was washed with water, dried, and evaporated under a reduced pressure. The residue, approx. 0.5 g., was purified by sublimation or distillation under a diminished pressure or recystallization from xylene. The colorless crystals thus obtained melted at 78~78.5°, b.p$_{0.5}$ 127~129°. There was no depression of the melting point on admixture with the compound obtained from ethyl 1-acetyl-2,3-dihydroindoxylate (XXII) by $LiAlH_4$ reduction. *Anal.* Calcd. for $C_{11}H_{13}ON$ (XX): C, 75.44; H, 7.48; N, 8.00. Found : C, 75.69; H, 7.04; N, 7.86.

Summary

When ethyl indoxylate was treated with lithium aluminum hydride, three compounds were obtained. Two of these compounds were identified as N-acetylanthranilic acid (V) and 2-methyl-2-(2′-methylindyl-3′)pseudoindoxyl (Ⅵ), and the remaining one was assumed to be bis(2-methyl-2-indolin-3-one) (Ⅶ). The mechanisms of their formation were discussed.

(Received April 26, 1956)

U.D.C. 547.677.4.07

52. **Michitoshi Ohta**: Azaditerpenoids. IV.[1] Synthesis of 1-Methoxycarbonyl-1,12-dimethyl-7-amino-1,2,3,4,9,10,11,12-octahydrophenanthrene.

(*Kowa Chemical Laboratories**)

In Part Ⅱ of this series,[2] it was shown that the permanganate oxidation of dehydroabietic acid and purification of the product as its methyl ester by chromatography afforded 1-methoxycarbonyl-1,12-dimethyl-7-acetyl-9-oxo-1,2,3,4,9,10,11,12-octahydrophenanthrene (Ⅲ) in 0.8% yield as a by-product. Later, this reaction condition was examined in order to increase the yield of (Ⅲ) and it was found that the oxidation of methyl dehydroabietate (I) with chromium trioxide in glacial acetic acid at about 80° afforded methyl 9-oxodehydroabietate (Ⅱ) in 25% yield, together with about 5% yield of (Ⅲ). Similar oxidation of (Ⅱ) was found to give (Ⅲ) in 14% yield. Recently, Zeiss, *et al.*[3] reported that oxidation of (I) in a large amount of glacial acetic acid with chromium trioxide at 70° gives (Ⅲ) in a good yield of 17~20%.

Heating of (Ⅲ) with equimolar amount of iodine in pyridine at 100° results in the formation of a corresponding pyridinium iodide but the substance remains uncrystallizable. Decomposition of this iodide by boiling with two moles of ethanolic sodium hydroxide affords 1-methoxycarbonyl-7-carboxy-9-oxo-1,12-dimethyloctahydrophenanthrene (Ⅳ), m.p. 200~202°. Use of an excess of ethanolic sodium hydroxide naturally results in the saponification of the ester at 1-position and a dicarboxylic acid of m.p. 290°(decomp.) is obtained. Attempted oxidation of (Ⅲ) with sodium hypobromite, followed by methylation of the acid so obtained with diazomethane, and purification of the methyl ester afforded rhomboprismatic crystals of m.p. 152.5~154°, which gave positive halogen test and whose analytical values agreed with $C_{20}H_{23}O_5Br$. These facts indicated that the desired oxidation of the acetyl group was accompanied with the introduction of bromine.

Reduction of (Ⅳ) by the Huang-Minlon method and recrystallization of the product from methanol-benzene mixture afforded crystals (V′) of m.p. 240~242°(sint. at around

---

* Shimotakaido, Suginami-ku, Tokyo (太田道敏).

[1] Part Ⅲ : J. Pharm. Soc. Japan, **75**, 445(1955).

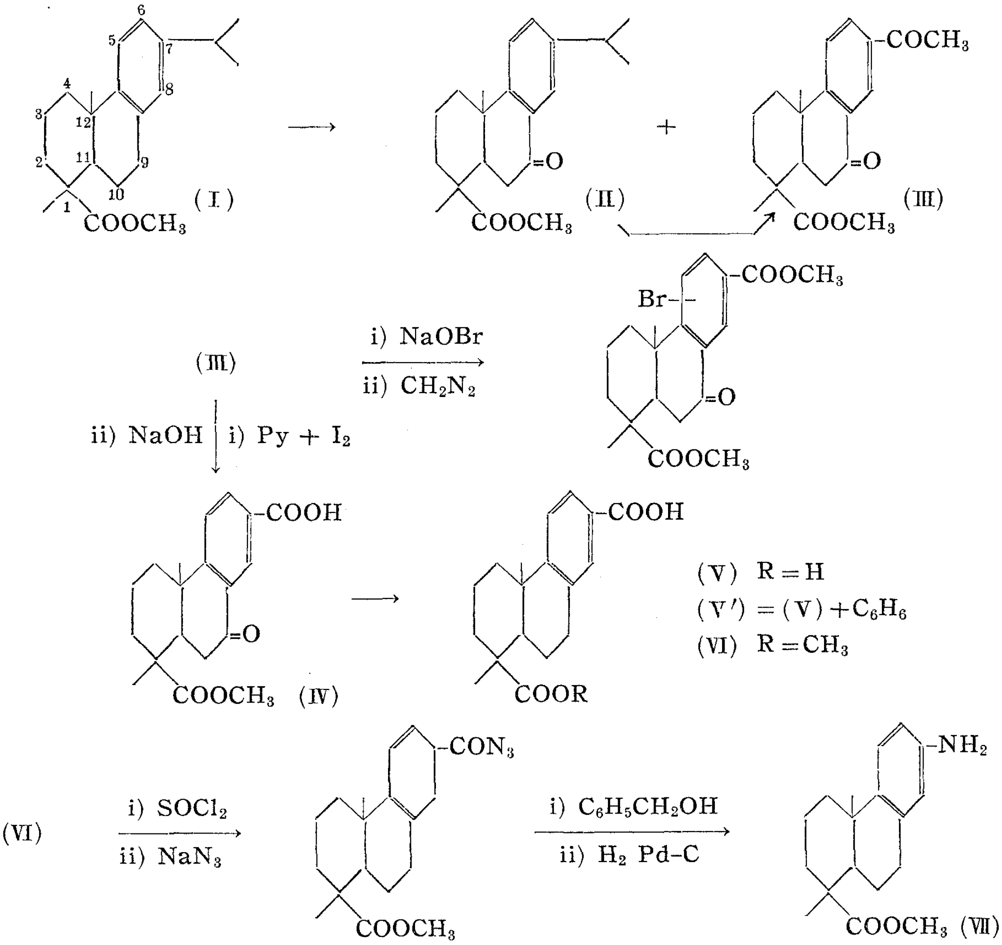
[2] M. Ohta : *Ibid.*, **75**, 289(1955).

[3] H. H. Zeiss, *et al.* : J. Am. Chem. Soc., **77**, 6707(1955).

142°). The analytical values obtained of a sample dried at 90° *in vacuo* agreed with those for an equimolar addition product of 1,7-dicarboxy-1,12-dimethyloctahydrophenanthrene (V) and benzene. After drying this substance at 140° under 1-mm. Hg vacuum there was no sintering at 142° and the analytical values agreed with those for (V). Therefore, (V′) must be (V) with 1 mole of benzene as a solvent of crystallization.

When the dimethyl ester of (V), obtained by treatment with diazomethane, is boiled with one mole of 0.1*N* ethanolic sodium hydroxide, the C_7-ester with less steric hindrance is preferentially saponified to form the monoester (VI) of m.p. 179~181°.

Conversion of (VI) to an acid chloride with thionyl chloride and its treatment with sodium azide in acetone afforded the acid azide of m.p. 96°(decomp.). Heating of this azide with benzyl alcohol at 100° converted it to benzylurethan, which remained uncrystallizable, and its catalytic reduction in ethanol acidified with hydrochloric acid, using palladium-charcoal as the catalyst, finally afforded the desired 1-methoxycarbonyl-1,12-dimethyl-7-aminoöctahydrophenanthrene (VII); yield from (VI), 83%. Derivation of (VI) to the acid amide through acid chloride and the Hofmann rearrangement of the amide gave (VII) in only about 30% yield. The Schmidt reaction of (VI) ended fruitless.



Deep gratitude of the author is expressed to Prof. E. Ochiai of the University of Tokyo for his unfailing guidance throughout the course of this work. The author is much indebted to the members of the elementary analysis room of this Laboratories and to Miss. R. Ohmori for her cooperation in these experiments.

Experimantal[4]

Chromium Trioxide Oxidation of Methyl Dehydroabietate (I)—A solution of 45 g. of CrO_3 dissolved in a mixture of 40 cc. of water and 200 cc. glacial AcOH was dropped into the solution of 30 g. (I) dissolved in 100 cc. glacial AcOH, while agitating on a water bath, during 50 mins., maintaining the temperature of the solution at 65~70°. The mixture was further heated at 78~83° for 4 hrs., allowed to stand over night, and excess CrO_3 was decomposed with MeOH. Glacial AcOH was distilled off under a reduced pressure, water was added to the residue, and this was extracted with benzene. The benzene extract was washed with dil. NaOH and water, dried over anhyd. Na_2SO_4, and benzene was distilled off. The residue was treated with Girard T reagent by the usual method and 20 g. of ketonic fraction was obtained. This was dissolved in 1:1 mixture of benzene and petr. ether and passed through a chromatographic column with 600 g. of Al_2O_3. Elution with the same solvent mixture afforded 7.7 g. (25%) of crude (II), m.p. 64°, and further elution with the same solvent added with a small amount of MeOH gave crude (III), m.p. 135~140°. The latter was dissolved in 10 cc. of hot MeOH, 4 cc. of 10% NaOH added, heated on a water bath for 1 min., and water added. This was extracted with benzene, the benzene extract was dried, and the solvent evaporated. The residue was recrystallized from MeOH to 1.5 g. (5%) of (III), m.p. 142~144°.

Chromium Trioxide Oxidation of Methyl 9-Oxodehydroabietate (II)—A solution of 21 g. CrO_3 dissolved in a mixture of 20 cc. of water and 100 cc. of glacial AcOH was added dropwise, with stirring, into a solution of 15 g. (II) dissolved in 35 cc. glacial AcOH, heated at 58~62° for 4 hrs., and allowed to stand at room temp. over night. This was treated as in the foregoing and 2.08 g. (14%) of (III), m.p. 142~144°, was obtained.

1-Methoxycarbonyl-7-carboxy-1,12-dimethyl-9-oxo-1,2,3,4,9,10,11,12-octahydrophenanthrene (IV)—A mixture of 1.05 g. I_2 added to a solution of 1.36 g. of (III) dissolved in 5 cc. pyridine was heated at 100° for 2 hrs. and allowed to stand over night at room temp. After the addition of 2 cc. water, pyridine was distilled off under a reduced pressure and the residue was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried over anhyd. Na_2SO_4, and $CHCl_3$ evaporated. The dark brown, syrupy residue was dissolved in 20 cc. EtOH, 8.28 cc. of *N* NaOH added, and the mixture was boiled on a water bath for 2 hrs. EtOH was evaporated under a reduced pressure, the residue was acidified with HCl, and extracted with ether. After drying over anhyd. Na_2SO_4, ether was distilled off and the residue was recrystallized from MeOH–*iso*-Pr_2O mixture to 0.99 g. (72%) of plate crystals, m.p. 195~200°. Two more recrystallizations from the same solvent mixture raised the m.p. to 200~202°. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.1; H, 6.7; COOH, 13.6. Found : C, 68.91; H, 6.93; COOH, 13.91. $[\alpha]_D^{15}$: +21.4°(c=2.096). U.V. λ_{max} mμ (log ε) : 224(4.61), 291(3.13), 301(3.12).

Sodium Hypobromite Oxidation of (III)—To a solution of NaOBr, prepared from 8 cc. of 20% NaOH and 0.6 cc. Br_2, 0.64 g. of (III) dissolved in 4 cc. dioxane was added dropwise, under stirring at room temp., by which a slight evolution of heat occurred and temperature of the reaction mixture reached 40°. After 10 mins., water was added and the mixture was extracted with ether. The aq. layer was acidified with HCl, extracted with ether, and ether was evaporated from the extract after drying over anhyd. Na_2SO_4. The residue was methylated with CH_2N_2 and recrystallized from MeOH to rhomboprisms, m.p. 152.5~154°, positive to Beilstein test. *Anal.* Calcd. for $C_{20}H_{23}O_5Br$: C, 56.7; H, 5.4. Found : C, 57.23; H, 5.26.

1,7-Dicarboxy-1,12-dimethyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (V)—To a solution of 0.87g. (IV) dissolved in 14 cc. diethylene glycol, 1 g. KOH and 1 cc. hydrazine hydrate were added and the mixture was heated at 130~140° for 1 hr. After attaching a downward condenser, the bath temp. was raised gradually, excess of hydrazine was allowed to distill off, and the mixture was heated at 210~220° for 2 hrs. When cooled, dil. HCl was added to the reaction mixture, extracted with ether, and the ether was evaporated after drying over anhyd. Na_2SO_4. The residue was recrystallized from MeOH-benzene mixture to 0.89 g. (89%) of (V′), m.p. 240~242°(sint. at ca. 142°). Analytical sample was dried at 90° for 4 hrs. *in vacuo*. *Anal.* Calcd. for $C_{24}H_{28}O_4$ (V′) : C, 75.8; H, 7.4; COOH, 23.7. Found : C, 75.60; H, 7.50; COOH, 23.93.

The sample was further dried at 140° for 1 hr. under 1 mm. Hg pressure; m.p. 240~242°. *Anal.* Calcd. for $C_{18}H_{22}O_4$ (V) : C, 71.5; H, 7.3; COOH, 29.8. Found : C, 71.16; H, 7.33; COOH, 30.22. $[\alpha]_D^{15}$: +74.5°(c=1.436). U.V. λ_{max} mμ (log ε) : 241(4.15), 280(3.15), 289(3.09).

1-Methoxycarbonyl-7-carboxy-1,12-dimethyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (VI)—To 1.66 g. of (V′) dissolved in ether, ethereal solution of CH_2N_2 was added to effect methylation. After decomposition of excess CH_2N_2 with AcOH, the ethereal solution was washed with dil. NaOH,

---

[4] The melting points are all uncorrected. Optical rotation and ultraviolet spectra were all measured in ethanolic solution.

dried over anhyd. Na_2SO_4, and ether was evaporated. The syrupy residue was dissolved in 40 cc. EtOH, 4.36 cc. of *N* NaOH was added, and the mixture was boiled on a water bath for 2 hrs. EtOH was distilled off under a reduced pressure, the residue was acidified with HCl, and extracted with ether. After drying over anhyd. Na_2SO_4, ether was evaporated, and the residue was recrystallized from dil. MeOH, affording 1.28 g. (93%) of plates, m.p. 178~180°. Two recrystallizations from the same solvent raised the m.p. to 179~181°. *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.1; H, 7.7; COOH, 14.2. Found : C, 72.43; H, 8.11; COOH, 14.42. $[\alpha]_D^{15}$: +69.1°(c=2.286). U.V. λ_{max} mμ (log ε): 241(4.15), 280(3.14), 288(3.07).

1-Methoxycarbonyl-1, 12-dimethyl-7-amino-1, 2, 3, 4, 9, 10, 11, 12-octahydrophenanthrene (VII)—A mixture of 0.78 g. (VI), 3 cc. $SOCl_2$, and 1 drop of pyridine was boiled for 1.5 hrs. on a water bath. Excess $SOCl_2$ was distilled off uuder a reduced pressure, dehyd. benzene was added, and the solvent removed under a reduced pressure. The residue was dissolved in 8 cc. acetone, a solution of 0.3 g. NaN_3 dissolved in 1.5 cc. water was added under ice chilling, and shaken for 15 mins. The acid azide, m.p. 96°(decomp.), that precipitated out on the addition of water was collected, dissolved in $CHCl_3$, dried over anhyd. Na_2SO_4, and the solvent was evaporated under a reduced pressure in a water bath of 40°. The residue was heated with 0.27 g. benzyl alcohol at 100° for 2 hrs., by which a vigorous reaction occurred at first but the evolution of N_2 became slack after 5 mins. This mixture was dissolved in 20 cc. EtOH, 0.07 g. of 10% Pd-C and 0.5 cc. conc. HCl added, and the mixture was submitted to catalytic reduction at ca. 50°, by which a little over 1 mole of H_2 was absorbed during 1 hr. After removal of the catalyst by filtration, EtOH was evaporated from the filtrate under a reduced pressure, the hydrochloride thereby obtained was dissolved in hot water, and a small amount of insoluble matter was filtered off. On cooling, the solution was basified with NaOH, extracted with ether, and the ether was evaporated after drying the extract over anhyd. Na_2SO_4. The residue was recrystallized from benzene-petr. ether mixture to 0.59 g. of needles, m.p. 102~104°, giving positive diazo reaction. Yield from (VI), 83%. Further recrystallization from the same solvent mixture raised m.p. to 104.5~106°. *Anal.* Calcd. for $C_{18}H_{25}O_2N$: C, 75.2; H, 8.8; N, 4.9. Found : C, 75.37; H, 8.73; N, 5.04. $[\alpha]_D^{10}$: +73.7°(c=1.534). U.V. λ_{max} mμ (log ε) : 237(3.96), 290(3.27).

Summary

7-Acetyl-9-oxo derivative (III) obtained by the oxidation of methyl dehydroabietate (I) with chromium trioxide converts to the corresponding carboxylic acid (IV) by the oxidation of C_7-acetyl group alone on treatment with iodine in pyridine and followed by treatment with sodium hydroxide. The ketone was reduced by the Huang-Minlon's method to 1,7-dicarboxy-1,12-dimethyloctahydrophenanthrene (V) and through its dimethyl ester, 1-monomethyl ester (VI) was prepared. The Curtius reaction of (VI) afforded the objective 1-methoxycarbonyl-1,12-dimethyl-7-amino-1,2,3,4,9,10,11,12-octahydrophenathrene.

(Received April 30, 1956)