Summary

Alkyl or aryl *o*-mercaptophenyl ketones, esters of *o*-mercaptobenzoic acid and S-esters of *o*-mercaptothiobenzoic acid were synthesized, expecting their strong chelating ability due to the presence of aromatic mercapto group and double bond of benzene ring. Alkyl or aryl *o*-mercaptophenyl ketones were unstable and could not be investigated in detail. Esters of *o*-mercaptobenzoic acid and S-esters of *o*-mercaptothiobenzoic acid formed a chelate with cobalt, nickel, and copper in a ratio of 3:1, 2:1, and 1:1, respectively. These ligands were sensitive to nickel and palladium.

(Received January 16, 1961)

UDC 547.677.2

6. **Hideaki Shirai and Noriichi Oda**: Studies on Phenanthrene Derivatives. IV.1) Syntheses of 2,3:5,6-Bismethylenedioxy- and 2,3:6,7-Bismethylenedioxyphenanthrene and Ultraviolet Absorption Spectra of Certain Methylenedioxyphenanthrenes.

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In a continuation of studies on phenanthrene derivatives, several methylenedioxyphenanthrenes were synthesized. This paper deals with the syntheses of 2,3:5,6-bismethylenedioxy- and 2,3:6,7-bismethylenedioxyphenanthrene, and the analysis of the ultraviolet absorption spectra of these synthesized phenanthrenes to obtain some knowledge of relationship between the spectra and the positions of methylenedioxy and methoxyl groups in the phenanthrene ring.

Syntheses of 2,3:5,6-Bismethylenedioxy- and 2,3:6,7-Bismethylenedioxyphenanthrene

2,3:5,6-Bismethylenedioxy- and 2,3:6,7-bismethylenedioxyphenanthrene were synthesized by the Pschorr reaction, starting from 6-nitropiperonal (I) and homopiperonylic acid (II). Condensation of (I) with (II) by the Perkin-Oglialoro reaction gave a mixture of two stereoisomers of α-(3,4-methylenedioxyphenyl)-2-nitro-4,5-methylenedioxycinnamic acid (III and IV). This mixture was submitted to silica-gel chromatography, and the high-melting form, assigned as *trans* (III), first eluted with ether. The lower-melting form, assigned as *cis* (IV), was obtained from the later eluate. On reduction, the *trans* isomer (III) gave the corresponding aminocinnamic acid (V), while the *cis* isomer (IV) gave the corresponding carbostyril (VI). (V) upon boiling in dehydrated ethanol produced the carbostyril (VI), as shown in Chart 1.

Aminocinnamic acid (V) was then submitted to the Pschorr reaction, from which three kinds of acidic materials, m.p. 243∼244° (VII), 293∼296° (decomp.) (VIII), and m.p. above 300° (IX) were obtained. (VII) was proved to be α-(3,4-methylenedioxyphenyl)-3,4-methylenedioxycinnamic acid from its ultraviolet absorption spectrum and mixed melting point determination with a specimen prepared from piperonal as will be described below. Such a side reaction i.e. elimination of the amino group, observed in Pschorr reaction, are well

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[*1] Hagiyama-cho, Mizuho-ku, Nagoya (白井秀明, 織田範一).

1) Part III: This Bulletin, 8, 727 (1960).

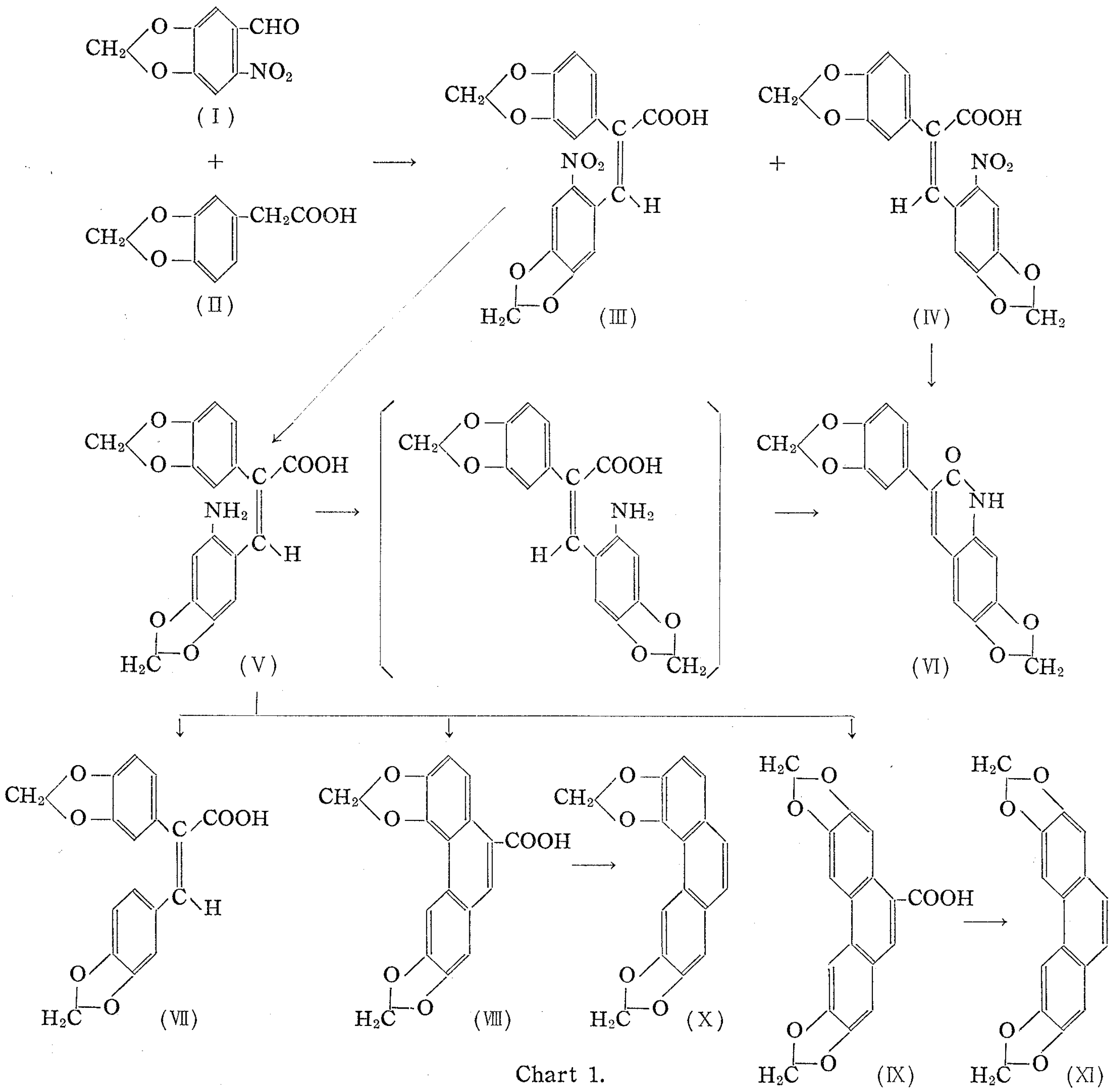

Chart 1.

known.[2] (VIII) and (IX) were decarboxylated by boiling with copper powder in quinoline, and yielded two phenanthrenes, m.p. 149° and m.p. 218~219°, respectively. According to the data of microanalysis and ultraviolet spectra, it is clear that these two compounds are bismethylenedioxyphenanthrene, but the location of methylenedioxy group in these two phenanthrenes was not determined.

Then, an unequivocal synthesis of 2,3:5,6-bismethylenedioxyphenanthrene (X) was carried out to prove the location of methylenedioxy group. Condensation of (I) with sodium 6-bromohomopiperonylate by the Perkin-Oglialoro reaction gave *trans*-*α*-(2-bromo-4,5-methylenedioxyphenyl)-2-nitro-4,5-methylenedioxycinnamic acid (XII). (XII) was converted to the corresponding aminocinnamic acid (XIII). The diazonium salt of (XIII) underwent easy cyclization to 1-bromo-3,4:6,7-bismethylenedioxy-10-phenanthrenecarboxylic acid (XIV), which was then dehalogenated and finally decarboxylated to 2,3:5,6-bismethylenedioxyphenanthrene (X). It has now been found that this phenanthrene is quite identical with the phenanthrene derivative of m.p. 149° mentioned above, on the basis of

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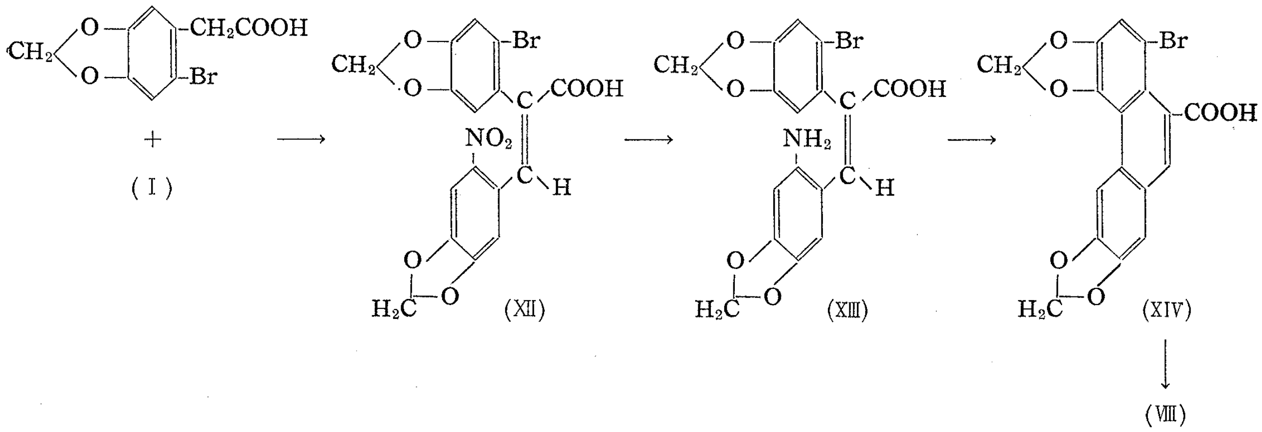
[2] D.F. DeTar : Org. Reactions, **9**, 420 (1957).

ultraviolet absorption spectra and mixed melting point determination. Therefore, the structure of the material of m.p. 218～219° must be 2,3:6,7-bismethylenedioxyphenanthrene (XI).



In order to determine the structure of deaminated by-product (VIII), α-(3,4-methylenedioxyphenyl)-3,4-methylenedioxycinnamic acid was synthesized, using piperonal as in the case of (III) and (IV). By fractional recrystallization from ethanol, the product was separated into two isomeric acids. The major product (m.p. 243～244°) was not depressed in its melting point when mixed with the afore-mentioned deaminated acid (VIII) and the minor product (m.p. 233～234°) seemed to be a stereoisomer of (VIII), but further experiments in this problem are in progress.

Ultraviolet Absorption Spectra

The ultraviolet absorption spectra of eight methylenedioxyphenanthrenes were measured in ethanolic solution and their characteristics are summarized in Table I. The full curves for the phenanthrenes are given in Figs. 1～5. All the curves showed the same general form as the spectrum of phenanthrene, and the spectra can be classified into

Table I. The Wave Length (in mμ) and the Lower the Intensity (log ε)

Phenanthrene	Group-I				Group-II			Group-III		
2,3-Methylenedioxy-	352	343	336	320	*	278		254		
	3.56	3.14	3.55	3.23		4.41		4.82		
3,4-Methylenedioxy-	356	348			312	282		249	*	
	3.41	3.30			3.88	4.04		4.65		
1-Methoxy-6,7-methylenedioxy-	357	340	324		310	*	*	256		
	3.85	3.72	3.38		3.93			4.73		
1-Methoxy-5,6-methylenedioxy-	368	350			320	308	294	252	246	
	3.54	3.57			4.11	4.08	4.20	4.68	4.62	
2-Methoxy-6,7-methylenedioxy-a)	356	340			285	268		254		
	3.34	3.30			4.10	4.11		4.62		
2-Methoxy-5,6-methylenedioxy-a)	361	344			310	288		266	253	234
	3.00	3.18			3.83	4.15		4.62	4.61	4.40
3-Methoxy-6,7-methylenedioxy-	358	341	*		286			254		
	2.85	3.04			4.42			4.78		
3-Methoxy-5,6-methylenedioxy-	374	356	*		318	306	*	257	*	
	3.62	3.57			4.25	4.16		4.79		
2,3:6,7-Bismethylenedioxy-	355	339			302	290		251	*	
	3.06	3.30			4.35	4.47		4.94		
2,3:5,6-Bismethylenedioxy-	368	349			322	311	290	260	*	
	3.47	3.60			3.93	3.93	4.15	4.69		

In some cases, no definite values of the maxima could be given, though an inflexion was apparent in the curve; such cases are denoted in the table by the asterisk (*). *a*) These spectra were reported in the preceding paper.1)

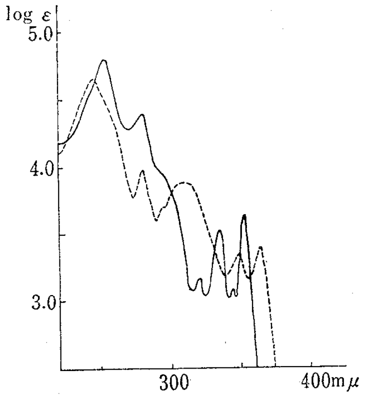


Fig. 1. Ultraviolet Absorption Spectra
—— 2,3-Methylenedioxyphenanthrene
------ 3,4-Methylenedioxyphenanthrene
(in EtOH)

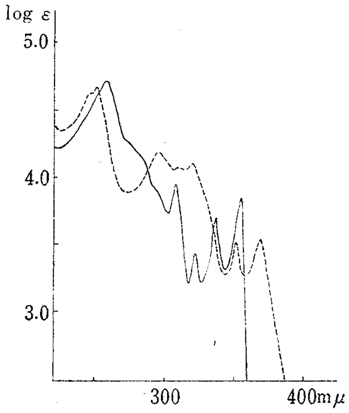


Fig. 2. Ultraviolet Absorption Spectra
—— 1-Methoxy-6,7-methylenedioxyphenanthrene
------ 1-Methoxy-5,6-methylenedioxyphenanthrene
(in EtOH)

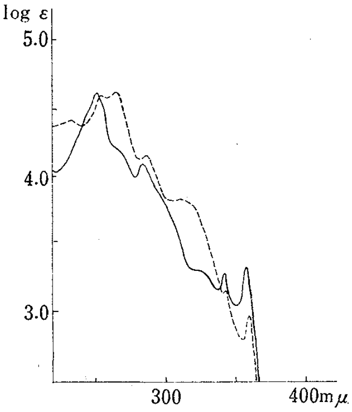


Fig. 3. Ultraviolet Absorption Spectra
—— 2-Methoxy-6,7-methylenedioxyphenanthrene
------ 2-Methoxy-5,6-methylenedioxyphenanthrene
(in EtOH)

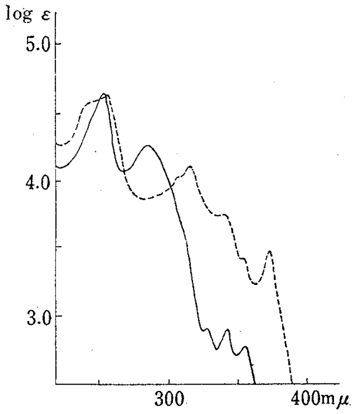


Fig. 4. Ultraviolet Absorption Spectra
—— 3-Methoxy-6,7-methylenedioxyphenanthrene
------ 3-Methoxy-5,6-methylenedioxyphenanthrene
(in EtOH)

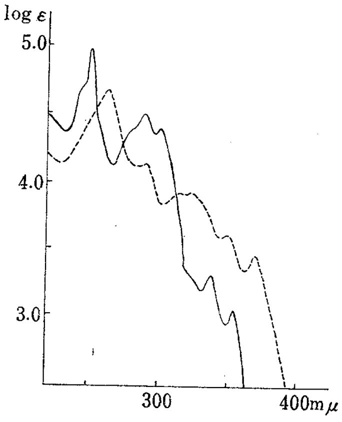


Fig. 5. Ultraviolet Absorption Spectra
—— 2,3:6,7-Bismethylenedioxyphenanthrene
------ 2,3:5,6-Bismethylenedioxyphenanthrene
(in EtOH)

three groups; Group-I (a series of several bands of low intensity in the neighbourhood of 350 mμ), group-II (a series of few bands of considerably greater intensity between ca. 280∼320 mμ), and group-III (more intense maxima at about 250 mμ).

There is a general shift towards a longer wave-lengths than those of phenanthrene, and the distinction of the maxima and minima tends to become less marked, many of the maxima and minima present in phenanthrene merging into inflexions. These effects are in accordance with the observations of Askew[3] on alkyl-substituted phenanthrenes.

It is interesting to note that the absorption maxima of group-I and group-II bands of 3,4-methylenedioxyphenanthrene derivatives were recorded at a longer wave-length than those of 2,3-methylenedioxyphenanthrene derivatives. The first maxima in group-I were most convenient for comparing these data. In Table II, wave-length shift was represented by subtracting the values of absorption maxima of 2,3-methylenedioxyphenanthrenes from those of 3,4-methylenedioxyphenanthrenes.

TABLE II.

Substituent		λ (mμ) of 1st max. of group-I.		
	Reverse numbering	2,3-Methylenedioxy derivative	3,4-Methylenedioxy derivative	Wave-length shift
None		352	356	+ 4
1-Methoxy	8	357	368	+11
2-Methoxy	7	356	361	+ 5
3-Methoxy	6	358	374	+16
6,7-Methylenedioxy	2, 3	355	368	+13
1,2-Dimethoxy[a]	7, 8	363	367	+ 4
2,3-Dimethoxy[a]	6, 7	355	365	+10
			average	+ 9

a) These spectra were reported by the senior author.[4]

Askew[3] already pointed out that the alkyl group introduced into 1-position of the phenanthrene ring mostly affected the wave-length shift than that in another positions. From Table I, similar effect would be seen in the case of methoxyl group by comparison of the spectra of 1-methoxyphenanthrenes and those of the derivatives having no methoxyl group.

Experimental[*2]

Syntheses of 2,3:5,6-Bismethylenedioxy- and 2,3:6,7-Bismethylenedioxyphenanthrene

***cis*- and *trans*-α-(3,4-Methylenedioxyphenyl)-2-nitro-4,5-methylenedioxycinnamic Acid (III and IV)**——A mixture of 4.9 g. of 6-nitropiperonal (I), 4.5 g. of homopiperonylic acid (II), 10 cc. of Ac_2O, and 5cc. of Et_3N was heated at 80° for 12 hr. After addition of 20 cc. of water and warming to decompose Ac_2O, the resulting mixture was evaporated *in vacuo* and the residue was extracted with 400 cc. of 5% NH_4OH. The basic solution was washed with Et_2O. After acidification of the solution with conc. HCl, separated acidic material was collected and dried. It was then dissolved in benzene and chromatographed on silica gel (100 mesh). By elution with Et_2O, the faster-moving band gave *trans*-nitrocinnamic acid (III), which was recrystallized from benzene. Yellow prisms, m.p. 216~217°. Yield, 4.2 g. *Anal.* Calcd. for $C_{17}H_{11}O_8N$: C, 57.15; H, 3.10; N, 3.92. Found : C, 56.98; H, 3.26; N, 4.22.

The slower-moving band gave *cis*-nitrocinnamic acid (IV), which was recrystallized from benzene. Light yellow plates, m.p. 212°. Yield, 0.8 g. *Anal.* Calcd. for $C_{17}H_{11}O_8N$: C, 57.15; H, 3.10; N, 3.92. Found : C, 57.06; H, 3.22; N, 3.88.

***trans*-α-(3,4-Methylenedioxyphenyl)-2-amino-4,5-methylenedioxycinnamic Acid (V)**——A solution of 1 g. of *trans*-nitrocinnamic acid (III) in 20 cc. of 5% NH_4OH was added gradually to a mixture of 4.4 g. of $FeSO_4 \cdot 7H_2O$, 10 cc. of water, and 12 cc. of 28% NH_4OH with continuous stirring. After addition, the mixture was heated on a water bath for 20 min. and then filtered. The filtrate and the washings were combined and acidified with conc. HCl to pH 5.0. The amino acid was collected and recrystallized from EtOH to colorless prisms, m.p. 170~171°(decomp.). Yield, 0.7 g. *Anal.* Calcd. for $C_{17}H_{13}O_6N$: C, 62.38; H, 4.00; N, 4.28. Found : C, 62.40; H, 4.30; N, 4.45.

3-(3,4-Methylenedioxyphenyl)-6,7-methylenedioxycarbostyril (VI)——i) From *cis*-α-(3,4-methylenedioxyphenyl)-2-nitro-4,5-methylenedioxycinnamic acid (IV) : A solution of 0.5 g. of *cis*-nitrocinnamic

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[*2] All melting points are corrected.

3) F. A. Askew : J. Chem. Soc., **1935**, 509.

4) H. Shirai : Yakugaku Zasshi, **63**, 517 (1943).

acid (IV) in 10 cc. of 5% NH_4OH was added into a mixture of 2 g. of $FeSO_4 \cdot 7H_2O$ in 5 cc. of water and 6 cc. of 28% NH_4OH with continuous stirring. The mixture was then heated on a water bath for 20 min. and filtered. The filtrate and the washings were combined, neutralized with conc. HCl, and extracted with benzene. After drying the benzene layer, the solvent was removed and the residue was recrystallized from AcOEt to colorless silky needles, m.p. above 300°. Yield, 0.3 g. *Anal.* Calcd. for $C_{17}H_{11}O_5N$: C, 66.02; H, 3.59; N, 4.53. Found : C, 65.98; H, 3.28; N, 4.40. IR (Nujol) cm^{-1} : $\nu_{C=O}$ 1670; ν_{C-O-C} 1231, 1044.

ii) From *trans*-α-(3,4-methylenedioxyphenyl)-2-amino-4,5-methylenedioxycinnamic acid (V) : A mixture of 0.1 g. of aminocinnamic acid (V) and 10 cc. of dehyd. EtOH was refluxed for 10 hr. After evaporation of the solvent, the residue was recrystallized from AcOEt to colorless silky needles, m.p. above 300°. Yield, 0.06 g. *Anal.* Calcd. for $C_{17}H_{11}O_5N$: C, 66.02; H, 3.59; N, 4.53. Found : C, 65.68; H, 3.20; N, 4.23. This compound was identical in its infrared spectrum with the compound prepared by the method (i).

2,3:5,6-Bismethylenedioxy-9-phenanthrenecarboxylic Acid (VIII) and 2,3:6,7-Bismethylenedioxy-9-phenanthrenecarboxylic Acid (IX)——A mixture of 3.5 g. of aminocinnamic acid (V), 70 cc. of MeOH, and 45 cc. of 20% H_2SO_4 was diazotized with 38 cc. of *N* $NaNO_2$ at 0°. After stirring for 30 min. at 0°, the reaction mixture was diluted with 50 cc. of water, 3 g. of Gattermann Cu was added to the mixture in small portions with continuous stirring, and the mixture was warmed on a water bath until a diazo-coupling test became negative. The cooled mixture was extracted with Et_2O. After washing and drying, Et_2O solution was evaporated and the residue was recrystallized fractionally from EtOH. 2,3:6,7-Bismethylenedioxy-9-phenanthrenecarboxylic acid (IX) separated first, as colorless prisms, m.p. above 300°. Yield, 0.7 g. *Anal.* Calcd. for $C_{17}H_{10}O_6$: C, 65.81; H, 3.25. Found : C, 65.71; H, 3.40.

2,3:5,6-Bismethylenedioxy-9-phenanthrenecarboxylic acid (VIII) was then obtained as the second fraction of colorless needles, m.p. 293~296° (decomp.). Yield, 0.24 g. *Anal.* Calcd. for $C_{17}H_{10}O_6$: C, 65.81; H, 3.25. Found : C, 65.25; H, 3.04.

On concentration of the mother liquor α-(3,4-methylenedioxyphenyl)-3,4-methylenedioxycinnamic acid (VII) was obtained as light yellow needles, m.p. 243~244°. Yield, 0.08 g. *Anal.* Calcd. for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87. Found : C, 65.21; H, 4.04.

2,3:5,6-Bismethylenedioxyphenanthrene (X)——A mixture of 0.1 g. of phenanthrenecarboxylic acid (VIII), 5 cc. of quinoline, and 0.1 g. of Gattermann Cu was heated in an oil bath at 180~200° for 10 min., and at 250~260° for 20 min. After cool, the mixture was diluted with Et_2O and extracted with dil. HCl until free from quinoline. The organic layer was evaporated, the residue was dissolved in benzene, and purified by chromatography on Al_2O_3. The phenanthrene was recrystallized from EtOH to colorless prisms, m.p. 149°. Yield, 0.03 g. *Anal.* Calcd. for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79. Found : C, 72.47; H, 4.18. Picrate : Brick red needles, (from EtOH), m.p. 153~154° (decomp.).

2,3:6,7-Bismethylenedioxyphenanthrene (XI)——This compound was prepared from 0.04 g. of the phenanthrenecarboxylic acid (IX), 2 cc. of quinoline, and 0.04 g. of Gattermann Cu in the same manner as for (X). The phenanthrene was recrystallized from benzene to colorless prisms, m.p. 218~219°. Yield, 0.02 g. Picrate : Brick red needles (from EtOH), m.p. 223° (decomp.).

***trans*-α-(2-Bromo-4,5-methylenedioxyphenyl)-2-nitro-4,5-methylenedioxycinnamic Acid (XII)**——A mixture of 1.9 g. of (I), 2.8 g. of sodium 6-bromohomopiperonylate, and 15 cc. of Ac_2O was heated at 110° for 12 hr. After addition of 30 cc. of water and warming to decompose Ac_2O, the resulting mixture was evaporated *in vacuo* and the residue was extracted with 200 cc. of 5% NH_4OH. The basic solution was washed with Et_2O. After acidification of the solution with conc. HCl, the cinnamic acid was recrystallized from EtOH to light yellow prisms, m.p. 239~240°. Yield, 2.3 g. *Anal.* Calcd. for $C_{17}H_{10}O_8NBr$: C, 46.81; H, 2.31; N, 3.21. Found : C, 46.44; H, 2.50; N, 3.20.

On concentration of the mother liquor, 2-nitro-4,5-methylenedioxycinnamic acid[5] was obtained as light yellow needles, m.p. 273~275° (decomp.). Yield, 0.08 g.

***trans*-α-(2-Bromo-4,5-methylenedioxyphenyl)-2-amino-4,5-methylenedioxycinnamic Acid (XIII)**——This compound was obtained from 1.7 g. of bromonitrocinnamic acid (XII), 20 cc. of 28% NH_4OH, and 7.5 g. of $FeSO_4 \cdot 7H_2O$ in the same manner as for (V). Light yellow prisms (from benzene), m.p. 209~210° (decomp.). Yield, 1.2 g. *Anal.* Calcd. for $C_{17}H_{12}O_6NBr$: C, 50.26; H, 2.98; N, 3.45. Found: C, 50.10; H, 3.88; N, 3.68.

1-Bromo-3,4:6,7-Bismethylenedioxy-10-phenanthrenecarboxylic Acid (XIV)——This compound was obtained from 1.5 g. of bromocinnamic acid (XIII), 30 cc. of MeOH, 17 cc. of 20% H_2SO_4, and 15 cc. of *N* $NaNO_2$ in the same manner as for (VII) and (VIII). Colorless prisms (from EtOH), m.p. above 300°. Yield, 0.5 g. *Anal.* Calcd. for $C_{17}H_9O_6Br$: C, 52.46; H, 2.33. Found : C, 52.56; H, 2.60.

2,3:5,6-Bismethylenedioxy-9-phenanthrenecarboxylic Acid (VIII)——A mixture of 0.5 g. of the

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5) G.R. Pettit, M.V. Kalnins : J. Org. Chem., 25, 1365 (1960).

above bromophenanthrenecarboxylic acid (XIV), 15 cc. of *N* NaOH, 5 cc. of EtOH, and 2 g. of copper bronze was refluxed for 39 hr. After cool, the mixture was filtered and the filtrate was acidified with conc. HCl. The precipitate was recrystallized from EtOH to almost colorless prisms, m.p. 294~296°(decomp.), which showed no depression when mixed with a specimen prepared from (V). Yield, 0.3 g. *Anal.* Calcd. for $C_{17}H_{10}O_6$: C, 65.81; H, 3.25. Found: C, 65.60; H, 3.51.

α-(3,4-Methylenedioxyphenyl)-3,4-methylenedioxycinnamic Acid (VII)——This compound was prepared from 1.5 g. of piperonal, 2 g. of sodium homopiperonylate, and 10 cc. of Ac_2O in the same manner as for (XII). The crude product was recrystallized from EtOH to colorless needles, m.p. 243~244°. Yield, 1.2 g. *Anal.* Calcd. for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87. Found: C, 65.08; H, 4.11. UV λ_{max}^{EtOH} mμ (log ε): 294 (4.12), 324 (4.20).

On concentration of the EtOH mother liquor, a small amount of colorless needles, m.p. 233~234°, was obtained. The structure of this substance is still unknown.

Determination of Ultraviolet Spectra——The ultraviolet spectra were measured in EtOH solution using Hitachi EPU-2A spectrophotometer.

The authors wish to express their deep gratitude to Prof. M. Tomita of Kyoto University for his guidance. Thanks are due to Mr. K. Machida and Mrs. I. Hamanaka, Kyoto University, for the measurements of infrared spectra. The authors also wish to thank Mrs. M. Hasegawa and Mr. T. Ueda of this School for carrying out the microanalyses.

Summary

2,3:5,6-Bismethylenedioxyphenanthrene (X) and 2,3:6,7-bismethylenedioxyphenanthrene (XI) were synthesized from 6-nitropiperonal (I) and homopiperonylic acid (II) by the Pschorr reaction. The structure of the compounds was determined by an unequivocal synthesis using 6-bromopiperonylic acid. The ultraviolet absorption spectra of several kinds of phenanthrenes possessing methylenedioxy group at 2,3- or 3,4-position were determined in ethanolic solution.

(Received February 6, 1961)

UDC 615.711.5:547.918

7. Daisuke Satoh, Hiroshi Ishii, Yohko Oyama, and Tamotsu Okumura: Studies on Digitalis Glycosides. XI.[*1] Isolation of Digipronin, Purpnin, and Purpronin.

(*Research Laboratory, Shionogi & Co., Ltd.*[*2])

From the leaves of Digitalis species, a number of noncardiac glycosides containing C_{21}-steroids as aglycones were isolated by several workers. These glycosides were known generally as the digitanol glycosides[1] and were classified into two types, the diginigenin type (basic formula I) and the pregnenolone type (basic formula II).[2] Diginin,[1,3] digi-

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[*1] Part X: H. Ishii, Y. Nozaki, T. Okumura, D. Satoh: Yakugaku Zasshi, **81**, 805 (1961)

[*2] Fukushima-ku, Osaka (佐藤大助, 石井 宏, 尾山蓉子, 奥村 保).

1) R. Tschesche, G. Buschauer: Ann., **603**, 59 (1957).

2) R. Tschesche: Proc. IVth International Congress Biochem., Vol. IV, 21 (1958).

3) W. Karrer: Festschrift für Barell, Basel, 236 (1936); C. W. Shoppee, T. Reichstein: Helv. Chim. Acta, **23**, 975 (1940); C. W. Shoppee: *Ibid.*, **27**, 246, 426 (1944); J. Press, T. Reichstein: *Ibid.*, **30**, 2127 (1947).