[CONTRIBUTION NO. 112 FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Studies in the Phenanthrene Series. IV. Phenanthrene-2-, 3- and 9-Aldehydes[1]

BY ERICH MOSETTIG AND JACOB VAN DE KAMP

The hitherto unknown mono-aldehydes of phenanthrene are of interest to us primarily for the promise they offer of synthesis of a variety of pharmacologically interesting substances, as phenanthryl-β-ethylamines, isoquinoline-like compounds and similar types.

Since we have available a satisfactory method for the preparation of three phenanthrenecarboxylic acids on a large scale, the 9-isomer from 9-bromophenanthrene,[2] the 2- and 3-isomers from the corresponding methyl ketones,[3] an aldehyde synthesis, starting from the carboxylic acids was given first consideration.[4] The Rosenmund method (catalytic reduction of acid chlorides) appeared to be the simplest and most convenient. By using decalin[5] as a solvent, phenanthrene-2-, 3-, and 9-aldehyde could be prepared in an average yield of 90% of the theoretical.[6]

Since in the Rosenmund method a simultaneous reduction of the phenanthrene nucleus is not impossible, and the re-oxidation of the aldehydes to the acids is not decisive, we prepared from the aldehydes—through the phenanthryl methyl alcohols, bromides and cyanides—the phenanthryl acetic acids. The latter were in every respect identical with the acids obtained from the 2-, 3- and 9-acetylphenanthrenes, respectively, by Willgerodt's method,[7] heating the ketones with yellow ammonium sulfide.[8]

Experimental

The phenanthroyl-2-, 3- and 9-chlorides were prepared by the action of five times the calculated amount of thionyl chloride on the phenanthrene-2-, 3-[9] and 9-carboxylic acids, respectively. The yield of acid chloride is quantitative. After evaporation of the excess of thionyl chloride the crystalline crude acid chloride was twice distilled in an

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[1] This investigation was supported by a grant from the Committee on Drug Addiction of the National Research Council from funds provided by the Bureau of Social Hygiene, Inc., and the Rockefeller Foundation.

[2] Mosettig and van de Kamp, THIS JOURNAL, **54**, 3328 (1932).

[3] Mosettig and van de Kamp, *ibid.*, **52**, 3704 (1930).

[4] Preliminary attempts to apply the Gattermann–Koch aldehyde synthesis to phenanthrene were not very encouraging and were soon abandoned without investigating this possibility systematically.

[5] Decalin and tetralin, among other solvents, have already been recommended in this procedure by Zetzsche and co-workers, *Helv. Chim. Acta*, IX, 177 (1926).

[6] When this work was nearly completed we learned that Shoppee [*J. Chem. Soc.*, 37 (1933)] prepared phenanthrene-9-aldehyde according to the method of Sonn and Müller, also starting from the acid chloride.

[7] Willgerodt, *J. prakt. Chem.*, [2] **84**, 383 (1911); [2] **80**, 192 (1909); [2] **81**, 74 (1910).

[8] The preparation of the phenanthryl acetic acids from the corresponding acetylphenanthrenes will be described in the following communication of this series.

[9] In the preparation of the phenanthrene-2- and 3-carboxylic acids by oxidation of the 2- and 3-acetylphenanthrenes, respectively, with a 2% sodium hypochlorite solution, the yield of the acids was made nearly quantitative by using about 50% excess of sodium hypochlorite.

oil pump vacuum. A nearly colorless distillate was obtained which solidified immediately on cooling. The acid chlorides were recrystallized from benzene by addition of petroleum ether.

TABLE I

PHENANTHROYL CHLORIDES, $C_{14}H_9COCl$

	M. p., °C.	Cl, %	
		Calcd.	Found
Phenanthroyl-2-chloride	101–101.5	14.74	14.78
Phenanthroyl-3-chloride	116–117[a]	...	...
Phenanthroyl-9-chloride	101.5–102[b]	14.74	14.82

[a] Fieser [THIS JOURNAL, **51**, 3101 (1929)] gives the m. p. 118°. [b] Shoppee (Ref. 6) gives the m. p. 102°.

Preparation of Phenanthrene-2-, 3- and 9-Aldehydes.—The freshly distilled acid chlorides were dissolved in decalin[10] (one part in four parts) in an apparatus described by Rosenmund and Zetzsche[11] of 350 cc. capacity. The 5% palladium–barium sulfate catalyst[12] was then added and a rapid stream of dry hydrogen passed into the solution. The hydrogen was taken from a tank and was carefully dried over a long column of Dehydrite. The reaction vessel was placed in an oil-bath, the temperature of which was maintained at 180–185°.

A faint development of hydrogen chloride was noticed starting at 70°. The evolution increased gradually, reaching a maximum at about 180°. In most cases the hydro-

TABLE II

CATALYTIC REDUCTION OF PHENANTHROYL-2-, 3- AND 9-CHLORIDES

Position of the —COCl	Amount of subs., g.	Amount of catalyst, g.[b]	Time,[a] hours	Yield, %
2	10	0.5	7	
2	35	+2.0	4.5	70
3	5	2.0	1.75	90
3	10	2.0	3	
3	20	2.5	4.75	90
3	20	+1.8	7	86
3	43	+3.0	13.5	Over 90
3	50	+3.0	11.25	90
3	56	+2.5	6	Over 90
9	10	1.0	2.5	
9	40	+1.5	4	
9	50	+2.0	5	90
9	75	+2.0	4.75	Over 90

[a] The time mentioned is the time from the beginning of the heating at room temperature to the point where the reaction was interrupted. It took from three-quarters to one hour to warm the oil-bath from room temperature to 180°.

[b] In the third column, + means that the catalyst from the preceding experiment was left in the reaction vessel, and that the amount mentioned was freshly added. This was done partly for preparative convenience and partly to utilize the costly palladium catalyst to the utmost.

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(10) Decalin, practical (Eastman Kodak), was allowed to stand over sodium for two days and was then distilled at reduced pressure, b. p. 95–96° (42 mm.).

(11) Rosenmund and Zetzsche, *Ber.*, **54**, 432 (1921).

(12) Schmidt, *Ber.*, **52**, 409 (1919). The palladous chloride was a C. P. grade purchased from Eimer and Amend, New York.

gen chloride formation dropped off quite suddenly and at the point where it became very faint the reaction was interrupted.

All experiments described in the above table were made with catalyst from the same batch. Another, freshly prepared, palladium–barium sulfate catalyst (prepared according to the directions of Schmidt) gave approximately the same yield of aldehyde but the time required for reaching a minimum hydrogen chloride evolution was somewhat shorter. Addition of a "Regulator" (to stop the reduction at the aldehyde stage) was not necessary. Whether this is due to the influence of the solvent used or to particular properties of the catalyst cannot be decided at present. An investigation to determine the relative effect of the solvent, and of the nature of the catalyst is under way, in which attempts to replace palladium with nickel are being made.

After allowing the reaction mixture to cool to room temperature, the decalin solution was decanted from the catalyst, diluted with ether and shaken with a saturated sodium bisulfite solution for twelve hours. The voluminous precipitate of bisulfite compound of the aldehyde was filtered off and thoroughly washed with ether. The bisulfite compound was suspended in water, decomposed with alkali, the aldehyde extracted into ether, the ether dried and evaporated. The aldehyde crystallized immediately. The aldehydes thus obtained still contained traces of decalin, which were washed out with petroleum ether. Finally the aldehydes were distilled in an oil pump vacuum.

Phenanthrene-2 and 3-aldehydes, $C_{14}H_9\cdot CHO$, are easily soluble in methyl or ethyl alcohol, from which solvents they can be recrystallized with the addition of a few drops of water; they can also be recrystallized from benzene by addition of petroleum ether. Phenanthrene-9-aldehyde is moderately soluble in alcohol, which solvent is very suitable for its purification. The aldehydes were characterized by their oximes and semicarbazones.

TABLE III

PHENANTHRENE-2-, 3- AND 9-ALDEHYDES, $C_{14}H_9CHO$

Position of —CHO group	Color and form	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2	White needles	59–59.5	87.34	87.49	4.89	4.98
3	White leaflets	79.5–80	87.34	87.11	4.89	4.88
9	White needles	100.5–101[a]	87.34	87.44	4.89	5.04

OXIMES, $C_{14}H_9CH{=}NOH$

Position of —CHO group	Color and form	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
2	White diamonds	194–195	6.34	6.37
3	White leaflets	145–145.5	6.34	6.43
9	White plates	157–157.5[a]	6.34	6.45

SEMICARBAZONES, $C_{14}H_9CH{=}N\cdot NHCONH_2$

Position of —CHO group	Color and form	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
2	White leaflets	281–282	15.97	15.96
3	White needles	274–275	15.97	16.01
9	White leaflets	221–222[a]	15.97	16.06

[a] Shoppee [*J. Chem. Soc.*, 37 (1933)] gives the m. p. of phenanthrene-9-aldehyde as 101°, of the 9-oxime 155°, of the 9-semicarbazone 222–222.5°.

Out of the original ether–decalin solutions from which the aldehydes had been extracted with sodium bisulfite, only the phenanthrenecarboxylic acids could be separated, the presence of which evidently was due to the fact that the reduction had not been carried to the very end. No alcohols or methylphenanthrenes could be detected.

Phenanthryl-2-, 3- and 9-methyl alcohols were prepared by catalytic reduction with platinum oxide catalyst (one part aldehyde in ten parts of absolute ethyl alcohol with

0.01 to 0.05 part of catalyst). The alcohols were purified by recrystallization from benzene by dilution with petroleum ether.

TABLE IV

PHENANTHRYL METHYL ALCOHOLS, $C_{14}H_9CH_2OH$

Position of —CH_2OH group	Color and form	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2	White needles	125–125.5	86.50	86.77	5.81	6.18
3	White prisms	103–103.5	86.50	86.47	5.81	5.76
9	White needles	149–149.5	86.50	86.35	5.81	5.83
3-BENZOYL DERIVATIVE						
	White needles	84.5–85	84.58	84.75	5.17	5.12

Phenanthryl-2-, 3- and 9-Methyl Bromides.—Into a solution of one part of the phenanthryl methyl alcohol in ten parts of absolute benzene a rapid stream of dry hydrogen bromide[13] was passed with cooling until saturation and then allowed to stand for one-half hour. The excess of hydrogen bromide was removed by passing a stream of dry air through the solution, after which the solvent was evaporated. The bromide crystallized upon cooling and was purified by distillation in an oil pump vacuum and by recrystallization from benzene; yield, quantitative.

Phenanthryl-2-, 3- and 9-Methyl Cyanides.—A solution of one part of the phenanthryl methyl bromide in 20 parts of ethyl alcohol was refluxed on a steam-bath with the

TABLE V

PHENANTHRYL METHYL BROMIDES, $C_{14}H_9CH_2Br$

Position of side-chain	Color and form	M. p., °C.	Bromine, % Calcd.	Bromine, % Found
2	White needles	111–111.5	29.49	29.51
3	White needles	114.5–115	29.49	29.52
9	White needles	103–103.5	29.49	29.64

PHENANTHRYL METHYL CYANIDES, $C_{14}H_9CH_2CN$

Position of side-chain	Color and form	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
2	White leaflets	106–106.5	6.45	6.52
3	White needles	84.5–85	6.45	6.63
9	White needles	96.5–97	6.45	6.66

PHENANTHRYLACETIC ACIDS, $C_{14}H_9CH_2COOH$

Position of side-chain	Color and form	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2	White needles	183.5–184.5	81.32	81.23	5.12	5.10
3	White leaflets	177–177.5	81.32	81.04	5.12	5.08
9	White leaflets	220–221	81.32	81.27	5.12	5.15

PHENANTHRYLACETIC ACID METHYL ESTERS, $C_{14}H_9CH_2COOCH_3$

Position of side-chain	Color and form	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2	White needles	78–78.5	81.56	81.29	5.64	5.79
3	Liquid*					
9	White diamonds	75–75.5	81.56	81.31	5.64	5.59

*3-METHYL ESTER PICRATE, $C_{23}H_{17}O_9N_3$

Color and form	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
Yellow needles	103.5–104	8.77	8.83

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[13] Houben and Boedler, Houben, "Die Methoden der organischen Chemie," Vol. III, 3d ed., 1930, p. 1156.

calculated amount (+5% excess) of potassium cyanide dissolved in as little water as possible, for three hours. Then the ethyl alcohol was evaporated, the residue shaken with ether, the ethereal solution of the nitrile dried and the ether evaporated. The residue which crystallized on standing was purified by distillation in an oil-pump vacuum and recrystallized from dilute alcohol; yield, nearly quantitative.

Phenanthryl-2-, 3- and 9-Acetic Acids.—The hydrolysis of the phenanthryl methyl cyanides was carried out by refluxing them for four hours with a 25% alcoholic potassium hydroxide solution. The phenanthrylacetic acids obtained, as well as their methyl esters, were identical in every respect with the ones prepared from the acetylphenanthrenes according to Willgerodt's method.[7]

Summary

1. Phenanthrene-2-, 3- and 9-aldehydes have been prepared by Rosenmund's procedure, catalytic reduction of the corresponding acid chlorides with palladium-barium sulfate.

2. Phenanthryl-2-, 3- and 9-methyl alcohols and phenanthryl-2-, 3- and 9-acetic acids are described.

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Some New Local Anesthetics Containing the Morpholine Ring. II[1]

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In a previous communication there were described several local anesthetics related to procaine and prepared from β-4-morpholine-ethanol and from γ-4-morpholine-propanol.[2] It has seemed of interest to extend this series to include other esters of these alcohols, hoping to obtain in this way compounds having more desirable properties. The first esters to suggest themselves were the cinnamates, forming analogs of apothesine (γ-diethylaminopropyl cinnamate).[3] The aryl urethans are also worthy of consideration in view of the success of Rider with similar compounds.[4]

In this investigation, the morpholine-alkyl cinnamate hydrochlorides were prepared by the interaction of the morpholine alcohols with cinnamoyl chloride in benzene solution.[5]

The phenylurethans were prepared by treating ethereal solutions of the alcohols with phenyl isocyanate followed by precipitation as the hydrochlorides with hydrogen chloride gas. The α-naphthylurethans were prepared similarly using α-naphthyl isocyanate. In the case of β-4-mor-

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[1] This work was made possible by assistance to the senior author from a grant made by the Rockefeller Foundation to Washington University for research in science.

[2] Gardner and Haenni, THIS JOURNAL, **53**, 2763 (1931).

[3] Wildman and Thorp, U. S. Patent 1,193,649; August 8, 1916.

[4] Rider, THIS JOURNAL, **52**, 2115, 2583 (1930).

[5] Since the completion of the experimental work on the preparation of these compounds, β-4-morpholine-ethyl cinnamate hydrochloride has been described by Leffler and Brill, *ibid.*, **55**, 365 (1933).