229. *Kationoid Reactivity of Aromatic Compounds. Part III. The Action of Piperidine on* meso*Benzanthrone.*

By William Bradley.

In Part I (J., 1932, 1254) Bradley and Robinson described the direct replacement of the nuclear hydrogen of several aromatic nitro-compounds by piperidine, and the present part deals with substitution by the same reagent in an aromatic carbonyl compound. From the standpoint of the present work the most reactive ketone is *meso*benzanthrone, which reacts slowly with piperidine even in the absence of condensing agents. The reaction rate is greatly accelerated by sodamide, and when oxygen is present the main product, 2-piperidino*meso*benzanthrone, may be obtained in almost theoretical yield. Experiments are described which indicate the stages in the substitution process. The first phase in the reaction is the formation of piperidide ions, and these react with free *meso*benzanthrone to form an anion which is easily oxidised by oxygen to 2-piperidino*meso*benzanthrone. The simple adduct, 2-piperidinodihydro*meso*benzanthrone, does not appear as an intermediate stage in the substitution process. There is no reaction at the carbonyl group. When oxygen is excluded, the reaction proceeds more slowly, and simple replacement of hydrogen by piperidine does not occur to any considerable extent. Instead, compounds are obtained which have the properties of hydroaromatic amines and are probably adducts of piperidine and *meso*benzanthrone.

*meso*BENZANTHRONE (I) shows two distinct types of reactivity conditioned by the character of the substituting agent. Nitration (Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 259) and halogenation (Cahn, Owen, and Simonsen, J., 1933, 444) occur in the *Bz*-nucleus. On the other hand the Grignard reagent affords 4-alkyl and -aryl derivatives (Allen and Overbaugh, *J. Amer. Chem. Soc.*, 1935, **57**, 740; Charrier and Ghigi, *Ber.*, 1936, **69**, 2211), and potassium hydroxide and potassium chlorate yield 2-hydroxy*meso*benzanthrone (Perkin and Spencer, J., 1922, **121**, 479). Again, in the presence of potassium hydroxide, aniline and *meso*benzanthrone give 2-anilino*meso*benzanthrone in small amount (Lüttringhaus and Neresheimer, *loc. cit.*), and both acetone and phenylacetonitrile react to form 2-derivatives (B.PP. 319593, 322253, 338764).

In the latter group of reactions involving 2- and 4-substitution, the orientation of the entering substituent with respect to the carbonyl group recalls the additive reactions of the same reagents with αβ-unsaturated carbonyl compounds; but, whilst in general the aliphatic adducts are stable, the *meso*benzanthrone derivatives are formed from the reactants with loss of hydrogen.

The formation of piperidino*meso*benzanthrone by the action of piperidine and sodamide on *meso*benzanthrone has already been described (Part I, *loc. cit.*), and advantage has been taken of the ease with which this derivative can be isolated to study the course of the substitution reaction.

*meso*Benzanthrone and piperidine react slowly at the boiling point of the latter and in the absence of condensing agents to form a basic derivative. The reaction is quicker in oxygen than in nitrogen, and is accelerated by potassium hydroxide and especially by sodamide.

The Reaction in Oxygen.—In toluene suspension, sodamide has little action on *meso*benzanthrone at 95—105°, at which temperature rapid substitution occurs in presence of piperidine. On the other hand, piperidine reacts with sodamide at this temperature with liberation of ammonia and formation of a suspension, which, cooled, reacts vigorously with *meso*benzanthrone at 50—55° to give an orange-yellow base. The first phase in the substitution is thus the formation of piperidide ions and the reaction of these with free *meso*benzanthrone.

The basic constituents of the reaction product occur free, and can be completely extracted with dry benzene or light petroleum. No basic compound occurs in the product as a sodium salt. When the reaction is carried out at 95—105°, the crude base is essentially 2-piperidino*meso*benzanthrone with very small amounts of stronger bases. The latter could not be purified completely, but their ability to reduce methylene-blue solution in the cold suggests that they are hydroaromatic amines.

Pre-formed sodium piperidide reacts easily with *meso*benzanthrone in oxygen even at the ordinary temperature, but in these circumstances the basic portion of the product consists largely of the stronger bases; in fact, these may form more than one half of the total amount of basic material.

The constitution of the 2-piperidino-derivative was established by its hydrolysis to 2-hydroxy*meso*benzanthrone, and by its formation from 2-acetoxy*meso*benzanthrone (Perkin and Spencer, *loc. cit.*) and piperidine.

2-Piperidino*meso*benzanthrone is relatively stable to hydrolysis. A suspension of sodium hydroxide in quinoline is almost without effect at 110°, but a slow reaction occurs with alcoholic potassium hydroxide at the same temperature. Fused potassium hydroxide readily hydrolyses the base at 250° with elimination of piperidine, but in these circumstances the main portion of the material is changed into a high-melting substance containing dibenzanthrone.

A characteristic feature of the substitution is the occurrence of phenols, mainly 2-hydroxy*meso*benzanthrone, in considerable amounts. The phenols result almost entirely by hydrolysis of the bases already formed, since it was shown in separate experiments that: (1) bases unaccompanied by phenols are formed when piperidine reacts with *meso*benzanthrone in the absence of condensing agents; (2) phenols are formed with bases when the reaction is carried out in nitrogen and in presence of sodamide; (3) the proportion of bases increased rapidly to a maximum in the early stages of the reaction and subsequently decreased, whilst the proportion of phenols increased steadily throughout the reaction, as found by careful comparisons of the amounts of phenols and bases formed in a series of experiments of different duration; (4) only traces of phenols result by the direct oxidation of *meso*benzanthrone with oxygen in presence of sodamide at the temperature at which rapid substitution occurs; (5) the phenols are formed in much greater amount when sodium hydroxide is added to the reactants.

The slow rate of direct oxidation of *meso*benzanthrone, together with the small yield of 2-piperidino*meso*benzanthrone obtained by heating 2-hydroxy*meso*benzanthrone with piperidine, indicate that little or no 2-piperidino*meso*benzanthrone is formed by this route in the substitution reaction.

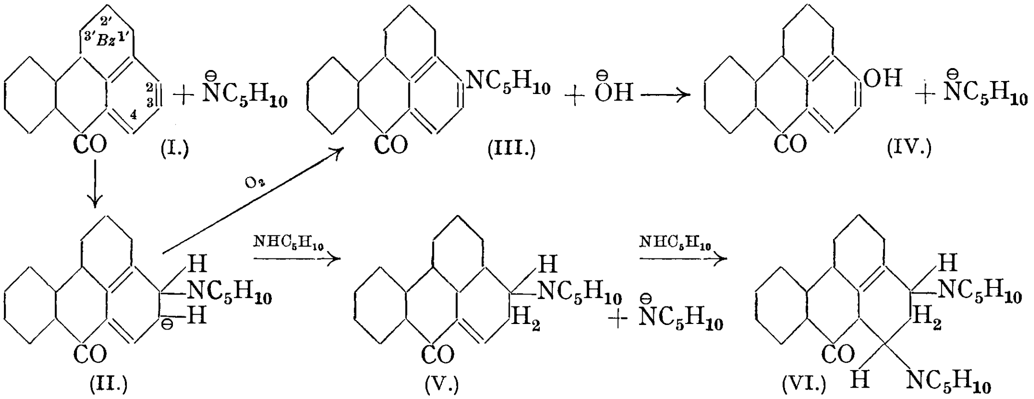
The Reaction in Nitrogen.—Under otherwise identical conditions the reaction between *meso*benzanthrone, piperidine, and sodamide proceeds much more slowly in nitrogen than in oxygen. Phenols are formed, and the bases occur free in the product and not as sodium salts. The carbonyl group of *meso*benzanthrone is clearly not involved in the reaction. The basic material is less homogeneous than that obtained in oxygen, and fractional extraction with hydrochloric acid from a solution in benzene shows it to consist of 2-piperidino*meso*benzanthrone and a stronger base. The former is usually present in very small amount. The stronger base is probably a hydroaromatic amine, since it reduces methylene-blue in the cold, and on heating, it hydrogenates azobenzene to hydrazobenzene and aniline. It has not yet been obtained pure. When it is freshly isolated and dried in a vacuum at the ordinary temperature, the nitrogen content (5·5%) is considerably higher than that of 2-piperidino*meso*benzanthrone (4·5%). Possibly it consists of a mixture of the adducts formed from 1 mol. of *meso*benzanthrone and 1 and 2 mols. of piperidine severally. The formulation of the stronger base as a *meso*benzanthrone derivative is supported by the occurrence of 2-hydroxy*meso*benzanthrone in the phenolic portion of the product, and by the formation of a green fluorescent solution when the base is fused with potassium hydroxide at 250°. No carboxylic acid was formed in this hydrolysis, a circumstance which indicates that the base contains no acyl piperidide grouping. On heating, the base decomposes with evolution of piperidine and formation of a yellow sublimate which dissolves in concentrated sulphuric acid with a cherry-red coloration such as is given by most derivatives of *meso*benzanthrone.

Attempts to obtain piperidino*meso*benzanthrone by dehydrogenating the crude base with azobenzene, iodine, benzoquinone, dilute chromic acid, or methylene-blue were unsuccessful.

That the basic character must be ascribed to the occurrence of piperidino-groups appears certain, since sodamide, apart from salt formation, has no action on piperidine at the b. p. of the latter during 2 or 3 hours.

The following scheme is suggested as the probable course of the reactions taking place between piperidine and *meso*benzanthrone in presence of sodamide :

$$NaNH_2 + NHC_5H_{10} \longrightarrow NaNC_5H_{10} + NH_3$$



The first stage in the reaction is the formation of piperidide ions, and these react with free *meso*benzanthrone to form the anion (II). When the reaction occurs in oxygen at 95—105°, (II) is oxidised to 2-piperidino*meso*benzanthrone (III), and sodium hydroxide formed simultaneously hydrolyses a portion of the product to 2-hydroxy*meso*benzanthrone (IV) and piperidine. In nitrogen, oxidation of (II) is inhibited. Instead, the anion reacts with piperidine to form the adduct (V), which is a strong base with reducing properties. The analytical figures suggest that (V) reacts further with piperidine to form a derivative which is richer in nitrogen (VI ?). When pre-formed sodium piperidide reacts with *meso*benzanthrone in oxygen at the ordinary temperature, the substitution reaction (I ⟶ II ⟶ III) and the addition reaction (I ⟶ II ⟶ V) proceed at comparable rates, and the product is a mixture of the bases (III) and (V). There is no evidence that (III) can be formed from (V) by dehydrogenation during the reaction.

EXPERIMENTAL.

*Constitution of the Piperidino*meso*benzanthrone*, m. p. 178°.—(a) The base (2·5 g.), prepared according to Bradley and Robinson (*loc. cit.*), was added to potassium hydroxide (20 g.) and water (2 c.c.) at 200°, and the temperature raised to 250° during 15 minutes. Piperidine was eliminated. The product, when added to water, partly dissolved to a brown solution with a strong green fluorescence; on being filtered and acidified, this solution afforded 0·5 g. of a phenol. Acetylated with acetic anhydride and sodium acetate, the phenol afforded 2-acetoxy-*meso*benzanthrone, m. p. 200—201° after recrystallisation from alcohol, alone or when mixed with an authentic specimen prepared according to Perkin and Spencer (*loc. cit.*). The alkali-insoluble portion of the product did not melt below 300°. It contained a considerable amount of dibenzanthrone, recognised by its violet colour, its bright red fluorescent solution in xylene, and its fluorescent reddish-violet solution in alkaline sodium hyposulphite (hydrosulphite).

(b) Piperidino*meso*benzanthrone (2·4 g.), stirred with a paste of potassium hydroxide (15 g.) and alcohol (30 c.c.) at 105—110° during 5 hours, gave 0·45 g. of 2-hydroxy*meso*benzanthrone, identified as the acetyl derivative.

(c) 2-Acetoxy*meso*benzanthrone (1·5 g.) was heated with piperidine (10 c.c.) at 200° during 8 hours. The precipitate obtained on pouring the product into water was collected, and extracted with hot concentrated hydrochloric acid. The deep orange solution, poured into water and basified with ammonia, afforded a canary-yellow precipitate which was collected, washed, dried, and recrystallised from light petroleum. The orange-yellow plates which separated melted at 178°, alone or when mixed with the base prepared by the action of sodamide and piperidine on *meso*benzanthrone (Found : N, 4·5. Calc. for $C_{22}H_{19}ON$: N, 4·5%).

The Action of Piperidine on meso*Benzanthrone in the Absence of a Condensing Agent.*—In the following experiments *meso*benzanthrone (9·2 g.) was boiled with piperidine (40 c.c.) under the conditions stated. In expts. 3 and 4 the apparatus used was wholly of Pyrex glass. The basic portion of the product was isolated by diluting the reaction mixture with water, collecting the precipitate, and extracting the bases with concentrated hydrochloric acid.

Expt. No.	Gas.	Time (hours).	Bases (g.).
1	N_2	4	0·08
2	O_2	6	0·2
3	N_2	170	0·15
4	O_2	90	0·8

Experiments in Oxygen.—In the following experiments unless stated otherwise the quantities of reactants used were : *meso*benzanthrone (9·2 g.), sodamide (4·0 g.), and piperidine (40 c.c.).

(a) *The action of sodamide on* meso*benzanthrone.* The reactants were stirred in toluene (40 c.c.) at 100—105° during 2 hours; there was no apparent change. Dry benzene was added, and from the solution *meso*benzanthrone (8·9 g.) was recovered. The material insoluble in benzene was sodamide. Less than 0·1 g. of phenolic compounds could be isolated.

(b) *Direct oxidation of* meso*benzanthrone in presence of sodium hydroxide.* Phenols (0·03 g.) resulted when *meso*benzanthrone was stirred with finely powdered sodium hydroxide (4 g.) in dry quinoline at 105—110° during 1·5 hours. *meso*Benzanthrone (9·05 g.) was recovered. In piperidine solution, *meso*benzanthrone and sodium hydroxide (5 g.) gave 0·04 g. of phenols. *meso*Benzanthrone (8·5 g.) was recovered.

(c) *Comparison of the amounts of base and phenols formed in various reaction times.* Piperidine, *meso*benzanthrone, and sodamide were stirred together in a three-necked flask provided with a mercury seal. The enclosed air was displaced by oxygen, and the temperature slowly raised by heating in an oil-bath. When the inner temperature reached 75—80° there was a rapid evolution of ammonia which continued for 3—4 minutes, accompanied by darkening of the reaction mixture. The product was a mobile black liquid. After the times stated, at an inner temperature of 85—90°, dry benzene was added, and the extraction continued until nothing more dissolved. The residue was in each instance a light brown powder which was partly soluble in water to a brown solution with green fluorescence. Acidification of the filtered solution gave phenols in the amount stated below. The main constituent of this fraction was 2-hydroxy*meso*benzanthrone. The material insoluble in benzene and water did not melt below 300°. Dibenzanthrone was absent, and no indication could be obtained of the presence of 2 : 2′-dibenzanthronyl. The benzene solution contained all the basic material and unchanged *meso*benzanthrone. The bases were isolated by evaporating the solution, extracting the residue with hot concentrated hydrochloric acid, and precipitating the filtered solution with ammonia after adding ice. The basic fraction consisted almost entirely of 2-piperidino*meso*benzanthrone, but when the crude base was dissolved in benzene and the solution was extracted with hydrochloric acid of increasing concentration, a portion more strongly basic than the main constituent could be separated with 1% hydrochloric acid. Piperidino*meso*benzanthrone was not extracted in considerable amount with acid more dilute than 10% . The stronger base was present only in small amount, but it could be isolated from the crude base obtained in each experiment. It was an oily orange-yellow substance soluble in 0·5% hydrochloric acid to an orange solution which reduced methylene-blue in the cold. Addition of more concentrated acid to the dilute solution caused precipitation of a dark, oily hydrochloride.

	Soluble in benzene.		Insoluble in benzene.	
Time (hours).	Base (g.).	Neutral (g.).	Phenols (g.).	Neutral (g.).
0·25	0·5	8·5	0·22	0·2
0·5	7·2	2·5	0·30	0·3
1·0	6·0	2·5	0·22	0·2
1·75	9·35	0·1	0·43	0·45
2·0	10·05	0·1	0·52	0·6
4·5	7·95	0·1	1·16	1·95
5·0	7·0	0·8	1·37	2·0
6·0	7·95	0·1	1·52	?

(d) *Effect of added sodium hydroxide on the amount of phenols formed in the reaction.* When finely powdered sodium hydroxide (2 g.) was added to the reactants, and the products were isolated after 1 hour, the yields obtained were : base (3·2 g.), phenols (1·45 g.).

Experiments in Nitrogen.—(a) *Comparative experiments in oxygen and in nitrogen. Effect of amount of sodamide.* In the following experiments *meso*benzanthrone (4·6 g.) and piperidine (20 c.c.) were used.

Gas.	Time (hours).	$NaNH_2$ (g.).	Bases (g.).
O_2	1·5	1·0	2·6
,,	1·5	1·0	2·8
N_2	1·5	1·0	0·95
O_2	3·0	1·0	2·6
,,	5·0	1·0	2·6
,,	1·5	2·0	3·4
N_2	1·5	2·0	1·7

(b) *Comparison of the amounts of bases and phenols formed in various reaction times.* In the experiments summarised below, the reactants were *meso*benzanthrone (9·2 g.), piperidine (40 c.c.), and sodamide (4 g.). The method of experiment was the same as that used in the oxygen experiments already described.

Expt. No.	Time (hours).	Bases (g.).	Phenols (g.).
1	1·0	2·65	0·2
2	4·0	2·5	0·2
3	6·0	2·5	0·25

(c) *Properties of the bases formed in nitrogen.* The crude base obtained in expt. 1 was washed with water after isolation, and dried over sulphuric acid in a vacuum [Found : N, 5·4, 5·5. Calc. for $C_{22}H_{21}ON$ (piperidinodihydro*meso*benzanthrone) : N, 4·5%. Calc. for $C_{27}H_{32}ON_2$ (dipiperidinotetrahydro*meso*benzanthrone) : N, 7·0%]. After several hours' drying at 100°, the nitrogen content was 4·5%.

A solution of the base in benzene was extracted with hydrochloric acid of increasing concentration. Almost the whole of the substance passed into 1% hydrochloric acid, forming an orange solution which reduced methylene-blue. The base remaining in the benzene solution was small in amount, and could only be readily extracted with concentrated hydrochloric acid. It appeared to be 2-piperidino*meso*benzanthrone. The stronger base was isolated, dried, and fused with azobenzene (10 g.) at 130—135° during 1 hour. The cooled melt, extracted with hot concentrated hydrochloric acid, afforded a solution from which benzidine hydrochloride crystallised on cooling. The salt was dissolved in hot water, and the solution filtered and mixed with dilute sulphuric acid. Benzidine sulphate was precipitated; yield, 0·6 g.

The crude base obtained in expt. 2 was treated as in the foregoing experiment, the more strongly basic fraction being fused with azobenzene (10 g.) at 130—135° during 1·5 hours. The cooled melt was dissolved in benzene and the solution extracted with 1% hydrochloric acid, and then with concentrated hydrochloric acid. The latter extract, diluted with water and basified with ammonia, gave a small amount of material, m. p. 80°, containing azobenzene. Attempts to separate a *meso*benzanthrone derivative by reducing the azobenzene to aniline were unsuccessful.

Low-temperature Experiments in Oxygen.—(a) *Sodamide and piperidine.* When piperidine (10 g.) was boiled with sodamide (3 g.) during 3 hours, and the suspension was cooled, mixed with water and excess of sodium nitrite, and then acidified with dilute acetic acid, nitrosopiperidine (9·0 g.), b. p. 190°/310 mm., was obtained. Piperidine (10 g.), which had not been heated with sodamide, gave on nitrosation 10·0 g. of nitrosopiperidine, b. p. 190°/310 mm.

(b) Piperidine (40 c.c.) was stirred with sodamide (4 g.) at 100° during ½ hour, then cooled, *meso*benzanthrone (9·2 g.) added, and stirring resumed at the ordinary temperature whilst a stream of oxygen was passed. After 24 hours the product was a viscous black mass. Almost all dissolved in cold benzene, and the solution, extracted with hydrochloric acid of increasing concentration, gave the following fractions : (1) soluble in 1% acid, 2·25 g.; (2) soluble in 5—10% acid, traces; (3) soluble in concentrated acid, 2·8 g. The stronger base was a brown solid with reducing properties. On heating, piperidine was evolved and a neutral yellow sublimate obtained which dissolved in concentrated sulphuric acid to an orange solution. When the base (1 g.) was fused with potassium hydroxide (20 g.) and water (2 c.c.) at 250° during 1 hour, piperidine was eliminated and a product obtained of which a small portion dissolved in water to a brown solution with greenish fluorescence. Only a trace of material was precipitated when the solution was acidified. The weaker base, an orange-yellow crystalline substance, m. p. 150—152°, gave pure 2-piperidino*meso*benzanthrone, m. p. 178°, when recrystallised from benzene.

The author is indebted to Imperial Chemical Industries Limited for grants and gifts of *meso*benzanthrone.

THE COLLEGE OF TECHNOLOGY, UNIVERSITY OF MANCHESTER. [*Received, May* 26*th*, 1937.]