On Kakishibu, V.
Methylation of Shibuol.

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In the third report[1] on this subject, the writers reported on the acetylation of shibuol in order to find the number of free hydroxyl groups in its molecule, by which to ascertain the manner of combination between the two molecules of phloroglucinol and gallic acid, and it was supposed that shibuol contained at least four hydroxyl groups in the molecule, tetracetyl shibuol being the result.

Methylation of shibuol by means of dimethyl sulphate for the same purpose as that of the acetylation was undertaken, However, the process of methylation on flavones and tannins could not be employed in our case. In the methylation of shibuol, the reaction should be conducted at a low temperature such as 10°, to avoid decomposition of the shibuol by hydrolysis.

1. METHYLATION OF SHIBUOL IN A SODIUM CARBONATE SOLUTION.

100 c.c. of purified shibu consaining 10% of shibuol were mixed with a solution of 115 grm. of sodium carbonate dissolved in 150 c.c, of water, and to the mixed solution a great excess of dimethyl sulphate was added gradually with constant stirring during an interval of two hours, and the reaction was completed by stirring briskly at ordinary temperature for three hours, and then the temperature raised to 80°, and the reaction

1 These Memoirs, A, **8**, 235 (1925).

product separated, on cooling, filtered, washed with water, alcohol, and then ether, dried on a vacuum desiccator. The yield was 10.5 grm.

This was a violet brown powder, insoluble in alcohol, acetic ester, acetone, and ether. The methoxyl-value was estimated to be 17.0%, which corresponds to the value of dimethyl shibuol.

II. METHYLATION OF SHIBUOL IN CAUSTIC SODA SOLUTION.

100 c.c. of a 10% kakishibu solution were mixed with an alkaline solution of 46 grm. of caustic soda dissolved in 50 c.c. of water, at a temperature of 5°. 100 grm. of dimethyl sulphate were added during an interval of one hour to the mixed solution above mentioned, which was cooled with ice cold water after the reaction was completed, the temperature of the reacting product was raised gradually to 60°, and kept there for 30 minutes, and then the solution was left to stand at ordinary temperature over night. The yellowish brown precipitate thus formed, was filtered, washed with cold water and dried on a porous plate and on a vacuum desiccator. The yield was 12 grm. It began to sinter at 220° and melted at 260° with decomposition.

It was soluble in alcohol, benzene, chloroform, acetic ester, and acetone, and also in dilute caustic alkali solution, but insoluble in water, and in ether. The analytical results agree well with these of trimethyl shibuol.

C=60.78 ; 60.83 ; H=5.31 ; 5.42 ; OCH_3=27.95.

C=61.07 ; H=5.38 ; OCH_3=27.84, Calc. for $C_{14}H_9O_4(OCH_3)_3$.

III. METHYLATION OF SHIBUOL IN DILUTE CAUSTIC SODA SOLUTION AT HIGH TEMPERATURE.

10 grm. of purified shibuol were dissolved in 325 grm. of a 20% caustic soda solution at 20°, to the mixture 100 grm. of dimethyl sulphate were added during an interval of 30 minutes, and the mixture left for one hour. The reaction mixture was then heated to 30° on a water bath, and a violent reaction was observed to take place instantly. After the reaction had been completed, the product was boiled for 30 minutes, and the precipitate (A) formed, separated by filtration from the mother liquor, washed with water, and treated with alcohol.

The product (A) was composed of two substances, one was insoluble in alcohol, and the other soluble in alcohol, acetone, and acetic ester; the former was a brown powder, sintering at 200°, and melting at 230°–240° ; and the latter substance was a pale yellow amorphous powder.

The mother liquor separated from the substance (A), on acidifying the solution with mineral acid, yielded a brown precipitate (B) which was purified from the alcohol solution, and was soluble in acetone, acetic ester, and acetic acid.

On analysis of the substances (A) and (B), the following results were obtained:

A. C=63.48; 63.44; H=5.40; 5.60; OCH_3=34.8.

B. C=61.70; 61.22; H=4.49; 4.82; OCH_3=23.5; Ash=0.2,

The substance (A) was determined to be tetramethyl shibuol, and the (B), trimethyl shibuol.

IV. METHYLATION OF SHIBUOL IN AN ACIDIC MEDIUM.

When shibuol was methylated with dimethyl sulphate in an alkaline medium, dimethyl and trimethyl shibuol resulted as reaction products; but the reaction which was carried out at high temperature, proceeded to form mostly di-or tri-methyl shibuols with some tetramethyl shibuol.

The writers, however, applying the methylation with dimethyl sulphate in an acidic medium, have succeeded in obtaining tetramethyl shibuol with fruitful results:

1 Mol of purified shibuol dissolved in a 10% caustic soda solution (5 mol of NaOH in water), and to the solution 12 mols. of dimethyl sulphate were added under cooling with ice-cold water with constant stirring. After standing the reaction mixture for 3~4 hours, 15 mols. of caustic soda in a concentrated solution were added and the mixture was left to stand at room temperature for one day. Tetramethyl shibuol, by this treatment, was separated in a reddish brick-coloured precipitate from the solution, and this was filtered and washed with water. The yield of the crude substance was 55 grm. from 50 grm. of shibuol, which corresponds to 92% of the theory.

It shrinks at 200° and melts at 220°. C=56.49; H=5.04; OCH_3=34.44; ash=3.9.

The crude tetramethyl shibuol was divided into two parts by their solubility in an acetone-alcohol solution, The crude substance was dissolved in cold acetone, and alcohol was added, whereupon the precipitate (C), was formed, separated from the solution by filtration, the solvent was then mainly expelled from the solution by distillation, and by adding alcohol to the residue, the second substance (D) was separated. Both substances were analysed:

	C	H	Ash	OCH_3
C.	60·19	5·77	2·06	34·85
	60·24	5·44	1·93	——
D.	62·48	6·42	0·1	38·10
	63·01	6.84	——	——

The tetramethyl derivative was observed as in the case of acetyl shibuol to be separated by means of a mixture of acetone and alcohol into the soluble and insoluble forms in the solvent. They show the same elementary composition and the methoxyl value, but they differ in solubility and ash-content from each other and such a relation of chemical & physical properties between the two substances is the same as that observed in shibuols and their acetyl compounds.

71 grm. of the crude tetramethyl shibuol by fractional precipitation of its acetone-alcohol solution, were divided into the following four fractions which show the melting points, and solubility in acetic ester, acetone, and alcohol.

	I	II	III	IV
Shrinks at	275°	260°	150°	90°
Melts at	288°*	270°	185°*	130°
Colour	light drown	light brown	reddish brick colour	yellowish brown
Acetone	soluble	soluble	soluble	soluble
Acetic ester	〃	〃	〃	〃
Alcohol (cold)	sparingly soluble	——	〃	〃
Ether	insoluble	——	sparingly soluble	somewhat soluble
Caustic soda	〃	——	〃	〃
Yield in grm.	31	7.5	11	8.5
Yield in %	53	13	19	15

*with decomposition.

V. METHYLATION OF TRIMETHYL SHIBUOL.

With 5 grm. of trimethyl shibuol dissolved in 30 c.c. of acetone, 10 grm. of methyl iodide, and 8 grm. of silver oxide were mixed, and the mixture was shaken in a sealed tube for 5 hours, and the reaction product separated from the silver iodide was purified from acetic ester. The yield was 6 grm.

It was a light brown powder and soluble in alcohol, acetone, and acetic ester, but insoluble in alkali solution, and melting at 208°–210° with decomposition. Analytical results agree with those for tetramethyl shibuol.

C=61·70; 61·89; H=5·70; 5·81; OCH_3=34·47; theory requires C=62·06; H=5·74; OCH_3=35·63 for $C_{11}H_8O_2(OCH_3)_4$.

VI. ACETYLATION OF TRIMETHYL SHIBUOL.

Trimethyl shibuol was acetylated with acetic anhydride and sodium acetate in a sealed tube heated at 140° for two hours. The reaction product was purified with acetone and then its acetyl value determined. CH_3CO=9.77% agrees with the theoretical value 11.16% for monoacetyl trimethyl shibuol. It was soluble in acetone and in acetic ester, but insoluble in water and in alcohol.

Shibuol when methylated gave a tetramethyl compound, a fact which indicates the presence of at least four free hydroxyl groups in the molecule, and harmonizes with the experimental results obtained by the acetylation.

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