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12. Eiji Ochiai, Toshihiko Okamoto, Masaaki Sekijima, Masao Nishikawa, and Kenji Shono : Syntheses of Alkylphenanthrenes. I.

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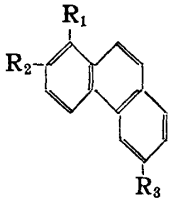
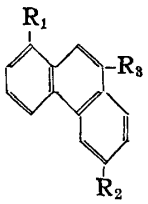
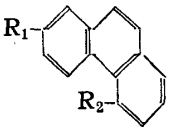
Previously we reported[1] that four alkylphenanthrenes were isolated as the dehydrogenation products of anhydroignavinol which was obtained by hydrolysis of ignavine. Recently, Sakai also reported[2] similar dehydrogenation of hypognavinol. One of the products was identified as 1,8-dimethylphenanthrene and the other two were the same as the dehydrogenation products from anhydroignavinol.

Because of the poor yield of dehydrogenation products, we could not continue further investigations with these alkylphenanthrenes. Therefore, it was decided to deduce the structures of the products by comparing the ultraviolet and infrared spectra of the dehydrogenation products with those of synthesized alkylphenanthrenes.[3]

Many papers concerning the syntheses of alkylphenanthrenes have been reported, but to get available data for our purpose, it was desirable to synthesize the possible alkylphenanthrenes and examine these samples by spectral method.

This paper deals with the syntheses of several di- and trisubstituted alkylphenanthrenes, the properties of which are shown in Table I.

Table I.

		R_1	R_2	R_3	m.p.(°C)	Picrate (m.p. °C)	Trinitrobenzene complex (m.p. °C)
	(I)	C_2H_5	H	$CH(CH_3)_2$	65.0~65.5	118~120	147~148
	(II)	$CH(CH_3)_2$	H	C_2H_5	61~63	—	151~152
	(III)	CH_3	CH_3	$CH(CH_3)_2$	109~110	140~141	157
	(IV)	CH_3	C_2H_5	C_2H_5	57~63	—	137~145
	(V)	C_2H_5	C_2H_5	CH_3	47~49	—	169~170
	(VI)	$CH(CH_3)_2$	CH_3	CH_3	41~43	159~161	186~188
	(VII)[a]	C_2H_5	CH_3	—	oil	—	112~113

a) E. E. Lewis and R. C. Elderfield (J. Org. Chem., **5**, 290) synthesized this compound by a different route.

Chart 1 gives the synthetic methods for these alkylphenanthrenes.

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1) This Bulletin, **2**, 388(1954).
2) S. Sakai : J. Pharm. Soc. Japan, **76**, 1056(1956).
3) E. Ochiai, M. Natsume : This Bulletin, **5**, 53(1957).

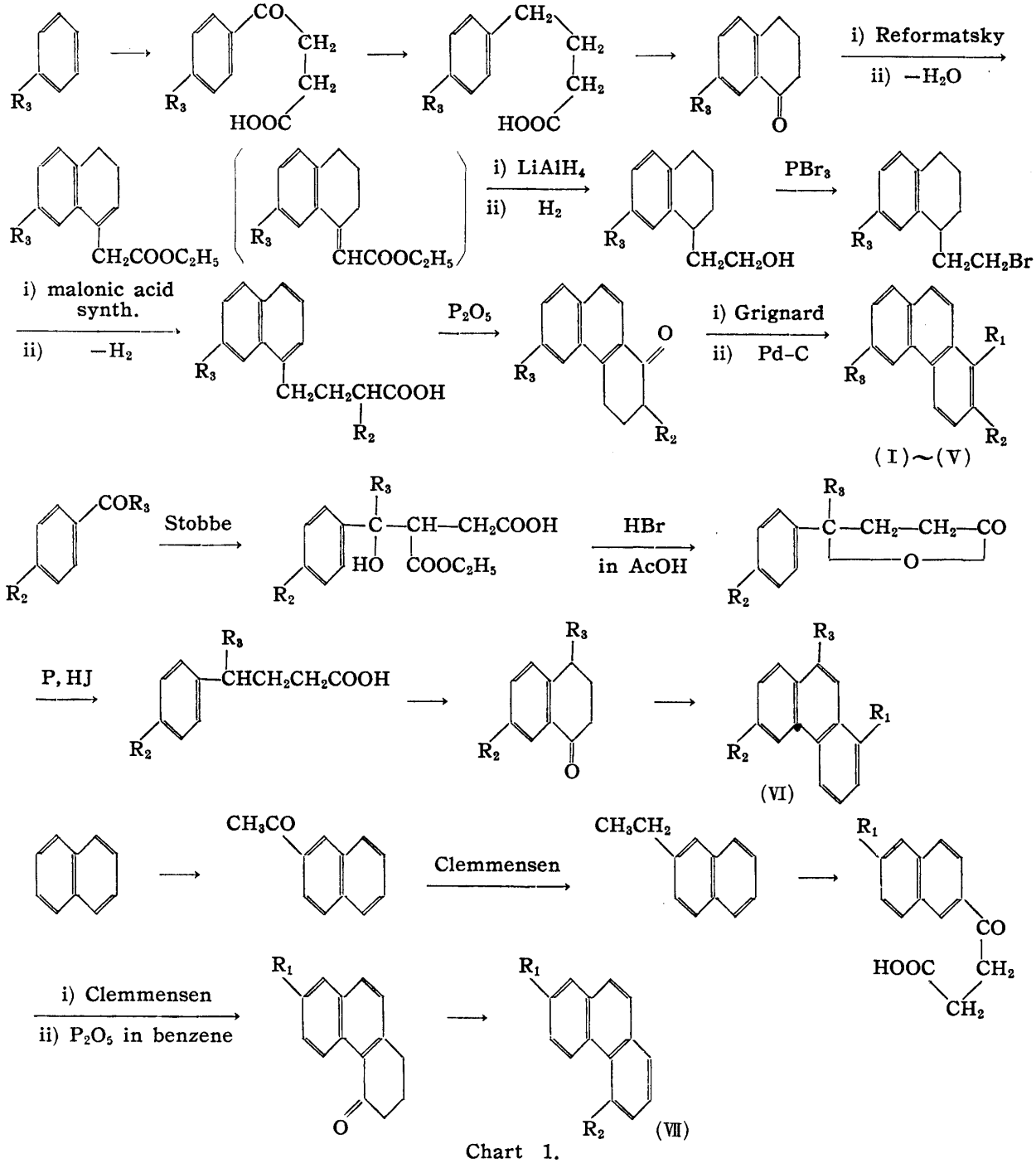

Chart 1.

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Experimental

1-Ethyl-6-isopropylphenanthrene (I)

3-*p*-Isopropylbenzoylpropionic Acid—Isopropylbenzene (b.p. 150~152°) was condensed with succinic anhydride in nitrobenzene by the use of $AlCl_3$ and recrystallized from benzene. m.p. 140~145°. Yield, 70~75%.

4-*p*-Isopropylphenylbutyric Acid—3-*p*-Isopropylbenzoylpropionic acid was reduced by the usual Clemmensen method and purified by distillation *in vacuo*, b.p_{11} 180~185°, m.p. 49~50°. Yield, 75~80%.

1,2,3,4-Tetrahydro-7-isopropyl-1-naphthalenone—The butyric acid was cyclized by heating with 90% H_2SO_4 on a steam bath. The product was purified by vacuum distillation, b.$p_{6\sim7}$ 160°, m.p. 37~37.5°. Yield, 53%.

Ethyl 3,4-Dihydro-7-isopropyl-1-naphthaleneacetate—To a mixture of 1,2,3,4-tetrahydro-7-isopropyl-naphthalenone (10 g.), Zn-Hg (40 g.), and I_2(0.2 g.) in 80 cc. of benzene-toluene (1:1) mixture was added dropwise 9 g. of ethyl bromoacetate, heating on a steam bath. After 2 hrs.' heating, the reaction mixture was treated with dil. HCl, benzene-toluene layer was separated, and aqueous layer was extracted with benzene. Benzene-toluene layer and benzene extract were combined, washed with dil. NH_4OH, and dried over anhyd. Na_2SO_4. After removal of the solvent, the residual oil was refluxed with Ac_2O(60 cc.) for about 1 hr. Excess of Ac_2O was decomposed with water, extracted with benzene, washed with Na_2CO_3 solution, dried, and concentrated. The residue was distilled *in vacuo*, b.$p_{6\sim7}$ 170~175°. Yield, 8 g.(65%).

***rac*-1,2,3,4-Tetrahydro-7-isopropyl-1-naphthaleneëthanol**—The ester was reduced with $LiAlH_4$ in ether solution and followed by hydrogenation with Pd-C as a catalyst. Distillation *in vacuo* gave an oil, b.$p_{7\sim8}$ 123~128°. Yield, 50%,

***rac*-1-(2-Bromoethyl)-1,2,3,4-tetrahydro-7-isopropylnaphthalene**—The alcohol was brominated with PBr_3 in benzene at room temperature and purified by vacuum distillation, b.$p_{7\sim8}$ 168~170°. Yield, ca. 90%.

7-Isopropyl-1-naphthalenebutyric Acid—Above bromo compound was added to sodium malonate solution (Na 0.4 g., dehyd. EtOH 10 cc., diethyl malonate 3.4 cc.), the mixture was allowed to stand at room temperature for about 1 hr., and then heated on a steam bath for 3 hrs. The reaction solution was concentrated, hydrolysed with 30% KOH solution on a steam bath, and 2.5 g. of the dicarboxylic acid was obtained. Decarboxylation of the acid was effected by heating at 160~180° for 30 mins. The product was dehydrogenated over Pd-C at 260~280°. After recrystallization from petr. ether, it showed m.p. 79~80°. Yield, 0.3 g.

1,2,3,4-Tetrahydro-6-isopropyl-1-phenanthrenone—To a solution of the above acid (0.25 g.) in benzene (15 cc.), P_2O_5(2.5 g.) was added and refluxed for 3 hrs. Excess of P_2O_5 was decomposed with water, benzene layer was washed with Na_2CO_3 solution, and concentrated to give 0.18 g. of an oil.

1-Ethyl-6-isopropylphenanthrene—To a Grignard reagent (Mg 0.2 g., EtBr 1.0 g., and ether 10 cc.) the cyclic ketone (0.18 g.) in ether (8 cc.) was added and the mixture was heated on a steam bath for 1 hr. Excess of Grignard reagent was decomposed, ether layer was separated, dried, and concentrated to give 0.15 g. of an oil. This was dehydrogenated over Pd-C at 260~280° for 2 hrs. and the product was extracted with benzene. After removal of the solvent ca. 100 mg. of the crude phenanthrene was obtained. The crude compound was purified as trinitrobenzene complex and recrystallization from MeOH gave yellow needles, m.p. 147~148°. Yield, 40 mg. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$(trinitrobenzene complex) : C, 65.07: H, 5.02. Found : C, 64.59; H, 5.44.

From this complex, few mg. of free 1-ethyl-6-isopropylphenanthrene was obtained by chromatography through Al_2O_3, with benzene-petr. benzine (1:1) mixture as a solvent, and was recrystallized from EtOH to colorless needles, m.p. 65.0~65.5°.

1-Isopropyl-6-ethylphenanthrene (II)

3-*p*-Ethylbenzoylpropionic Acid—Ethylbenzene was condensed with succinic anhydride. Recrystallization from benzene gave colorless needles, m.p. 103~104°. Yield, 31%.

4-*p*-Ethylphenylbutyric Acid—Above acid was reduced by the Clemmensen method, b.p_6 178~180°, m.p. 71~73°. Yield, 84%.

1,2,3,4-Tetrahydro-7-ethyl-1-naphthalenone—The butyric acid was cyclized by the use of 90% H_2SO_4; b.p_{20} 163~164°. Yield, 64%.

Ethyl 3,4-Dihydro-7-ethyl-1-naphthaleneacetate—The above ketone was condensed with ethyl bromoacetate by the Reformatsky method and then dehydrated with Ac_2O. b.p_7 170~175°. Yield, 86%.

***rac*-7-Ethyl-1,2,3,4-tetrahydro-1-naphthaleneëthanol**—Reduction of the ester with $LiAlH_4$ gave an oil, b.p_7 180~183°. Yield, 72%. This was hydrogenated over Pd-C to the alcohol, b.p_7 160~170°. Yield, 91%.

***rac*-1-(2-Bromoethyl)-7-ethyl-1,2,3,4-tetrahydronaphthalene**—The alcohol was brominated by the usual way, b.p_2 150~154°. Yield, 32%.

7-Ethyl-1-naphthalenebutyric Acid—Above bromo compound was condensed with diethyl malonate by the usual method, decarboxylated, and dehydrogenated. Recrystallization from petr. ether gave colorless needles, m.p. 99~101°. Yield, 11%.

6-Ethyl-1,2,3,4-tetrahydro-1-phenanthrenone—The butyric acid was cyclized in the usual way. Yield, 61%. *p*-Nitrophenylhydrazone : m.p. 245~248°(decomp.).

6-Ethyl-1-isopropylphenanthrene—The cyclic ketone was reacted with *iso*-PrMgBr and dehydrogenated over Pd-C. Yield, 29%. The crude product was purified by recrystallization of its trinitrobenzene complex from MeOH and the free phenanthrene was obtained in the same way as for (I).

Recrystallization from MeOH gave colorless needles, m.p. 61~63°. Trinitrobenzene complex : Yellow needles, m.p. 151~152°. *Anal*, Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$(trinitrobonzene complex) : C, 65.07; H, 5.02. Found : O, 64.81; H, 5.17.

1,2-Dimethyl-6-isopropylphenanthrene (III)

7-Isopropyl-α-methyl-1-naphthalenebutyric Acid—*rac*-1-(2-Bromoethyl)-1,2,3,4-tetrahydro-7-isopropylnaphthalene ($b.p_{7\sim8}$ 168~170°) was condensed with ethyl methylmalonate, hydrolysed, decarboxylated, and dehydrogenated. Yield, 22%.

1,2,3,4-Tetrahydro-3-isopropyl-7-methyl-1-phenanthrenone—The acid was cyclized in the usual way. Yield, 82%. 2,4-Dinitrophenylhydrazone : m.p. 228~230°(decomp.).

1,2-Dimethyl-6-isopropylphenanthrene—The cyclic ketone was methylated and dehydrogenated to the phenanthrene. Yield, 34%. The crude product was purified by recrystallization as trinitrobenzene complex from MeOH, m.p. 153~155°. Free compound was recrystallized from MeOH to colorless needles, m.p. 109~110°. Picrate : m.p. 140~141°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$(trinitrobenzene complex) : C, 65.07; H, 5.02. Found : C, 64.65; H, 4.96.

2,6-Diethyl-1-methylphenanthrene (IV)

α,7-Diethyl-1-naphthalenebutyric Acid—*rac*-1-(2-Bromoethyl)-7-ethyl-1,2,3,4-tetrahydronaphthalene ($b.p_2$ 150~154°) was condensed with ethyl ethylmalonate by the usual method, hydrolysed, decarboxylated, and dehydrogenated. Yield, 16%.

2,6-Diethyl-1,2,3,4-tetrahydro-1-phenanthrenone—The acid was cyclized in the usual way. Yield, 40%.

2,6-Diethyl-1-methylphenanthrene—The cyclic ketone was methylated and dehydrogenated to the phenanthrene. Yield, 67%. The crude compound was purified as trinitrobenzene complex, m.p. 137~145°. The free phenanthrene was recrystallized from MeOH to colorless needles, m.p. 57~63°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$(trinitrobenzene complex) : C, 65.07; H, 5.02. Found : C, 64.46; H, 4.46.

1,2-Diethyl-6-methylphenanthrene (V)

3-*p*-Toluoylpropionic Acid—Toluene was condensed with succinic anhydride by the usual method, m.p. 126~128°. Yield, 34%.

4-*p*-Tolylbutyric Acid—The acid was reduced by the Clemmensen method, $b.p_5$ 178~180°, m.p. 59~61°. Yield, 81%.

1,2,3,4-Tetrahydro-7-methyl-1-naphthalenone—Above acid was cyclized by the usual method. $b.p_{10}$ 142~144°, m.p. 35~38°. Yield, 57%.

Ethyl 3,4-Dihydro-7-methyl-1-naphthaleneacetate—The ketone was condensed with ethyl bromoacetate, dehydrated with Ac_2O, $b.p_{10}$ 170~180°. Yield, 49%.

***rac*-1,2,3,4-Tetrahydro-7-methyl-1-naphthaleneëthanol**—The ester was reduced with $LiAlH_4$ and followed by catalytic hydrogenation, $b.p_5$ 155~156°. Yield, 61%.

***rac*-1-(2-Bromoethyl)-1,2,3,4-tetrahydro-7-methylnaphthalene**—The alcohol was brominated in the usual way, $b.p_5$ 155~158°. Yield, 32%.

α-Ethyl-7-methylnaphthalenebutyric Acid—The bromo compound was condensed with ethyl ethylmalonate, hydrolysed, decarboxylated, and dehydrogenated. Yield, 5%.

2-Ethyl-1,2,3,4-tetrahydro-6-methyl-1-phenanthrenone—Above acid was cyclized by the usual method, oil. Yield, 62%.

1,2-Diethyl-6-methylphenanthrene—The ketone was ethylated by the usual method and dehydrogenated over Pd-C to the phenanthrene. The crude phenanthrene was purified as trinitrobenzene complex, m.p. 169~170°. The free compound was recrystallized from MeOH to colorless needles, m.p. 47~49°. Yield, 20%. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_6N_3$(trinitrobenzene complex) : C, 65.07; H, 5.02. Found : C, 64.84; H, 3.93.

1-Isopropyl-6,9-dimethylphenanthrene (VI)

Stobbe Condensation of 4'-Methylacetophenone—K (4.3 g.) was dissolved in 100 cc. of *tert*-BuOH (b.p. 82°), to this solution were added diethyl succinate (26 g.) and 4'-methylacetophenone (13.4 g.), and the mixture was refluxed for 45 mins. in N_2 stream. The reaction solution was treated with dil. HCl, the alcohol was removed by distillation under a reduced pressure, and the residue was extracted with benzene. The product was taken up in 3% KOH solution from the benzene extract and the half ester separated when the alkaline solution was acidified. Yield, 22.5 g.

4-*p*-Tolyl-γ-valerolactone—The crude half ester (22.5 g.), glacial AcOH (90 cc.), and conc. HBr (70 cc.) were mixed and refluxed for 3 hrs. The reaction solution was distilled off under a reduced pressure to give an oil. This oil was dissolved in benzene, washed with Na_2CO_3 solution, concentrated, and distilled *in vacuo*, $b.p_8$ 167~168°. Yield, 12.5 g.

4-*p*-Tolylvaleric Acid—A mixture of the above lactone (12.0 g.), P (10.0 g.), and HI (d 1.70)(120 g.) was refluxed for 6 hrs., diluted with water, and extracted with benzene. The benzene solution was treated with Na_2CO_3 solution and the alkaline solution was acidified to separate an oil, $b.p_9$ 173~174°. Yield, 4.5 g.

1,2,3,4-Tetrahydro-4,7-dimethyl-1-naphthalenone—The acid was cyclized in the usual way. Yield, 59%.

Ethyl 3,4-Dihydro-4,7-dimethylnaphthaleneacetate—The ketone was condensed with ethyl bromoacetate by Reformatsky method and dehydrated with Ac_2O. $b.p_5$ 185~200°. Yield, 73%.

***rac*-1,2,3,4-Tetrahydro-4,7-dimethyl-1-naphthaleneëthanol**—The ester was reduced with $LiAlH_4$ and followed by catalytic hydrogenation. $b.p_5$ 190~195°. Yield, 59%.

***rac*-1-(2-Bromoethyl)-1,2,3,4-tetrahydro-4,7-dimethylnaphthalene**—Above alcohol was brominated by the usual method. $b.p_5$ 190~200°. Yield, 43%.

4,7-Dimethyl-1-naphthalenebutyric Acid—Above bromo compound was condensed with ethyl malonate, hydrolysed, decarboxylated, and dehydrogenated. The acid was recrystallized from petr. ether, m.p. 107~109°. Yield, 36%.

1,2,3,4-Tetrahydro-6,9-dimethyl-1-phenanthrenone—The butyric acid was cyclized to the ketone, oil. Yield, 59%.

1-Isopropyl-6,9-dimethylphenanthrene—Above ketone was reacted with *iso*-PrMgBr and dehydrogenated to the phenanthrene. The crude product was purified as trinitrobenzene complex, m.p. 186~188°. Free phenanthrene was purified by chromatography and recrystallized from MeOH to colorless needles, m.p. 41~43°. Yield, 16%. Picrate : m.p. 159~161°. *Anal.* Calcd. for $C_{19}H_{20}\cdot C_6H_3O_7N_3$ (picrate) : C, 62.88; H, 4.86; N, 8.81. Found : C, 62.57; H, 5.05; N, 9.18.

2-Ethyl-5-methylphenanthrene (VII)

2′-Acetonaphthone—Naphthalene was condensed with AcCl by the usual method and β-isomer was separated by vacuum distillation and fractional crystallization from EtOH. β-Acetyl compound was obtained as colorless plates, m.p. 52.0~53.5°. Yield, 31~34%.

2-Ethylnaphthalene—Above compound was reduced by the Clemmensen method. $b.p_{7\sim8}$ 108~111°. Picrate : m.p. 76~78°. Yield, 73~78%.

3-(6-Ethyl-2-naphthoyl)propionic Acid—The bromide was condensed with succinic anhydride by the usual method. The product was recrystallized from acetone, m.p. 170~171°. Yield, 40%.

6-Ethyl-2-naphthalenebutyric Acid—Above acid was reduced by the Clemmensen method and recrystallized from benzene, m.p. 119~121°. Yield, ca. 80%.

1,2,3,4-Tetrahydro-7-ethyl-4-phenanthrenone—The butyric acid was cyclized by the usual method and recrystallized from petr. ether, m.p. 46~48°. Yield, 74%. Semicarbazone : m.p. 220°.

2-Ethyl-5-methylphenanthrene—The cyclic ketone was methylated by the usual method and dehydrogenated to the phenanthrene. The crude product was purified as trinitrobenzene complex, m.p. 112~113°. The free phenanthrene was obtained as an oil. Yield, ca. 50%. *Anal.* Calcd. for $C_{17}H_{16}\cdot C_6H_3O_6N_3$ (trinitrobenzene complex) : C, 63.73; H, 4.42; N, 9.70. Found : C, 63.67; H, 4.64, N, 9.82.

Summary

Di- and trialkylphenanthrenes were synthesized. 1-Ethyl-6-isopropyl-, m.p. 65.0~65.5° (picrate : m.p. 118~120°, trinitrobenzene complex : m.p. 147~148°). 6-Ethyl-1-isopropyl-, m.p. 61~63° (trinitrobenzene complex : m.p. 151~152°). 1,2-Dimethyl-6-isopropyl-, m.p, 109~110° (picrate : m.p. 140~141°, trinitrobenzene complex : m.p. 157°). 2,6-Diethyl-1-methyl-, m.p. 57~63° (trinitrobenzene complex : m.p. 137~145°). 1,2-Diethyl-6-methyl-, m.p. 47~49° (trinitrobenzene complex : m.p. 169~170°). 1-Isopropyl-6,9-dimethyl-, m.p. 41~43° (picrate : m.p. 159~161°, trinitrobenzene complex : m.p. 186~188°). 2-Ethyl-5-methyl-, oil, (trinitrobenzene complex : m.p. 112~113°).

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