Retene Investigations

XVIII. The Mannich Reaction with Monohydroxy Derivatives of Phenanthrene and Retene

K. J. KARRMAN and EINAR BLADH

Department of Organic Chemistry, University, Lund, Sweden

The condensation of ammonia or a primary or secondary amine with formaldehyde and an organic compound containing at least one hydrogen atom of pronounced reactivity is known as the Mannich reaction. At this reaction the active hydrogen atom is replaced by an aminomethyl or substituted aminomethyl group according to the formula:

$$AH + CH_2O + R_1R_2NH \rightarrow ACH_2NR_1R_2 + H_2O$$

This type of reaction has found during recent years wide application in organic preparations in several different classes of organic compounds, above all on ketones. The Mannich reaction has been less investigated with phenols, where, however, the o- and p-hydrogen atoms are sufficiently active to enter into this reaction. Thus, p-cresol gives a mono- and a disubstituted product [1] and phenol mono-di-and tri-substituted derivatives [1,2].

In the naphthalene series 1-naphthol gives substitution in the 2-position (not, however, in the 4-position as far as I have found in the literature), while 2-naphthol is substituted in the 1-position [3].

As for monohydroxy derivatives in the phenanthrene series no information exists in the literature concerning their ability to enter into the Mannich reaction. Due to this the present investigation was carried out. It comprises the following phenols: 2- and 3-hydroxyphenanthrene, 2- and 3-hydroxyretene and 4-methyl-3-hydroxyretene. Piperidine and morpholine, with, to a lesser degree, dimethylamine have been the amines mainly used.

The standard preparation has been the following. The phenol in question was dissolved in glacial acetic acid and an excess of formalin and amine was
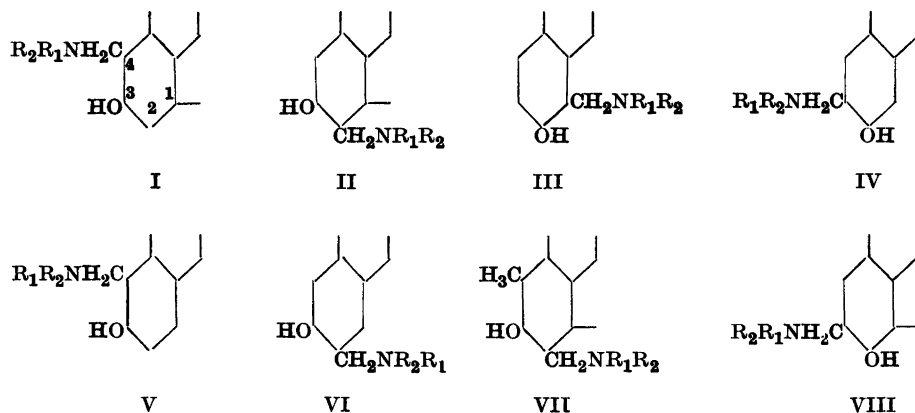
Fig. 1. Possible isomeres.

added at room temperature, after which the reaction mixture was allowed to stand 15—20 hours. Then the reaction product was precipitated with water and purified in various ways. This resulted in 2- and 3-hydroxyphenanthrene and 3-hydroxyretene reacting easily under formation of monoderivatives, whereas 2-hydroxyretene and 4-methyl-3-hydroxyretene did not react under the standard conditions. Reaction, however, could be obtained with 2-hydroxyretene, if the reaction mixture was boiled for several hours. A monosubstituted derivative was then formed.

It must be considered highly probable that substitution occurs in that benzene ring, to which the hydroxyl group is attached and as there are no free *para* positions in relation to this group, only *ortho* positions are available for substitution. The phenols in question can then give rise to eight different compounds (Fig. 1), namely 3-hydroxyretene I and II, 2-hydroxyphenanthrene III and IV, 3-hydroxy-phenanthrene V and VI, 4-methyl-3-hydroxyretene VII and 2-hydroxyretene VIII. The three phenols first named, which easily react, only give one reaction product, even if theoretically two isomeres could be formed from each phenol. As 4-methyl-3-hydroxyretene does not react, while 3-hydroxyretene gives a monoderivative, there is reason to suspect, that the last-mentioned compound is substituted in the 4-position with the group -$CH_2NR_1R_2$. If this position, however, is occupied (as in case the of 4-methyl-3-hydroxyretene) no reaction takes place. This assumption has been shown to be correct (see further). As, furthermore, 2-hydroxyphenanthrene gives a monoderivative, while 2-hydroxyretene, having occupied 1-position, does not react under the standard conditions, there is reason to suppose, that 2-hydroxyphenanthrene is substituted in the 1-position.
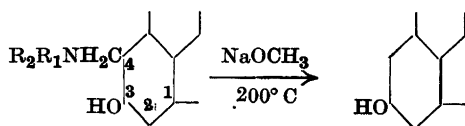
Fig. 2. Reaction with sodium methoxide.

This has also been found to be the case. Both these examples constitute yet another contribution to the well-known fact, that the two *ortho*-positions in a hydroxyl-substituted phenanthrene nucleus are not equivalent.

In order to clear up the structure of the Mannich bases obtained we have considered it suitable to try to transform these to the corresponding methyl-derivatives. This involves a cleavage of the carbon-nitrogen bond according to the formula:

$$HOArCH_2NR_1R_2 \rightarrow HOArCH_3 + R_1R_2NH$$
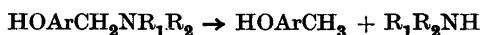
This metod has been launched by Caldwell and Thompson [4] for the preparation of phenols, methyl substituted in the nucleus. They performed the cleavage by hydrogenation over copper-chromit catalyst in dioxane solution. We have tried to use their method but obtained an viscous oil and well crystallizing hydrocarbons, which were not subjected to a closer examination, as they were of no interest in this connection.

Instead, attempts were made to cleave the carbon-nitrogen bond by heating the compound in question with sodium methoxide in methanol solution in an autoclave at 130—200 °C. Cornforth, Cornforth and Robinson [5] have, namely, in this manner treated 2,7-dihydroxy-1,8-bispiperidinomethylphenanthrene and obtained the corresponding 1,8-dimethyl derivative. In our case, however, this method resulted in a cleavage of the carbon-carbon bond, thus giving back the original phenol (see Fig. 2). This process is therefore of no value for the determination of the structure. Morpholinomethyl-2-hydroxy-retene is, however, an exception. It remains unchanged when heated with sodium methoxid for 14 hours at 200 °C. In this connection it is of interest to point out, that 2-hydroxyretene only reacts with formaldehyde and morpholine under rigorous conditions in contrast to the other phenols.

Mc Cleary and Roberts [6] have recently found that Mannich bases of phenols in the benzene series react with thiols under formation of thioethers according to the formula:

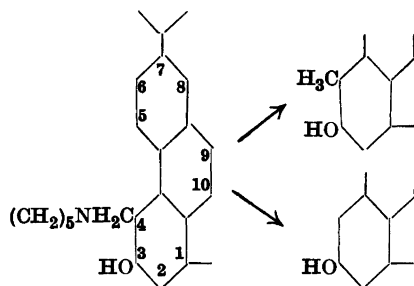$$HOC_6H_4CH_2N(CH_3)_2 + HSR \rightarrow HOC_6H_4CH_2SR + (CH_3)_2NH$$

Fig. 3. Hydrogenation over Raney nickel.

By hydrogenation of the thioethers thus obtained the desired methyl derivatives should be obtained. Preliminary attempts have shown, however, that our Mannich bases react with thiols under cleavage of the carbon-carbon bond. The process is thus of no interest for the determination of the structure. It should be noted, however, that morpholinomethyl-2-hydroxyretene is in this case also extremely stable and remains unchanged.

The result of attempts to cleave the carbon-nitrogen bond with cyanogen bromide was that under normal reaction conditions no reaction was obtained. Harder conditions resulted in oily, indefinite products.

By hydrogenation in dioxane solution over Raney-nickel at 150—180°C and 140—160 at the undesirable, original phenol (cleavage of the carbon-carbon bond) was obtained together with much resinous products. Reduction of the hydrogen pressure to 80—100 at (with the same temperature as before) resulted as previously in oily products and original phenol, but in this case also the desired methylphenol could be isolated. By systematic and tedious methods of purification it was possible to isolate in each special case from the complicated reaction mixture so much of the methylphenol, that its identity could with certainty be established. By the last-mentioned hydrogenation the following two reactions (illustrated in Fig. 3 for piperidinomethyl-3-hydroxyretene) occur.

The hydrogenations gave the following results. Morpholinomethyl-3-hydroxyretene gave a methyl-3-hydroxyretene, which proved to be identical with 4-methyl-3-hydroxyretene. The latter has been quite recently prepared [7]. By hydrogenation of the corresponding piperidino derivative the same methylphenol is obtained. Morpholinomethyl-3-hydroxyphenanthrene gave a methylphenol, which is not described in the literature. With regard to the preceding results it could be expected that it was 4-methyl-3-hydroxyphenanthrene. This compound has been prepared by us from 3-hydroxyphenanthrene-

4-aldehyde by reduction according to Clemmensen. This compound is identical with that obtained by hydrogenation of morpholinomethyl-3-hydroxyphenanthrene. The Mannich reaction with both 3-hydroxy-retene and -phenanthrene thus results in substitution in the 4-position.

Morpholino- (and piperidino-) methyl-2-hydroxyphenanthrene gave one and the same methylphenol, identical with 1-methyl-2-hydroxy-phenanthrene, already described in the literature [8]. This compound has been prepared by us through reduction according to Clemmensen of 2-hydroxyphenanthrene-1-aldehyde.

2-Hydroxyretene has only one free ortho position and it must therefore be considered highly probable that substitution occurs in the 3-position at the Mannich reaction. As, however, we have hitherto not succeeded in preparing 3-methyl-2-hydroxy-retene, we have not performed any hydrogenations with this Mannich base.

As we have found, that 3-hydroxyretene with occupied 4-position does not enter into the Mannich reaction it was of a certain interest to investigate, whether 3-hydroxyretene, substituted in another position, would react. For this purpose use was made of 9-(or 10) bromo-3-hydroxyretene and 3-hydroxyretene-9-(or 10) sulfonic acid, which both gave the expected products.

Whereas morpholine and piperidine respectively easily react with 3-hydroxyretene and formaldehyde we, in spite of varying reaction conditions, failed to obtain reaction with aliphatic amines, such as dimethylamine.

In the Mannich bases here described the hydroxylgroup and the substituted aminomethyl group are placed in ortho position and chelation between them is probable [9]. Thus the reactivity of the hydroxylgroup is diminished. It does not react, i. g., with acetic anhydride, not even at boiling. If, on the other hand, sodium hydroxide is added acetylation of the hydroxyl group with acetic anhydride easily occurs at room temperature; benzoylation is also easy to perform in alkaline medium. It is remarkable, that these Mannich bases are not attacked by boiling acetic anhydride under formation of the corresponding hydroxymethyl derivatives. Attempts to methylate showed that both dimethyl sulphate and diazomethane do not react with the hydroxylgroup. Snyder and Brewster [10] have quite recently found that phenolic Mannich bases with the substituents in *ortho* position cannot be methylated. *m*-Nitrobenzazid in boiling xylene for several hours does not react with the hydroxyl group. We have made attempts to replace the hydroxyl group with an amino group by heating morpholino- (and piperidino-) methyl-3-hydroxyretene with ammonium chloride, glacial acetic acid and anhydrous sodium acetate in an autoclave at 260 °C. The result was that 3-acetaminoretene was formed in a high

yield, which indicates that the substituted aminomethyl group has been split off and the hydroxyl group aminated.

As these Mannich bases are tertiary amines we have tried to prepare their methiodides but always without result. Snyder and Brewster [10] have not succeeded in preparing the quaternary salts of, *i. g.*, 1-dimethylaminomethyl-2-hydroxynaphthalene.

EXPERIMENTAL

Preparation of the Mannichs bases. Derivatives

4-Morpholinomethyl-3-hydroxyretene, $HOC_{18}H_{16}CH_2N(CH_2)_4O$. 3-Hydroxyretene (10 g, 0.04 mole) with the melting point $161-163$ °C was dissolved in 250 ml of glacial acetic acid by gentle warming. The solution was then cooled to 20 °C whereupon a mixture of 10 ml (0.12 mole) of morpholine and 10 ml (0.1 mole) of 30 % formalin was added in portions. The solution thus obtained was stirred for a short while and then allowed to stand for $15-20$ hours at room temperature. Then it was poured into two liters of cold water whereby a milky precipitate was formed. On addition of 200 ml 5 % sodium hydroxide the precipitate coagulates and is then easy to filter. After washing with diluted sodium hydroxide and water, and drying, 12 g (85 %) of a yellow-white powder was obtained. Recrystallized from a mixture of 96 % ethanol and acetone (5 : 1) 4.6 g of beautiful rectangular plates are obtained which melt at $176-177$ °C.

Calc.	C	79.0	H	7.79	N	4.01
Found	»	78.7	»	7.66	»	4.09

The picrate, $HOC_{18}H_{16}CH_2N(CH_2)_4O.HOC_6H_2(NO_2)_3$ was obtained from the components in ethanol solution in the form of yellow needles with the melting point $159-160$ °C.

Calcd.	C	60.2	H	5.22
Found	»	59.5	»	5.23

4-Morpholinomethyl-3-benzoxyretene, $C_6H_5COOC_{18}H_{16}CH_2N(CH_2)_4O$, was prepared by benzoylation according to Schotten-Baumann. The crude product was recrystallized from ethanol and obtained as white, transparent, prismatic crystals, melting at $182-183$ °C.

Calcd.	C	79.4	H	6.89
Found	»	79.0	»	6.84

4-Morpholinomethyl-3-acetoxyretene, $CH_3COOC_{18}H_{16}CH_2N(CH_2)_4O$, was obtained through shaking a suspension of the Mannichs base in diluted sodium hydroxide with acetic anhydride at room temperature. Recrystallization from ethanol gave thick plates. M. p. $172.5-173.5$ °C.

Calcd.	C	76.7	H	7.47
Found	»	76.8	»	7.51

Morpholinomethyl-3-hydroxy-9- (or 10)bromoretene, $HO(Br)C_{18}H_{15}CH_2N(CH_2)_4O$. 3-Hydroxy-9-(or 10) bromoretene (1.0 g) was dissolved in 40 ml of glacial acetic acid. A mixture of 1.5 ml of morpholine and 1.5 ml of 30 % formalin was added under stirring at room temperature. After 24 hours 200 ml of 1 % sodium hydroxide was added and the white precipitate formed was filtered off an washed with water. The crude product (1.0 g) was recrystallized from 96 % ethanol, and the pure compound obtained as thin plates with the melting point of 161—162 °C. Yield 0.3 g.

Calcd.	C	63.8	H	5.84	Br	19.3
Found	»	63.7	»	5.83	»	20.2

4-Piperidinomethyl-3-hydroxyretene, $HOC_{18}H_{16}CH_2(CH_2)_5$. To 3-hydroxyretene (10 g., 0.04 mole, m. p. 161—163 °C) dissolved in 250 ml of glacial acetic acid was added in portions while stirring a mixture of 10 ml (0.12 mole) of piperidine and 10 ml (0.1 mole) of 30 % formalin at room temperature. After 15—20 hours two liters of 1 % sodium hydroxide was added whereby a yellowish-white precipitate and a sticky oil is obtained, the later solidifying gradually. After washing with water and drying, the product (11 g) was recrystallized from 96 % ethanol. Yield 4.8 g of thin, rectangular plates melting at 155—156 °C.

Calcd.	C	82.9	H	8.42	N	4.03
Found	»	83.5	»	8.33	»	4.13

The picrate, $HOC_{18}H_{16}CH_2N(CH_2)_5 \cdot 2\ HOC_6H_2(NO_2)_3$ was obtained from the components in ethanol solution as garnet red needles, which melt at 148.5—149.5 °C. It is of interest that this picrate contains two molecules of picric acid while all the other picrates described in this paper only contain one. The colour of the picrate (garnet red) is also quite different from that of all the other picrates (yellow).

Calcd.	C	53.7	H	4.38
Found	»	53.4	»	4.36

4-Piperidinomethyl-3-benzoxyretene, $C_6H_5COOC_{18}H_{16}CH_2N(CH_2)_5$. The benzoylation was performed according to Schotten-Baumann. Recrystallization from ethanol gave hexagonal plates melting at 139—140 °C.

Calcd.	C	82.4	H	7.36
Found	»	81.2	»	7.20

Piperidinomethyl-3-hydroxyretene-9- (or 10) sulfonic acid, $HO_3S(HO)C_{18}H_{15}CH_2N(CH_2)_5$. The sulfonic acid (0.5 g), 0.5 ml of piperidine and 0.5 ml of 30 % formalin were dissolved in 10 ml of glacial acetic acid at room temperature. The reaction mixture was treated as before and a white powder was obtained.

Calcd.	N	3.28	S	7.49
Found	»	3.15	»	7.31

Morpholinomethyl-2-hydroxyretene, $HOC_{18}H_{16}CH_2N(CH_2)_4O$. 2-Hydroxyretene (5.0 g, 0.02 mole, m. p. 199—201 °C), 2.0 g (0.025 mole of morpholine and 5 ml (0.05 mole) of

30 % formalin were dissolved in 200 ml of glacial acetic acid and refluxed for 5 hours. After cooling, the solution was poured into 1 liter of 1 % sodium hydroxide, the precipitate formed filtered off and thoroughly washed with water. After drying, 6 g of a yellowish-white powder was obtained, which on recrystallization from a mixture of ethanol and acetone (5 : 1) gave thin, transparent plates, m. p. 176—177 °C. Yield 3.0 g.

$$\begin{array}{lllll} \text{Calcd.} & \text{C} & 79.0 & \text{H} & 7.79 \\ \text{Found} & » & 78.9 & » & 7.62 \end{array}$$

The picrate, $HOC_{18}H_{16}CH_2N(CH_2)_4O \cdot HOC_6H_2(NO_2)_3$ was obtained from the components in ethanol solution in the form of yellow needles, which melt at 230 °C (decomposition).

$$\begin{array}{lllll} \text{Calcd.} & \text{C} & 60.2 & \text{H} & 5.22 \\ \text{Found} & » & 59.2 & » & 5.13 \end{array}$$

4-Morpholinomethyl-3-hydroxyphenanthrene, $HOC_{14}H_8CH_2N(CH_2)_4O$. To 3-hydroxyphenanthrene (5.0 g, 0.026 mole, m. p. 114—116 °C) dissolved in 100 ml of glacial acetic acid was added a mixture of 5 ml (0.06 mole) of morpholine and 5 ml (0.05 mole) of 30 % formalin under stirring. The reaction mixture was left one day at room temperature and then poured into 1 % sodium hydroxide. The precipitate thus formed was washed with much water and dried. The crude product is a white powder and amounts to 6 g. Recrystallization from 96 % ethanol gave 3 g of long, needle-shaped crystals melting at 146—147 °C.

$$\begin{array}{lllllll} \text{Calcd.} & \text{C} & 77.8 & \text{H} & 6.53 & \text{N} & 4.77 \\ \text{Found} & » & 76.9 & » & 6.27 & » & 4.82 \end{array}$$

The picrate, $HOC_{14}H_8CH_2N(CH_2)_4O \cdot HOC_6H_2(NO_2)_3$ was prepared in the usual manner in ethanol solution. Yellow needles, decomposition at 181—183 °C.

$$\begin{array}{lllll} \text{Calcd.} & \text{C} & 57.6 & \text{H} & 4.25 \\ \text{Found} & » & 57.1 & » & 4.32 \end{array}$$

1-Morpholinomethyl-2-hydroxyphenanthrene, $HOC_{14}H_8CH_2N(CH_2)_4O$. 2-Hydroxyphenanthrene (0.20 g, m. p. 168 °C), 0.2 ml of morpholine and 0.2 ml of 30 % formalin were dissolved in 8 ml of glacial acetic acid and left for one day at room temperature. Precipitation with 1 % sodium hydroxide in the usual manner gave 0.25 g of a white powder. By recrystallization from 96 % ethanol the pure compound was obtained as lustrous scales. Melting point 194—195 °C. Yield 0.22 g.

$$\begin{array}{lllll} \text{Calcd.} & \text{C} & 77.8 & \text{H} & 6.53 \\ \text{Found} & » & 77.0 & » & 6.50 \end{array}$$

The picrate $HOC_{14}H_8CH_2N(CH_2)_4O \cdot HOC_6H_2(NO_2)_3$ was prepared in ethanol solution. Yellow needles melting at 205 °C (decomp.).

$$\begin{array}{lllll} \text{Calcd.} & \text{C} & 57.6 & \text{H} & 4.25 \\ \text{Found} & » & 56.7 & » & 4.21 \end{array}$$

1-Piperidinomethyl-2-hydroxyphenanthrene, $HOC_{14}H_8CH_2N(CH_2)_5$. 2-Hydroxyphenanthrene (0.50 g, m. p. 168 °C), 0.5 ml of piperidine and 0.5 ml of 30 % formalin were dissolved in 25 ml of glacial acetic acid. After one day at room temperature 200 ml of 1 % sodium hydroxide were added and the precipitate formed drawn off, washed and dried. Yield 0.70 g. Recrystallization from 96 % ethanol gave 0.57 g of long needles with the melting point 153—154 °C.

Calcd.	C	82.5	H	7.29	N	4.81
Found	»	81.4	»	7.11	»	4.76

The picrate, $HOC_{14}H_8CH_2N(CH_2)_5 . HOC_6H_2(NO_2)_3$ from ethanol. Yellow needles. M. p. 198 °C (decomp.).

Calcd.	C	60.0	H	4.66
Found	»	58.5	»	4.60

Amination. 4-Piperidinomethyl-3-hydroxyretene (1.00 g), 1.0 g of ammonium chloride, 1.7 g of anhydrous sodium acetate and 1.0 g of glacial acetic acid were heated together in a sealed tube at 250 °C for 14 hours. The reaction product was filtered off, washed with water and dried, giving 0.78 g of a brown powder. On recrystallization from toluene 0.43 g of a white substance was obtained, melting at 239—241 °C.

$CH_3CONHC_{18}H_{17}$	Calcd.	C	82.4	H	7.28	N	4.81
	Found	»	83.1	»	7.32	»	4.87

Mixing the product with an authentic sample of 3-acetaminoretene did not result in any depression of the melting point. By boiling for some hours with acetic anhydride the diacetate was formed, m. p. 222—223 °C (*cf.* Karrman and Sihlbom [11] 221.5—222 °C).

4-Morpholinomethyl-3-hydroxyretene treated in the same manner also gave 3-acetaminoretene.

Attempts to determine the structure of the Mannichs bases

1. *With cyanogen bromide.* 4-Piperidinomethyl-3-hydroxyretene (0.5 g) and cyanogen bromide (0.2 g) were dissolved in ether. No noticeable reaction was observed. The solution was boiled for a few minutes; after evaporation of the solvent a yellow resinous oil remained. 4-Morpholinomethyl-3-benzoxyretene (0.2 g) and cyanogen bromide (0.05 g) dissolved in 5 ml of ether and 10 ml of 96 % ethanol were boiled for twenty minutes. After evaporation of the solvent the unchanged substance was recovered. This was again treated with cyanogen bromide in chloroform in a sealed tube at 100 °C for six hours. Unchanged substance together with a resinous oil was obtained.

2. *With sodium methoxide.* To a solution of 0.65 g of 4-piperidinomethyl-3-hydroxyretene in 10 ml of methanol in a tube 1.0 g of sodium was added. When the later has dissolved the tube was sealed and heated to 170—180 °C for two and a half hours. The viscous reaction product was treated with diluted hydrochloric acid and extracted twice with 20 ml of ether. The ether solution was dried with anhydrous sodium sulphate; after evaporation of the solvent 0.54 g of a substance, m. p. 162—163 was left behind.

On mixing with an authentic sample of 3-hydroxyretene no depression of the melting point was observed.

$$\text{Calcd.} \quad \text{C} \quad 85.0 \qquad \text{H} \quad 7.25$$
$$\text{Found} \quad \text{\textit{»}} \quad 85.5 \qquad \text{\textit{»}} \quad 7.03$$

The above experiment was repeated at 190—200 °C and a heating time of 43 hours. Only resinous products were obtained. Under milder conditions (130 °C, 20 hours) 3-hydroxyretene was formed in a high yield (80 per cent).

4-Morpholinomethyl-3-hydroxyretene (0.5 g), 10 ml of methanol and 1.0 g of sodium in a sealed tube at 130 °C for 14 hours gave 3-hydroxyretene in a yield of 75 per cent.

A mixture of 4-morpholinomethyl-3-hydroxyphenanthrene (0.5 g), 14 ml of methanol and 1 g of sodium was heated to 200 °C for 14 hours. The reaction product was treated with diluted hydrochloric acid and after drying the precipitate was recrystallized twice from a mixture of bensene and ligroin. M. p. 119—120 °C, picrate, m. p. 159 °C. The compound was identical with 3-hydroxyphenanthrene. The same result was obtained with 4-piperidinomethyl-3-hydroxyphenanthrene.

4-Morpholinomethyl-2-hydroxyphenanthrene was treated exactly as the 3-isomer above. The reaction resulted in a complicated mixture, from which 2-hydroxyphenanthrene could be isolated as the picrate, m. p. 156—158 °C. The picrate was dissolved in benzene and filtered through aluminium oxide giving pure 2-hydroxyphenanthrene. M. p. 168 °C.

3. *With thiols.* 4-Piperidinomethyl-3-hydroxyretene (0.20 g) and 0.3 g of isoamylthiol were heated together in a sealed tube for 6 hours at 130 °C. The reaction product was poured into water and the precipitate formed recrystallized from ligroin. Yield 0.1 g, m. p. 161—163 °C. The compound was identical with 3-hydroxyretene.

Hydrogenations

1. *Over copper chromite* [12]. 4-Piperidinomethyl-3-hydroxyretene (0.7 g), 15 ml of dioxane and 0.5 g of catalyst were heated to 180 °C for 3 hours at a hydrogen pressure of 200 at. After removal of catalyst, solvent and basic compounds, 0.6 g of a brown crystalline mass was obtained. Purification by repeated recrystallizations from ethanol gives 0.1 g of coulerless plates, m. p. 85—87 °C.

$$\text{Found} \quad \text{C} \quad 91.8 \qquad \text{H} \quad 7.45 \qquad \sum \quad 99.3$$

The product is thus a hydrocarbon, probably a mixture of chiefly retene and dihydroretene.

2. *Over Raney-nickel* [13]. 1-Morpholinomethyl-2-hydroxyphenanthrene (2.0 g), 125 ml of dioxane and about 1 g of catalyst are hydrogenated at 185 °C for 3 hours under 100 at. Then the catalyst is filtered off and the solvent removed giving 2.3 g of a brown oil. This was dissolved in ether, gaseous hydrochloric acid was passed into the solution, the precipitate formed drawn of, the solution dried with anhydrous sodium sulphate and carbonate and evaporated to dryness. 1.3 g of a half-solid mass was obtained which on attempts at recrystallization from benzene-ligroin only gave an oil. The solution was then diluted with more solvent and filtered through aluminium oxide (Brockmann) and then partly evaporated, whereby a mixture of oil and crystals were obtained. The crystals were separated and recrystallized from benzene-ligroin; yield 0.11 g m. p. 195.5—197 °C.

(According to the literature [8] 1-methyl-2-hydroxyphenanthrene melts at 196—197 °C.) Mixed with an authentic sample of 1-methyl-2-hydroxyphenanthrene no depression of the melting point could be observed.

The picrate, $HOC_{14}H_8CH_3 \cdot HOC_6H_2(NO_2)_3$, had a m. p. of 162—164 °C.

$$
\begin{array}{llll}
\text{Calcd.} & \text{C} & 57.7 & \text{H} & 3.45 \\
\text{Found} & \text{»} & 58.4 & \text{»} & 3.44
\end{array}
$$

4-Morpholinomethyl-3-hydroxyphenanthrene (2.6 g), 75 ml of dioxane and about 1 g of catalyst were hydrogenated at 150 °C for 3 ½ hours. Hydrogen pressure 80 at. From the reaction mixture the catalyst and the solvent were removed leaving behind 2.8 g of a brown oil. This oil was dissolved in ether and gaseous hydrochloric acid passed into the solution. The precipitate was filtered off and the solution dried and evaporated to dryness, giving 1.4 g of a brown oil. This oil was dissolved in a mixture of benzene and ligroin and filtered through aluminium oxide; after removing of the solvent 1.2 g of a brown oil remained. The oil was dissolved in benzene and picric acid added, giving a solid picrate, which melted at 140—145 °C. After one recrystallization from benzene the m. p. was 144—146 °C. This product, dissolved in benzene, was filtered through aluminium oxide (Brockmann), the solvent removed, and a white product was obtained, 0.2 g, m. p. 90.5—92 °C. Crystallization from a mixture of benzene and hexane gave 0.1 g with the melting point 92—93 °C. Further recrystallizations did not change the melting point. The product was a methyl-3-hydroxyphenanthrene according to the analysis.

$$
\begin{array}{lllll}
C_{15}H_{12}O & \text{Calcd.} & \text{C} & 86.6 & \text{H} & 5.81 \\
& \text{Found} & \text{»} & 86.5 & \text{»} & 6.05
\end{array}
$$

For comparision 4-methyl-3-hydroxyphenanthrene was prepared from 3-hydroxyphenanthrene-4-aldehyde by reduction according to Clemmensen. The aldehyde (0.40 g m. p. 92—93.4 °C) was dissolved in 20 ml of absolute ethanol whereupon 5 ml of concentrated hydrochloric acid and about two grams of amalgamated zinc were added. The originally yellow reaction mixture, gradually grows ligther during reflux and was after two hours colourless. After cooling it was poured into water and the precipitate crystallized from 96 % ethanol. Yield 0.25 g, m. p. 91.5—92.5 °C.

$$
\begin{array}{lllll}
C_{15}H_{12}O & \text{Calcd.} & \text{C} & 86.6 & \text{H} & 5.81 \\
& \text{Found} & \text{»} & 85.7 & \text{»} & 5.67
\end{array}
$$

The methyl-3-hydroxyphenanthrene obtained by hydrogenation did not depress the melting point of 4-methyl-3-hydroxyphenanthrene prepared as above.

Also the picrates and the benzoylderivatives have been prepared and the melting points compared as is seen in table 1.

4-Morpholinomethyl-3-hydroxyretene (7.5 g), 100 ml of dioxane and about 2 g of catalyst at 160 °C for two hours. Hydrogen pressure 100 at. The further treatment of the reaction mixture showed that it was much more difficult here to isolate definite chemical compounds than in the preceeding cases. However, through systematic recrystallizations, purification over picrates and chromatographic separation with aluminium oxide among others 0.3 g of 3-hydroxyreten and 0.3 g of 4-methyl-3-hydroxyretene m. p.

4

Table 1. Comparision of the methylphenols.

Substance	M. p.	Picrate m. p.	Benzoylderiv. m. p.
4-Methyl-3-hydroxyphenan-threne	91.5—92.5	154—156	142—143
Methyl-3-hydroxyphenan-threne from hydrogenation	92—93	153—155	141—142

127 °C were obtained. The last mentioned compound gave a *picrate* m. p. 139—140 °C (Karrman[7] 139—140 °C) and a benzoylderivative m. p. 150—151° Karrman[7] 151—152°). The corresponding piperidino-derivative gave the same result by hydrogenation.

SUMMARY

Mannich bases have been prepared from 2- and 3-hydroxyphenanthrene and 2- and 3-hydroxyretene. These phenols with the exception of 2-hydroxy-retene condense easily with formaldehyde and piperidine or morpholine in glacial acetic acid solution at room temperature under the formation of mono-derivatives. 2-Hydroxyretene reacts only under more rigorous conditions.

By hydrogenation at a pressure of 80—100 at over Raney-nickel among other things a cleavage of the carbon-nitrogen bond occurs under the forma-tion of the corresponding methylphenols. In this way 4-methyl-3-hydroxy-retene was obtained from morpholino- (and piperidino-) methyl-3-hydroxy-retene and 4-methyl-3-hydroxyphenanthrene from morpholino-methyl-3-hydroxyphenanthrene. 1-Methyl-2-hydroxyphenanthrene was obtained by the hydrogenation of morpholino- (and piperidino-) methyl-2-hydroxyphen-anthrene. Thus the structure of these Mannich bases has been fully established. It is very probable that the Mannich base of 2-hydroxyretene is substituted in the 3-position.

The reactivity of the hydroxyl group and substituted aminomethyl group was shown to be diminished, which probably is due to chelation.

LITERATURE

1. Décombe, J. *Compt.rend.* **196** (1933) 866.
2. Bruson, H. A., and Mac. Mullen, C. W. *J. Am. Chem. Soc.* **63** (1941) 270.
3. Caldwell, W. T., and Thompson, T. R. *J. Am. Chem. Soc.* **61** (1939) 2354.

4. Caldwell, W. T., and Thompson, T. R. *J. Am. Chem. Soc.* **61** (1939) 765.
5. Cornforth, J. W., Cornforth, R. H., and Robinson, R. *J. Chem. Soc.* (1942) 682.
6. Mc Cleary, R. F., and Roberts, S. M. *C. A.* **41** 3819.
7. Karrman, K. J. *Svensk Kem. Tid.* **61** (1949) 221.
8. Hill, P., Short, W. F., and Higginbottom, A. *J. Chem. Soc.* (1936) 317.
9. Snyder, H. R., and Brewster, J. H. *J. Am. Chem. Soc.* **70** (1948) 4230.
10. Snyder, H. R., and Brewster, J. H. *J. Am. Chem. Soc.* **71** (1949) 1058.
11. Karrman, K. J., and Sihlbom, L. *Svensk Kem. Tid.* **57** (1945) 284.
12. *Neuere Methoden der präparativen organischen Chemie* I p. 122.
13. *Organic Syntheses* **21** 15.