U. D. C. 547.677.2.07

9

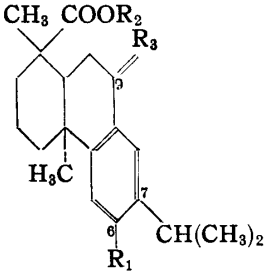
13. Eiji Ochiai and Mitsutaka Natsume : Sytheses of Alkylphenanthrenens. II.[1]

(*Pharmaceutical Institute, Medical Faculty, University of Tokyo**)

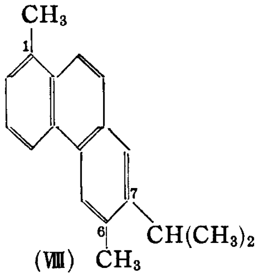
In the previous paper,[1] the syethesis of several types of alkylphenanthrenes was reported, which was undertaken in order to clarify the structure of the alkylphenanthrenes obtained as the products of selenium dehydrogenation reaction from anhydroignavinol[2] and hypognavinol.[3] We present in this paper the syntheses of 7-isopropyl-1,6-dimethylphenanthrene (VIII) from dehydroabietic acid (I) and also 1,7-dimethyl-6-ethyl- (XIX) and 1,7-dimethyl-6-isopropylphenanthrene (XXI) from agathic acid.

7-Isopropyl-1,6-dimethylphenanthrene

It has been shown[4] that the 6-chloromethyl derivative of dehydroabietic acid can be easily obtained by Blanc's chloromethylation method.[5] This methyl 6-chloromethyldehydroabietate was reduced to 6-methyl derivative by catalytic hydrogenation over palladium-carbon and the methyl derivative was dehydrogenated with selenium to 7-isopropyl-1,6-dimethylphenanthrene.



	R_1	R_2	R_3
(I)	H	H	H_2
(II)	CH_2Cl	H	H_2
(III)	CH_2Cl	CH_3	H_2
(IV)	COOH	H	H_2
(V)	$COCH_3$	CH_3	H_2
(VI)	COOH	H	O
(VII)	CH_3	CH_3	H_2



(VIII)

6-Isopropyl-1,7-dimethyl- and 6-Ethyl-1,7-dimethylphenanthrenes.

Ruzicka, *et al.*[6] reported the preparation of triene ester (XIV) from agathic acid (IX) and the ester was converted to pimanthrene by dehydrogenation. We followed their method with some modification and the triene ester (XIV) was easily obtained.

On the Friedel-Crafts acetylation in *sym*-tetrachloroethane, (XIV) afforded only one product which was proved to be 6-acetyl derivative on the following grounds. The product showed two maxima in ultraviolet spectrum at 258 mμ (log ε 4.13) and 292 mμ (log ε 3.35). Comparing these data with those of succesively 2′-methylated acetophenone series[7] (Table I), it is clear that the compound is not a 2′,6′-disubstituted acetophenone. The possibility of 8- or 5-acetyl derivative is thus excluded, and moreover, acetylation at 5-position is sterically hindered.

6-Acetyl compound (XV) was converted to (XX) by the Clemmensen reduction and (XV) was also methylated, dehydrated, and catalytically reduced to give (XVIII). Dehydrogenation of (XX) and (XVIII) gave the desired phenanthrenes (XXI) and (XIX).

---

* Hongo, Tokyo (落合英二, 夏目充隆).

1) Part I. E. Ochiai, *et al.* : This Bulletin, **5**, 48(1957).

2) E. Ochiai, T. Okamoto, T. Sugasawa, S. Sakai : *Ibid.*, **2**, 388(1954).

3) S. Sakai : J. Pharm. Soc. Japan, **76**, 1054(1956).

4) Y. T. Pratt : J. Am. Chem. Soc., **73**, 3803(1951).

5) Bull. soc. chim. France, [4] **33**, 313(1923).

6) Helv. Chim. Acta, **24**, 223(1941).

7) E. A. Braude, F. Sondheimer : J. Chem. Soc., **1955**, 3754.

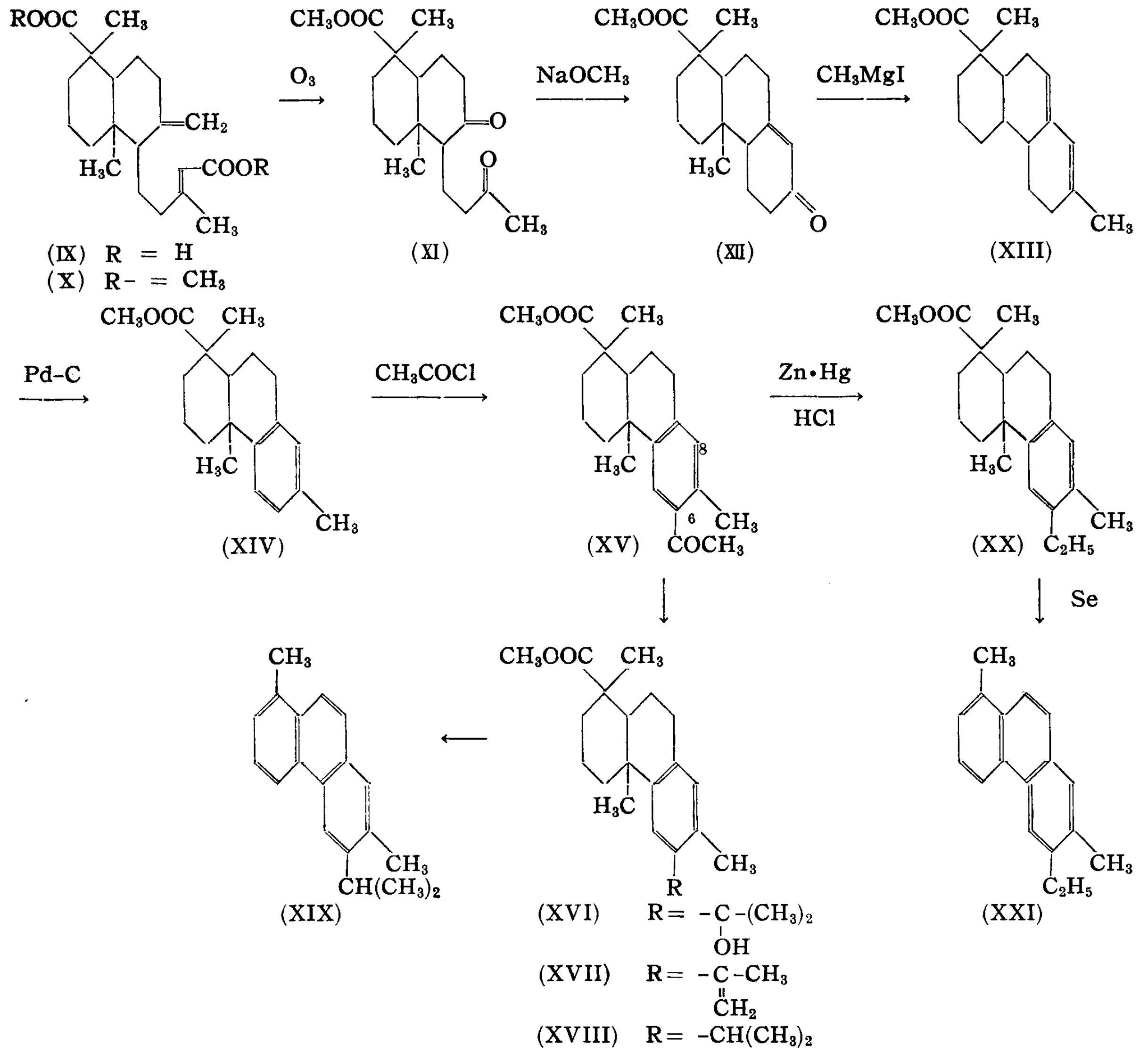


Table I.

	λ_{max} mμ (log ε)
Acetophenone	243 (4.12), 279 (3.08)
2′-Methylacetophenone	242 (3.94), 281 (3.08)
2′,6′-Dimethylacetophenone	251 (3.75), 281*(2.95)

* Inflexion

We are greatly indebted to Mr. M. Ohta, Kowa Chemical Loboratories, for supplying us sample of dehydroabietic acid. The microanalyses were carried out by the members of the Central Analysis Room of this Institute and by Mr. Nara and Mr. Yamaguchi of Kowa Chemical Laboratries, to all of whom our thanks are due.

Experimental

7-Isopropyl-1,6-dimethylphenanthrene : Methyl 6-Chloromethyldehydroabietate (III)—The ester was obtained as described by Pratt[4] and recrystallized from MeOH to colorless prisms, m.p. 112~116°.

Methyl 6-Methyldehydroabietate (VII)—The chloromethyl compound (0.24 g.) was hydrogenated over Pd-C (prepared from 0.1 g. of carbon and 3 cc. of 1% $PdCl_2$) in alkaline-EtOH solution (50cc. of EtOH and a small amount of $Ba(OH)_2 \cdot 8H_2O$), and quantitative volume of H_2 (16 cc.) was consumed at 30°. After filtration of the catalyst, the reaction solution was concentrated to a syrup, diluted with Et_2O, washed with 5% HCl solution and then with 5% K_2CO_3 solution, and dried over anhyd. Na_2SO_4. The distillation of the solvent gave 0.21 g. of a crude product. Repeated recrystallization from MeOH gave colorless pillars (VII), m.p. 122~123°. Yield, 50 mg. *Anal.* Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.93; H, 9.48.

7-Isopropyl-1,6-dimethylphenanthrene (VIII)—Above compound (100 mg.) was dehydrogenated with Se (150 mg.) at 310~330° for 3.5 hrs. and the reaction product was extracted with ether. After removal of the solvent, 57 mg. of crude crystals (m.p. 85~90°) was obtained. Purified by chromatographic method on Al_2O_3 using petr. benzine as a solvent and recrystallized from MeOH to colorless needles, m.p. 102~103°. Yield, 18 mg.

Trinitrobenzene complex: Yellow needles, m.p. 184~185°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$: C, 65.07; H, 5.02; N, 9.11. Found: C, 64.40; H, 4.62; N, 9.21.

Picrate: Orange-yellow needles, m.p. 169.5~170.5°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_7N_3$: C, 62.87; H, 4.86; N, 8.80. Found: C, 63.31; H, 4.75; N, 9.45.

6-Isopropyl-1,7-dimethyl- and 3-Ethyl-1,7-dimethyl-phenanthrenes.: The Diketo Ester (XI)—White needles, m.p. 219°, obtained after the description of Ruzicka *et al.*

Modified Cyclization Reaction of (XI) to (XII)—The diketo ester (1.0 g.) was added to the solution of MeOH (75 cc.) and Na (1.0 g.) and heated on a steam bath for 5 mins. After rapid cooling, the reaction solution was diluted with H_2O to ca. 200 cc., the resultant precipitate was collected by filtration, and then disolved in Et_2O. Dried over anhyd. Na_2SO_4 and the solvent was distilled off to a crystalline product(0.68 g.), m.p. 107~110°. Recrystallization from petr. benzine gave colorless pillars, m.p. 115~117°. Yield, 0.51 g. The purest sample showed m.p. 117~118°, $[\alpha]_D^{15}$ 51.1°($CHCl_3$). U.V. λ_{max}^{EtOH} 240, 292 mμ (log ε 4.28, 2.06). Semicarbazone: m.p. 235°(decomp.).

Grignard Reaction of (XII)—(XII) (0.97 g.) was methylated with MeMgI in Et_2O solution. The crude product was purified by chromatography on Al_2O_3 using petr. benzine as a solvent. Recrystallization from MeOH gave 0.59 g. of colorless plates, m.p. 71~73°. U.V. λ_{max}^{EtOH} 239 mμ (log ε 4.32).

Partial Dehydrogenation of (XIII)—(XIII) (0.80 g.) was dehydrogenated over Pd-C (prepared from 300 mg. of carbon and 6.5 cc. of 10% $PdCl_2$) at 200~210° for 30 mins. The crude product (XIV) (0.61 g.) was purified by repeated recrystallization from MeOH and showed m.p. 98°. U.V. λ_{max}^{EtOH} 269, 277 mμ (log ε 3.20, 3.21). *Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.69; H, 9.14. Found: C, 79.76; H, 9.30.

Friedel-Crafts Reaction of (XIV)—The triene ester (XIV) (1.1 g.) was reacted with AcCl (0.35 g.) in *sym*-tetrachloroethane (8 cc.) with $AlCl_3$ (1.0 g.) under ice cooling. After stirring for 1 hr., the reaction solution was allowed to stand over night at room temperature, poured into ice water, and steam distilled. The residual oil was taken up in Et_2O, washed with Na_2CO_3 solution, dried over anhyd. Na_2SO_4, and concentrated to give 1.25 g. of a syrup. The crude product was separated into two portions by chromatography on Al_2O_3 with petr. benzine and then benzene as solvent. The petr. benzine fraction (0.60 g.) contained the starting material and the benzene fraction (0.52 g.), the desired substance. The latter was recrystallized from MeOH and afforded colorless dice (XV) (0.37 g.), m.p. 133~134°. U.V. λ_{max}^{EtOH} 258, 292 mμ (log ε 4.13, 3.35). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.53; H, 8.91.

Grignard Reaction of (XV)—A solution of the acetyl compound (0.30 g.) in Et_2O (5 cc.) was added to a suspension of 0.125 g. of Mg and 1.00 g. of MeI in Et_2O (5 cc.). After the usual treatment the resultant syrup(ca. 0.35 g.)was purified by alumina chromatography using petr. benzine as a solvent. The first crop was the recovered material (0.07 g.) and the second was the product (0.23 g.). Recrystallization from petr. benzine gave colorless pillars (0.18 g.), m.p. 127~127.5°. U.V. λ_{max}^{EtOH} 270, 279 mμ (log ε 3.04, 3.02). *Anal.* Calcd. for $C_{22}H_{32}O_3$: C, 76.69; H, 9.36. Found: C, 76.69; H, 9.69.

Dehydration of (XVI)—A solution of (XVI) (0.18 g.) in glacial AcOH (1.8 cc.) was heated on a steam bath for 10 mins. Diluted with water, the separated product was taken up in Et_2O and 0.16 g. of the crude product was recrystallized from MeOH to colorless needles, m.p. 114°. U.V. λ_{max}^{EtOH} 270, 279 mμ (log ε 3.07, 3.06). *Anal.* Calcd. for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26. Found: C, 81.07; H, 9.74.

Catalytic Reduction of (XVII)—(XVII) (0.15 g.) in AcOH (15 cc.) absorbed quantitative volume of H_2 (11 cc.) over Pd-C (prepared from 0.2 g. of carbon and 5 cc. of 1% $PdCl_2$). Colorless needles, m.p. 105~106°. Yield, 96 mg. U.V. λ_{max}^{EtOH} 270, 279 mμ (log ε 3.01, 3.05). *Anal.* Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83. Found: C, 79.99; H, 10.42.

6-Isopropyl-1,7-dimethylphenanthrene (XIX)—(XVIII) (100 mg.) was dehydrogenated with Se at 310~340° for 2 hrs. The crude product was purified by alumina chromatography, and separated into two fractions. The first fraction (20 mg.), eluted with petr. benzine, showed U.V. absorption spectrum of an alkylphenanthrene and gave trinitrobenzene complex of yellow needles (from MeOH), m.p. 188°. The second fraction (52 mg.) gave U.V. spectrum of a naphthalene derivative; trinitrobenzene complex: m.p. 149°; picrate: m.p. 123~124°. Latter fraction (26 mg.) was again dehydrogenated over Pd-C at 280~300° for 1 hr. and converted to the above alkylphenanthrene (11 mg.) and 10 mg. of oil (XIX) was recovered from 24 mg. of trinitrobenbene complex by passing through Al_2O_3 (15 cc.) with petr. benzine.

Picrate: Orange needles, m.p. 178~179°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$ (trinitrobonzene complex): C, 65.07; H, 5.02; N, 9.11. Found: C, 64.89; H, 6.00; N, 8.89.

Clemmensen Reduction of (XV)—The acetyl compound (XV) was reduced by the Clemmensen method in the usual way and recrystallized form MeOH, m.p. 107~109°. *Anal.* Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.03; H, 9.79.

6-Ethyl-1,7-dimethylphenanthrene (XXI)—(XX) (72 mg.) was dehydrogenated with Se (120 mg.) at 300~310° for 2 hrs. and further at 330° for 1 hr. The crude product was extracted with ether and 44 mg. of brown syrup was obtained, which gave 22 mg. of the crystalline fraction by alumina chromatography using petr. benzine as a solvent. 22 mg. of (XXI) was changed to its trinitrobenzene complex and then to a picrate, recrystallized, and the free phenanthrene was recovered through Al_2O_3 chromatography with petr. benzine. Recrystallization from MeOH gave 9 mg. of colorless scales, m.p. 70~71°. Trinitrobenzene complex: Yellow needles (from MeOH), m.p. 170.5~171.5°. *Anal.* Calcd. for $C_{18}H_{18} \cdot C_6H_3N_3O_6$: C, 64.42; H, 4.73. Found: C, 64.64; H, 5.05.

Picrate: Orange needles (from MeOH), m.p. 160~161°.

Summary

Three alkylphenanthrenes were derived by the selenium dehydrogenation of resinic acid derivatives. 7-Isopropyl-1,6-dimethylphenanthrene, m.p. 102~103° (trinitrobenzene complex: m.p. 184~185°, picrate: m.p. 169.5~170.5°). 6-Isopropyl-1,7-dimethyl-, oil, (trinitrobenzene complex: m.p. 188°, picrate: m.p. 178~179°). 6-Ethyl-1,7-dimethyl-, m.p. 70~71° (trinitrobenzene complex: m.p. 170.5~171.5; picrate: m.p. 160~161°).

(Received November 16, 1956)

U.D.C. 547.831.6

14. Eiji Ochiai und Chikara Kaneko: Polarisation der heterozyklischen Ringe mit aromatischem Charakter. CXV. Über eine neue Nitrierung des Chinolin-N-oxydes.

(*Pharmazeutisches Institut d. Mediz. Fakultät, Universität Tokyo**)

Bei der Nitrierung des Chinolin-N-oxydes mit Salpeter-Schwefelsäure haben Ochiai und Okamoto[2] eine sehr auffällige Tatsache bemerkt, dass die Reaktionsrichtung von der Reaktionstemperatur abhängig ist. Nitrierte man Chinolin-N-oxyd bei 0° zu 10° so wurde die α-Stellung der Benzol-Hälfte zuerst substituiert und nur 5- und 8-Nitroderivate erhalten, wie beim Chinolin selbst der Fall ist. Steigerte man die Reaktionstemperatur über 40°, so trat die Reaktivität der 4-Stellung ein und bei 65~70° ergab es hauptsächlich das 4-Nitroderivat. Dieser Temperatureffekt weist darauf hin, dass der polare Effekt der N-Oxydgruppe erst über 40° eingreift und bei 65~70° die Hauptrolle spielt. Hierbei muss man jedoch die Beteiligung der konz. Schwefelsäure an der Reaktion berücksichtigen, die den Elektronenzustand der N-Oxydgruppe ändern würde, wie schon Hirayama und Kubota[3] UV-spektrographisch erwähnten.

Wir dachten daher die Nitrierung von Chinolin-N-oxyd in möglichst neutralem Medium zu untersuchen. Zu diesem Zweck haben wir zuerst die Nitrierung mit Acetylnitrat in Essigsäureanhydrid-Lösung probiert. Chinolin-N-oxyd wurde nämlich in Essigsäureanhydrid gelöst, unter Eiskühlung und Umrühren einen Überschuss von Acetylnitrat zugesetzt und bei Zimmertemperatur stehengelassen. Bei der Aufarbeitung der Reaktionslösung haben wir gelbe Prismen vom Zers. Pkt. 295~297° als ein einziges

---

* Hongo Tokyo (落合英二, 金子主税).

[1] CXIV. Mitteilung: Dieses Bulletin, **3**, 454(1955).

[2] E. Ochiai, T. Okamoto: J. Pharm. Soc. Japan, **70**, 384(1950).