by adding 0.15 g. of *o*-formamidobenzaldehyde oxime to 2 cc. of conc. H_2SO_4 at a low temperature was allowed to stand at room temperature for 3 hr., poured into 20 cc. of ice water, and neutralized with $NaHCO_3$. The solution was extracted with $CHCl_3$ and quinazoline 3-oxide was obtained on removal of $CHCl_3$ and by recrystallization from acetone, m.p. 150°. Yield, 0.1 g.

The products prepared by the above methods (1) to (5) were identified with an authentic sample of quinazoline 3-oxide by mixed m.p. determination.

Reaction between (I) or (II) and *p*-Nitrobenzaldehyde—(1) A mixture of 0.5 g. of (I), 0.3 g. of *p*-nitrobenzaldehyde, and 5 cc. of EtOH was refluxed on a steam bath for 2 hr. When cool, yellow crystals separated out, m.p. 160~164° (0.2 g.), and recrystallization from EtOH gave pale yellow plates, m.p. 164°. *Anal.* Calcd. for $C_{15}H_{12}O_4N_4$: C, 57.69; H, 3.85; N, 17.95. Found: C, 57.87; H, 4.03; N, 18.18.

EtOH was removed from the filtrate by distillation, yellow needles were obtained, and recrystallized from acetone to quinazoline 3-oxide, m.p. 150~152° (0.08 g.). The product was identified with an authentic sample by mixed m.p. determination.

(2) A mixture of 0.1 g. of *p*-nitrobenzaldehyde and 1 cc. of EtOH was refluxed on a steam bath for 2 hr. After cool, yellow crystals were obtained, m.p. 160° (0.13 g.), and (III) was obtained by recrystallization from EtOH, m.p. 164°.

Decomposition of (III) with conc. Sulfuric Acid—A mixture prepared by adding 0.5 g. of (III) to 4 cc. of conc. H_2SO_4 at a low temperature was allowed to stand at room temperature for 20 hr. By pouring the mixture into 50 cc. of ice water, *p*-nitrobenzaldehyde oxime, m.p. 130°, 0.18 g., was obtained, after recrystallization from benzene. The crystals were identified with an authentic sample by mixed m.p. *Anal.* Calcd. for $C_7H_6O_2N_3$: N, 16.86. Found: N, 17.03. After basification

with NH_4OH, the filtrate was extracted with $CHCl_3$ (100 cc.), $CHCl_3$ was distilled off, and quinazoline 3-oxide was obtained by recrystallization from acetone, m.p., 152° (0.11 g.). It was not depressed on admixture with an authentic sample.

Reaction of Quinazoline 3-Oxide and *p*-Nitrobenzaldehyde Oxime (Preparation of (III))—A mixture of 0.05 g. of quinazoline 3-oxide, 0.05 g. of *p*-nitrobenzaldehyde oxime, and 2 cc. of EtOH was refluxed on a steam bath for 10 min. After cool, a crystalline substance, m.p. 164° (0.086 g.), was obtained and was purified by recrystallization from benzene, m.p. 164°, undepressed on admixture with the former sample of (III). *Anal.* Calcd. for $C_{15}H_{12}O_4N_4$: N, 17.93. Found: N, 17.76.

Thermal Analysis—Results obtained from thermal analyses by the usual method are given below.

Quinazoline 3-oxide and *p*-nitrobenzaldehyde oxime

Quinazoline 3-oxide (%)	Quinazoline 3-oxide (mg.)	*p*-Nitrobenzaldehyde oxime (mg.)	Softening Point (°C)	m.p. (°C)
0			127	127
10.1	2.313	20.553	85	120.5
15.5	3.248	17.706	85	120
19.9	3.222	12.967	85	135
25.4	6.426	18.967	84.3	142
27.3	5.445	14.498	85	145
38.2	8.523	13.764	105	162.5
45.0	4.340	5.344	163.5	164
50.0	4.024	4.027	145	164
53.8	4.811	4.129	122	162
60.4	6.054	3.969	122	154.5
72.5	7.400	2.805	122	154.0
75.0	7.464	2.508	121	152
81.5	4.883	1.109	123	143
89.3	8.820	1.060	123	145
100.0			153	153

Quinazoline 3-oxide and (II)

Quinazoline 3-oxide (%)	Quinazoline 3-oxide (mg.)	(II) (mg.)	Softening Point (°C)	Decomp. Point (°C)
0			165	169
4.4	0.718	16.321	145	160~162
6.5	1.172	18.981	139	160
8.9	0.805	6.411	137	155
14.0	1.319	8.576	138	155
16.9	1.066	5.254	138	156~158
21.7	1.800	6.959	139	155~157
28.4	1.778	4.488	139	155
41.0	4.763	7.089	139	145~147
42.4	3.010	4.092	140	145
45.0	2.962	3.621	142	145
46.2	2.883	3.793	125	145
50.6	2.334	2.277	112	145
59.6	4.656	3.533	107	129
62.8	4.167	2.485	106	117
69.9	4.759	2.200	105~107	107
71.2	6.823	2.759	105	112~115
79.9	7.892	1.988	107	135
84.9	4.546	0.823	120	141
100.0			m.p. 153	

Summary

On the evidence of the following experimental results the chemical structures (I) and (II) were assigned respectively to the intermediates, $C_{16}H_{15}O_3N_5$(I) and $C_8H_9O_2N_3$(II), which were prepared by the reaction of quinazoline and hydroxylamine.

(1) On alkaline decomposition, (II) gave formic acid, ammonia, and *o*-aminobenzal-

dehyde oxime.

(2) By the action of hydroxylamine and sodium acetate mixture, (II) formed *o*-formamidobenzaldehyde oxime.

(3) Quinazoline 3-oxide was obtained by terating (I) or (II) with acetone or *p*-nitrobenzaldehyde, by formylation of *o*-aminobenzaldehyde oxime with formic acid or ethyl orthoformat, and by dehydration of *o*-formylaminobenzaldehyde oxime with conc. sulfuric acid.

(4) (I) behaved like (II) toward ferric chloride, acetone, and sodium hydroxide and was proved to be a molecular compound of quinazoline 3-oxide and (II).

Also, based on the chemical structure of the intermediates, the mechanism of the specific hydroxylamine reaction shown in Chart 3 is proposed.

(Received December 5, 1958)

UDC 615.412-011 : 537.221

90. **Jun Hasegawa**: Studies on Tablets. IV.[1] Frictional Electrification of Crystalline Medicines.

(*Faculty of Pharmaceutical Sciences, University of Tokyo**)

It is a well known phenomenon that in two insulators like silk, glass, fur, or ebonite, when rubbed with each other and separated, a static charge of opposite signs is produced on their surface. With recent advances in industrial processes several undesirable side effects due to static charge such as adhesion of small dust particles to synthetic fibers became evident.

The effect of this phenomenon is also found in the fields of pharmacy. When crystalline Aspirin is crushed and mixed in a mortar, the powder adheres so firmly to the surface of the tools employed that its removal is very difficult. When medicines are sieved or filled in bottles by automatic machines, adhesion of crystals to wire nets, container surfaces, or to each other may be so great as to hinder or even make it impossible to complete the process. When crystals of Aspirin are washed with benzene after acetylation in the course of manufacture, static charges from friction appear between the crystals and the container.

Depending upon the amount, the electrical capacity of apparatus, and the electrical resistance to leakage, thousands of volts may be formed and becomes a dangerous fire hazard.[2]

Dry crystals may adhere to the glass wall of ampules giving an erronous impression of wetness. The effect of static electricity may also be observed in tablet manufacture.

In spite of the many side effects of static electricity, as described above, very few reports on the phenomenon have been presented. It is the purpose of this study to present model experiments on frictional electrification of crystalline medicine and to discuss preventive measures against formation of static charges when handling powders.

The author wishes to express his gratitude to Prof. H. Nogami of this University for his kind guidance and encouragement and to Prof. Y. Suge and Dr. Z. Otaki, Laboratory of Applied Physics, University of Tokyo, for their helpful suggestions and technical guidance throughout this study.

* Hongo, Tokyo (長谷川 淳).

1) Part III: This Bulletin, **5**, 15(1957).

2) N. Makino, *et al.*: Bull. Electro-Technical Lab., **16**, 273.