129. Studies on the Synthesis of Dibenzochinolizine-Derivatives (VI).

A Synthesis of 4', 5'-Dimethoxy-1, 2, 5, 6, 7, 8, 3'', 4'', 5'', 6''-decahydro-(1', 2' : 3, 4 ; 1'', 2'' : 5, 6-dibenzochinolizine)).*

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One of the present authors (S. S.) and his collaborators have been engaged in synthesizing the six (B—G) out of the seven theoretically possible dibenzochinolizine-type of compounds, of which little or nothing had been known at the time they commenced the work in this field. ("A" represents the skeleton of berberine and palmatine, the well-known natural alcaloids, the syntheses of which from benzyl-tetrahydroisoquinoline-derivatives had already been recorded).

By the present day they were successful in preparing those compounds having skeletons B¹⁾, C²⁾, D³⁾, E⁴⁾ and F⁵⁾, but all attempts to synthesize the one having skeleton G ended fruitless.

Considering this reason we were led to notice the following facts, that those compounds built up by condensation of two hydro-isoquinolines (A, B and C) are fairly stable in the air, but those formed by condensation of each one of hydro-quinoline- and hydro-isoquinoline-unit (D and E) are readily oxidized in the air. From this facts it is to be deduced, that the compound constructed by condensation of two hydro-quinoline-units, therefore having skeleton G, will be quite unstable in the air; and that all our attempts to synthesize this type of com-

*) S. Sugasawa: XXXIII. Communication upon "Studies on the Synthesis of Nitrogen-Ring-Compounds."

1) Sugasawa and Kakemi: Proc. **15** (1939), 52; Ber. **72** (1939), 980.

2) Sugasawa, Kakemi and Kazumi: Proc. **15** (1939), 223; Ber. **73** (1940), 782.

3) Sugasawa and Kakemi: Proc. **14** (1938), 214; Ber. **71** (1938), 1860; Sugasawa and Yoshikawa: J. Chem. Soc. **1933**, 1585.

4) Sugasawa, Kodama and Inagaki: Proc. **16** (1940), 473; Ber. **74** (1941), 455.

5) Sugasawa and Ohki: Proc. **18** (1942), 287.

pound ended only in the production of intractable tar will probably due to the unstability of this skeleton.

As is reported in the preceeding paper we and Nakata have, however, succeeded in synthesizing dimethoxy-hexahydro-benzochinolinizine (VIII in that paper) and found that, though this compound is fairly unstable in the air, its methiodide forms stable, well-defined crystalline substance. This tells the possibility of existence of the skeleton G, in case one of the two benzo-groups will be completely reduced. which view was supported by our present synthesis.

Bz-tetrahydroquinaldine was prepared according to Basu¹⁾ and its methiodide (I) was condensed with veratraldehyde in the presence of piperidineacetate, giving 2-(3', 4'-dimethoxystyryl)-Bz-tetrahydroquinoline-methiodide (II)²⁾, from which N-methyl-2-(3', 4'-dimethoxyphenethyl)-decahydroquinoline (III) was readily prepared by catalytic reduction over Adams-Pt. The corresponding dihydroxy-compound (IV) now underwent the dehydrogenation according to Robinson and Sugasawa³⁾.

The methylation of the dehydrogenation-product (crude V) by means of diazomethane in ether-alcoholic solution gave oily methoxy-methiodide (crude VI). On standing the dilute alcoholic solution of this compound much oily substance separated first, followed by a small amount of star-shaped crystals. By being purified further from the same solvent the latter forms prisms of d. p. 128-129°, and the corresponding metho-picrate separates in long yellow needles from dilute alcohol. The results of analyses of these substances conform with the formula $C_{20}H_{23}O_2N.X$ ($X=I$ or $C_6H_2O_7N_3$), therefore the tetradehydro-compound of (VI), for which we provisionally propose formula (VI').

The oily substance first separated probably comprises the mixture of isomers of (VI: $X=I$), from which is the formation of (VI') explicable through dehydrogenation. Indeed, when the former was treated with air in the presence of Pd-black or better with chloranil, certain amount of (VI') was again isolated from the dehydrogenation-product.

The tertiary base (VII), 4', 5'-dimethoxy-1, 2, 5, 6, 7, 8, 3'', 4'', 5'', 6''-

1) Ann. **512** (1934), 131; **514** (1934), 292.

2) Ann. **530** (1937), 131.

3) J. Chem. Soc. **1932**, 789.

decahydro- (1', 2' : 3, 4; 1'', 2'' : 5, 6-dibenzochinolizine), was obtained by heating (VI, X=Cl) and distilling the residue in vac. Freshly distilled it forms faint yellow viscous oil, which gradually darkens; and red-brown tarry substance separated immediately, when its solution in organic solvents was shaken in the air.

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(Experimental).

3-(3', 4' - Dimethoxystyryl) - Bz - tetrahydroquinoline - methiodide (II) : Bz-tetrahydroquinaldine-methiodide (I, 33g), veratraldehyde (20 g) and piperidine-acetate (ca. 6 g) were dissolved in absolt. alcohol (45 cc) and the whole was heated for 10 hrs. From the reaction-mixture was alcohol removed in vac. and to the solid remained was acetone added. The methiodide (II) was then obtained in yellow crystalline powder, which was purified from SO₂acid alcohol, forming yellow needles of d. p. 222°, yield 60% of the theoretical. (C₁₉H₂₁O₂N.CH₃I requires C 54.95, H 5.5, N 3.2; Found C 55.15, H 5.7, N 3.5).

N-Methyl-2-(3', 4'-dimethoxyphenethyl)-decahydroquinoline (III): The foregoing methiodide in alcoholic suspension was reduced catalytically by means of hydrogen activated upon Adams-Pt.; for the completion of the reduction occasional addition of fresh catalyst was necessary. The base (III) was obtained as faint yellow viscous oil of b.p.₄₋₅ 218–222°. (C₂₀H₃₁O₂N requires C 75.7, H 9.8, N 4.45; Found 75.8, H 10.0, N 4.85).

Picrate: Minute grains from alcohol, m. p. 107–108°. (C₂₀H₃₁O₂N.C₆H₃O₇N₃ requires C 57.3, H 6.2, N 10.25; Found C 57.1, H 6.2, N 10.05).

The base (III) was demethylated to the corresponding phenolic base (IV) by boiling with hydroiodic acid. Since none of its derivatives obtained crystalline, it was used directly in the next stage.

4', 5'-Dimethoxy-5, 6, 3'', 4'', 5'', 6''-hexahydro-(1', 2' : 3, 4; 1'', 2'' : 5, 6-dibenzochinolizine)-methiodide (VI'): The phenolic base (IV)-hydroiodide (2 g) and potassium acetate (0.5 g) were dissolved in alcohol (40 cc), filtered and the filtrate was treated with chloranil (1.2 g) in alcoholic suspension (350 cc). The dehydrogenation proceeded just as in the similar cases and the product was worked up as usual.

The crude 4', 5'-dihydroxy-1, 2, 5, 6, 7, 8, 3'', 4'', 5'', 6''-decahydro-(1', 2' : 3, 4; 1'', 2'' : 5, 6-dibenzochinolizine)-metho-salt (V) thus obtained, from which no definite acetyl-derivative was produced, was then methylated by means of diazomethane in ether-alcoholic solution and the methylated product was converted into the corresponding methiodide (VI), which separated as viscous oily substance. The latter was now dissolved in dilute alcohol acidified with a little hydroiodic acid. On standing the greater part of the methiodide separated as oil, but after a few days a small amount of star-shaped crystals deposited on the wall, which was collected (0.3 g from 4 g methiodide) and purified from the same solvent, forming light yellow prisms of d. p. 128–129°. The corresponding metho-picrate was prepared as usual and purified from dilute alcohol, forming

long yellow needles of d. p. 114° . Both substances analysed correctly as tetrahydro-derivatives of (VI), for which the formula (VI': $X=I$ or $C_6H_2O_7N_3$) was provisionally proposed.

	C		H		N
$C_{20}H_{26}O_2NI \cdot 3H_2O$ requires	48.7		6.5,		2.9
Found in subst. dried at 60° , 15 hrs.	48.95,	48.85	6.4,	6.4,	3.2
$C_{20}H_{26}O_2N \cdot C_6H_2O_7N_3 \cdot H_2O$ requires	55.9,		5.35,		10.05
Found in subst. dried at 60° , 15 hrs.	56.05,	55.95,	5.45,	5.0,	10.05.

Dehydrogenation of (VI): 1) The oily methiodide (VI) separated first from the alcoholic solution was dissolved in alcohol containing Pd-black and the air was bubbled through the boiling solution for 5 hrs. Alcohol was then removed from the filtered solution and the syrupy residue was purified from dil. HI-acid alcohol, giving light yellow star-formed crystals of d. p. $128-129^{\circ}$, which was proved to be identical with the afore-mentioned specimen.

2) The oily methiodide (VI: $X=I$) was converted into the corresponding methochloride (0.35 g) which was then treated in alcoholic solution with chloranil (0.5 g) in alcohol (150 cc). The whole was kept standing over night, the excess of chloranil was filtered (0.15 g being recovered) and the filtrate was evaporated in the atmosphere of hydrogen. The residue was then extracted with dil. hydrochloric acid, filtered and the filtrate was added with potassium iodide, causing light brown precipitate, from which the same methiodide of d. p. $128-129^{\circ}$ was obtained in the same manner.

Further dehydrogenation of this crystalline methiodide by means of alcoholic iodine ended in the production of dark brown mass, from which nothing definite was isolated.

The tertiary base (VII), 4', 5'-dimethoxy-1, 2, 5, 6, 7, 8, 3'', 4'', 5'', 6''-decahydro-(1' 2': 3, 4; 1'', 2'': 5, 6-dibenzochinolizine), was prepared by heating the methochloride (VI: $X=Cl$) at 300° and distilling the residue in vac. A faint yellow very viscous oil came over at $280-290^{\circ}$ bath-temp. and 3 mm. (H_2 -atmosphere) which is, however, quite unstable in the air and its dehydrogenation to the dehydro-compound having skeleton (G) was attempted without the least success.

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