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Studies on the Synthesis of Munjistin. II.1,2

Synthesis of 3-O-Methyllydamnoncanthal.

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In the previous paper,1,2 it was reported that damnoncanthal (1-methoxy-3-hydroxy-2-anthraquinonecarboxaldehyde) (I) was synthesized from damnoncanthol (1-methoxy-2-hydroxymethyl-3-hydroxyanthraquine) (II), and that nor-damnoncanthal (1,3-dihydroxy-2-anthraquinonecarboxaldehyde) (III) and munjistin (1,3-dihydroxy-2-anthraquinonecarboxylic acid) (IV) were synthesized directly from lucidin (2-hydroxymethyl-1,3-dihydroxyanthraquine) (V). 3-O-Methyllydamnoncanthal (VI), m.p. 185° ~ 186° was obtained as a pre-step product en route to 1,3-O-dimethylmunjistin (VII),a though the melting point of VI was reported to be 125° VIII,3 prepared from I by the methylation with dimethyl sulfate and potassium carbonate in acetone. It is therefore the purpose of this paper to ascertain the melting point of VI which was shown at 185° ~ 186°.

When lucidin (V)1,5 was repeatedly dissolved in 90% ethanol and either concentrated or refluxed for 6 hours, the substance of m.p. 180° (decomp.) was obtained. Since the substance of m.p. 180° (decomp.) could be synthesized to 2-ω-O-ethyl-1,3-O-dimethyllucidin (IX),4 m.p. 141° ~ 142°, which was derived from 2-ω-O-ethyl-3-O-methyllucidin,4 the structure of substance, m.p. 180° (decomp.), should be indicated to be 2-ω-O-ethylcucidin (X). V was refluxed in acetic acid solution to afford its alcoholic acetate, 2-ω-O-acetyl-lucidin (XI), m.p. > 300° (decomp.), which was confirmed by methylation to 2-ω-O-acetyl-1,3-O-dimethyllucidin (XII), m.p. 173° ~ 174° as reported in the literature.5

On selective acetylation by means of boro-triacetate and acetic anhydride, V gave 2-ω,3-O-diacetyllucidin (XIII), m.p. 152° ~ 153°, which was also confirmed by methylation to 1-O-methy1-2-ω,3-O-diacetyllucidin (XIV), m.p. 156° ~ 157°, as reported in the literature.3,5 On the other hand, V gave XIII directly by the treatment with acetic anhydride. V was methylated directly to lucidin trimethyl ether (XIV), m.p. 162°, which was confirmed to be identical with 2-methoxymethyl-1,3-dimethoxanthraquine, prepared from II.5 It was reported that XIII gave 1,3-O-dimethyllucidin (XVI), m.p. 175°,4,5 on hydrolysis with 3% methanolic sulfuric acid. On oxidation with active manganese dioxide,3 XVI gave 3-O-methyllydamnoncanthal (VII), m.p. 185° ~ 186°. Treatment of I by the method described in the literature5 also afforded VI as a sole product. Infrared spectrum of VI in Nujol

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mull showed the presence of aldehyde absorption at 1704 cm\(^{-1}\), and the corresponding absorption to the literature\(^3\) was not observed at 1700\(\sim\)1710 cm\(^{-1}\) region assigned to C-O stretchings in free aldehyde.

**Experimental**

2-\(\omega\)-O-Ethylidin (X) — V (0.2 g) was refluxed in 90% EtOH (100 ml) for 6 hr. The solution was concentrated to separate crystalline solid which was repeatedly recrystallized from EtOH to pale yellow needles of m.p. 180\(\theta\) (decomp.). Its paper chromatogram using filter paper, Toyo Roshi No. 50, and BuOH saturated with 28% NH\(_2\)OH as a developing solvent showed Rf. 0.84. *Anal. Calcd.* for C\(_{17}\)H\(_{14}\)O\(_2\): C, 68.45; H, 4.73. Found : C, 68.88; H, 4.32.

2-\(\omega\)-O-Ethyl-1,3-O-dimethylidin (IX) — It was prepared from X by usual way, m.p. 141\(\sim\)142\(\theta\). The identity of IX with that described in the literature\(^5\) was established m.p. determination by admixture. *Anal. Calcd.* for C\(_{19}\)H\(_{18}\)O\(_3\): C, 69.92; H, 5.56. Found : C, 70.04; H, 5.62.

2-\(\omega\)-O-Acetylidin (XI) — V (0.6 g) was refluxed in AcOH (60 ml) for 1 hr. The solution was concentrated to separate crystalline solid which was repeatedly recrystallized from AcOH together with charcoal to yellow needles of m.p. >300\(\theta\) (decomp.). *Anal. Calcd.* for C\(_{21}\)H\(_{18}\)O\(_3\): C, 65.38; H, 3.87. Found : C, 65.45; H, 3.81. IR \(\nu^{\text{max}}\) cm\(^{-1}\) : 3370 (OH), 1730 (alcoholic acetate), 1663 (non-chelated C=O), 1638 (chelated C=O), 1600 and 1588 (phenyl).

2-\(\omega\)-O-Acetyl-1,3-O-dimethylidin (XII) — A mixture of XI (1.2 g), Ag\(_2\)O (6 g), CH\(_2\)I (5 ml) and Me\(_2\)CO (80 ml) was refluxed for 10 hr. Recrystallization from EtOH in the presence of charcoal, afforded pale yellow needles of m.p. 173\(\sim\)174\(\theta\), which was identified by mixed melting point, IR spectrum with that prepared by the method of Venkataraman\(^5\) from 2-bromourubidin dimethyl ether. *Anal. Calcd.* for C\(_{25}\)H\(_{20}\)O\(_4\): C, 67.05; H, 4.75. Found : C, 67.29; H, 4.45. IR \(\nu^{\text{max}}\) cm\(^{-1}\) : 1728 (alcoholic acetate), 1674 (non-chelated C=O), 1583 (phenyl).

2-\(\omega\)-O-Diacetylidin (XIII) — i) A mixture of V (1 g), boroacetic anhydride (2.5 g), and Ac\(_2\)O (10 ml) was refluxed for 10 min. The crystalline precipitate separated after cooling was digested in H\(_2\)O. The resulting precipitate was recrystallized from dill. AcOH to yellow needles of m.p. 151\(\sim\)153\(\theta\). *Anal. Calcd.* for C\(_{21}\)H\(_{18}\)O\(_3\): C, 64.40; H, 3.98. Found : C, 64.05; H, 4.24.

ii) A mixture of V (0.3 g) and Ac\(_2\)O (30 ml) was refluxed for 1 hr., and poured into H\(_2\)O. The precipitate separated was recrystallized from dill. AcOH together with charcoal to yellow needles of m.p. 151\(\sim\)153\(\theta\), which showed no depression by mixed melting point with that described above. *Anal. Calcd.* for C\(_{21}\)H\(_{18}\)O\(_3\): C, 64.40; H, 3.98. Found : C, 64.80; H, 4.01.

1-0-Methyl-2-\(\omega\)-O-diacetylidin (XIV) — A mixture of XIII (0.5 g), Ag\(_2\)O (2.5 g), CH\(_2\)I (3 ml) and Me\(_2\)CO (60 ml) was refluxed for 10 hr. Recrystallization from MeOH added with charcoal afforded pale yellow needles of m.p. 156\(\sim\)157\(\theta\), which was established by mixed m.p. determination with an authentic sample.\(^5\)

**Lucidin Trimethyl Ether (XV) —** A mixture of V (0.5 g), Me\(_2\)SO\(_4\) (2.5 g), K\(_2\)CO\(_3\) (10 g) and Me\(_2\)CO (100 ml) was refluxed for 20 hr. Recrystallization from MeOH afforded pale yellow needles of m.p. 162\(\theta\), which was established m.p. determination with an authentic sample.\(^5\)

3-0-Methylidamcanthal (VI) — i) A mixture of XVI (0.5 g), active MnO\(_2\) (2.5 g) and AcOEt (150 ml) was refluxed for 0.5 hr. Recrystallization from MeOH with charcoal afforded pale yellow needles of m.p. 185\(\sim\)186\(\theta\). *Anal. Calcd.* for C\(_{17}\)H\(_{15}\)O\(_3\): C, 68.91; H, 4.08. Found : C, 69.14; H, 4.40. IR \(\nu^{\text{max}}\) cm\(^{-1}\) : 1704 (Aryl-CHO), 1675 and 1663 (non-chelated C=O), 1580 (phenyl).

ii) I was methylated with either Me\(_2\)SO\(_4\), K\(_2\)CO\(_3\) and Me\(_2\)CO or Ag\(_2\)O, Mel and Me\(_2\)CO. The product was recrystallized from MeOH to yellow needles of m.p. 185\(\sim\)186\(\theta\), the identity of which with that described above was established by a mixed m.p. determination and IR spectra in Nujol. *Anal. Calcd.* for C\(_{17}\)H\(_{15}\)O\(_3\): C, 68.91; H, 4.08. Found : C, 69.04; H, 3.99.

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**Summary**

Synthesis of 3-O-methylidamcanthal (VI), m.p. 185\(\sim\)186\(\theta\), was described.

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