These recalculated coefficients are in good agreement with Cowperthwaite and La Mer's at concentrations 0.005 to 0.05 m, and with the author's at 0.05 to 1.5 m. Log $\gamma_{\pm}$ *vs.* $\sqrt{m}$ are shown in Fig. 1.

It would be of great interest to obtain values of the partial molal heat of dilution of zinc sulfate at concentrations here studied, on account of the difference between the calorimetric values given by Lange and collaborators[8] and the results of La Mer and Cowperthwaite, obtained by application of the Gibbs-Helmholtz equation.[9] But as $\bar{L}_2$ in the case of zinc sulfate depends about equally upon the precision with which $(E^{0\prime} - E^0)$ and $\mathrm{d}(E^{0\prime} - E^0)/\mathrm{d}T$ can be determined, it is obvious that more than the three temperatures investigated in the present paper, are necessary to obtain values of $\bar{L}_2$ which are sufficiently accurate[10] to be compared with those determined calorimetrically. The final answer to the questions must therefore await a more extended investigation.[11]

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(8) E. Lange, J. Monheim and A. L. Robinson, THIS JOURNAL, **55**, 4733 (1933).

(9) V. K. La Mer and I. A. Cowperthwaite, *ibid.*, **55**, 1004 (1933).

(10) The partial molal heat of dilution varies considerably with the temperature, according to some unpublished calculations of $\bar{C}_p - \bar{C}_p^0$ for zinc sulfate at concentrations studied; hence it is necessary to make use of a sufficient number of temperatures.

(11) According to a communication from Professor La Mer, W. H. Wood, working with Dr. Cowperthwaite, has been reinvestigating the e. m. f. of the cell at 5° temperature intervals from 0 to 50° from high dilution to one molal; the results have not yet been published.

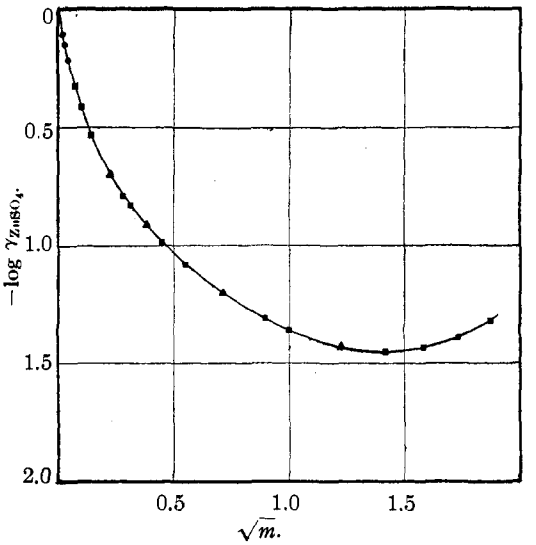

Fig. 1.—Mean stoichiometric activity coefficients of zinc sulfate at 25°: ●, Measurements of Cowperthwaite and La Mer; ■, Bray; ▲, Kielland.

Summary

The electromotive force of the cell Zn (satd. amalgam) | $ZnSO_4(m)$, $PbSO_4(s)$ | Pb (satd. amalgam) has been measured at 15, 25 and 35° for concentrations of zinc sulfate of 0.0512, 0.150, 0.510 and 1.501 molal. The activity coefficients of zinc sulfate are given for these concentrations and temperatures.

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[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Studies in the Phenanthrene Series. XIII. 9,10-Dihydrophenanthrene and Amino Alcohols Derived from It[1,2]

BY ALFRED BURGER AND ERICH MOSETTIG

The important investigations of Schroeter and his co-workers[3] have shown that phenanthrene yields by catalytic hydrogenation (elevated temperature and pressure) and by reduction with sodium and amyl alcohol, three well-defined hydrogenation products, namely, 9,10-dihydrophenanthrene, 1,2,3,4-tetrahydrophenanthrene and 1,2,3,4,5,6,7,8-octahydrophenanthrene, in amounts which depend upon the mode of reduction. These investigators determined the structure of the hydrocarbons beyond any doubt by synthetic methods, thus ridding the literature of the great confusion prevailing in the series of hydrogenated phenanthrenes up to that time. While the octahydro[4] and tetrahydro compounds may be isolated quite conveniently from the

(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan.

(2) See preliminary note, THIS JOURNAL, **57**, 2731 (1935).

(3) Schroeter, *Ber.*, **57**, 2025 (1924); Schroeter, Müller and Huang, *ibid.*, **62**, 645 (1929).

(4) For a convenient preparative method of octahydrophenanthrene, see van de Kamp and Mosettig, THIS JOURNAL, **57**, 1107 (1935).

reaction mixture and purified easily, the isolation and purification of the dihydro compound offers considerable difficulty. Neither the known reductive methods nor the synthetic method[3] is practicable for the preparation of 9,10-dihydrophenanthrene, which was needed in large amounts for systematic chemical and pharmacological investigations.

Through the extensive studies of Adkins and his collaborators on catalytic hydrogenation,[5] the great practical value of the "chromite" catalyst has been demonstrated. Copper–chromium oxide (or copper–chromium–barium oxide) proves to be particularly useful in cases where only partial or selective hydrogenation is desired. It has been known for a long time that the 9,10-double bond in phenanthrene is characteristically different from the other double bonds in this ring system. It behaves, to some extent, like an olefinic double bond (bromination, nitration), and it could be expected, therefore, that by employing the chromite catalyst in the reduction of phenanthrene, only or chiefly the 9,10-double bond would be attacked, leaving the benzenoid double bonds of the terminal nuclei intact. This expectation is fully realized; phenanthrene, reduced at 220° under a pressure of 2000–3000 lb./sq. in. (136–204 atm.), using copper–chromium–barium oxide as catalyst, yields practically pure 9,10-dihydrophenanthrene in very satisfactory amounts (up to 80%). The rate of reduction is apparently dependent to some extent upon the age of the catalyst. Phenanthrene can be recovered easily in the form of the picrate, and no higher hydrogenated phenanthrenes can be found in the reaction mixture. Efforts to bring the reduction to completion by varying experimental conditions were without success.

We found that anthracene, which is well known to be more reactive on the meso-positions than phenanthrene, is reduced under similar conditions, using chromite catalyst, at a decidedly lower temperature (160°) and in a considerably shorter time, yielding 9,10-dihydroanthracene only. The hydrogenation of anthracene at room temperature and atmospheric pressure, using noble catalysts, has been investigated carefully by Fries and Schilling.[6] The reduction of phenanthrene under similar conditions has not been reported, as far as we know. Phenanthrene, purified by the method of Cohen and Cormier,[7] distilled over sodium, treated with maleic anhydride,[8] recrystallized and resublimed, resists catalytic reduction under ordinary conditions (platinum oxide in glacial acetic acid). Synthetic phenanthrene, prepared by Pschorr's method, however (or as we later found, phenanthrene purified through the stages, 9-bromophenanthrene ⟶ 9-cyanophenanthrene ⟶ 9-phenanthroic acid ⟶ phenanthrene), absorbs hydrogen readily under those conditions.[9] We are now engaged in reinvestigating the course of the catalytic reduction of phenanthrene and of partially hydrogenated phenanthrenes under various conditions, a study that seems to be of interest as a complement to the investigation of Fries and Schilling[6] on the course of the reduction of anthracene. It may also be of importance in connection with the 1,4-dihydrophenanthrene (from the lithium addition product) of Schlenk and Bergmann,[10] for the structure of which, in our opinion, sufficient proof has not been offered.

The Friedel–Crafts reaction on 9,10-dihydrophenanthrene, employing acetyl and propionyl chlorides, proceeds smoothly in nitrobenzene solution as well as in carbon disulfide, giving in very satisfactory yields the expected ketones. It should be recalled that the same reaction on phenanthrene itself can be carried out successfully only in nitrobenzene solution, while in carbon disulfide chiefly oily and uncharacterizable products are obtained.[11] The formation of these is undoubtedly due to the interference of the 9,10-double bond.[12] Another remarkable difference between phenanthrene and 9,10-dihydrophenanthrene lies in their power to direct substituents. Whereas with phenanthrene in the Friedel–Crafts reaction, the acetyl or propionyl group enters mainly the 3-position, substitution in position-2 being a minor side reaction,[12,13] in 9,10-dihydrophenanthrene these groups are directed solely into the 2-position. Dihydrophenanthrene behaves in this respect as a diphenyl rather than as phenanthrene. The

(5) Adkins and Connor, THIS JOURNAL, **53**, 1091 (1931); Adkins and Folkers, *ibid.*, **53**, 1095 (1931); Connor, Folkers and Adkins, *ibid.*, **54**, 1138 (1932); Folkers and Adkins, *ibid.*, **54**, 1145 (1932); Adkins, Wojcik and Covert, *ibid.*, **55**, 1669 (1933).

(6) Fries and Schilling, *Ber.*, **65**, 1494 (1932).

(7) Cohen and Cormier, THIS JOURNAL, **52**, 4363 (1930).

(8) Clar, *Ber.*, **65**, 852 (1932).

(9) Mosettig and Krueger, unpublished results.

(10) Schlenk and Bergmann, *Ann.*, **463**, 84 (1928).

(11) Mosettig and van de Kamp, THIS JOURNAL, **52**, 3704 (1930).

(12) See Mosettig and van de Kamp, *ibid.*, **54**, 3328 (1932).

(13) Mosettig and Czerwin, unpublished results.

structural proof for the acylation products mentioned was carried out by converting them into 2-acetyl-9,10-phenanthrene quinone and 2-propionyl-9,10-phenanthrene quinone, respectively.

Name of compound Derivatives of 9,10-dihydrophenanthrene	Solvent	Appearance	Yield, %	M. p., °C. (all hydrochlorides with dec.)	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
2-ω-Chloroacetyl-- [a]	Petrol. ether	Pale yellow		100–101	$C_{16}H_{13}OCl$	74.84	74.53	5.11	4.88		
2-Propionyl—	MeOH	Colorless prisms	74	62–63	$C_{17}H_{16}O$	86.39	86.54	6.83	6.85		
-Semicarbazone	EtOH	Colorless needles		213–214	$C_{18}H_{19}ON_3$					14.33	14.49
2-α-Bromopropionyl—	Ether–petr. ether	Pale yellow	84	85–86	$C_{17}H_{15}OBr$	64.75	64.60	4.80	5.09		
2 - [2 - (Dimethylamino) - 1 - oxo-ethyl]—·HCl	EtOH–Et_2O	Yellow	60	213–215	$C_{18}H_{20}ONCl$					4.64	4.71
2 - [2 - (Diethylamino) - 1 - oxo-ethyl]—·HCl	EtOH–Et_2O	Yellow	94	173–176	$C_{20}H_{24}ONCl$					4.25	4.36
2 - [2 - Piperidino - 1 - oxo - ethyl]—	Dil. MeOH	Pale yellow		86–87	$C_{21}H_{23}ON$					4.59	4.32
- Hydrochloride	EtOH–Et_2O	Colorless	98	240–252	$C_{21}H_{24}ONCl$					4.10	4.36
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - oxo - ethyl]—·HCl [b]	EtOH–Et_2O	Yellow	64	238–239	$C_{25}H_{24}ONCl$					3.60	3.62
2 - [2 - (Dimethylamino) - 1 - oxo-propyl]—·HCl	EtOH–ether	Colorless	86	210–214	$C_{19}H_{22}ONCl$					4.44	4.59
2-[2-(Diethylamino)-1-oxo-propyl]—·$HClO_4$	EtOH–Et_2O	Almost colorless	57	138–140	$C_{21}H_{26}O_5NCl$					3.44	3.55
2 - [2 - Piperidino - 1 - oxo - propyl]—·HCl	EtOH–Et_2O	Colorless		208–213	$C_{22}H_{26}ONCl$					3.94	4.05
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - oxo - propyl]—·$HClO_4$	EtOH	Almost colorless	47	230–231	$C_{26}H_{26}O_5NCl$					3.00	3.06
2 - [2 - (Dimethylamino) - 1 - hydroxy-ethyl]—·HCl	EtOH–Et_2O	Colorless	98	170–172	$C_{18}H_{22}ONCl$	71.14	71.30	7.31	7.38	4.61	4.54
2 - [2 - (Dimethylamino) - 1 - acetoxy-ethyl]—·HCl	EtOH–Et_2O	Colorless		216–217	$C_{20}H_{24}O_2NCl$					4.05	3.93
2 - [2 - (Diethylamino) - 1 - hydroxy-ethyl]—·HCl	EtOH–Et_2O	Colorless	95	184–186	$C_{20}H_{26}ONCl$	72.36	71.97	7.90	7.79	4.22	4.12
2 - [2 - (Diethylamino) - 1 - acetoxy-ethyl]—·HCl	EtOH–Et_2O	Colorless		145–150	$C_{22}H_{28}O_2NCl$					3.73	3.98
2-[2-Piperidino-1-hydroxy-ethyl]—	EtOH	Colorless needles		124	$C_{21}H_{25}ON$	82.03	82.22	8.20	8.18	4.56	4.69
-Hydrochloride	EtOH–Et_2O	Silky leaflets	86	242	$C_{21}H_{26}ONCl$					4.08	3.90
2-[2-Piperidino-1-acetoxy-ethyl]—·HCl	EtOH–Et_2O	Colorless		212–213	$C_{23}H_{28}O_2NCl$					3.63	3.75
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - hydroxy - ethyl]—	Dil. MeOH	Colorless		101–102	$C_{25}H_{25}ON$	84.46	84.47	7.10	7.10		
-Hydrochloride	MeOH	Colorless	75	244–246	$C_{25}H_{26}ONCl$	76.59	76.81	6.69	6.95	3.58	3.81
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - acetoxy - ethyl]—·HCl	EtOH–Et_2O	Colorless		197–199	$C_{27}H_{28}O_2NCl$					3.23	3.36
2 - [2 - (Dimethylamino) - 1 - hydroxy-*n*-propyl]—	EtOH–water	Colorless		90–91	$C_{19}H_{23}ON$	81.08	81.19	8.24	8.29	4.98	5.04
-Hydrochloride	EtOH–Et_2O	Glittering rods	99	225–227	$C_{19}H_{24}ONCl$					4.41	4.41
2 - [2 - (Dimethylamino) - 1 - acetoxy-*n*-propyl]—·HCl	EtOH–Et_2O	Glittering rods		210–211	$C_{21}H_{28}O_2NCl$					3.90	4.02
2 - [2 - (Diethylamino) - 1 - hydroxy-*n*-propyl]—·HCl	EtOH–Et_2O	Silky leaflets	90	209–210	$C_{21}H_{28}ONCl$	72.90	73.24	8.16	8.11	4.05	4.01
2 - [2 - (Diethylamino) - 1 - acetoxy-*n*-propyl]—·HCl	EtOH–Et_2O	Colorless		189–190	$C_{23}H_{31}O_2NCl$					3.61	3.61
2-[2-Piperidino-1-hydroxy-*n*-propyl]—	Dil. MeOH	Colorless needles		104–106	$C_{22}H_{27}ON$	82.18	81.80	8.47	8.55	4.36	4.54
-Hydrochloride	EtOH–Et_2O	Colorless		249–250	$C_{22}H_{28}ONCl$					3.92	4.06
2-[2-Piperidino-1-acetoxy-*n*-propyl]—·HCl	EtOH–Et_2O	Colorless		192–194	$C_{24}H_{30}O_2NCl$					3.51	3.53
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - hydroxy - *n*-propyl]—	EtOH	Colorless		136–138	$C_{26}H_{27}ON$					3.79	4.10
-Hydrochloride	EtOH–Et_2O	Colorless	90	226–228	$C_{26}H_{28}ONCl$	76.90	76.54	6.96	7.15	3.45	3.59
2-[2-(1,2,3,4-Tetrahydroisoquinolino) - 1 - acetoxy - *n*-propyl]—·HCl	EtOH–Et_2O	Colorless		190–192	$C_{28}H_{30}O_2NCl$					3.13	3.28

[a] Obtained in poor yield by Friedel–Crafts reaction with chloroacetyl chloride.

[b] As a by-product in the exchange of the bromine with tetrahydroisoquinoline a red resin is formed, which on treatment with dilute alkali, yields 9,10-dihydrophenanthrene-2-carboxylic acid. Compare Mosettig and Robinson, THIS JOURNAL, **57**, 2188 (1935), footnote g.

In addition, the methyl ester of the carboxylic acid obtained by oxidation of the acetyl derivative with sodium hypochlorite was dehydrogenated with selenium, whereby 2-phenanthroic acid was formed.[14]

From the 2-acetyl- and 2-propionyl-9,10-dihydrophenanthrenes, amino alcohols of the type $-CHOHCH_2NR_2$ and $-CHOHCH(CH_3)NR_2$ were synthesized, *via* the bromo ketones and amino ketones, in a manner described previously in communications of this series. The pharmacological study of these compounds in comparison with their non-hydrogenated analogs, is expected to give some information concerning the influence of saturation of the 9,10-double bond on the physiological effectiveness in this series.

Experimental

Preparation of 9,10-Dihydrophenanthrene.[15]—One hundred and twenty grams of phenanthrene in 260 cc. of absolute alcohol with 10 g. of chromite catalyst was heated to 220° and kept at this temperature for eight to ten hours under a hydrogen pressure of 2000–3200 lb./sq. in. (136–218 atm.). Phenanthrene was removed from the reaction mixture as the picrate; the crude dihydrophenanthrene was purified by vacuum distillation (b. p. at 60 mm., 212–213°, yield 78-84%). This product was used for further reactions. By freezing it (5° overnight) and treating it with methyl alcohol at the same temperature, a pure dihydrophenanthrene was obtained. It is advantageous to use freshly prepared catalyst, since it was observed that with a catalyst that had been stored for about a year, the reduction proceeded considerably slower, and more catalyst had to be added to attain the same results.

2-Acetyl- and 2-Propionyl-9,10-dihydrophenanthrene.—A cold solution of 2 moles of aluminum chloride in 800 cc. of dry nitrobenzene was added gradually to an ice-cold solution of 1 mole of dihydrophenanthrene and 1.2 moles of acetyl or propionyl chloride, respectively, in 360 cc. of nitrobenzene. The mixture was allowed to stand at room temperature overnight, poured onto ice and hydrochloric acid and worked up in the customary way. The crude ketones were distilled in an oil pump vacuum and purified through the semicarbazones or oximes.

Structural Proofs.—Three grams of the acetyl compound was heated for four hours, with an excess of dilute sodium hypochlorite solution at 70°; yield of carboxylic acid, 1.9 g. One gram of the oily methyl ester (prepared from the acid with diazomethane) was heated with 2 g. of selenium in a sealed tube to 280–300° for twenty hours. The reaction product was treated with ether, and the ethereal solution was extracted with cold dilute potassium hydroxide solution. The acid obtained was identified as 2-phenanthroic acid by direct comparison with an authentic specimen of this acid (mixed melting point of acids and methyl esters).

One gram of the acetyl compound in 10 cc. of warm glacial acetic acid was treated with a solution of 1.2 g. of chromic acid in 2 cc. of water. After a few minutes the quinone crystallized out and was purified by high vacuum sublimation, m. p. 223–224° (dec.). The mixed melting point with an authentic sample of 2-acetyl-9,10-phenanthrene quinone showed no depression.

The propionyl-9,10-dihydrophenanthrene was oxidized in the same manner. The orange-red quinone was sublimed in a high vacuum; m. p. 215–217° (dec.).

Anal. Calcd. for $C_{17}H_{12}O_2$: C, 77.24; H, 4.58. Found: C, 77.25; H, 4.81.

The mixed melting point with 2-propionyl-9,10-phenanthrene quinone of the same m. p. (obtained by chromic acid oxidation of 2-propionylphenanthrene)[13] showed no depression.

Preparation of Amino Alcohols.—The bromination of the ketones was carried out in absolute ether (cooling with cold water). The yield of the bromoacetyl compound was 55%, that of the bromopropionyldihydrophenanthrene, 84%. The exchange of the bromine atom with the amino groups was effected by allowing the reactants to stand in benzene solution overnight. The hydrochlorides of the amino ketones (in two cases the perchlorates) were readily hydrogenated in 90% alcohol or methyl alcohol solutions, using a platinum oxide catalyst. The amino alcohols were acetylated in pyridine solution with acetic anhydride.

Summary

A convenient large scale method for the preparation of 9,10-dihydrophenanthrene by catalytic reduction of phenanthrene at elevated temperature and pressure, using chromite catalyst, is described.

By the Friedel–Crafts reaction, 2-acetyl- and 2-propionyl-9,10-dihydrophenanthrenes are obtained in good yields.

From the acetyl and propionyl derivatives amino alcohols of the type $C_{14}H_{11}CHOHCH_2NR_2$ and $C_{14}H_{11}CHOHCH(CH_3)NR_2$ (NR_2 being the dimethylamino-, the diethylamino, the piperidino and the 1,2,3,4-tetrahydroisoquinolino group) have been synthesized for pharmacological studies.

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(14) The cleavage of the ester groups in this process is remarkable. Similar observations with selenium dehydrogenation of esters have been made recently also by Ruzicka [*Helv. Chim. Acta*, **19**, 419 (1936)].

(15) Additional experimental data, reference 2.