cerophosphate, 0.02 M, 0.01 M, and 0.05 M, respectively. After 1 hr keeping at 30°, crystals were collected by centrifugation and recrystallized from aq. MeOH producing needles of mp 88°.

Synthesis of O,S-Difuroylmercaptoethanol——To a mixture of 20 ml of pyridine and 7.8 g of furoyl chloride under cooling and stirring, 1.56 g of ME was added slowly. After 30 min, reaction mixture was poured into ice-water and crystals were filtered, washed with $NaHCO_3$ solution and recrystallized from EtOH giving needles of mp 88—89°. Both NMR and IR spectra (Fig. 1 and 2) were identical with those of the product mentioned above. *Anal.* Calcd. for $C_{12}H_{10}O_5S$: C, 54.14; H, 3.79. Found: C, 54.34; H, 3.98.

O,S-Dibenzoylmercaptoethanol——SBT was dissolved into 10 vol. of 40% MeOH and ME was added in alkaline medium. After standing, oil separated was dissolved into $CHCl_3$, washed with water and dried over Na_2SO_4, and the solvent was distilled off. Both NMR and IR spectra of this oil were identical with those of O,S-dibenzoylmercaptoethanol synthesized from benzoyl chloride and ME in pyridine.

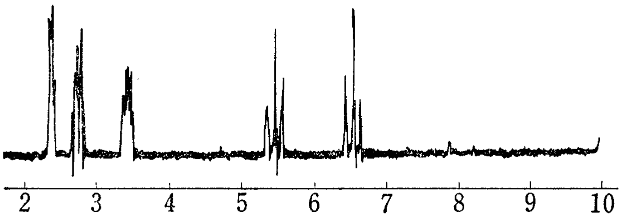

Fig. 1. NMR Spectrum of O,S-Difuroylmercapto-ethanol

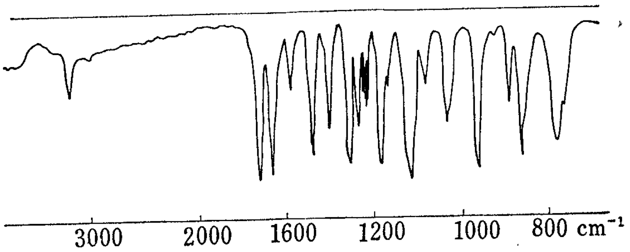

Fig. 2. IR Spectrum of O,S-Difuroylmercapto-ethanol

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Studies on the Synthesis of Munjistin. IV.[1] Synthesis of Munjistin through 1,4-Dihydroxy-2-methylanthraquinone

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In the previous communication[3] the synthesis of munjistin (I), namely 1,3-dihydroxy-2-anthraquinonecarboxylic acid, had been reported. The purpose of the communication was concerned with the identification of synthetic I with the one derived from damnacanthal (II) (3-hydroxy-1-methoxy-2-anthraquinonecarbaldehyde), a natural pigment of *Damnacanthus* spp.

The present paper is to report the details of the synthesis of I. The discrepancy between the observed value and the theoretical value of the analyses of the synthetic specimens of I[4] and 1,2,4-trihydroxy-3-anthraquinonecarboxylic acid (III)[5-7] has now been discriminated.

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1) Part III: Y. Hirose, *Chem. Pharm. Bull.* (Tokyo), **11**, 533 (1963).
2) Location: *5-1 Ōe-hon-machi, Kumamoto.*
3) S. Nonomura and Y. Hirose, *Yakugaku Zasshi*, **75**, 1305 (1955).
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6) D.R.P., 272301 (Friedländer, **11**, 592 (1915)).
7) D.R.P., 260765 (Friedländer, **11**, 592 (1915)).

The procedures to 1,4-dihydroxy-2-anthraquinonecarboxylic acid (IV) starting from condensation of *m*-cresol and phthalic acid anhydride were carried out by the method of K. Keimatsu and T. Hirano.[8] 4-Bromo-1-hydroxy-3-methylanthraquinone (V) was obtained from 2-(5-bromo-2-hydroxy-4-methylbenzoyl)benzoic acid (VI) by an improved reaction condition of the literature[8] in which 7% fuming sulfuric acid was used. When the conversion of V to 1,4-dihydroxy-2-methylanthraquinone (VII) was carried out at 150—160° as shown in the literature,[8] a product assumed to be 1,4-dihydroxy-2-methylanthraquinonesulfonic acid (VIII)[9] was obtained, while at 110—120° VII was obtained in 50% yield. Melting point 149—149.5° of 1,4-diacetyloxy-2-methylanthraquinone (IX) in the literature[8] was amended to 214—215°.

IV did not give III at 5—10° using commercially available manganese dioxide according to D.R.P. method,[6] and the use of the freshly prepared one[10] at $<0°$ gave satisfactory results. On reduction of sodium dithionide III afforded I identical with that derived from II and isolated from *Rubia chinensis* REGEL et MAACK var. *glabrescens* KITAGAWA.[11] Oxidation of 1,3-dimethoxy-2-hydroxymethylanthraquinone (X)[12] and 1,3-dimethoxy-2-anthraquinonecarbaldehyde (XI)[13] by chromium trioxide gave 1,3-di-O-methylmunjistin (XII) which was also prepared from I by methylation with methyl iodide or dimethyl sulfate.

Experimental

4-Bromo-1-hydroxy-3-methylanthraquinone (V)——To a solution of fused B_2O_3 (5 g) in conc. H_2SO_4 (50 ml) was added with stirring 2-(5-bromo-2-hydroxy-4-methylbenzoyl)benzoic acid (110 g). The stirring was continued for 3 hr heating on a water bath while the reaction mixture was changed from dark green color to deep red. The reaction mixture was poured on ice. The precipitated solid was washed with 3% Na_2CO_3 and then hot water. It was recrystallized from AcOH to afford orange, granular crystals, mp 184—185°. *Anal.* Calcd. for $C_{15}H_9O_3Br$: C, 56.80; H, 2.84. Found: C, 57.07; H, 2.86. IR cm^{-1}: 1670, 1632.

1,4-Dihydroxy-2-methylanthraquinone (VII)——V (2.5 g) was added in small portions to a solution of fused B_2O_3 (6 g) in conc. H_2SO_4 (25 ml) at 110—120°. The reaction mixture was kept at 110—120° for 3 hr and poured on ice after cooling. The precipitated solid was heated with water. Insoluble residue was treated with 5% NaOH. This solution was acidified with dil. HCl. The precipitated solid was recrystallized from AcOH and then MeOH to orange needles, mp 183—185°. *Anal.* Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96. Found: C, 70.58; H, 4.40. IR cm^{-1}: 1626.

1,4-Diacetyloxy-2-methylanthraquinone (IX)——Prepared from VII by the method of K. Keimatsu and T. Hirano.[8] Pale yellow needles. mp 214—215° (from MeOH). *Anal.* Calcd. for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17. Found: C, 67.55; H, 4.37. IR cm^{-1}: 1674, 1768.

1,4-Dihydroxy-2-anthraquinonecarboxylic Acid (IV)——Prepared from V and VII by the method of K. Keimatsu and T. Hirano.[8] Orange-brown needles, mp 254° (decomp.) (from AcOH and then toluol) (lit.,[8] mp 249—250°). *Anal.* Calcd. for $C_{15}H_8O_6$: C, 63.39; H, 2.84. Found: C, 63.39; H, 3.01. IR cm^{-1}: 1710, 1630.

Pseudopurpurin (III) (1,2,4-trihydroxy-3-anthraquinonecarboxylic Acid)——IV (5 g) was dissolved adding in small portions to conc. H_2SO_4 (50 ml). To this solution was added in small portions with stirring freshly prepared MnO_2(12 g) cooling at $<0°$. The stirring was continued for 2.5 hr at $<0°$. The reaction mixture was poured on ice. The green, precipitated solid was added in 5% $NaHSO_3$ (100 ml) and allowed to stand at room temperature overnight. The solution was made acidic with dil. HCl and warmed at 80—90° for 5 min. The deposited solid was recrystallized from $CHCl_3$ to bright red-brown plates, mp 229.5—230.5° (decomp.). *Anal.* Calcd. for $C_{15}H_8O_7$: C, 60.01; H, 2.69. Found: C, 59.51; H, 2.77. IR cm^{-1}: 3450, 1705, 1625.

Munjistin (I) (1,3-dihydroxy-2-anthraquinonecarboxylic Acid)——To a solution of III (0.15 g) in 28% NH_4OH (1 ml), 4% $Na_2S_2O_4$ (10 ml) was added in small portions at 20° with intermittent shaking 10 min changing the reaction mixture color from red to transparent yellow-brown. The reaction mixture was

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[8] K. Keimatsu and T. Hirano, *Yakugaku Zasshi*, **51**, 698 (1921).
[9] Unpublished.
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[11] M. Aritomi, *Memories of Faculty of Education, Kumamoto University*, **12**, Sec. I, 13 (1964).
[12] Y. Hirose, *Chem. Pharm. Bull.* (Tokyo), **8**, 422 (1960).
[13] Y. Hirose, *Chem. Pharm. Bull.* (Tokyo), **11**, 532 (1963).

carefully made acidic with 1% HCl at 0°. The depositing precipitate was recrystallized from Me_2CO to yellow plates, mp 232° (decomp.). *Anal.* Calcd. for $C_{15}H_8O_6$: C, 63.39; H, 2.84. Found: C, 63.57; H, 2.99. IR cm^{-1}: 3250, 3080, 1688, 1626. This product was identified with an authentic sample of I derived from II,³⁾ and a sample¹⁰⁾ isolated from *Rubia chinensis* Regel et Maack var. *glabrescence* Kitagawa by mixed mp determination and IR comparison.

Methyl 1,3-Dimethoxy-2-anthraquinonecarbonate (XIII) (1,3-di-O-methylmunjistin 2-methyl ester)—— (1) A mixture of I (0.5 g), Ag_2O (3 g), CH_3I (3 ml), and Me_2CO (100 ml) was refluxed for 10 hr. (2) A mixture of I (0.5 g), K_2CO_3 (10 g), $MeSO_4$ (3 ml), and Me_2CO (100 ml) was refluxed for 10 hr.

The product obtained by treatment as shown in (1) and (2) run was recrystallized from MeOH to give pale yellow needles, mp 147—148°. *Anal.* Calcd. for $C_{18}H_{14}O_6$: C, 66.25; H, 4.32. Found: C, 66.66; H, 4.47. IR cm^{-1}: 1734, 1678, 1664.

1,3-Di-O-methylmunjistin (XII) (1,3-dimethoxy-2-anthraquinonecarboxylic Acid)——1) XIII (0.2 g) was refluxed with 2% ethanolic KOH (50 ml) for 3 hr. The product obtained by the usual way was recrystallized from MeOH to pale yellow needles, mp 212—213°. *Anal.* Calcd. for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87. Found: C, 64.95; H, 3.91. IR (Nujol) cm^{-1}: 1760, 1720, 1700, 1673, 1646. IR ($CHCl_3$) cm^{-1}: 1760, 1720, 1689. IR (dioxane) cm^{-1}: 1750, 1682. IR ($CHCl_3$+1 gtt. piperidine) cm^{-1}: 1674.

2) To a solution of 1,3-dimethoxy-2-anthraquinonecarbaldehyde (XI)¹³⁾ (200 mg) in AcOH (1) : $(AcO)_2O$ (1) (10 mg) was added dropwise with stirring a solution of CrO_3 (100 mg) in AcOH (10 ml) and H_2O (0.1 ml) at 55—60°, and the stirring was continued keeping at this temperature for 2 hr when the reaction was complete changing the reaction mixture color from brown to green. The reaction mixture was poured into hot water (500 ml) and left at room temperature overnight. The depositing precipitate was recrystallized from MeOH to pale yellow needles, mp 212—213°. The IR spectrum of this product was shown to be superimposable with that of the foregoing product (XII), and their mixed mp showed no depression.

3) To a solution of 1,3-dimethoxy-2-hydroxymethylanthraquinone (X)¹²⁾ (200 mg) in AcOH (1) : $(AcO)_2O$ (1) (10 ml) was added dropwise with stirring a solution of CrO_3 (200 mg) in AcOH (10 ml) and H_2O (0.1 ml) at 55—60°. The product obtained by the working as described above was shown to be identical with the foregoing product by mixed mp determination and IR comparison.

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Studies on Peptides. XVII. Synthesis of N-(Nᵅ-Acetylseryltyrosylserylmethionylglutamylhistidylphenylalanylarginyl)-5-methoxytryptamine and Its Physiological Properties on Frog Melanocyte *in vitro*¹˒²⁾

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Recently we have replaced the acetyl group of melatonin⁴˒⁵⁾ which is known as the most powerful but nonspecfic inhibitior of α-melanocyte-stimulating hormone (MSH)⁶⁾ with a histi-

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1) The Part XVI of this series: *Chem. Pharm. Bull.* (Tokyo), **16**, 919 (1968).
2) The peptides and peptide derivatives mentioned in this communication are of the L-configuration and their abbreviated designations are those recommended by IUPAC-IUB commission for biological nomenclature in July 1965 and July 1966: *Biochemistry*, **5**, 2485 (1966); **6**, 362 (1967).
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