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162. **Shoji Hara and Yoko Tokushige**: Syntheses of Alkylphenanthrenes.[*1] V.

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Previously, Ochiai and one of the authors (S.H.) reported the synthesis of 1,7-dimethyl-6-propylphenanthrene[3] (II) which was found to be identical with the alkylphenanthrene (m.p. 89~90°) obtained by selenium dehydrogenation reaction of anhydroignavinol[1] and hypognavinol,[2] derived from natural aconite alkaloids.

A small amount of an oily alkylphenanthrene[4,5] (trinitrobenzene complex, m.p. 173~175°) was isolated from the dehydrogenation mixture of anhydroignavinol and hypognavinol. In the case of anhydroignavinol, another oily alkylphenanthrene[4] (trinitrobenzene complex, m.p. 175~177°) was obtained in addition to the above oil. When the ring opening of the carbon skeleton (I) in the assumed structure of the aconite alkaloids occurred at positions marked with *a*, 1,3,8-trisubstituted phenanthrene derivative would be formed. These considerations agreed also with the investigation of the ultraviolet[4] and infrared spectra[*1,*3] of the alkylphenanthrenes derived from natural alkamines.

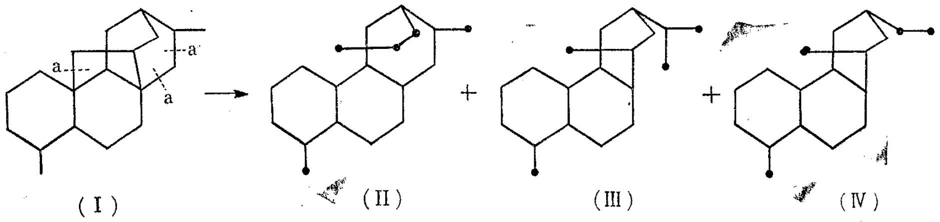

Chart 1.

In order to clarify the structure of these alkylphenanthrenes, two kinds of 1,3,8-trisubstituted derivatives were synthesized. As expected, 1,8-dimethyl-3-ethylphenanthrene (IV) was identical with the alkylphenanthrene (trinitrobenzene complex, m.p. 173~175°) derived from natural alkaloids by admixture of the trinitrobenzene complexes of both samples and further by the comparison of their ultraviolet and infrared spectra. The other alkylphenanthrene (trinitrobenzene complex, m.p. 175~177°) was identified with 1,8-dimethyl-3-isopropylphenanthrene (III).

For the preparation of these alkylphenanthrenes, 3-methyl-4-bromoacetophenone[6] (V), synthesized from *o*-bromotoluene, was reacted with methylmagnesium iodide. The resulting carbinol was dehydrated and hydrogenated over palladium-charcoal affording 1-bromo-2-methyl-4-isopropylbenzene (VII). On the other hand, (V) was converted to 1-bromo-2-methyl-4-ethylbenzene (VIII) by the Clemmensen method. (VII) and (VIII) thus obtained were respectively reacted with magnesium by heating in benzene for 6 hours. Ethylene oxide was introduced into these benzene solutions and phenethyl alcohol derivatives (IXa, b),

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[*1] This paper constitutes Part V of a series entitled "Syntheses of Alkylphenanthrenes" by E. Ochiai. Part IV: This Bulletin, **5**, 113(1957).

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[*3] Oily alkylphenanthrene (trinitrobenzene complex: m.p. 173~175°): IR $\nu_{max}^{CS_2}$ cm^{-1}: 865, 812, 757.

1) E. Ochiai, T. Okamoto: This Bulletin, **7**, 556(1959).
2) S. Sakai: *Ibid.*, **7**, 55(1959).
3) E. Ochiai, T. Okamoto, S. Hara, S. Sakai, M. Natsume: *Ibid.*, **6**, 327(1958).
4) E. Ochiai, T. Okamoto, T. Sugasawa, S. Sakai: *Ibid.*, **2**, 388(1954).
5) S. Sakai: Yakugaku Zasshi, **76**, 1054(1956).
6) M. Schöpf: Ber., **24**, 3766(1891).

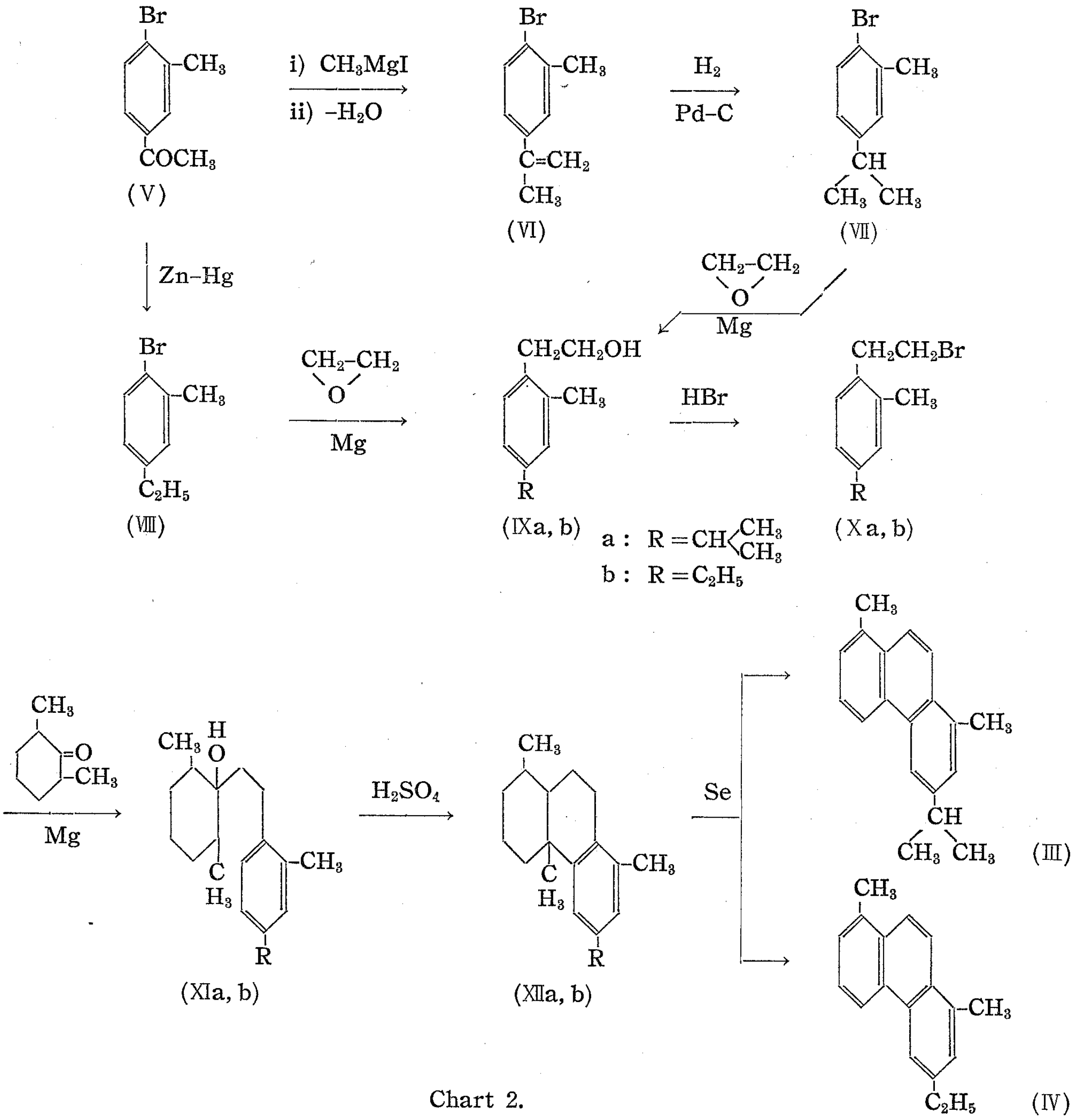

Chart 2.

Table I.

	m.p. (°C)	Trinitrobenzene Complex m.p. (°C)	Picrate m.p. (°C)	IR $\nu_{max}^{CS_2}$ cm^{-1}		
(III)	74～76	182～183	162～163	870	814	757
(IV)	52～53	176～177.5	161～162	865	812	754

		UV								
(III)	λ_{max}^{EtOH} mμ	253	260	283.5	295	308	330	337	345	353.5
	(log ε)	4.78	4.81	4.21	4.33	4.38	2.76	2.87	2.68	2.80
(IV)	λ_{max}^{EtOH} mμ	254	260	283.5	295	308	331	337	346	353.5
	(log ε)	4.78	4.84	4.20	4.28	4.31	2.75	2.87	2.68	2.82

		UV								
(III)	λ_{min}^{EtOH} mμ	233	255	280	289	301	329	332	344	349
	(log ε)	4.34	4.77	4.18	4.12	4.14	2.76	2.75	2.67	2.57
(IV)	λ_{min}^{EtOH} mμ	233	255	280	289	301	328	333	344	350
	(log ε)	4.21	4.77	4.16	4.12	4.14	2.74	2.74	2.65	2.59

were obtained in appreciable yields, identified as their phenylurethan derivatives. *m*-Cymene and 1-methyl-3-ethylbenzene were found to be the by-products in these reactions. The bromides (Xa, b), derived from (IXa, b) by bromination, were condensed with 2,6-dimethylcyclohexanone[7,8] by the Grignard reaction and the products (XIa, b) were dehydrated and cyclyzed to octahydrophenanthrene derivatives (XIIa, b). Dehydrogenation of these two compounds by heating with selenium at 340° yielded the desired alkylphenanthrenes (III, IV) as crystalline substances. The physical properties of synthesized phenanthrene derivatives are shown in Table I.

Experimental

All m.p.s are uncorrected. Beckman Model DU and Hitachi Model EPS II spectrophotometers were used for determination of ultraviolet spectra. Baird Infrared spectrophotometer was used for infrared spectra which were measured in CS_2 solution.

1-Bromo-2-methyl-4-isopropenylbenzene (VI)—To the Grignard reagent prepared from MeI (23.2 g.) and Mg (4.0 g.) in dehyd. Et_2O (40 cc.), 16.7 g. of 3-methyl-4-bromoacetophenone[6] (V) (UV : $\lambda_{\max}^{\mathrm{EtOH}}$ 255 mμ) in dehyd. Et_2O (30 cc.) was added. The mixture was allowed to stand overnight and heated under reflux for 3 hr. After the usual treatment, the carbinol was extracted with Et_2O. The dried extract was evaporated yielding oily residue (18 g.), which was heated at 150° (bath temp.) for 20 min. to effect dehydration. Azeotropic removal of H_2O was effected with benzene and the residue was distilled *in vacuo*. Pale yellow oil, b.p$_5$ 103~105°; yield, 13.8 g. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ : 253, 276.

1-Bromo-2-methyl-4-isopropylbenzene (VII)—A mixture of 13.8 g. of isopropenyl derivative (VI) in AcOH (40 cc.) was reduced in H_2 at an ordinary pressure over 50% Pd-C (2.5 g.) and 1335 cc. of H_2 uptake was observed (90% of calcd. amount) in 1 hr. After removal of the catalyst, the solvent was distilled off *in vacuo* and the residue was dissolved in Et_2O. Et_2O layer was washed with 5% K_2CO_3 solution and H_2O, dried, and evaporated. Distillation of the residue (13.0 g.) afforded an oil, b.p$_{20}$ 113~115°), which was redistilled *in vacuo* to colorless oil, b.p$_{15}$ 109~111°; yield, 12.5 g. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ : 263, 270, 277.

2-Methyl-4-isopropylphenethyl Alcohol (IXa)—A mixture of the bromide (VII) (12.5 g.), Mg (1.5 g.), and Et_2O (50 cc.) was heated under reflux for 6 hr. Since the reaction did not proceed, dehyd. benzene (20 cc.) was added to this and the mixture was further refluxed for 6 hr. After dissolving Mg completely, ethylene oxide (4.6 g.) in dehyd. Et_2O (16 cc.) was added to the foregoing mixture. The reaction mixture, which changed to gel immediately, was allowed to stand overnight. The excess reagent was destroyed by HCl and the mixture was extracted with Et_2O. The extract (12.0 g. of brownish oil) was distilled *in vacuo*, giving two main fractions : (a) b.p$_{28}$ 75~80°, 5.0 g.; (b) b.p$_3$ 104~107°, 5.2 g.; residue, 2.2 g.

The first fraction was distilled at an ordinary pressure. Colorless oil, b.p. 173° (*m*-cymene). The second fraction was distilled *in vacuo* to colorless oil, b.p$_2$ 99~102° (bath temp. 110~120°); yield, 4.4 g. Phenylurethan (recrystallized from hexane) : Needles, m.p. 93~94°. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε) : 259 (2.82), 266 (2.84), 275 (2.78). *Anal.* Calcd. for $C_{19}H_{23}O_2N$: C, 76.73; H, 7.80; N, 4.71. Found : C, 76.93; H, 7.88; N, 5.06.

1-(2-Bromoethyl)-2-methyl-4-isopropylbenzene (Xa)—A mixture of the alcohol (IXa) (2.0 g.), 48% HBr (4.2 g.), and conc. H_2SO_4 (0.72 cc.) was heated under reflux for 4.5 hr. Resultant dark brownish solution was extracted with Et_2O. Et_2O layer was washed with 5% Na_2CO_3 solution and H_2O, dried over anhyd. Na_2SO_4, and evaporated. Distillation of the residue (2.0 g.) afforded an oil, b.p$_6$ 115~117° (bath temp., 135~140°), which was redistilled *in vacuo*. Colorless oil, b.p$_2$ 91~92° (bath temp., 110°); yield, 1.6 g. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε) : 267.5 (2.72), 276.5 (2.68).

1-(2-Methyl-4-isopropylphenethyl)-2,6-dimethylcyclohexanol (XIa)—To the solution of phenethylmagnesium bromide derivative prepared from the bromo compound (Xa) (1.55 g.) and Mg (0.18 g.) in dehyd. Et_2O (12 cc.), 2,6-dimethylcyclohexanone[7,8] (1.0 g.) in dehyd. Et_2O (3 cc.) was added and the mixture was set aside overnight. After 5 hr. of heating under reflux, the solution was treated in the usual manner, extracted with Et_2O, and dried Et_2O solution was evaporated. Vacuum distillation of residual oil (2.05 g.) afforded recovered dimethylcyclohexanone (0.65 g.) and pale yellow viscous oil, b.p$_{0.002}$ 150~160° (bath temp.). Yield, 0.85 g.

1,4a,8-Trimethyl-6-isopropyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIIa)—Ice-cold 85% H_2SO_4 (3.5 cc.) was added to the alcohol (XIa) (850 mg.) and the mixture was shaken for 20 min. The resulting dark red mixture was extracted with hexane and the hexane layer was washed with 85%

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[7] F. E. King, T. J. King : J. Chem. Soc., **1954**, 1373.
[8] W. S. Johnson, H. Posvic : J. Am. Chem. Soc., **69**, 1361 (1947).

H_2SO_4 and H_2O. The dried solution was evaporated and the residual oil (700 mg.) was distilled in vacuum. Colorless viscous oil, $b.p_{0.1\sim0.2}$ 145~155° (bath temp.); yield, 430 mg. UV λ_{max}^{EtOH} mμ (log ε): 268 (2.67), 276 (2.64). *Anal.* Calcd. for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 87.52; H, 10.72.

1,8-Dimethyl-3-isopropylphenanthrene (III)—The octahydrophenanthrene derivative (XIIa) (400 mg.) was heated with Se (500 mg.) at 340°±5° for 5 hr. Two portions of Se, 200 and 130 mg., were added to the reaction mixture after 3 and 4 hr. from the start of heating. The product was extracted with hexane and isolated as a brown syrup (330 mg.), which gave 220 mg. of yellow viscous oil by chromatography over alumina (20 g.) using hexane as a solvent. The crude phenanthrene was changed to its trinitrobenzene complex and recrystallized repeatedly from MeOH. Trinitrobenzene complex: Yellow needles, m.p. 174~176° (150 mg.). Free phenanthrene was obtained by passing the trinitrobenzene complex through Al_2O_3 with hexane-benzene. Recrystallization from MeOH gave colorless prisms, m.p. 74~76°. The pure phenanthrene was converted to its trinitrobenzene complex again as yellow needles (from MeOH), m.p. 182~183°. *Anal.* Calcd. for $C_{25}H_{23}O_6N_3$: C, 65.07; H, 5.02; N, 9.11. Found: C, 65.18; H, 5.01; N, 9.23.
Picrate: Orange yellow needles (from MeOH), m.p. 162~163°.

1-Bromo-2-methyl-4-ethylbezene (VIII)—A mixture of 3-methyl-4-bromoacetophenone[6] (V) (15 g.) and Zn-Hg, prepared from Zn (50 g.), $HgCl_2$ (2.5 g.), conc. HCl (2.5 cc.), and H_2O (50 cc.), was heated in conc. HCl (53 cc.) and H_2O (40 cc.) under reflux and 25 cc. of conc. HCl was added every 3 hr. After heating for 10 hr., the mixture was cooled, saturated with NaCl, and extracted with Et_2O. Concentration of the Et_2O solution and distillation of the residue (13 g.) afforded an oil, $b.p_{35}$ 123° (6.7 g.), which was redistilled *in vacuo*. Colorless oil, $b.p_5$ 81° (reported[9] b.p. 220~221°, obtained from 1-ethyl-3-methylbenzene by bromination). Yield, 6.5 g. UV λ_{max}^{EtOH} mμ: 263, 270, 278.

The following compounds were prepared by the same method as described in the above reaction steps.

2-Methyl-4-ethylphenethyl Alcohol (IXb)—From the bromo compound (VIII) (6.5 g.), Mg (0.77 g.), ethylene oxide (2.8 g.). (a) 1-Ethyl-3-methylbenzene: b.p. 157°, 0.5 g. (b) Colorless oil, $b.p_3$ 117° (bath temp., 140~150°), 1.2 g. Phenylurethan (recrystallized from hexane): Needles, m.p. 84~85°. *Anal.* Calcd. for $C_{18}H_{21}O_2N$: C, 76.29; H, 7.47; N, 4.94. Found: C, 75.87; H, 7.36; N, 5.05.

1-(2-Bromoethyl)-2-methyl-4-ethylbenzene (Xb)—From the alcohol derivative (IXb) (1.0 g.), 48% HBr (2.1 g.), and conc. H_2SO_4 (0.36 cc.). Colorless oil, $b.p_4$ 109° (bath temp., 120~140°); yield, 1.05 g.

1-(2-Methyl-4-ethylphenethyl)-2,6-dimethylcyclohexanol (XIb)—From the bromo compound (Xb) (1.05 g.), Mg (0.12 g.), and 2,6-dimethylcyclohexanone (0.65 g.). Pale yellow oil, $b.p_{0.002}$ 140~150° (bath temp.); yield, 0.57 g.

1,4a,8-Trimethyl-6-ethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIIb)—From the cyclohexanol derivative (XIb) (570 mg.) and 85% H_2SO_4 (3 cc.). Colorless viscous oil, $b.p_{0.1}$ 140~160° (bath temp.); yield, 300 mg. UV λ_{max}^{EtOH} mμ (log ε): 268 (2.70), 276 (2.66). *Anal.* Calcd. for $C_{19}H_{28}$: C, 88.99; H, 11.01. Found: C, 89.47; H, 10.73.

1,8-Dimethyl-3-ethylphenanthrene (IV)—From the octahydrophenanthrene derivative (XIIb) (290 mg.) and Se (800 mg.). Trinitrobenzene complex: Yellow needles (from MeOH), m.p. 176~177.5°; yield, 70 mg. *Anal.* Calcd. for $C_{24}H_{21}O_6N_3$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.55; H, 4.66; N, 9.25.
The free phenanthrene was recrystallized from MeOH. Colorless prisms, m.p. 52~53°. Picrate: Orange-yellow needles (from MeOH), m.p. 161~162°.

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Summary

1,8-Dimethyl-3-ethyl- and 1,8-dimethyl-3-isopropyl-phenanthrenes were synthesized. These alkylphenanthrenes were identified with the two alkylphenanthrenes obtained by selenium dehydrogenation reaction of anhydroignavinol and hypognavinol, the aconite alkaloids.

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[9] Malhe: Bull. soc. chim. France, **29** [4] 293.