wings were C_{34} to C_{36}, those in both blood and larva, C_{21} to C_{27}, and those in mulberry leaf, C_{16} to C_{20}. Large hydrocarbons, C_{32}, C_{34}, C_{38}, C_{40} and C_{41}, were found in the wings.

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113. Abdul-Mohsen M.E. Omar*1 and Shun-ichi Yamada*2 : Studies on Thioamides. III.*3 A New Synthetic Method of the 3,4-Dihydroisoquinoline Derivatives by the Cyclodesulfurization of Thioamides.

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In a preliminary step towards the realization of our exploratory project on using thioamides in the synthesis of the 3,4-dihydroisoquinoline nucleus, the present authors have recently accomplished the cyclization of several N-(2-arylethyl) thioamides with the general acidic condensing agents,[1] as reported for the cyclodehydration of N-phenethylamides under the Bischler-Napieralski reaction conditions,[2] and got the required 1-substituted-3,4-dihydroisoquinoline derivatives in good yield.

In continuation of this project, investigations were directed to take advantage of the presence of the active sulfur atom in these thioamides and attempt their cyclization, independently from the classical Bischler-Napieralski reaction and under milder conditions, by employing the common desulfurizing agents which can act as Lewis acids on such active centers. A part of the successful results of this investigation has been published, in a brief communication,[3] in advance to the present full detailed demonstration of the nature of this new type of ring closure as well as its establishment in the synthesis of the 3,4-dihydroisoquinoline derivatives.

Choosing N-homoveratrylthiobenzamide (Ia) as a model compound of the N-(2-arylethyl) thioamides series, several experiments were carried out to effect its cyclization with silver nitrate,[4~6] mercuric cyanide,[7] mercuric acetate,[8~10] mercuric oxide,[11~17] metallic mercury, iodine,[18,19] triethyl phosphite,[20~25] calomel, ethylmercuric chloride,

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methyl iodide,[26~31] zinc chloride or stannic chloride in various polar and non polar solvents, as reported for desulfurization of many organic sulfur compounds whose structure does not allow cyclization of the desulfurized products, but the results were always disappointing due to quantitative conversion of the starting thioamide (Ia) to the corresponding acid amide (XII) in some cases or quantitative recovery of Ia in the others as summarized in Table I. Moreover, when either Raney nickel or degassed Raney nickel was employed under different conditions,[32] the starting thioamide (Ia) was always recovered in large amounts together with minor yields of N-benzylidene-3,4-dimethoxyphenethylamine whose structure was established by being identical in infrared spectra with the authentic sample prepared from equimolecular amounts of homoveratrylamine and benzaldehyde according to the reported method.[33]

The first signs of success were achieved when experiments started with mercuric chloride.[34~40] This reagent proved to possess a great efficiency in cyclizing the thioamide (Ia) smoothly and fulfilling the desired purpose.

However, during the establishment of the reaction conditions with mercuric chloride, it was found that the yield of cyclized 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) was greatly influenced by the variations in the molar ratio of the reactants as well as by the nature of solvent. In acetonitrile, the maximum yield of IVa was obtained when three moles of mercuric chloride were stirred with one mole of the thioamide (Ia) under reflux for seven hours. This yield could not be reached when either one or two moles of mercuric chloride were used for each mole of Ia even under reflux for sixty-five hours. In addition, the presence of a further excess of mercuric chloride was proved to be without any effect in this cyclodesulfurization reaction as evidenced from the constant yield of IVa from the reactions of either three, four, five or six moles of mercuric chloride with one mole of Ia under reflux for seven hours. In benzene or dimethylformamide on the other hand, the reaction could not be brought to completion with three or four moles of mercuric chloride and the yield of IVa was remarkably poor after seven hours of reflux. When reflux was extended to thirteen

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Table I. Unsuccessful Cyclodesulfurization of N-Homoveratrylthiobenzamide (Ia) with Various Desulfurizing Agents

D. A.[a]	Moles of D. A. per mole of Ia	Reaction conditions		Products (%)	
		Solvent	Reflux period (hr.)	Recovd. Ia	Prodcd. XII
$AgNO_3$	1.7	MeOH	0.5	—	Quant.[a]
〃	1	abs. EtOH	1.0	—	〃
〃	3	CH_3CN	r.t. 2.0	—	〃
$Hg(CN)_2$	3	〃	3.0	unidentified[b]	
$Hg(OOCCH_3)_2$	3	〃	9.25	—	Quant.[a]
HgO	3	EtOH	5.0	—	〃
Hg	excess	pyridine	4.0	Quant.[a]	—
I_2	2	abs. EtOH	r.t. 24.0	〃	—
$(C_2H_5O)_3P$	2	EtOH	1.0	〃	—
〃	7	nitrobenzene	(170°) 1.5	Charring resid.	
〃	1	pyridine	1.5	Quant.[a]	—
〃	4	toluene	1.5	〃	—
〃	4	xylene	1.5	〃	—
〃	1	DMF	1.5	〃	—
〃	excess	——	2.0	〃	—
Hg_2Cl_2	2	CH_3CN	6.0	〃	—
C_2H_5HgCl	3	〃	7.0	〃	—
〃	3	DMF	5.0	〃	—
CH_3I	3	EtOH	2.0	〃	—
$ZnCl_2$	3	CH_3CN	10.0	〃[c]	—
〃	3	〃	20.0	94[c]	—
$SnCl_4$	1	〃	9.0	mixture of Ia and XII	
Raney Ni	excess	abs. EtOH	5.5	48	others[d]
〃	〃	abs. EtOH /N_2	7.5	70	〃[d]
Degassed Raney Ni	〃	acetone	3.5	94	〃[d]

a) Abbreviations: D.A.=desulfurizing agent. Quant.=quantitative.
b) Dirty residue which exhibited a weak band of C=N in IR was produced.
c) Traces of isoquinoline were detected by UV.
d) Schiff's base was produced in 35.8, 19.5% and traces respectively.

hours in benzene, IVa was obtained in high yield as shown in Table II, but it was still inferior to that produced in case of using acetonitrile. In this manner, both benzene and dimethylformamide were proved to be inefficient to provide the proper medium for this cyclodesulfurization reaction and, in accordance with the nature of reaction in both solvents, it was thought that the insolubility of mercuric chloride in benzene is responsible for the retardation of cyclization in the reacting heterogeneous mixture while in dimethylformamide, the production of mercuric sulfide, a product which was not obtained during cyclization in acetonitrile or benzene, may be the principal factor for worsening the yield of the required product in this solvent.

Experimentally, the reaction of three moles of mercuric chloride with one mole of N-homoveratrylthiobenzamide (Ia) in acetonitrile under reflux for seven hours accompanied with various changes in the color of the original reaction solution from yellow to white turbid, yellow with evolution of hydrogen chloride gas at the beginning of reflux and finally to deep yellow golden solution with a white creamy amorphous powder suspended in it. This powder was found to be inorganic product whose components are mercury, sulfur and chlorine. The preliminary analysis of this product proved the presence of mercury in excess than the equivalent amount of sulfur but the actual percentage of each component was difficult to determine because of the several variations in the results of the elemental analysis.

Evaporation of the golden yellow reaction solution afforded a golden yellow frothy

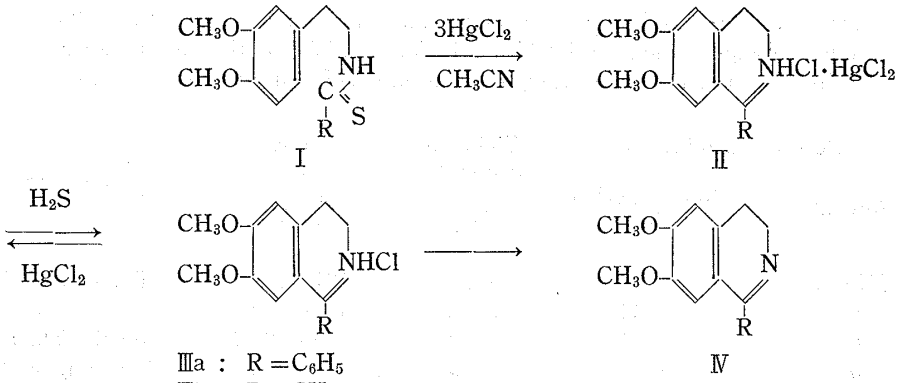
Table II. The Maximum Yield of Cyclized 1-Phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) by Using Different Molar Ratios of Mercuric Chloride and N-Homoveratrylthiobenzamide (Ia) in Various Solvents

Moles of $HgCl_2$ per mole of Ia	Reaction conditions: Solvent	Reaction conditions: Reflux period (hr.)	Yield of crude IV (%)	Crude base m.p. (°C)	Other products[a]
1	CH_3CN	7	24.7	121~123	Th. am. & Ac. am.[b]
1	〃	36	33.8	120~122	〃
1	〃	65	40.0	120~121.5	mostly Th. am.
2	〃	7	55.5	122~123	Th. am. & Ac. am.
2	〃	16	73.8	121~123	〃
2	〃	36	73.8	121~123	〃
2	〃	65	75.6	120~121	〃
3	〃	2	62.2	119~121	〃
3	〃	3	66.6	119~121	〃
3	〃	4	77.8	118~120	〃
3	〃	5	84.4	119~121	〃
3	〃	6	84.4	120~122	〃
3	〃	7	84.8	122~123	Ac. am.
4	〃	7	86.2	122~123	〃
5	〃	7	85.1	121~123	〃
6	〃	7	85.3	120~122	〃
3	benzene	7	56.5	120~121.5	〃
3	〃	10	67.7	119~121	〃
3	〃	13	79.0	118~120	〃
4	〃	7.25	57.1	120~122	〃
3	DMF	1	45.1	114~116	〃
3	〃	7	20.0	114~116	〃
3	〃	(at 100°) 7	33.8	117~119	〃
4	〃	(at 110°) 7	33.8	116~118	〃

a) Identified by IR spectra in $CHCl_3$ and TLC.
b) Abbreviations: Th. am.=the thioamide (Ia), Ac. am.=the acid amide (XII).

residue which on recrystallization from ethanol gave the corresponding 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (IIa) identified by analysis, similarity in infrared and ultraviolet spectra as well as by mixed melting point with the authentic sample prepared by stirring equimolecular amounts of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (IIIa) and mercuric chloride in acetonitrile at room temperature for two hours. This complex, when treated with hydrogen sulfide gas in acetonitrile containing few drops of dil. aqueous hydrochloric acid gave black precipitate of mercuric sulfide. The filtration of such precipitate followed by evaporation of the filtrate yielded yellowish white needles which proved to be the isoquinoline hydrochloride (IIIa) by similarity in infrared and ultraviolet spectra as well as by mixed melting point with the previously prepared authentic sample.[1] Treating an aqueous soltion of IIIa with dil. aqueous sodium hydroxide solution afforded the required 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) as fine white prisms which were identical in infrared and ultraviolet spectra and showed no melting point depression with the authentic sample.[1] The reaction sequence is illustrated in Chart 1.

The infrared spectra of the isoquinoline hydrochloride mercuric chloride complex (IIa), the isoquinoline hydrochloride (IIIa) as well as 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline mercuric chloride complex (V), prepared from equimolecular amounts of the free isoquinoline base (IVa) and mercuric chloride, were found to be different in many respects when measured in the solid state as demonstrated in Fig. 1. The examina-



IIIa : R = C_6H_5
IIIb : R = CH_3
IIIc : R = $C_6H_5CH_2$

Chart 1.

tion of these spectra could not lead to definite conclusion on the actual structure of IIa because variations in band positions were observed in many regions indicating that mercuric chloride is not attached to a specific functional group of the organic product but involved in the whole electronic vicinity of the molecule. In addition, the insolubility of this product in almost all the organic solvents except dimethylformamide and acetonitrile, of which the former obscures the spectra in many desired regions and the solubility in the latter is not enough to produce clear spectra, made it difficult to determine the spectra in solutions.

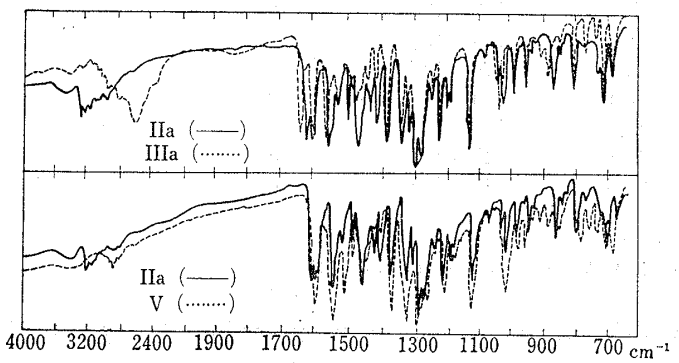


Fig. 1.

Reaching these results, it became of interest to synthesize the possible intermediates of this cyclodesulfurization reaction, by performing experiments under moderate conditions which would not allow cyclization of N-homoveratrylthiobenzamide (Ia), in order to establish the reaction mechanism. In this respect, a mixture of equimolecular amounts of Ia and mercuric chloride was stirred in acetonitrile at room temperature for two hours to afford a white voluminous chalky powder which on recrystallization from ethanol gave transparent needles whose infrared spectra exhibited a shift of 50 cm^{-1} to the lower frequency in the N-H stretching vibration band and showed several other differences in the regions where the C=S group of the thioamide (Ia) is absorbed as demonstrated in Fig. 2. The elemental analysis of this product indicated its structure as being the corresponding N-homoveratrylthiobenzamide mercuric chloride adduct (VI) whose composition involves the combination of equimolecular amounts of Ia and mercuric chloride.

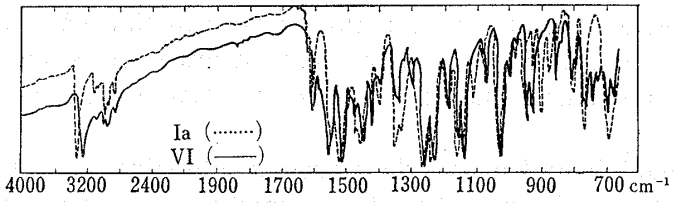


Fig. 2.

Furthermore, when mixtures of either two or three moles of mercuric chloride and one mole of Ia were treated under the above conditions, the thioamide mercuric chloride adduct (VI) was obtained as the sole product in every case as evidenced from elemental analysis, identity in the infrared spectra as well as by mixed melting point of each product with the other.

In the above experiments, although it was proved that the thioamide mercuric chloride adduct (Ⅵ) is the first intermediate in this cyclodesulfurization reaction, it was believed that according to the nature of reaction at room temperature, the insolubility of this adduct in acetonitrile will be effective in preventing it from further reaction with excess mercuric chloride and hence it remains unchanged. Therefore, our efforts were directed to trap the actual intermediates by performing experiments under reflux and interrupting their progress at various intervals to check the nature of the different products.

Unfortunately, as shown in Table Ⅲ, these attempts were fruitless to realize the desired purpose because in most experiments, the 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (Ⅱa) was the prominent product. In addition, yellow short rods (Ⅶ) were obtained in almost all experiments and identified as being a complex of two moles of the isoquinoline hydrochloride (Ⅲa) and one mole of mercuric chloride by analysis, chemical confirmation as shown in Chart 2, as well as by similarity in the infrared spectra with the authentic sample prepared from different routes as demonstrated in Chart 3.

Table Ⅲ. Separation of the Different Cyclodesulfurization Reaction Products from the Reactions of N-Homoveratrylthiobenzamide (Ia) with Various Moles of Mercuric Chloride in Acetonitrile

Exp. No.	Moles of $HgCl_2$ per mole of Ia	Reflux period (hr.)	Product (%)					
			Recovd. Ia	Ⅱa	Ⅲa	Ⅵ	Ⅶ	Other products[a]
1	1	65	20	6.3	13	—	31.6	Th. am. & Ac. am.[b]
2	2	7	—	24.0	—	3.2	32.3	〃
3	2	65	—	52.9	—	—	12.1	〃
4	3	1	—	24.6	—	10.	4.4	Ac. am.
5	3	2	—	64.4	—	—	2.0	〃
6	3	3	—	66.6	—	—	2.7	〃
7	3	4	—	72.3	—	—	2.0	〃
8	3	5	—	78.6	—	—	2.0	〃
9	3	6	—	81.7	—	—	—	〃
10	3	7	—	81.5	—	—	1.4	〃

a) These products were obtained after passing H_2S in the dirty residue which could not be purified or characterized by IR spectra. Identification of these products was made by IR and TLC.
b) Abbreviations: Th. am.=the thioamide (Ia), Ac. am.=the acid amide (Ⅻ).

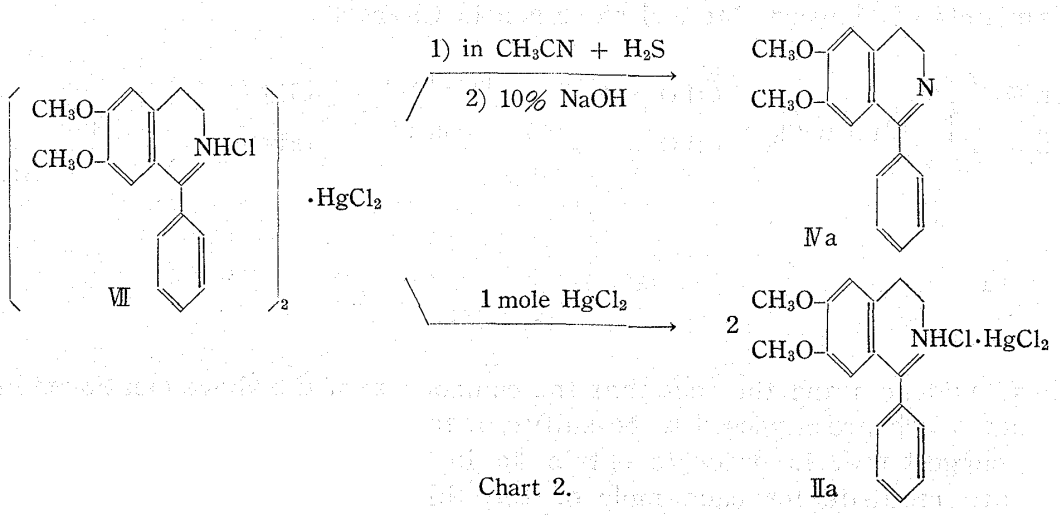


Chart 2.

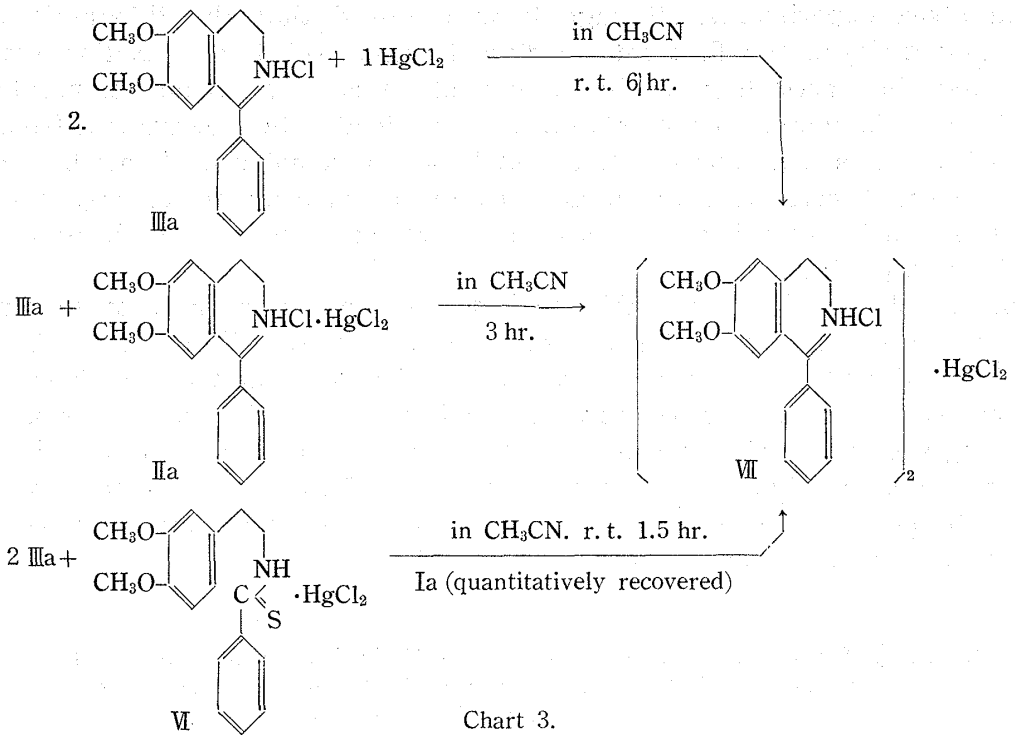


Chart 3.

As shown in Table Ⅲ, the yield of Ⅱa was increasing and the yield of Ⅶ was inversely decreasing when the molar ratio of mercuric chloride per mole of Ia increased. Moreover, in some experiments (No. 2 and 4), the N-homoveratrylthiobenzamide mercuric chloride adduct (Ⅵ) was trapped in minute amounts.

On the other hand, the production of Ⅶ was always favored when the ratio of Ⅲa and mercuric chloride or its thioamide adduct (Ⅵ) in the reaction mixture was 2:1 and the reaction of two moles of Ⅲa with one of Ⅵ at room temperature, gave one mole of Ⅶ and quantitative recovery of Ia (Chart 3). Moreover, the further reaction of Ⅶ with one mole of mercuric chloride afforded Ⅱa as shown in Chart 2.

This demonstrates that when sufficient mercuric chloride to form Ⅱa is present in the reaction mixture, Ⅱa is formed as the principal product (Exp. No. 4~10 in Table Ⅲ) while in presence of insufficient amount of mercuric chloride, the yield of Ⅶ increases (Exp. No. 1~3 in Table Ⅲ).

In other experiments, when the isoquinoline hydrochloride mercuric chloride complex (Ⅱa) was reacted with thioamide (Ia), it gave Ⅵ and Ⅶ at room temperature but when refluxed, no thioamide mercuric chloride adduct (Ⅵ) was produced and only small amounts of Ⅶ were obtained as shown in Chart 4.

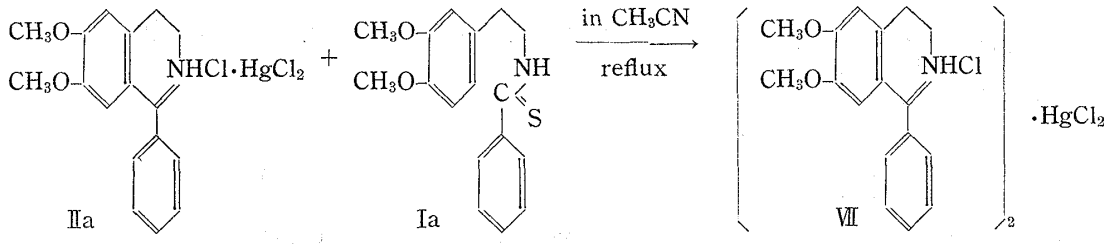


Chart 4.

These evidences and the fact that the components of the above mentioned inorganic by-product which are supposed to be sulfur, mercury and chloride with a rough ratio of 1:2:2, suggest that in order to obtain Ⅱa in good yield, three moles of mercuric chloride are requisite for each mole of the thioamide (Ia), of which, one mole of

mercuric chloride is employed for making the isoquinoline hydrochloride complex (IIa) and the residual two moles are consumed to cyclize Ia.

In illustrating these findings, a mechanism for the cyclodesulfurization of N-homoveratrylthiobenzamide (Ia) was tentatively proposed as shown in Chart 5.

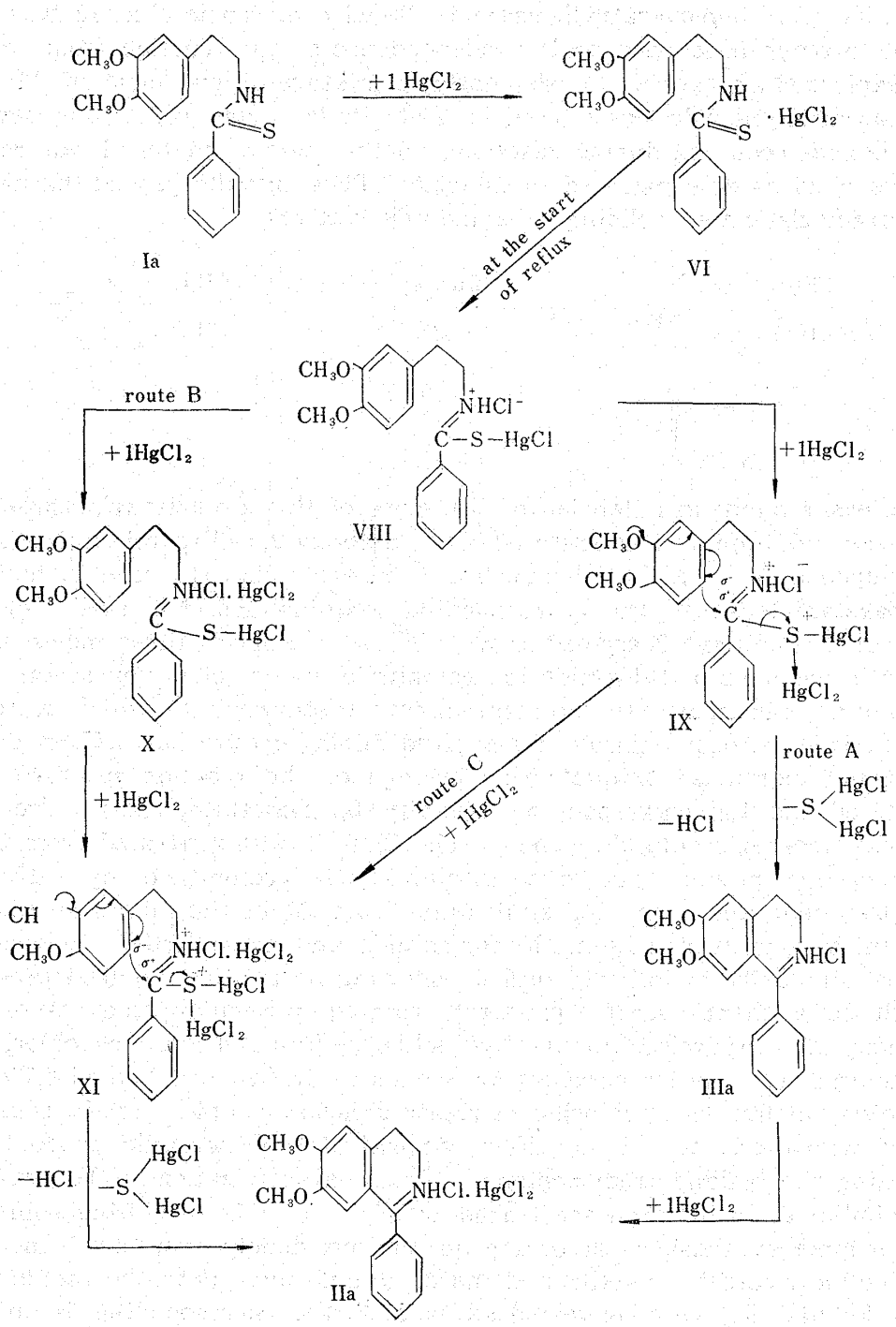
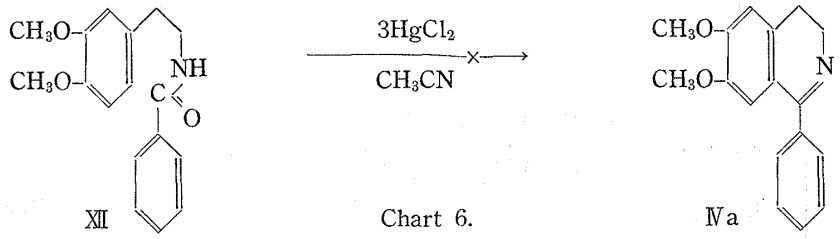


Chart 5.

In each of the proposed routes of this cyclodesulfurization reaction mechanism, three moles of mercuric chloride are used for every mole of Ia. In addition, the thioamide mercuric chloride adduct (VI) was considered as the first intermediate which undergoes enolization at the start of reflux to give the corresponding N-protonated-S-mercuric chloride iminothiol (VIII). This VIII can be cyclized according to either of

the three routes to afford IIa. However, both route B and C are still more favorable than route A because if A becomes effective, the reaction will be brought to completion with two moles of mercuric chloride and the product will be only the isoquinoline hydrochloride (IIIa) which is not in agreement with the experimental results.

Following the establishment of the proper cyclodesulfurization reaction conditions, the cyclization of N-homoveratrylbenzamide (XII) with mercuric chloride was checked in an attempt to reach conclusion on the independence of our reaction from the classical Bischler-Napieralski reaction. Consequently, a mixture of one mole of XII and three moles of mercuric chloride was stirred in acetonitrile under reflux for seven hours, when no changes occurred during reaction and the starting material was recovered in quantitative yield as demonstrated in Chart 6. These results proved that our reaction is only characteristic for cyclizing thioamide derivatives.



XII Chart 6. IVa

On the other hand, in extension of the scope of this cyclodesulfurization reaction to synthesize additional 1-substituted-6,7-dimethoxy-3,4-dihydroisoquinoline derivatives, the cyclization of both N-homoveratrylthioacetamide (Ib) and N-homoveratrylphenylthioacetamide (Ic) to the corresponding isoquinolines (IVb) and (IVc) was tried under the same conditions described above. Thus, by stirring three moles of mercuric chloride with one mole of thioamide in acetonitrile under reflux for seven hours, the reaction was accompanied with the same characteristic changes which were observed in case of Ia and hydrogen chloride gas evolved during cyclization. When the isolation of the organic mercurial products was attempted, the reaction mixture in case of Ib was filtered and the corresponding 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (IIb) (Chart 1) was separated from its mixture with the inorganic product, due to its insolubility in acetonitrile, by extraction with dimethylformamide and then recrystallization from either the minimum amount of the same solvent or a mixture of dimethylformamide and acetonitrile. IIb was identified by analysis, similarity in infrared and by showing no melting point depression when mixed with the authentic sample prepared from equimolecular amounts of 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (IIIb) and mercuric chloride by stirring in acetonitrile at room temperature for one hour. In case of 1-benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (IIc), its separation was effected by evaporating the filtrate after removal of the inorganic product and then recrystallizing the residue from acetone. The characterization of IIc was made by analysis, similarity in infrared spectra as well as by mixed melting point with the authentic sample synthesized according to the previously mentioned methods from the isoquinoline hydrochloride (IIIc) and mercuric chloride. Both the mercuric chloride complexes (IIb) and (IIc) were converted as usual to the corresponding isoquinoline hydrochlorides (IIIb) and (IIIc), then the free bases (IVb) and (IVc) were finally obtained by treating the hydrochlorides with either aqueous sodium hydroxide solution in case of IIIb or saturated sodium bicarbonate solution in case of IIIc.

As mentioned above, it became certain that this cyclodesulfurization reaction is very effective to synthesize various types of 3,4-dihydroisoquinoline derivatives, and we are now investigating the scope of this new type of ring closure for the synthesis of other heterocyclic compounds.

Experimental[*4]

General Procedure for the Isolation of Desulfurized Products from the Reactions of N-Homoveratrylthiobenzamide (Ia) with Desulfurizing Agents Other Than Mercuric Chloride. a) When the Products are Either the Starting Thioamide (Ia) or the Corresponding Acid Amide (XII)——A mixture of the calculated amount of both Ia and the chosen desulfurizing agent was stirred in the recorded solvent (Table I) under reflux for the specified period. The reaction mixture was then diluted with extra solvent, acidified with few drops of 10% aq. HCl, saturated with H_2S and the produced metal sulfide was filtered. The filtrate was evaporated and the residue was dissolved in H_2O and then extracted with ether. The ether extracts were washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent removed to give either Ia or N-homoveratrylbenzamide (XII) or mixture of both. These were identified by similarity in IR with the authentic samples as well as by TLC in $CHCl_3$, Rf 0.55 (Ia), 0.3 (Ib) (developed by dil. aq. $KMnO_4$ solution).

The original aq. solution was made distinctly alkaline with 10% aq. NaOH and extracted repeatedly with ether. The ether was washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent removed to leave nothing.

b) When the Products are Mixtures of N-Benzylidene-3,4-dimethoxyphenethylamine and the Starting Thioamide (Ia)——After the mixture of either Raney Ni or degassed Raney Ni and the thioamide (Ia) were allowed to react as specified in Table I, Raney Ni was filtered and the filtrate was evaporated to leave a semi-crystalline residue, m.p. 96~112°, which showed a weak band at 1640 cm^{-1} in addition to the usual bands of Ia in IR. This product was recrystallized from benzene-hexane to afford the pure sample of Ia as fine yellow crystals, m.p. 118~119.5°, identified by IR and TLC. The mother liquor was evaporated to leave a yellow oil whose IR spectrum was similar to that of the authentic sample prepared as described below.

N-Benzylidene-3,4-dimethoxyphenethylamine from Homoveratrylamine and Benzaldehyde——This compound was synthesized according to the reported method,[33] by adding the equivalent amount of freshly distilled benzaldehyde to homoveratrylamine when an exothermic reaction occurred and slight turbidity appeared. The mixture was heated on a water bath for 30 min. to give clear solution. The product was again heated on water bath *in vacuo* to remove the starting reactants and then dried over P_2O_5 overnight to afford yellow oil which exhibited very strong band at 1640 cm^{-1} ($\nu_{C=N}$) in IR. Yield 87%. Picrate from MeOH, yellow crystals, m.p. 162~166°, which on recrystallization from MeOH gave orange yellow needles, m.p. 164~166°.

General Procedure for the Cyclodesulfurization of N-Homoveratrylthiobenzamide (Ia) with Mercuric Chloride to Give Directly 1-Phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) without Isolation of the Intermediate Organic Mercurials——To a solution of 500 mg. (1.66 mmoles) of Ia in anhyd. CH_3CN, benzene or DMF was added the solution of estimated molar ratio of $HgCl_2$ in the same solvent (in case of benzene, $HgCl_2$ was used in suspension) and the mixture was stirred under reflux as specified in Table II. The original pale yellow clear solution soon developed a slight white turbidity which gradually increased at the start of reflux to become a white voluminous powder. This powder was again consumed in solution and HCl gas evolved vigorously as long as reflux continued till the end when a golden yellow solution with creamy white amorphous powder was produced. The reaction mixture was diluted with extra amount of solvent (in case of benzene, EtOH was used for this purpose), few drops of 10% aq. HCl and saturated with H_2S till no more black HgS was formed. HgS was filtered and the filtrate was evaporated to leave a yellowish white viscous residue which was dissolved in H_2O and extracted thoroughly with ether The ether extracts were washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent was removed *in vacuo* to leave a minute amount of either the starting thioamide (Ia), the corresponding acid amide (XII) or mixture of both as evidenced from IR in $CHCl_3$ and TLC in $CHCl_3$, Rf 0.55 (Ia) and 0.25 (XII) (developed with dil. aq. $KMnO_4$ solution).

The aqueous layer was made distinctly alkaline with 10% aq. NaOH to afford a white milky emulsion from which the cyclized 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) was obtained by repeated extraction with ether, washing the ether with H_2O, drying it over anhyd. Na_2SO_4 and removal of the solvent under reduced pressure. The produced base IVa was identical in all respects with the previously prepared authentic sample.[1]

The Separation and Identification of the Individual Reaction Products from the Cyclodesulfurization of N-Homoveratrylthiobenzamide (Ia) with Three Moles of Mercuric Chloride in Acetonitrile—— After the performance of reaction as mentioned in the general procedure, the resulted golden yellow solution with creamy white amorphous powder was filtered, the powder washed well with fresh CH_3CN and the washings were added to the filtrate. This filtrate was evaporated under reduced pressure to give golden yellow frothy residue which on recrystallization from 95% EtOH afforded 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (IIa) as golden yellow prisms, m.p. 190.5~192°, identified by analysis, similarity in IR and UV spectra as well as by mixed melting point with the authentic sample prepared as described in the next experiment. *Anal.* Calcd. for $C_{17}H_{18}O_2NCl_3Hg$: C, 35.49; H, 3.15; N, 2.43;

[*4] All melting points are not corrected and TLC were prepared from silica gel.

Cl, 18.49; Hg, 34.87. Found: C, 35.40; H, 3.19; N, 2.65; Cl, 18.35; Hg, 35.19. UV $\lambda_{max}^{CH_3CN}$ mμ (log ε): 240 (4.47), 283 (4.08), 313 (4.0), 371 (3.94). When IIa was dissolved in CH_3CN containing few drops of 10% aq. HCl and saturated with H_2S till no more black HgS was formed, it gave, after filtration of such HgS and evaporation of the solvent, a yellowish white residue which on recrystallization from EtOH–ether yielded 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (IIIa) as fine yellowish white needles, m.p. 212~213°, whose IR and UV spectra were similar to the previously prepared authentic sample.[1] UV $\lambda_{max}^{CH_3CN}$ mμ (log ε): 255 (4.39), 282 (4.10), 312 (4.12), 368 (4.10). The treatment of an aqueous solution of IIIa with 10% aq. NaOH followed by extraction of the formed milky emulsion with ether gave the cyclized 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline base (IVa) as fine white prisms, m.p. 121~123°, which was identical in IR and UV spectra with the authentic sample.[1] UV $\lambda_{max}^{CH_3CN}$ mμ (log ε): 233 (4.5), 273 (3.7), 284 (3.7), 309 (3.9). The IR spectra of these products are shown in Fig. 1.

The original white creamy amorphous powder slightly darkened but did not melt until 290°. This product was completely insoluble in H_2O, all organic solvents, dil. and concd. mineral acids even when boiled with aqua regia. In attempt to detect its components, the addition of 20% aq. NaOH gave a black precipitate which was partially soluble in dil. mineral acids indicating that it was a mixture of both HgS and HgO. When the acidic solution of this black precipitate was saturated with H_2S, it gave additional amount of HgS to prove that the amount of Hg is larger than equimolar amount of S in the inorganic product. The treatment of the original alkaline filtrate with HNO_3 and the addition of aq. $AgNO_3$ solution afforded a voluminous white precipitate of AgCl. When this inorganic product was dried at 100° and 4 mm. and subjected to analysis to know its actual percent of its components Hg, S and Cl, it gave variable results in every attempt which rendered the determination of its structure difficult.

Synthesis of 1-Phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline Hydrochloride Mercuric Chloride Complex (IIa)——To a solution of 250 mg. (0.82 mmole) of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (IIIa) in 20 ml. of anhyd. CH_3CN (IIIa was slightly insoluble in CH_3CN) was added a solution of 225 mg. (0.82 mmole) of $HgCl_2$ in 20 ml. of of the same solvent and the mixture was stirred at room temperature or under reflux for 1 hr., when a golden yellow solution was formed and remained unchanged during the reaction period. CH_3CN was evaporated to yield a golden frothy residue which on being recrystallized from 95% EtOH or by dissolution in CH_3CN and reprecipitation by ether afforded IIa as fine golden yellow prisms, m.p. 190~192°. Yield 95%. *Anal.* Calcd. for $C_{17}H_{18}O_2NCl_3Hg$: C, 35.49; H, 3.19; N, 2.43; Cl, 18.49. Found: C, 35.49; H, 3.22; N, 2.65; Cl, 18.63. UV $\lambda_{max}^{CH_3CN}$ mμ (log ε): 240 (4.47), 283 (4.08), 313 (4.0), 371 (3.94).

In some experiments especially those performed at room temperature, a product which exhibited several variations in IR spectra from that of IIIa, when measured in the solid state as KBr tablets, was obtained but later identified as being the diamorphous of IIIa by analysis, mixed melting point as well as by being superimposable with the authentic asmple when their IR spectra were measured in CH_3CN solution.

Synthesis of 1-Phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline Mercuric Chloride Complex (V)——A solution of 200 mg. (0.75 mmole) of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVa) in 10 ml. of anhyd. CH_3CN was mixed with a solution of 200 mg. (0.75 mmole) of $HgCl_2$ in 10 ml. of the same solvent and the mixture was stirred under reflux for 2.25 hr., when on addition of $HgCl_2$ solution, the original colorless isoquinoline solution became yellow and developed a white precipitate which was filtered, washed with fresh CH_3CN and dried, m.p. 191~192°. Recrystallization of this product from 99% EtOH afforded 225 mg. of white prisms, m.p. 190~191.5°, which was different from either IIIa or IIa in IR (Fig. 1). The evaporation of the mother liquor followed by recrystallization of the residue from the same solvent yielded additional 65 mg. of the same product, m.p. 190~191°, as evidenced from IR and UV spectra as well as mixed melting point test. Yield 72.5%. A sample for analysis was twice recrystallized from 99% EtOH to give white prisms, m.p. 192~194°. *Anal.* Calcd. for $C_{17}H_{17}O_2NCl_2Hg$: C, 37.88; H, 3.16; N, 2.6; Cl, 13.17. Found: C, 37.66; H, 3.06; N, 2.43; Cl, 13.46. UV $\lambda_{max}^{CH_3CN}$ mμ (log ε): 237 (4.43), 314 (3.95), 373 (3.87).

Preparation of N-Homoveratrylthiobenzamide Mercuric Chloride Adduct (VI)——A solution of 590 mg. (2.16 mmoles) of $HgCl_2$ in 25 ml. of anhyd. CH_3CN was added to a solution of 650 mg. (2.16 mmoles) of N-homoveratrylthiobenzamide (Ia) in 25 ml. of the same solvent and the mixture was stirred at room temperature for 2.25 hr., when soon a white voluminous precipitate appeared and gradually increased during stirring. This precipitate was filterered and dried to give a white chalky powder weighing 1.13 g., m.p. sintered at 148 and melted at 149°, Yield 91%. A sample for analysis was twice recrystallized from excess 95% EtOH to give VI as transparent white prisms, m.p. 149~149.5°, whose IR spectrum exhibited several differences from that of the starting thioamide (Ia) as illustrated in Fig. 2. *Anal.* Calcd. for $C_{17}H_{19}O_2NCl_2HgS$: C, 35.64; H, 3.34; N, 2.44. Found: C, 35.79; H, 3.45; N, 2.26.

In other experiments, when either 2 or 3 moles of $HgCl_2$ were used for each mole of Ia under the above mentioned conditions, VI was always the sole product in every case as evidenced from IR spectra as well as mixed melting point of each product with the other.

The solubility Properties of VI——i) Insoluble in cold EtOH but dissolves in large amount of the solvent when warmed. ii) Soluble in excess of cold CH_3CN and on warming it gives a yellow solution with

the separation of some white amorphous powder. iii) Completely insoluble in cold and warm benzene, $CHCl_3$, hexane, ligroin, petr. ether and or ether. iv) Insoluble in cold but soluble in hot ethyl acetate leaving white particles which did not dissolve on further warming.

Separation and Identification of the Individual Products when the Cyclodesulfurization of N-Homoveratrylthiobenzamide (Ia) is carried out in Presence of Insufficient Amount of Mercuric Chloride—— In all experiments, after a solution of 500 mg. (1.66 mmoles) of Ia in 25 ml. of anhyd. CH_3CN was mixed with the calculated amount of $HgCl_2$ in 25 ml. of the same solvent and the mixture was stirred under reflux as summarized in Table Ⅲ, the resulted golden yellow solution with the creamy amorphous powder was filtered, the inorganic product was washed well with fresh CH_3CN and the washings were added to the filtrate. This filtrate was made slightly turbid by the addition of excess ether and left at room temperature for at least 2 hr., when Ⅶ separated as the first product in the form of yellow short rods, m.p. 227~228°, which on being recrystallized by dissolution in cold CH_3CN and reprecipitation with ether gave the analytically pure sample of Ⅶ as short rods, m.p. 228~229.5°, whose structure was found to be composed of 2 moles of 1-pheny-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲa) and 1 mole of $HgCl_2$. *Anal.* Calcd. for $C_{34}H_{36}O_2N_2Cl_4Hg$: C, 46.44; H, 4.13; N, 3.19. Found : C, 46.36; H, 4.20; N, 3.44. UV $\lambda_{max}^{CH_3CN}$ mμ (log ε) : 241 (4.67), 252 (4.56), 285 (4.33), 313 (4.39), 371 (4.28).

The original CH_3CN filtrate after separation of Ⅶ was half evaporated under reduced pressure and at a temperature not higher than 30°, made turbid by addition of excess ether and left at room temperature until the separation of products became complete. This treatment gave Ⅱa as golden yellow prisms, m.p. 190.5~192°, which were identified as in the previous experiments. After the isolation of these products, the remained ones were separated by either evaporating the filtrate to dryness *in vacuo* and recrystallizing the residue from the proper solvent as in case of N-homoveratrylthiobenzamide mercuric chloride adduct (Ⅵ) and 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲa) or by passing H_2S in acidified solution of the residue in CH_3CN when it was dirty and difficult to recrystallize as in case of recovering the thioamide (Ia) or obtaining the resulted acid amide (Ⅻ).

In some experiments, the separation of products was not effected completely and one resultant was sometimes slightly contaminated with traces of the other. In this respect, the mixture was re-dissolved in cold CH_3CN and reprecipitated again by addition of ether and the method repeated until pure products were obtained.

Experimental Identifications of Ⅶ (Chart 2)——i) By treatment with H_2S : A solution of 100 mg. of Ⅶ in excess CH_3CN was acidified with few drops of 10% HCl and saturated with H_2S till no more black HgS was formed. HgS was filtered and the filtrate was evaporated to leave a yellowish viscous residue which was dissolved in H_2O and extracted repeatedly with ether. The ether layer was washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent was evaporated *in vacuo* to leave nothing. The aqueous layer was made distinctly alkaline with 10% aq. NaOH and extracted repeatedly with ether. The evaporation of this ether after being washed and dried as above, afforded 60 mg. of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline base (Ⅳa) as white prisms, m.p. 120~122°, which was identical in IR and UV spectra and showed no melting point depression when mixed with the authentic sample.[1] Yield. Quantitative.

ii) By reaction with one mole of $HgCl_2$: A solution of 200 mg. (about 0.23 mmole) of Ⅶ in 20 ml. of anhyd. CH_3CN was mixed with a solution of 65 mg. (0.23 mmole) of $HgCl_2$ in 10 ml. of the same solvent and stirred under reflux for 7 hr. The resulted golden yellow solution was half evaporated and then treated with enough ether to cause slight turbidity and left at room temperature overnight to give 230 mg. of golden yellow prismatic crystals, m.p. 188.5~190.5°. The mother liquor was evaporated to 1/4 and treated with excess ether as above and left at room temperature overnight to afford another 30 mg. of the same product, m.p. 188~190°, which proved to be 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquionline hydrochloride mercuric chloride complex (Ⅱa) by similarity in IR and UV as well as by showing no melting point depression when mixed with the authentic sample prepared in the previous experiments. The overall yield of Ⅱa was 260 mg. or quantitative.

Synthesis of Ⅶ from Different Routes (Chart 3)——i) From two moles of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲa) and one mole of mercuric chloride : To a solution of 200 mg. (0.66 mmole) of Ⅲa in 30 ml. of anhyd. CH_3CN was added a solution of 90 mg. (0.33 mmole) of $HgCl_2$ in 10 ml. of the same solvent and the mixture was stirred at room temperature for 6 hr., when some yellow crystals appeared during stirring. These crystals were filtered, dried (200 mg.) and identified as being Ⅶ, m.p. 228~230°, by IR and UV as well as by showing no melting point depression when mixed with the authentic sample. The filtrate was evaporated to 1/4 and made turbid with excess ether and left at room temperature overnight to give another 60 mg. of Ⅶ, m.p. 229~230°, which was same to the authentic sample in all respects. Evaporation of the mother liquor afforded a contaminated sample of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (Ⅱa) weighing 20 mg. The overall yield of Ⅶ was 260 mg. or 96%.

ii) From equimolecular amounts of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride mercuric chloride complex (Ⅱa) and 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲa) : A solution of 135 mg. (0.46 mmole) of Ⅱa in 15 ml. of anhyd. CH_3CN was mixed with a solution of 70 mg. (0.46 mmole) of Ⅲa in 15 ml. of the same solvent and the mixture was stirred at room temperature for 3 hr. The resulted

yellow solution was evaporated to leave a yellow prismatic residue which on recrystallization from the minimun amount of CH_3CN afforded yellow rods, m.p. 230°, whose IR and UV spectra were same to the authentic sample and showed no melting point depression when mixed with it. The treatment of the mother liquor as mentioned above gave successively additional 40, 10 and 5 mg. of Ⅶ which were identical with the previously prepared sample in all respects. The overall yield of Ⅶ was 190 mg. or 92.7%.

iii) From two moles of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲa) and one mole of N-homoveratrylthiobenzamide mercuric chloride adduct (Ⅵ): A mixture of 260 mg. (0.86 mmole) of Ⅲa and 245 mg. (0.43 mmole) of Ⅵ was stirred in 40 ml. of anhyd. CH_3CN at room temperature for 1.5 hr. The resulted clear yellow solution was treated with enough ether to cause slight turbidity and then left at room temperature for 4 hr. to give 270 mg. of Ⅶ as yellow short rods, m.p. 228~230°, which were similar in all physical properties with the samples prepared above. The treatment of the mother liquor as described above afforded another 85 mg. of Ⅶ, m.p. 228~230°. The final mother liquor was evaporated to dryness and extracted with benzene. Removal of benzene yielded 130 mg. or quantitative yield of N-homoveratryl-thiobenzamide (Ia) as semi-crystalline residue which was practically pure when checked by IR in $CHCl_3$ as well as TLC when it exhibited a single spot in $CHCl_3$, Rf 0.48. The overall yield of Ⅶ was 355 mg. or 94.2%.

Preparation of 1-Methyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVb) from the Cyclodesulfurization of N-Homoveratrylthioacetamide (Ib) with Three Moles of Mercuric Chloride——A solution of 1 g. (4.2 mmoles) of Ib in 20 ml. of anhyd. CH_3CN was mixed with a solution of 3.42 g. (12.6 mmoles) of $HgCl_2$ in 30 ml. of the same solvent and the mixture was stirred under reflux for 7 hr., when upon addition of the $HgCl_2$ solution, a pinkish precipitate appeared and soon changed to white creamy powder which increased gradually during reflux and a vigorous evolution of HCl gas was detected. The final reaction mixture was diluted with extra amount of CH_3CN, acidified with few drops of 10% aq. HCl and saturated with H_2S till no more black HgS was formed. The filtration of HgS followed by evaporation of the solvent gave viscous yellow residue which was dissolved in H_2O and and extracted repeatedly with benzene. The benzene layer was washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent evaporated to leave traces of yellowish oil whose IR spectra in $CHCl_3$ was identical with the authentic acid amide. The aqueous layer was made distinctly alkaline with 10% aq. NaOH and the produced white emulsion was extracted thoroughly with benzene. The benzene was washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and evaporated *in vacuo* to afford the cyclized 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline base (Ⅳb) as white prisms, m.p. 102~105°, which on recrystallization from benzene-hexane gave the analytically pure sample, m.p. 104~105°, whose IR and UV spectra were identical with the authentic sample[1] and showed no melting point depression when mixed with it. Yield of the cyclized product was 81.7%.

Separation of 1-Methyl-6,7-dimethoxy-3,4-dihydroisoquinoline Hydrochloride Mercuric Chloride Complex (IIb)——After a solution of 500 mg. (2.1 mmoles) of Ib in 20 ml. of anhyd. CH_3CN was allowed to react with a solution of 1.7 g. (6.3 mmoles) of $HgCl_2$ in 20 ml. of the same solvent under the above conditions, the reaction mixture was filtered and the precipitate washed well with fresh CH_3CN, dried to give 1.45 g. of creamy white amorphous powder which melted but did not become clear at 244°. This powder was extracted with hot DMF and the extract was evaporated to a half to afford after cool 400 mg. of yellow prisms, m.p. 245~247°(decomp.). The repeated evaporation of the filtrate followed by addition of CH_3CN to cause turbidity and then leaving the mixture in refrigerator for several hours, gave additional 200, 70 and 60 mg. of the same product, m.p. 244~245.5°(decomp.) which did not show melting point depression when mixed with each other and were identical in IR with the authentic sample prepared as in the next experiment. Yield 70%. A sample for analysis was recrystallized from CH_3CN-DMF (7:1) to afford pale yellow prisms, m.p. 246~247°(decomp.). *Anal.* Calcd. for $C_{12}H_{16}O_2NCl_3Hg$: C, 28.08; H, 3.14; N, 2.73; Hg, 39.09; CH_3O, 12.01. Found: C, 28.0; H, 3.28; N, 2.76; Hg, 39.21; CH_3O, 11.98.

Synthesis of 1-Methyl-6,7-dimethoxy-3,4-dihydroisoquinoline Hydrochloride Mercuric Chloride Complex (IIb)——A solution of 250 mg. (0.92 mmole) of 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲb) in 20 ml. of anhyd. CH_3CN was stirred with a solution of 250 mg. (0.92 mmole) of $HgCl_2$ in 20 ml. of the same solvent at room temperature for 1 hr. when soon a white voluminous powder was produced and increased during stirring. The filtration of this powder followed by its recrystallization from CH_3CN-DMF (1:7) afforded 400 mg. of pale yellow square crystals, m.p. 246~247° (decomp.), which was identical with the above prepared sample of Ⅱb in IR spectra. The evaporation of the filtrate and the recrystallization of residue from the same solvent gave another 70 mg. of Ⅱb, m.p. 245~247° (decomp.), whose physical characters were identical with the previously prepared Ⅱa. The overall yield of Ⅱa was 470 mg. or 95%.

Preparation of 1-Benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline (IVc) from the Cyclodesulfurization of N-Homoveratrylphenylthioacetamide (Ic) with Three Moles of Mercuric Chloride——A solution of 1 g. (3.11 mmoles) of Ic in 25 ml. of anhyd. CH_3CN was treated with a solution of 2.6 g. (9.33 mmoles) of $HgCl_2$ in 50 ml. of the same solvent and the mixture was stirred under reflux for 7 hr., when on mixing the solution of reactants, a yellowish turbid solution was produced and changed gradually to yellow and at the end of reflux gave white amorphous powder. The resulted mixture was acidified with few drops of 10% aq. HCl, saturated with H_2S and the produced HgS was filtered. Evaporation of the filtrate left a yellowish viscous caramel which was dissolved in H_2O and extracted thoroughly with benzene. This benzene was washed

well with H_2O, dried over anhyd. Na_2SO_4, filtered and the solvent removed to leave traces of the acid amide which was identified by IR spectra in $CHCl_3$ and by TLC. The aqueous layer was made distinctly alkaline, under cooling with ice, with satd. aq. $NaHCO_3$ to afford a white emulsion which was rapidly extracted with ether. The ether layer was washed well with H_2O, dried over anhyd. Na_2SO_4, filtered and evaporated under reduced pressure and at low temperature to afford the cyclized isoquinoline (Ⅳc) as white needles, m.p. 95~97°, which on attempted recrystallization from benzene-hexane mixture underwent slight oxidation and exhibited a strong carbonyl band at 1680 cm^{-1} in IR. When another sample of the cyclized product was recrystallized from abs. ether, it gave aggregate creamy needles, m.p. 98~100°, which were similar to the previously prepared sample[1] in all respects. Yield 85~90%.

Separation of 1-Benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline Hydrochloride Mercuric Chloride Complex (IIc)——After a mixture of the above amounts of reactants was stirred under reflux in anhyd. CH_3CN for 7 hr., the reaction mixture was filtered and the filtrate was evaporated to leave yellow frothy residue which on recrystallization from acetone yielded 720 mg. of yellowish white crystals, m.p. 170~172.5°. The repeated evaporation of the filtrate and recrystallization of the residue from acetone afforded another 210, 300 and 200 mg. of the same product, m.p. 171~173°, which were similar in IR and showed no melting point depression when mixed with each other or with the authentic sample prepared as described in the next experiment. The overall yield of Ⅱc was 78%. A sample for analysis was twice recrystallized from acetone to give yellowish white prisms which melted at 171~173°. *Anal.* Calcd. for $C_{18}H_{20}O_2NCl_3Hg$: C, 36.68; H, 3.42; N, 2.38; Hg, 34.04. Found : C, 36.55; H, 3.25; N, 2.42; Hg, 34.6.

Synthesis of 1-Benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline Hydrochloride Mercuric Chloride Complex (IIb)——A solution of 175 mg. (0.63 mmole) of $HgCl_2$ in 10 ml. of anhyd. CH_3CN was added to a solution of 200 mg. (0.63 mmole) of 1-benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (Ⅲb) in 10 ml. of the same solvent and the mixture was stirred at room temperature for 1 hr. The resulted yellow solution was evaporated and the produced yellow frothy residue was recrystallized from acetone to afford 300 mg. of Ⅱc as pale yellowish white prisms, m.p. 171~172°, which showed no melting point depression when mixed with the above prepared sample and was similar in IR with it. The mother liquor was evaporated and recrystllized from acetone to give additional 40 mg. of Ⅱc whose physical properties were identical with the previously prepared sample. Overall yield was 340 mg. or 91.6%.

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Summary

A new type of ring closure has been established for the synthesis of some 1-substituted-6,7-dimethoxy-3,4-dihydroisoquinoline derivatives through desulfurization of N-(3,4-dimethoxyphenethyl)thioamides. Mercuric chloride proved to be the only effective desulfurizing agent which produces the optimum yield of cyclized products when three moles of it are used for each mole of thioamide in acetonitrile. A reaction mechanism was tentatively proposed from the intermediates. Several organic mercurial products such as Ⅱ, Ⅵ and Ⅶ were also obtained.

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