58. The New Syntheses of Hydroxydroserone (The Pigment of *Drosera Whittakeri*), Phthiocol (The Pigment of Human Tubercle Bacillus), and Naphthopurpurin; and the Studies of the related Compounds.

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In the previous papers^{1) 2) 3)} on the constitution of Shikonin, the several synthetical procedures of naphthazarin, naphthopurpurin, and their derivatives, and also their comparative properties were reported.

Subsequent experiments gave some interesting results, and suggested the syntheses of hydroxydroserone^{4) 5)} [c], the pigment of plant *Drosera Whittakeri*, and phthiocol⁶⁾ [f], the pigment of human Tubercle Bacillus. In this paper, these results may be summarized as follows.

1) It was confirmed that; [A] naphthazarin and any naphthoquinone* which contains no OH group in β -position of the quinone ring do not react with Na-bicarbonate, on the other hand; [B] naphthopurpurin, and any naphthoquinone* which contains the same OH group as mentioned above react, not only with Na-bicarbonate, but also with Na-salts of certain weak acids, such as acetate etc. These behaviours are applicable for the separation of the compounds of the above two systems [A] [B], because, when their solutions in water insoluble solvent are shaken with aq. solution of Na-salts as above mentioned, only the compounds of [B] system pass, into the aq-layer forming Na compounds. The Na compounds are generally crystallisable, and the quantitative determinations of Na as Na_2SO_4 proved to be mono-Na compounds; the position of Na is considered probably to be β in the following examples, compounds formed:—

<p>[a].</p>	<p>[b].</p>	<p>[c].</p>	<p>[d].</p>
<p>$\text{C}_{10}\text{H}_5\text{O}_5\text{Na}$. Brown red needles. Na. found 9.93 ,, calc. 10.04</p>	<p>$\text{C}_{11}\text{H}_7\text{O}_5\text{Na}$. Brown red needles. 9.28 9.50</p>	<p>$\text{C}_{11}\text{H}_7\text{O}_5\text{Na} \cdot 2\text{H}_2\text{O}$. Dark-brown needles. 8.49 8.27</p>	<p>$\text{C}_{10}\text{H}_5\text{O}_5\text{Na}$. Red needles. 11.71% 11.71%</p>

1) 2) Kuroda and Wada: Proc., **12** (1936), 239; **13** (1937), 163.

3) Kuroda and Wada: Sci. Pa. Inst. Ph. Ch. Res., (1938), 1741.

4) Winzor; J. Chem. Soc., **338** (1935).

5) Kuroda and Wada: Sci. Pa. Inst. Ph. Ch. Res. (1938), 1760.

6) Anderson and Newman: J. Biol. Chem., **103** (1933), 405.

*) Naphthoquinone (contains no acidic group such as CO_2H , SO_3H).

2) A simple and improved method for synthesis of naphthopurpurin was found as follows: when a bluish solution of naphthazarin in 0.5% NaOH aq. was heated on the water bath for about one hour in contact with air using only a mechanical stirrer, naphthopurpurin was easily formed showing its reddish colour in the NaOH aq-sol. From the solution acidified with dil HCl, almost pure naphthopurpurin was isolated by the aid of Na-bicarbonate and organic solvent as above mentioned: yield was nearly quantitative, leaving unchanged naphthazarin in the solvent: the above principle was applied to the other napho-quinones as follows:*

3) The H of OH group in β position of the quinone ring was also noted to be active, namely that it is possible to be alkylated with alcohol and dry HCl gas: the experiments were carried out in the following compounds.

With CH₃OH and HCl, methylation was successful in the case of [a] (the product mp. 178° found C, 60.16; H, 3.60% Calc. C, 60.00; H, 3.64%) and [b] whereas it was negative in the case of [c]. Furthermore, the treatment was applied to another quinone [d] Rapanone, which was studied by Dr. Kawamura¹⁾ who proposed the formula [d] for it, with which though anticipated Na-compound by the aid of Na-bicarbonate was obtained and methylation with CH₃OH, HCl in the above Na-compound was successful, yet only monomethyl ether (mp. 95° CH₃O, found 8.1% calc. 8.8% for which the present author proposed the formula [e]) was obtained, whereas di-methyl-ether was produced with diazo-methane.

In view of the above experimental results, it was thought that the alkyl group in β position of quinone ring, the above mentioned, in acidic medium may hinder some reaction for OH group in its ortho position. It was moreover very interesting to be observed that by many chemists as well as by the present author,²⁾ in Thiele Winter's

*) See page 228.

1) Rep. Jap. Sci. Ass., **377** (1937).

2) Kuroda and Wada: Sci. Pa. Inst. Ph. Ch. Res., **1740** (1938).

method¹⁾ which was carried out in acidic medium, namely $(\text{CH}_3\text{CO})_2\text{O}$ and H_2SO_4 , alkyl group in β position of quinone ring also hinders the introduction of OAc group into the quinone ring.

It was then anticipated that, in the case of an alkaline medium, on the contrary, some different influence may occur; with this idea therefore the author's method in which alkali was used for the preparation of naphthopurin as above mentioned, was applied to the

compound which was synthesized by the author, from

maleic acid and tolu-hydro-quinone or, from citraconic acid and hydro-quinone. The methyl naphthazarin (0.5 g) in 0.5% Na-OH aq. sol (150 c.c.) was treated in the similar manner in the case of naphthazarin itself: fortunately a very interesting and characteristic compound, hydroxy droserone [c] which was previously synthesized by the author²⁾ according to the literature³⁾ was produced. (in a good yield mp. 198° alone or mixed with authentic specimen; its acetyl-der. mp. 152°)

As the result of the above experiment, the synthesis of phthiocol was attempted. As the pigment is considered as a very important and interesting substance for a biological significance, several synthetic studies^{4) 5) 6) 7)} had been reported, however the processes were either rather complicated, or gave only poor yield.

In the present work the starting material (2 g) which

had been obtained from β methyl naphthalene and CrO_3 was treated with 0.5% Na-OH aq. (600 c.c.) in a same way as previously mentioned. After acidifying with HCl, the main product separated in reddish yellow crystals; the product dissolved in ether or benzene was treated with Na-bicarbonate, and the aq. layer was acidified; then crude phthiocol crystallized out. From aqueous mother liquor, some quantity of phthiocol was isolated by the aid of ether and Na-bicarbonate (yield 70%). For analysis, the specimen was purified by sublimation and recrystallized from 50% CH_3OH (yellow needles mp. 173° found C, 70.03; H, 4.39%. Calc. C, 70.22; H, 4.26%). Mono-acetyl derivative (white crystal mp. 106° , found C, 67.82; H, 4.42% Calc. C, 67.82; H, 4.34%) was easily obtained when the pigment was treated with $(\text{CH}_3\text{CO})_2\text{O}$ and H_2SO_4 . Triacetomethyl naphthalene (mp. 158° in white crystal) was easily obtained when the pigment was treated with Zn., $(\text{CH}_3\text{CO})_2\text{O}$ and Na-acetate.

- 1) Ann., **311** (1900), 345.
- 2) Kuroda and Wada: Sci. Pa. Inst. Ph. Ch. Res., (1938), 1741.
- 3) Winzer: J. Chem. Soc., **338** (1935).
- 4) Anderson and Newman: J. Biolo. Chem., **103** (1933), 405.
- 5) Madinavetia: An. Soc. espan fisic y quim., **31** (1933), 750.
- 6) Anderson: J. Biolo. Chem., **105** (1934), 279.
- 7) Hooker: J. Amer. Chem. Soc., **1168** (1936).

Moreover the following compounds were synthesized and some interesting experiments are now in progress.

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1) Baker: J. Chem. Soc., **1602** (1938).