The authors are indebted to Prof. Y. Hosoya, Osaka City Medical College, and to Mr. Nishikawa, Ukiha Hygienic Laboratory, for their supplies of a part of the materials, and wish to thank Messrs. Horai, Funakoshi, and Miss Tada for their voluntary participation in the weighing of samples.

Summary

The ninhydrin reagent for use in the quantitative determination of amino acids separated by paper chromatography was reëxamined and modified, and the conditions under which the reagent could be used most advantageously were determined. The potency of the ascorbic acid contained in the reagent was stabilized by the use of 2% aqueous solution of metaphosphoric acid, and the blank test value and the range of variation in the determined value were minimized. This modified method surpasses the original in that it is less expensive, less sensitive to ammonia, and easier to use, than the latter.

(Received March 18, 1957)

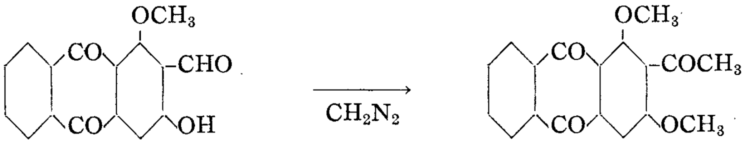
UDC 547.673.6

6-4

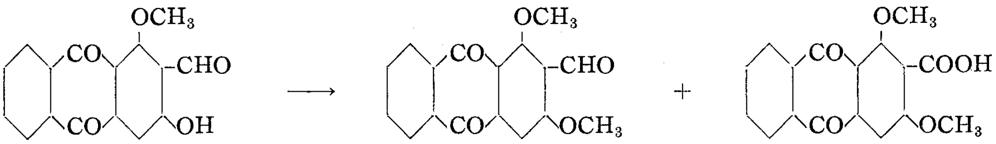
Susumu Nonomura : Chemistry of Damnacanthus Genus. V.* Some Derivatives of Damnacanthal — Munjistin Dimethyl Ether.

(*Pharmaceutical Faculty, University of Kumamoto***)

In a previous experiment[1] damnacanthal dissolved in acetone was methylated with diazomethane but the product (m.p. 175°) thereby obtained was not found to be a simple methyl ether derivative. This time, the product was prepared again and examined. It was proved that the aldehyde group of damnacanthal was changed into a methyl ketone group and the hydroxyl group was methylated. Its infrared absorption spectrum seemed quite reasonable for this structure.



In order to prepare the monomethyl ether of damnacanthal, it was heated with dimethyl sulfate and anhydrous potassium carbonate in acetone. The product was recrystallized from acetone and divided into two kinds of crystals. The one was a crude damnacanthal monomethyl ether (m.p. ca. 125°) and the other a damnacanthic acid monomethyl ether (m.p. 263°), i.e. munjistin dimethyl ether, which is a new substance.[2] Perhaps damnacanthal has been oxidized or it is a product of Cannizzaro reaction and the carboxyl group of munjistin is not esterified on account of the steric hindrance.



---

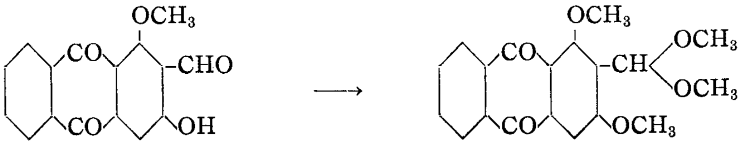
* Part IV. S. Nonomura : J. Pharm. Soc. Japan, **75**, 1305(1955).

** Ōe-machi, Kumamoto (野々村進).

[1] Part III. S. Nonomura : J. Pharm. Soc. Japan, **75**, 227(1955).

[2] E. Schunck, *et al.* : J. Chem. Soc., **33**, 422(1878).

On the other hand, damnacanthal was methylated with methyl iodide and silver oxide. The product (m.p. 145°) was a trimethyl ether of damnacanthal.



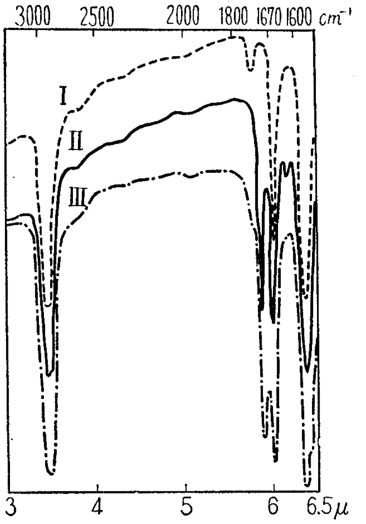


Fig. 1. Infrared Spectra (in Nujol)

I. Damnacanthal trimethyl ether
II. Methyl ketone derivate
III. Damnacanthal monomethyl ether

The infrared spectra of these methyl derivatives are also quite reasonable.

The absorption maxima of the methyl derivative produced by diazomethane are at 1705 and 1660 cm^{-1}. The band at 1705 cm^{-1} is assigned to the methyl ketone and the one at 1660 cm^{-1} to the non-chelated carbonyl of the anthraquinone. The absorption maxima of damnacanthal monomethyl ether are at 1685 and 1668 cm^{-1}, the former being assigned to the free aldehyde group and the latter to the non-chelated carbonyl. The absorption maximum of damnacanthal trimethyl ether is only at 1668 cm^{-1}, for the apsorption of non-chelated carbonyl.

The infrared spectra of damnacanthal anil and damnacanthal hydrazone are represented in Fig. 2. The absorption maximum of damnacanthal anil is only at 1668 cm^{-1}, for the absorption of non-chelated carbonyl.

One of the absorption maxima of damnacanthal hydrazone is also at 1660 cm^{-1} for the non-chelated carbonyl, and other absorptions at 3280 and 3150 cm^{-1} which are assigned to amino groups. The absorption of 3-hydroxyl in these dammacanthal derivatives, like damnacanthal itself,[3] has shifted to the longer wave length on account of chelation with the carbonyl of aldehyde or its derivative and does not appear.

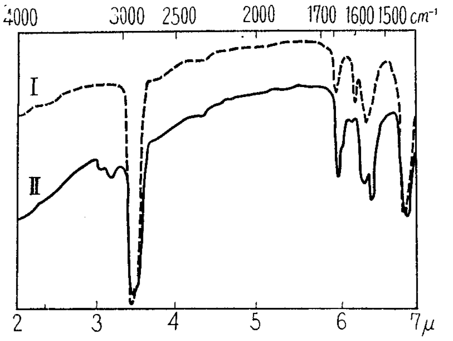


Fig. 2. Infrared Spectra (in Nujol)

I. Damnacanthal anil
II. Damnacanthal hydrazone

---

[3] Part IV. S. Nonomura, Y. Hirose: J. Pharm. Soc. Japan, **75**, 1307(1955).

The author is grateful to Prof. Dr. S. Shibata, University of Tokyo, for his encouragement and to Mr. H. Kozuma, Shin-Nihon-Chisso-Hiryo Co. Ltd., for carrying out the infrared spectral determination. The author's thanks are also due to Miss E. Kawagishi, Miss A. Horie, and Mr. N. Ogata for their help in preparing samples, and to Miss S. Norimatsu for carrying out elemental microanalyses.

Experimental

Methylation with Diazomethane; Methyl Ketone Derivative—To a solution of damnacanthal (0.5 g.) in acetone (50 cc.) was added a solution of CH_2N_2 in ether (prepared from 5 g. N-nitrosomethylurea). After 1 hr. the solvent was distilled off and the residue was recrystallized from MeOH. Pale yellow needles, m.p. 175°, soluble in EtOH, ether, acetone, and MeOH. *Anal.* Calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55; CH_3O, 20.95. Found : C, 70.04, 69.96; H, 4.85, 4.87; CH_3O (Zeisel), 20.30.

Damnacanthal Trimethyl Ether—Damnacanthal (0.5 g.) was heated with MeI (25 g.) and Ag_2O (1 g.) for 1 hr., Ag_2O was filtered off, and the filtrate was distilled. The crystalline residue was recrystallized from MeOH to pale yellow needles, m.p. 145°. *Anal.* Calcd. for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30; CH_3O, 36.26. Found : C, 66.79; H, 5.40; CH_3O, 35.69.

Methylation with Dimethyl Sulfate—A solution of damnacanthal (0.5 g.) in acetone (100 cc.) was heated with Me_2SO_4 (3 cc.) and anhyd. K_2CO_3 (10 g.) for 5 hrs. The carbonate was filtered off and washed with acetone until the filtrate became colorless. The filtrate was evaporated, water and HCl were added to the residue, and a yellow precipitate formed. K_2CO_3 filtered off from the acetone solution was acidified with dil. HCl and the orange precipitate here formed was added to the yellow precipitate mentioned above. The combined precipitate was recrystallized from acetone to pale yellow crystals. The mother-liquor afforded orange needles. The former is a monomethyl ether and the latter damnacanthic acid methyl ether (=munjistin dimethyl ether).

Damnacanthal Monomethyl Ether—Pale yellow needles, m.p. 125°. This is a crude monomethyl ether but difficult to purify. Elemental analysis and methoxyl determination were carried out, but there was a little too large error.

Munjistin Dimethyl Ether (Damnacanthic Acid Methyl Ether)—Orange needles (from acetone), m.p. 263~265°. *Anal.* Calcd. for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87; CH_3O, 19.88. Found : C, 65.52; H, 4.08; CH_3O, 19.12.

Summary

Methylation of damnacanthal with diazomethane gave a methyl ketone derivative, while methylation with dimethyl sulfate and anhydrous potassium carbonate gave a monomethy ether and munjistin dimethyl ether (m.p. 263~265°), and methylation with methyl iodide and silver oxide gave a trimethyl ether. The infrared absorption spectra of these methyl derivatives and other derivatives of damnacanthal were measured.

(Received March 25, 1957)