

# The Properties of Hydroxy Naphthoquinones<sup>1,2</sup>

Chika Kuroda (黒田チカ)

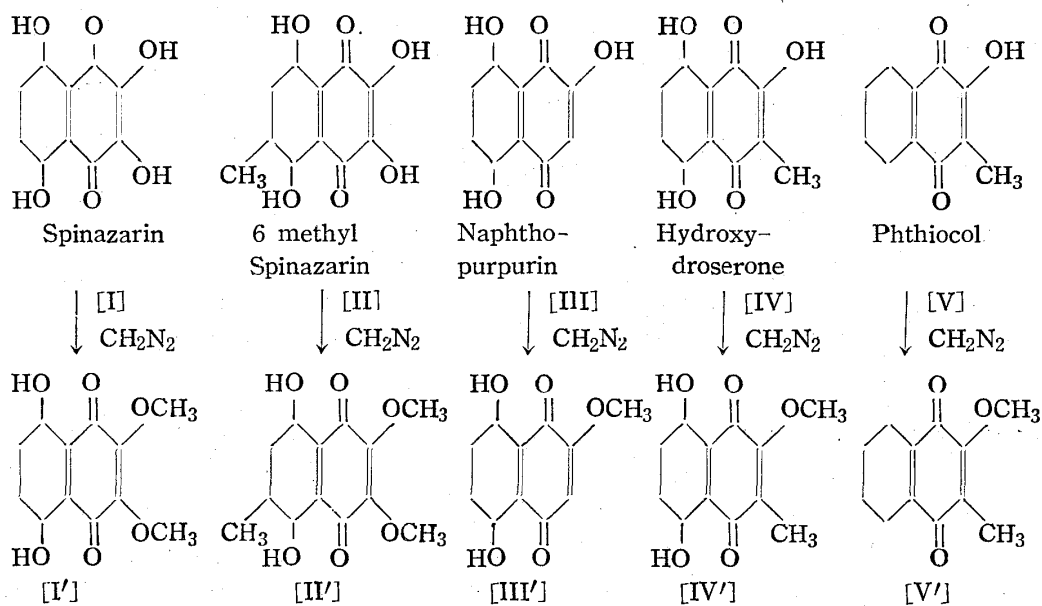
Department of Chemistry, Faculty of Science,  
Ochanomizu University

In the subsequent experiments of the hydroxy naphthoquinones concerning Shikonin<sup>1)</sup> and Spinochrome<sup>2)</sup>, the following interesting results were observed which will be a subject of this paper.

## 1. Method of methylation with diazomethane.

According to the special property of the above compounds for diazomethane the following peculiar method for methylation was wanted.

In this work methylation with diazomethane is very important, however, sometimes the anticipated product was very poor in yield or nothing was formed owing to side reaction; and the result was indefinite. Similar experience with difficulty was recorded previously; the methylation of hydroxydroserone [IV] was carried out by A. K. Macbeth, J. R. Prince and F. L. Winzor<sup>3)</sup> with diazomethane in etherial solution yielding only a crystalline product which was not the anticipated methyl ether (10% nitrogen was found in analysis). As the result of the present author's effort in several experiments, the most suitable conditions were found for obtaining the anticipated methyl ether in theoretical yields as shown in the following compounds [I], [II], [III], [IV] and [V].



<sup>1</sup> Contribution from Department of Chemistry, Faculty of Science, Ochanomizu University, No. 6

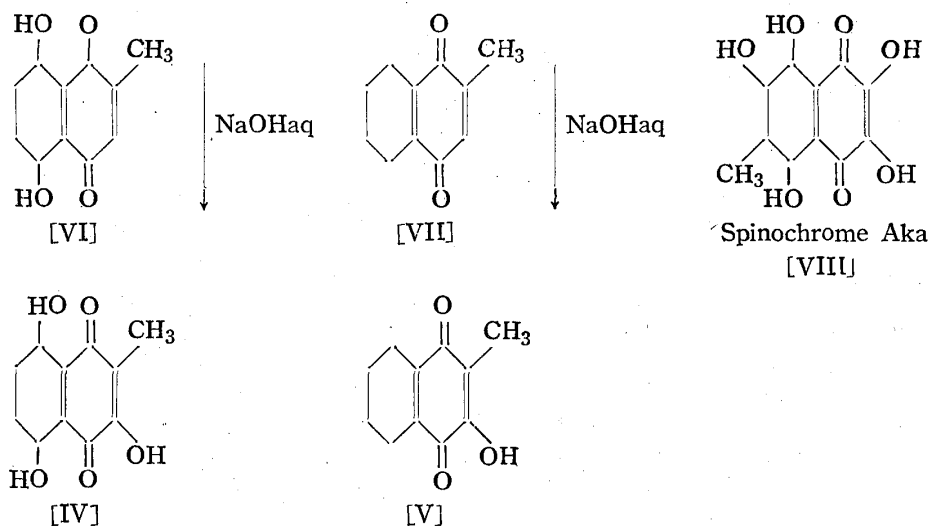
<sup>2</sup> This work has been partly carried out at Institute of Physical and Chemical Research, Tokyo.

*Note.* The new compounds [I], [II] synthesized<sup>4)</sup> by the present author are related with the Spinochromes (the pigment from the Spines of Sea Urchins). Therefore they are named Spinazarin and 6-methyl-spinazarin respectively.

In each case the solid substance, without dissolving in any solvent was directly methylated with etherial solution of diazomethane. The detail of the procedure will be shown in experimental part. All the above methyl ethers, except [V'] (see page 87) resemble naphthazarin in their appearances, and dissolve with blue colour in caustic alkali, but give no reaction with bicarbonates of alkali or alkali earth metals, sodium acetate or phosphate.

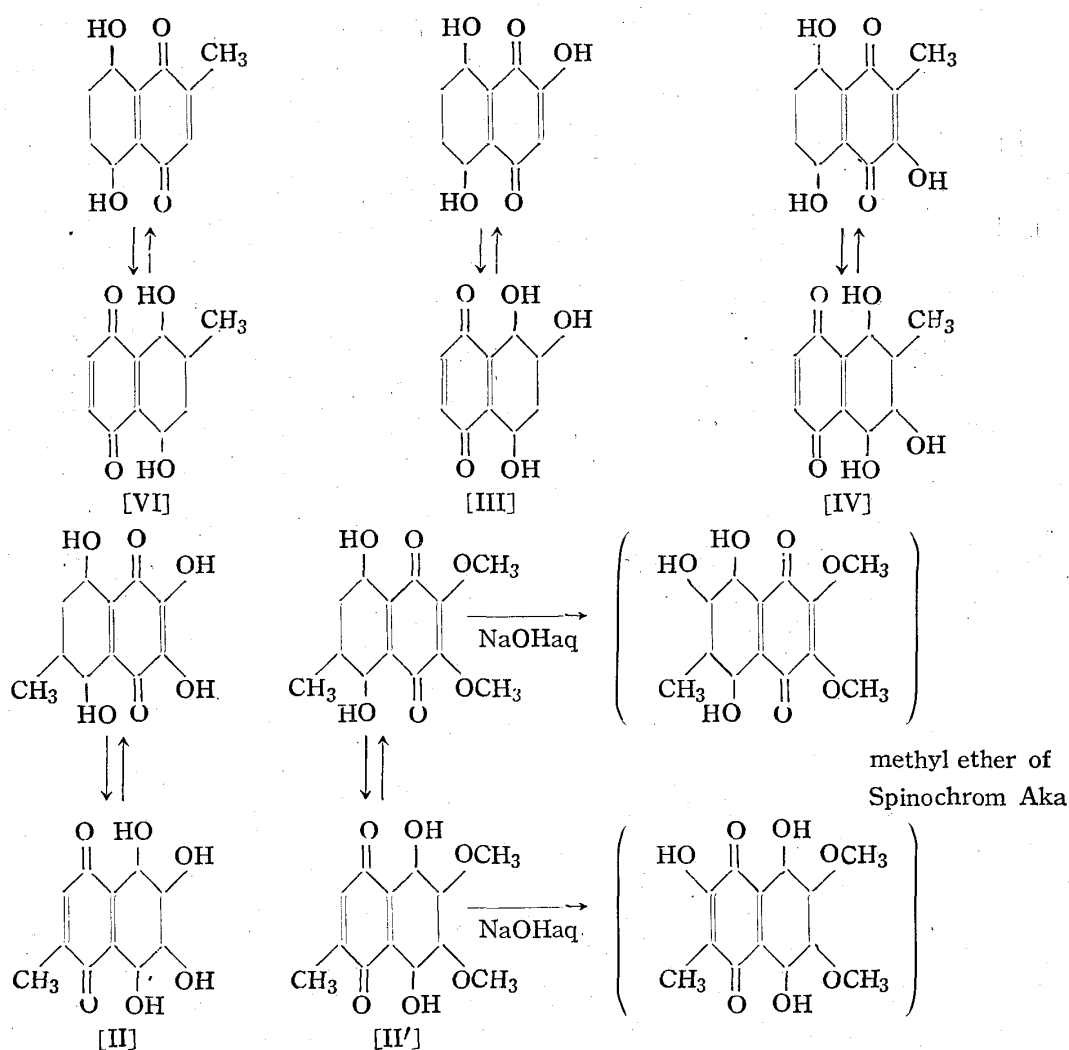
## 2. Demethylation with hot dilute caustic alkali.

The interesting phenomena of the above methyl ethers with aqueous caustic alkali were observed; it was attempted at first to synthesize Spinochrome Aka, [VIII] (the formula proposed by Kuroda and Ohshima<sup>5)</sup>, 6 methyl 7 hydroxy Spinazarin) from 2,3 dimethyl ether of 6 methyl Spinazarin [II'] as follows. In the previous work by Kuroda<sup>6)</sup> hydroxydroserone [IV] and Phthicol [V] were synthesized from  $\beta$  methyl-naphthazarin [VI] (2 methyl 5,8 dihydroxy naphthoquinone 1:4) and 2 methyl naphthoquinone 1:4, [VII] respectively, by treating with hot aqueous caustic alkali solution. From the above fact it was shown that, when

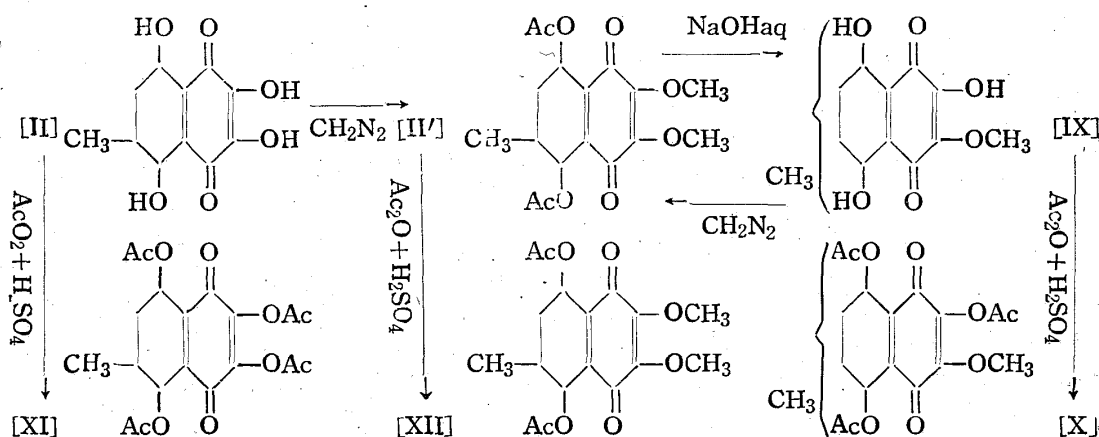


naphthoquinone 1:4 in which a methyl group exists in the position 2 is heated with aqueous dilute caustic alkali, the formation of a new OH group in position 3 is possible.

Generally, the derivatives of 5,8 dihydroxy naphthoquinone 1:4 are considered to exist in the tautomeric forms as shown in the following examples [VI], [III] and [IV]; therefore, it was likewise considered that [II] and [II'] might exist in the following tautomeric forms. It was then anticipated that if the above alkali method is applied to [II'] the methyl ether of Spinochrome Aka, namely 2:3 dimethyl ether of 6 methyl 7



hydroxy Spinzarin may be synthesized. On the contrary, another reaction was observed; namely by heating it with 1% caustic soda solution on the water bath, the liquid slowly changed in colour from blue to purple red. After one hour when the product was acidified and purified, a reddish crystalline compound (mp.  $188^{\circ}$ ) was obtained. The compound was proved to be [IX] by 1) the result of analysis, 2) chemical behaviours, and 3) the relation between its derivatives as follows.

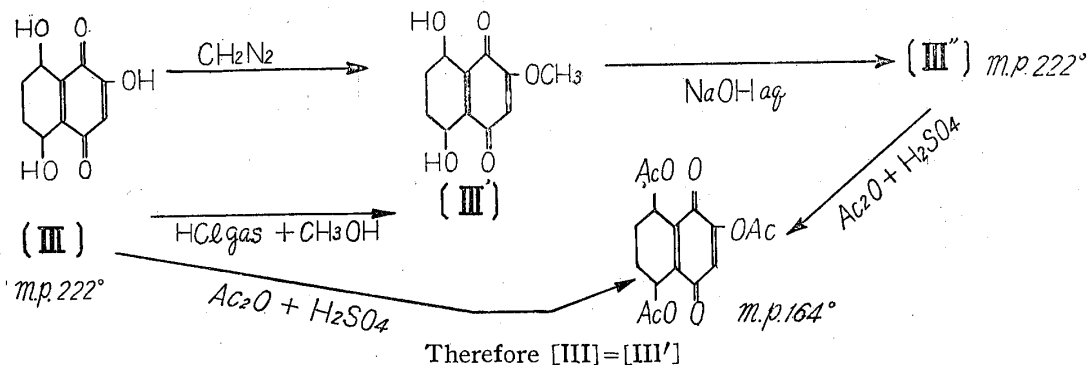


Then it was proved that in this case the  $\text{CH}_3$  group from one of  $\text{OCH}_3$  in the quinone ring of the compound [II'] was split off. To confirm this reaction, the method was applied to the following examples, [I'] [III'] [IV'] [V'] then, the demethylation was observed.

The demethylation was slow taking about over one hour in the cases of [I'] [II'] [IV'] and [V'] as in the case of [II'] whereas the reactions were instantaneous in the cases of 2:3 dimethoxynaphthoquinone and 2 methoxy naphthoquinone which were prepared by Kuroda.

All the demethylated products thus obtained dissolve in aqueous caustic alkali with reddish purple as in the case of naphthopurpurin, and also are soluble in aqueous solution of bicarbonates of alkali or alkaline earth metals, and sodium acetate or phosphate with purple colour.

The relations are also proved as shown below.



*Note.* For the compound [I'] which was previously<sup>8)</sup> mentioned, the analytical values are given here, mp. of [II] is higher than that of previous specimen (mp.  $117^\circ$ ) obtained by Kuroda<sup>9)</sup>.

### Experimental

Methylation with diazomethane. The solid substance was spread out on a watch glass or a crystalline dish, and ethereal solution of diazomethane was poured on the substance from a pipette, then after a vigorous reaction accompanied with sudden evaporation of nitrogen gas and ether, the anticipated methyl ether separated out at once in crystalline state.

[I']. Spinazarin dimethyl ether. Dried Spinazarin (0.05 g) was divided into several portions (about 6-7) and each portion was spread out on a watch glass or a dish respectively and methylated by the way as mentioned above. The crystalline product was collected by the aid of ether, and the ethereal solution was treated with sodium bicarbonate aqueous solution to remove another product which reacted with the bicarbonate; the remaining ethereal solution was shaken with a minimum amount of dilute sodium hydroxide aqueous solution; when the bluish alkaline solution thus obtained was acidified, the anticipated methyl ether separated out (yield nearly theoretical) in reddish crystalline state. When the

product was purified with acetone, it crystallized (in brown thin trigonal-plates with dark greenish metallic lustre) mp. 133.5°. Analytical results; Sub. 3.939, 3.798; CO<sub>2</sub>, 8.340, 8.038; H<sub>2</sub>O, 1.503, 1.421 mg; C, 57.74, 57.72; H, 4.27, 4.19%. Calc. C, 57.60; H, 4.19%.

The following methyl ethers [II'] [III'] [IV'] and [V'] were obtained by nearly the same way as in the case of [I'].

The product [II'] was recrystallized from dilute acetic acid. It separated in brown needles with dark brownish metallic lustre mp. 122°.

Analytical results; sub. 2.550; CO<sub>2</sub>, 5.495; H<sub>2</sub>O, 1.060 mg; Found C, 58.80; H, 4.65%. Calc. C, 59.09; H, 4.55%.

[III']. The product was purified from acetone (mp. 183°). Analytical results; sub. 3.234, 3.188; CO<sub>2</sub>, 7.113, 7.029; H<sub>2</sub>O, 1.066, 1.069 mg; C, 59.98, 60.13; H, 3.69, 3.75%. Calc. C, 60.00; H, 3.10%.

[IV']. When the product [IV'] from [IV] was purified from methanol, it separated out in red needles mp. 113–114°. Analytical results; sub. 3.177; CO<sub>2</sub>, 7.183; H<sub>2</sub>O, 1.306 mg; C, 61.66; H, 4.60%. Calc. C, 61.54; H, 4.27%.

Demethylation; [IX] from [II']. When the methyl ether [II'] (0.05 g) dissolved in 1% dilute sodium hydroxide aqueous solution (2 cc) was heated on the water bath, the demethylation was slow by changing in colour from blue to red. After over one hour the product was acidified and extracted with ether. The ethereal solution was shaken with sodium bicarbonate aqueous solution. When the soluble part in the latter was acidified, a crystalline product separated. When the product was purified with methanol a new substance [IX] was obtained (orange yellow prisms mp. 188°). Analytical results; sub. 3.58; CO<sub>2</sub>, 7.602; H<sub>2</sub>O, 1.360 mg; C, 57.77; H, 4.24%. Calc. C, 57.60; H, 4.00%.

[II'] from [IX]. When the compound [IX] was methylated with diazomethane, the product was proved to be identical with original methyl ether [II'] (mp. 122° in specimen alone or mixed sample with authentic sample).

[XII] from [II']. The above compound was acetylated with acetic anhydride and conc. sulphuric acid then the product was proved to be [XII]. When it was purified from ether yellow needles were obtained mp. 126°. Analytical results; sub. 3.904; CO<sub>2</sub>, 8.378; H<sub>2</sub>O, 1.760 mg; C, 58.53; H, 4.78%. Calc. C, 58.62; H, 4.78%.

[X] from [IX]. [IX] was acetylated with acetic anhydride and conc. sulphuric acid in usual manner; when the product was purified from dilute acetic acid it was obtained in beautiful yellow crystal mp. 148°, analytical results; sub. 2.637; CO<sub>2</sub>, 5.56; H<sub>2</sub>O, 1.006 mg; C, 57.52; H, 4.27%. Calc. C, 57.45; H, 4.26%.

[III] from [III']. The methyl ether [III] (0.05 g) was heated with sodiumhydroxide aqueous solution for one hour on the water bath. The product was treated by the same manner as in the case of [II']. The

demethylated part (the soluble part in sodium bicarbonate) was purified with benzene and was recrystallized from acetone, a reddish substance (needle crystal) was obtained and proved to be identical with [III] (mp. 222° in the specimen alone or in mixed sample with authentic sample.) Analytical results; sub. 3.087; CO<sub>2</sub>, 6.891; H<sub>2</sub>O, 0.861 mg; C, 58.23; H, 3.12%. Calc. C, 58.25; H, 2.91%.

The acetyl derivative (acetylation was carried out with acetic anhydride and conc. sulphuric acid of the above compound was also proved to be identical with the acetyl derivative of [III]; (mp. 164° in the specimen alone or in the mixed sample with authentic sample).

#### The results of methoxy determinations.

	Name	substance mg	AgI mg	CH <sub>3</sub> O %	
				Calc.	Exp.
[ I' ]	Spinazarin-dimethyl ether (2:3)	3.452	6.637	24.81	25.42
[ II' ]	6-Methyl-Spinazarin dimethyl ether (2:3)	4.315	7.623	23.49	23.34
[XII]	6-Methyl-Spinazarin dimethyl ether (2:3) diacetate (5:8)	3.415	4.514	17.82	17.46
[III']	Hydroxy Droserone mono-methyl ether (2)	3.232	3.358	13.25	13.73
[ IX ]	6-Methyl-Spinazarin mono-methyl ether (2 or 3)	1.078	1.231	12.41	12.55
[ V' ]	Phthiocol methyl ether	3.333 3.057	3.838 3.548	15.35	15.21 15.33

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#### Literature

- 1) C. Kuroda and M. Wada: Sci. Pap. Phys. and Chem. Res., 34, 1740 (1938).
- 2) C. Kuroda and H. Ohshima: Proc. Imp. Acad., 16, 214 (1940).
- 3) A. K. Macbeth, J. R. Prince and F. L. Winzor: J. Chem. Soc., 336 (1935).
- 4) C. Kuroda and H. Ohshima: Proc. Imp. Acad., 16, 216 (1940).

The compounds III IV and V are synthesized by C. Kuroda: Proc. Imp. Acad., 15, 227 (1939) and see Page 90 in this paper.

The compounds [IV'] and [V'] are new, for mp. of [II'] see Page 91.

- 5) Kuroda and Ohshima: Proc. Imp. Acad., 16, 293 (1940) and see Kuroda and Iwakura: Proc. Imp. Acad., 18, 74 (1942).

- 6) C. Kuroda: Proc. Imp. Acad., 15, 227 (1939).

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This method was found by C. Kuroda previously, see, Proc. Imp. Acad., 15, 227 (1939).

- 8) C. Kuroda and H. Ohshima: Proc. Imp. Acad., 16, 216 (1940).
- 9) C. Kuroda: Proc. Imp. Acad., 16, 216 (1940).