Another portion of the amino ketone was obtained from the filtrate in the usual way. The amino ketone hydrochloride was separated from small amounts of high-melting, very insoluble, crystalline by-products by crystallization from alcohol. The ether–benzene solution of the indifferent by-products was evaporated and the residue sublimed in a high vacuum at 90–100°, whereby half of it remained as a tar in the distilling flask. The distillate was separated by crystallization from alcohol. The molecular compounds (m. p. 119 and 107°, respectively) are less soluble than the corresponding phenanthrols. In order to avoid distillation, the residue was repeatedly crystallized from alcohol and ligroin in another experiment; the results were essentially the same. The total yield of crystalline reaction products was about 50%.

Amino Alcohols.—The amino ketone hydrochlorides of the 3,4-series could be hydrogenated in methyl alcoholic solution with a platinum oxide catalyst to the corresponding amino alcohols without any complication. The success of the hydrogenation of the amino ketone hydrochlorides of the 1,2-series with platinum oxide depends apparently upon uncontrollable factors. In some cases the calculated amount of hydrogen was absorbed, and the amino alcohols could be isolated in a pure state; in other cases considerably more hydrogen, up to two moles, was absorbed and the amino alcohol hydrochlorides could be separated from the reaction mixture only in small amounts. However, satisfactory results were obtained consistently by hydrogenating the free amino ketones in methanol solution.

Summary

The synthesis of a series of amino alcohols derived from tetrahydrophenanthrene is described. This new type of amino alcohol is characterized by having the alcoholic hydroxyl and the nitrogen directly attached to the phenanthrene nucleus.

The synthesis is effected by exchanging the bromine atoms in 1-keto-2-bromo-1,2,3,4-tetrahydrophenanthrene and in 3-bromo-4-keto-1,2,3,-4-tetrahydrophenanthrene with the dimethylamino, diethylamino, piperidino and tetrahydroisoquinolino group, and reducing the resulting amino ketones catalytically to the corresponding amino alcohols.

UNIVERSITY, VIRGINIA RECEIVED JULY 12, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis of Phenanthrene and Hydrophenanthrene Derivatives. II. The Hydrocarbon Synthesis[1]

BY LOUIS F. FIESER AND EMANUEL B. HERSHBERG

The most prominent synthetical routes to members of the phenanthrene series were developed in order to provide methods of identifying degradation products of certain opium alkaloids, resin acids and natural products containing the aetiocholane ring system. The Pschorr synthesis,[2] the phenanthrene syntheses of Bardhan and Sengupta[3] and of Bogert,[4] which employ a common intermediate, and the method of cyclizing suitable arylbutyric acids, which has received particular elaboration in the hands of R. D. Haworth,[5] have been employed further by Cook, in the course of his important work on the cancer problem for the preparation of polynuclear hydrocarbons containing the phenanthrene nucleus.[6] The interest in synthetic compounds of possible sex hormone activity has provided a further impetus for the exploitation of the known methods and for the development of new avenues of approach.

The diene reaction of Diels and Alder has until very recently[6a] found little application to the problem.

Although hydrophenanthrene derivatives would be expected to result from the addition of dienes to β-naphthoquinones, a successful reaction of this type has been reported only in the case of one alkylated quinone,[7] and the reaction is not such as to lend itself to general application. A difficulty in the case of the ortho quinones is that they are perhaps too reactive, and too prone to enter into complicating side reactions. 3,4-Dihydronaphthalene-1,2-dicarboxylic acid anhydride (I), which is but one example of a class of compounds readily available by the Bougault synthesis,[8] is far more stable than the quinones, and, being a cyclic derivative of maleic anhydride, is of a type theoretically amenable to condensation with di-

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[1] Preliminary communication: THIS JOURNAL, **57**, 1508 (1935).

[2] Pschorr, *Ber.*, **29**, 496 (1896).

[3] Bardhan and Sengupta, *J. Chem. Soc.*, 2520, 2798 (1932).

[4] Bogert, *Science*, **77**, 289 (1933).

[5] Haworth and co-workers, *J. Chem. Soc.*, 1125, 1784, 2248, 2717, 2720 (1932); 454 (1934).

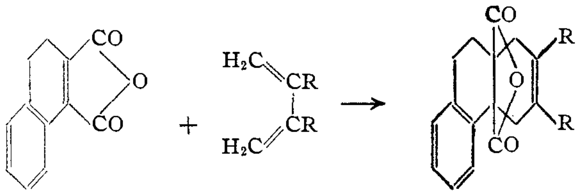
[6] Cook, *ibid.*, 1472 (1932); Cook and Hewett, *ibid.*, 398 (1933); Cook, Haslewood and Robinson, *ibid.*, 667 (1935); Cook and Haslewood, *ibid.*, 767 (1935).

[6a] Barnett and and Lawrence, *J. Chem. Soc.*, 1104 (1935).

[7] Fieser and Seligman, THIS JOURNAL, **56**, 2690 (1934).

[8] Fieser and Hershberg, *ibid.*, **57**, 1851 (1935).

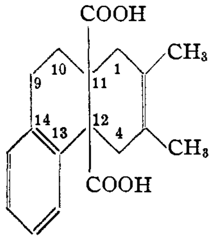
enes. It has been found that such condensations proceed in a highly satisfactory manner. The addition is rather slow, even with a large excess of diene and at a temperature of 100°, but the reaction proceeds smoothly to give in excellent yield nicely crystalline addition products of the type II.



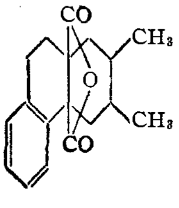
I II

The adducts from I with butadiene and 2,3-dimethylbutadiene have been prepared, together with the 2,3-dimethylbutadiene adducts from the anhydrides of 3,4-dihydrophenanthrene-1,2-dicarboxylic acid[8] and 1,2-dihydrophenanthrene-3,4-dicarboxylic acid.[8] The reaction appears to be one of quite general application.

Thus far we have studied most extensively the hydrophenanthrene derivative obtained from I with 2,3-dimethylbutadiene (II, R = CH_3), and the corresponding acid, 2,3-dimethyl-1,4,9,10,11,12-hexahydrophenanthrene-11,12-dicarboxylic acid (III).



III



IV

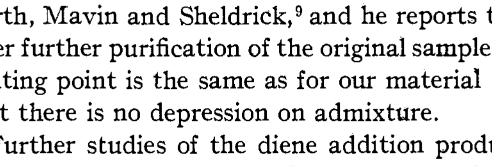
The di-potassium salt of the acid (III) is obtained by warming the anhydride with 6 *N* potassium hydroxide, the anhydride ring being rather resistant to hydrolysis. When the anhydride is heated with methyl alcoholic potassium hydroxide it is converted into a monomethyl ester of the acid III. The dimethyl ester, prepared with the use of diazomethane, is highly resistant to hydrolysis, as would be expected from the tertiary character of both ester groups. Attempts to differentiate between the two groups by partial hydrolysis have not yet been successful. The only method found suitable for effecting a hydrolysis is to fuse the ester with potassium hydroxide, and under these conditions both ester groups are hydrolyzed.

The double bond of the anhydride (II) is easily saturated by catalytic hydrogenation, giving IV. The properties of this substance and of the corresponding acid are similar to those of the unsaturated compounds.

The first attempts to eliminate the anhydride grouping of the adduct and to obtain an aromatic hydrocarbon met with little success. At the high temperature required for dehydrogenation with selenium a reversal of the Diels–Alder reaction apparently occurred, giving the original components or their products of dehydrogenation. The saturation of the double bond did not prevent this reversal, for similar results were obtained with the dihydro compound IV. The two additional hydrogen atoms may in this case be the first eliminated in the selenium treatment. Sulfur apparently is too active a reagent, for both the adduct (II) and its dihydro derivative were converted into a sulfur-containing compound of m. p. 73–74°. The dibasic acids could not be decarboxylated in quinoline solution with copper, for they lost water under these conditions and reverted to the anhydrides. The monomethyl ester of the adduct likewise lost methyl alcohol and suffered cyclization. It seemed necessary to conduct the decarboxylation in a strongly alkaline medium, and the desired result was achieved by fusing the adduct (II) with potassium hydroxide at 320–400° and distilling the product. Hydrocarbon fractions were obtained in this manner in good yield, but the reaction apparently does not follow a single course. Simple decarboxylation of the dipotassium salt would give a hexahydrophenanthrene derivative, but the preparations obtained boiled over a 9° range and the composition corresponded most closely to that of a mixture of the hexahydro and tetrahydro compounds. The material is resistant to hydrogenation in the presence of platinum, and there is but little absorption of hydrogen using palladium. We at first[1] took this as an indication that the principal hydrocarbon present is the 1,2,3,4-tetrahydro derivative, but although such a substance may indeed be present, we were unable to isolate a picrate and we are inclined now to regard the material as a mixture of tetra- and hexa-hydro compounds.

The nature of the gases evolved further points to the occurrence of reactions other than simple decarboxylation. When the dipotassium salt was fused with excess alkali a considerable amount of hydrogen was liberated; when the pure salt was subjected to dry distillation the formation of a large volume of carbon monoxide was noted. In the presence of an excess of potassium hydroxide at the high reaction temperature the cleavage of carbon monoxide, potassium formate or potassium oxalate from the molecule would be obscured by secondary changes, and the course of the reactions is still uncertain. The dihydro compound IV reacted with potassium hydroxide only at a considerably higher temperature, but it gave in good yield a mixture of tetra- and hexa-hydrophenanthrenes. The adduct from I and butadiene (II, R = H) gave a hydrocarbon boiling over a narrow range and having the composition of a hexahydrophenanthrene.

Although the method of fusion with alkali follows a complicated course and gives mixtures of hydrocarbons of varying degree of saturation, these mixtures are entirely suitable for the preparation of the completely aromatic hydrocarbons. The different fractions are dehydrogenated smoothly by selenium, giving pure phenanthrene derivatives in good yield. Phenanthrene itself was prepared by the present synthesis, and in the dimethyl series we obtained a hydrocarbon to which the structure of 2,3-dimethylphenanthrene (V) can be assigned on the basis of the oxidation of the substance to pyromellitic acid (VI).



V VI

Dr. R. D. Haworth has kindly compared our hydrocarbon with the material synthesized by Haworth, Mavin and Sheldrick,[9] and he reports that after further purification of the original sample the melting point is the same as for our material and that there is no depression on admixture.

Further studies of the diene addition products and further applications of the new phenanthrene synthesis are in progress.

Experimental Part[10]

1. The Diels–Alder Reaction

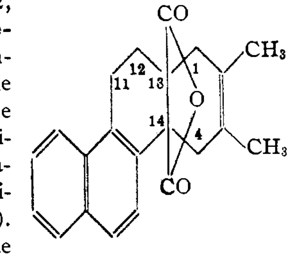
2,3 - Dimethyl - 1,4,9,10,11,12 - hexahydrophenanthrene-11,12-dicarboxylic Acid Anhydride.—For the condensation of 3,4-dihydronaphthalene-1,2-dicarboxylic acid anhydride with 2,3-dimethylbutadiene, 30 g. of the anhydride was heated in a sealed tube with 20–25 g. of the freshly distilled diene in a steam bomb at 100° for twenty to twenty-five hours. The anhydride soon went into solution and after the first five to ten hours it no longer crystallized on cooling the tube. At the end of the reaction the contents of the tube were taken up in ether, treated with Norite and the residue left on distillation of the solvent was distilled, b. p. 175–185° at 1 mm. The colorless oil obtained slowly crystallized, giving a solid, m. p. 92–94°; yield, 94–97%. Recrystallization from benzene-ligroin gave diamond-shaped prisms of the adduct, m. p. 95–96°. The anhydride is very readily soluble in benzene or ether and readily soluble in alcohol or ligroin.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.45. Found: C, 76.56; H, 6.44.

The first experiment, identical with the above but carried out some months earlier, gave a product melting at 75–76°. The sample had been ground for analysis, and when it was reëxamined, subsequent to the later experiments, the melting point was found to have risen to 95–96°.

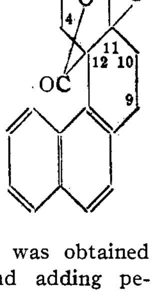
1,4,9,10,11,12 - Hexahydrophenanthrene - 11,12 - dicarboxylic Acid Anhydride.—The addition of butadiene was definitely slower and it was found advisable to use 5–6 molecular equivalents of the diene and to continue the heating for eighty-five hours. The anhydride distilled at 160–170° at 1 mm.; yield, 63%; colorless prisms, m. p. 83.5–84°, from benzene-ligroin.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.56; H, 5.55. Found: C, 75.61; H, 5.97.



2,3 - Dimethyl - 1,4,11,12, 13,14 - hexahydrochrysene-13,14-dicarboxylic Acid Anhydride.—Because of the sparing solubility of the starting material the addition of 2,3-dimethylbutadiene was carried out in dioxane solution (45 hours). The yield in one small scale experiment was good; colorless prisms from cyclohexane, m. p. 196–196.5°. It is only slightly less soluble than the anhydrides described above.

Anal. Calcd. for $C_{22}H_{20}O_3$: C, 79.47; H, 6.07. Found: C, 79.51; H, 6.21.



5,6 - Benz - 1,4,9,10,11,12 - hexahydrophenanthrene - 11,12 - dicarboxylic Acid Anhydride.—A mixture of 10 g. of 1,2-dihydrophenanthrene - 3,4 - dicarboxylic acid anhydride, 15 cc. of dioxane and 14 g. of butadiene (added in portions on successive days) was heated in a sealed tube at 100° for 160 hours. The bright yellow color of the starting material faded during this time, but the solution retained a dull yellow color due to a by-product. A part of the adduct crystallized on cooling the tube and more was obtained by concentrating the mother liquor and adding petroleum ether; yield, 76%. The anhydride is readily soluble in benzene and crystallizes well from benzene-

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[9] Haworth, Mavin and Sheldrick, *J. Chem. Soc.*, 454 (1934).

[10] See Note 4 of the first paper (Ref. 8).

ligroin, forming large, colorless prisms, m. p. 161.5–162°. On attempted distillation at the pressure of the oil pump the material became highly yellow-colored as the result of the partial reversal of the diene addition.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.92; H, 5.30. Found: C, 78.82; H, 5.39.

The **2,3-dimethyl derivative** of the above compound was obtained in a similar manner in dioxane solution; yield, 68%, colorless prisms, m. p. 128–128.5°.

Anal. Calcd. for $C_{22}H_{20}O_3$: C, 79.49; H, 6.07. Found: C, 79.38; H, 6.40.

2. Characterization of the Anhydrides

2,3-Dimethyl-1,4,9,10,11,12-hexahydrophenanthrene-11,12-dicarboxylic Acid (III).—A mixture of 2 g. of the anhydride and 15 cc. of 6 *N* potassium hydroxide was heated at the boiling point until the solid had dissolved (ten minutes), stronger alkali was added and the dipotassium salt was allowed to crystallize. On acidifying a solution of the salt in cold water the acid was precipitated. The acid is very readily soluble in alcohol and crystallizes only slowly on diluting the solution with water; it is very sparingly soluble in benzene. To obtain a pure sample the acid was dissolved in a small quantity of acetone and the solvent was largely displaced by adding successive portions of benzene and evaporating the solution. The acid then crystallized slowly as colorless microcrystals melting sharply at 176–177° with loss of water.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.95; H, 6.73. Found: C, 71.97; H, 6.81.

Monomethyl Ester.—The anhydride was recovered unchanged after being refluxed with methyl alcohol for four hours. To prepare the ester a solution of 3 g. of the anhydride in 150 cc. of methyl alcohol containing 1 equivalent of potassium hydroxide was refluxed for twelve hours. The solution was diluted with water and neutralized, the product separating as an oil which slowly solidified. Recrystallization from benzene–ligroin gave 2 g. of colorless prisms, m. p. 157–159° with loss of alcohol and formation of the anhydride.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.57; H, 7.07. Found: C, 72.52; H, 7.15.

Dimethyl Ester.—This was prepared by the action of diazomethane on either the acid or the monomethyl ester. Crystallized from methyl alcohol, in which it is moderately soluble, the ester formed prisms, m. p. 93.5–94°.

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.13; H, 7.37. Found: C, 73.20; H, 7.53.

The ester was not appreciably hydrolyzed by boiling a mixture of the material (0.2 g.) with 10 cc. of 6 *N* potassium hydroxide and 2 cc. of alcohol for four hours. A paste of the ester with 50% potassium hydroxide was heated carefully until the material was partially converted into a hard potassium salt. This was extracted with water from the unchanged ester, and the acid obtained on acidification was identified as the original dibasic acid in a very pure form.

2,3-Dimethyl-1,2,3,4,9,10,11,12-octahydrophenanthrene-11,12-dicarboxylic Acid Anhydride (IV).—The hydrogenation of the addition product II proceeded smoothly in glacial acetic acid solution with Adams catalyst, the dihydro compound forming transparent octahedra from ligroin, m. p. 117–118°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.00; H, 7.11. Found: C, 76.24; H, 7.17.

The **acid**, prepared and purified as above, crystallized with one-half molecule of benzene which was retained on drying the sample at room temperature. The substance melted at 183–184°; loss in weight on melting, 18.3% (calcd., 16.7%).

Anal. Calcd. for $C_{18}H_{22}O_4{\cdot}(C_6H_6)^1/_2$: C, 73.81; H, 7.44. Found: C, 74.05, 74.06; H, 7.53, 7.70.

3. Decarboxylation

In a typical experiment a mixture of 5.7 g. of the (dimethyl) adduct II, 11 g. of potassium hydroxide, and 10 cc. of water in a Pyrex distilling flask with a sealed-on receiver was warmed until the at first molten anhydride had been converted into the solid potassium salt. The mixture was then heated in a nitrate bath to about 200° to distil off the bulk of the water and the temperature was raised to 325–350°, collecting the oily distillate and some water in the receiver. After bringing the bath to a temperature of 400–420° to complete the distillation, the product was dried in ether and fractionated. The total yield of colorless hydrocarbon suitable for dehydrogenation and boiling over a range of about 9° was 70–85% of the theoretical amount; middle fraction, b. p. 201–204° at 24 mm. The composition of the product was between that of the tetrahydro and hexahydro derivatives as shown in the following analyses of typical preparations.

Anal. Calcd. for $C_{16}H_{18}$: C, 91.37; H, 8.63; for $C_{16}H_{20}$: C, 90.50; H, 9.50. Found: preparation (a), C. 91.25, 91.31; H, 8.99, 9.12; (b) C, 90.86; H, 9.11.

No absorption of hydrogen by the hydrocarbon mixture was noted in alcoholic solution using Adams catalyst. With palladinized calcium carbonate the amount of hydrogen absorbed corresponded to approximately half that calculated for the presence of one reactive double bond, as in a pure hexahydro compound. The tetrahydro derivatives, if present, appear to resist hydrogenation.

The pyrolysis of the dry di-potassium salt (CO evolved) gave a yellow hydrocarbon fraction, b. p. 213–218° at 24 mm., in 64% yield.

When the dimethyloctahydrophenanthrene dicarboxylic acid anhydride (IV) was submitted to a similar fusion with excess alkali, the decomposition occurred only at a higher temperature (about 395°), and the reaction was conducted at a bath temperature of 400–420°. The hydrocarbon fraction, b. p. 200–210° at 24 mm., was obtained in 80% yield. The composition was about the same as above, indicating a mixture. (Found: C, 91.04, 91.02; H, 9.10, 9.24.)

The unmethylated adduct from butadiene (II, R = H) on fusion with alkali as above gave after redistillation a colorless liquid, b. p. 179–180° at 23 mm., in 55% yield. This apparently homogeneous **hexahydrophenanthrene** formed no picrate.

Anal. Calcd. for $C_{14}H_{16}$: C, 91.26; H, 8.74. Found: C, 91.23; H, 8.93.

On dehydrogenation of this material with selenium, there was obtained in 86% yield a hydrocarbon, m. p. 96.5–97.5°, identical with **phenanthrene** from coal tar.

4. Dehydrogenation

2,3-Dimethylphenanthrene.—Various hydrocarbon mixtures obtained as described above were submitted to dehydrogenation with entirely similar results. After heating 2.1 g. of a mixture of the tetra- and hexahydrides with 3 g. of selenium, added in portions, at 310° for twenty hours, the melt solidified completely on cooling. After extracting and distilling the product, one crystallization from methyl alcohol gave 1.6 g. (78%) of plates, m. p. 77–78°. On recrystallization from alcohol or petroleum ether the hydrocarbon formed fluorescent plates, m. p. 78–78.5°.

Anal. Calcd. for $C_{16}H_{14}$: C, 93.16; H, 6.85. Found: C, 92.86; H, 7.08.

The **picrate** formed light yellow needles from alcohol, m. p. 146–147°. The **quinone** crystallized from glacial acetic acid as glistening orange plates, m. p. 237.5–238.5° (**quinoxaline derivative**, m. p. 208–209°).

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.32; H, 5.13. Found: C, 81.23; H, 5.37.

In a letter to one of us Dr. R. D. Haworth states that the original specimen of 2,3-dimethylphenanthrene picrate prepared by his method[9] melts, after two recrystallizations from alcohol, at 144–145°; the regenerated hydrocarbon melts at 79–80°, and the styphnate (Found: C, 58.47; H, 3.95) melts at 137–148° (the m. p. given as 165–167° by a typographical error should have been 145–147°). Dr. Haworth compared his hydrocarbon, picrate, quinone and quinoxaline derivative with ours and observed no depressions; the constants are all in close agreement.

A mixture of 0.5 g. of 2,3-dimethylphenanthrene, 1 cc. of concentrated nitric acid, and 2 cc. of water was heated at 180–200° for twelve hours. As the reaction was not complete, an additional 1 cc. of acid was introduced and the tube was reheated. On concentrating the clear yellow solution and adding fuming nitric acid, the oxidation product was caused to separate. The crude acid was heated at 250° and the anhydride was sublimed in vacuum and crystallized from dioxane, giving prisms containing dioxane of crystallization. After drying at 150° in vacuum to remove the solvent, the substance melted at 277–279° and gave no depression when mixed with a sample of pyromellitic anhydride purified in the same way.

Summary

A new synthesis of phenanthrene has been developed which, in its simplest complete form, involves the following steps: (1) the preparation of γ-phenylbutyric ester, for example, by the condensation of benzene with succinic anhydride, followed by Clemmensen reduction and esterification; (2) condensation with oxalic ester; (3) cyclization to the anhydride of 3,4-dihydronaphthalene-1,2-dicarboxylic acid (the Bougault reaction, as applied by von Auwers and Möller); (4) the addition of butadiene (Diels–Alder reaction); (5) decarboxylation by fusion with alkali (a reaction which may yield a mixture of hydrophenanthrenes, but in which the carbon skeleton is not disturbed); (6) dehydrogenation.

The yields throughout are excellent, and pure products are obtainable at every step except (5). Some variation is possible in step (4), and the compounds required in (1) are already available in wide variety. Successful experiences with reactions (2), (3) and (4), using γ-arylbutyric esters of both the benzene and naphthalene series, indicate that the synthesis probably is capable of wide application.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS.
RECEIVED AUGUST 19, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Oxidation of Carbon Monoxide Catalyzed by Nitrogen Dioxide[1]

BY R. H. CRIST AND O. C. ROEHLING

The oxidation of carbon monoxide is recognized as being of the chain type. The rate at high temperatures is explosive and exhibits the familiar pressure limits.[1] The explosive reaction as shown by Dixon, and Weston and Garner is changed by the presence of water vapor and hydrogen. A homogeneous reaction outside of the explosive region has not been measured. However, studies of a heterogeneous reaction have been made by Bodenstein and Ohlmer in a quartz vessel at 308°, the rate being proportional to the oxygen and inversely proportional to the carbon monoxide and by Langmuir, who found similar results with platinum at 700°. McKinney[2] studied the oxidation at 80° on platinum oxide. The explosive system has been shown by Semenoff and his coworkers[1] to be very sensitive to traces of nitrogen dioxide.

The present investigation is concerned with this reaction under conditions such that the rate of the oxidation in the presence of nitrogen dioxide is measurable. Preliminary experiments show[3]

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[1] For a discussion of this reaction and the literature see Hinshelwood, "Kinetics of Chemical Change in Gaseous Systems," Oxford Univ. Press., 1933, and Semenoff, "Chemical Kinetics and Chain Reactions," The Clarendon Press, Oxford, 1935.

[2] McKinney, THIS JOURNAL, **56**, 2577 (1934).

[3] Crist and Roehling, *Science*, **80**, 338 (1934).