[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

Investigations in the Retene Field. XI. The Synthesis of Retopyridines (Naphthoquinolines) from 3-Aminoretene*

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Polycyclic nitrogen heterocycles, structurally akin to important polycyclic hydrocarbons, have recently attracted considerable interest, because of the discovery that certain dibenzacridines[1,2,3] and dibenzocarbazoles[4,5] possessed definite cancerigenic or tumorigenic activity, that some phenanthridine derivatives exhibited trypanocidal action,[6] while others functioned as antiseptics.[7]

Bachmann, Cook, *et al.*,[2] therefore, prepared and studied a number of benzacridine derivatives. Further, the active search now under way for satisfactory morphine substitutes of equal or greater analgesic power but non-habit-forming, emphasizes the desirability of learning more about the pharmacological properties of polycyclic systems composed of a nitrogen heterocycle fused with a phenanthrene nucleus. With this in mind, Mosettig and his co-workers[8,9,10,11] have described the synthesis of a number of naphthoquinolines, naphthisoquinolines, dibenzoquinolines and dibenzisoquinolines.

In the present communication, the preparation of an analogous retopyridine (VIIa or VIIb), or methylisopropylnaphthoquinoline, as well as an homologous retopicoline, from 3-aminoretene, is described. These syntheses were undertaken not only for the reasons just recited and the relation of such structures to alkaloidal types, but also because retene is a natural product, formed by the degradation of various resins and resin acids. It is not impossible that the methyl and isopropyl groups present on the naphthoquinolines derived therefrom, or hydrogenation products of the latter, may influence their physiological effects. The presence and location of alkyl groups in certain polycyclic hydrocarbons have been shown to have considerable bearing upon carcinogenic and other properties.[12,13]

3-Aminoretene (VI) was prepared by Adelson and Bogert,[14] under the name of 6-aminoretene, but the recent investigations of Ruzicka and Kaufmann,[15] Campbell and Todd[16] and Fieser and Clapp,[13] have made it evident that the amino group is probably in position 3.

Adelson and Bogert used acetylretene as the initial material for their synthesis, and at first we made it that way. Subsequent experience, however, convinced us that it was more satisfactory to prepare it from β-3-retoylpropionic acid (II), another of the synthetic processes developed by Adelson and Bogert.[17]

Ethyl retoylpropionate (III) was converted into its oxime (IV), which yielded the ethyl retylsuccinamate (V) by a Beckmann rearrangement with phosphorus pentachloride. Alkaline or acid hydrolysis of this gave a 37% yield of the desired aminoretene. By this process, the overall yield of the aminoretene from 100 g. of retene was 11 g.; whereas, by the acetylretene method, the yield was only 10 g. and the operations were much more troublesome.

The conversion of the aminoretene into the naphthoquinoline was effected by the usual Skraup reaction, in much the same way as carried out by Mosettig and Krueger[8] in their valuable work in this field.

The constitution of the retopyridine (VIIa or VIIb) has not been determined as yet. If (VIIa) represents its structure, it resembles a 1,2-benzanthracene, carrying a meso-methyl, with a pyridine replacing one of its benzene cycles, and it would therefore be of interest to test its carcinogenic properties. Fieser and Clapp[13] have shown that 3-retoylpropionic acid cyclizes with position 2 and not 4. If the quinoline formation from 3-

* Presented in abstract before the Division of Organic Chemistry at the Cincinnati Meeting of the American Chemical Society, April 10, 1940.

(1) Barry, Cook, Haslewood, Hewitt, Hieger and Kennaway, *Proc. Roy. Soc.* (London), **B117**, 318 (1935).

(2) Bachmann, Cook, Dansi, de Worms, Haslewood, Hewitt and Robinson, *ibid.*, **B123**, 343 (1937).

(3) Rondini and Corbellini, *Tumori*, **20**, 106 (1936).

(4) Boyland and Brues, *Proc. Roy. Soc.* (London), **B122**, 429 (1937).

(5) Andervont, *U. S. Pub. Health Repts.*, **54**, 1529 (1939).

(6) Browning, Morgan, Robb and Walls, *J. Path. Bact.*, **46**, 203 (1938).

(7) Morgan, Walls, Browning, Gulbransen and Robb, *J. Chem. Soc.*, 389 (1938).

(8) Mosettig and Krueger, (a) THIS JOURNAL, **58**, 1311 (1936); (b) *J. Org. Chem.*, **3**, 317 (1938).

(9) Mosettig and May, THIS JOURNAL, **60**, 2962 (1938).

(10) Stuart and Mosettig, *ibid.*, **62**, 1110 (1940).

(11) Krueger and Mosettig, *J. Org. Chem.*, **5**, 313 (1940).

(12) Newman and Joshel, THIS JOURNAL, **62**, 972 (1940).

(13) Fieser and Clapp, unpublished results.

(14) Adelson and Bogert, THIS JOURNAL, **58**, 653 (1936).

(15) Ruzicka and Kaufmann, *Helv. Chim. Acta*, **23**, 288 (1940).

(16) Campbell and Todd, THIS JOURNAL, **62**, 1287 (1940).

(17) Adelson and Bogert, *ibid.*, **59**, 1776 (1937).

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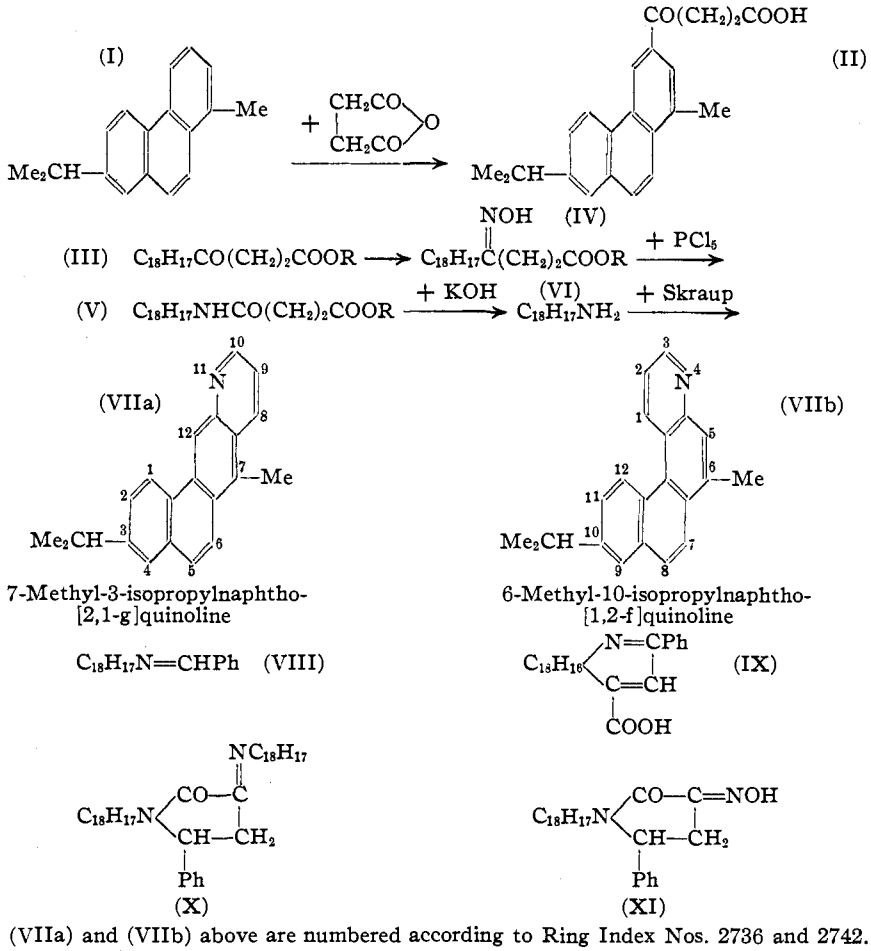

(VIIa) and (VIIb) above are numbered according to Ring Index Nos. 2736 and 2742.

aminoretene follows a similar course, the naphthoquinoline produced should have this formula (VIIa).

A closer analogy, however, is the case of 3-aminophenanthrene itself which, as Mosettig and Krueger[8] have shown, gives the (VIIb) type when subjected to the Skraup quinoline reaction. In this connection the possible orienting influence of the methyl group must not be ignored. For a further discussion of orienting factors in determining the course of cyclization reactions, see Mosettig and Krueger's article.[8]

By the Doebner and von Miller reaction,[18] the aminoretene yielded the expected retopicoline, when paraldehyde was used as the source of the requisite acetaldehyde. Purified through its picrate, and removal of the picric acid by adsorption on alumina, it was obtained in white plates, m. p. 110–111° (cor.). Its hydrochloride crystallized from water in fine hair-like pale yellow needles, carrying 3 moles of water which could not be removed without decomposition.

This naphthoquinaldine offers alluring possibilities for the synthesis of new dyes (including photosensitizers), drugs, etc., and we hope to be able to conduct some explorations in this new territory.

By the Doebner reaction,[19] with benzaldehyde and pyruvic acid, either a benzalaniline (VIII), a diketopyrrolidine anil (X), or a cinchoninic acid (IX), should result. When this reaction was run on 3-aminoretene, the product was insoluble in alkali and not identical with synthetic benzalaminoretene. The conclusion that it must be therefore the retoanil of a retophenyl diketopyrrolidine (X) was supported by its analysis, and that of its picrate, as well as its conversion into the analogous oxime (XI).

Acknowledgments.—We are deeply indebted to the Committee of the Joseph Henry Fund, of the National Academy of Sciences, for financial assistance in the purchase of the retene necessary for this investigation; and to the Hooker Electrochemical Company of Niagara Falls, N. Y., for a generous supply of anhydrous aluminum chloride. We are also under obligations to Mr. Saul Gottlieb, of these laboratories, by whom the analyses were carried out.

Experimental

The retene used in these experiments was purified by distillation at 263–268° under a pressure of 25 mm. As thus prepared, it was sufficiently pure for our purposes. By three crystallizations from alcohol, it was obtained in glistening white plates, m. p. 97–98° (cor.).

(18) Doebner and v. Miller, *Ber.*, **16**, 2464 (1883).

(19) (a) Doebner, *ibid.*, **20**, 277 (1887); (b) Borsche, *ibid.*, **41**, 3884 (1908); (c) Adams and Johnson, THIS JOURNAL, **45**, 1307 (1923).

All melting points were taken with thermometers checked against a set of total immersion thermometers certified by the U. S. Bureau of Standards, and the determinations were carried out in a Thiele melting point apparatus.

β-3-Retoylpropionic acid (II) was prepared by the process of Adelson and Bogert,[17] with the modifications which follow; yield, 54%; m. p. 194–196° (cor.). Adelson and Bogert found 194–196° (cor.); Fieser and Clapp[13] have reported 198–199.5° (cor.).

The benzene used was dried over sodium, after distilling off a 15% forerun, and Eastman Kodak Co. succinic anhydride was employed. The presence of any moisture or alcohol in the reactants resulted in a product which was extremely difficult to purify. The purity of the crude product was also dependent upon the character of the aluminum chloride used. It was found necessary to discontinue the steam distillation as soon as the odor of benzene was no longer apparent, or some of the product was lost. By thoroughly mixing the crude acid with powdered potassium carbonate before adding water and boiling, the time consumed in making the potassium salt was reduced to thirty minutes. In the crystallization of the acid, it was found better to add the fully dried crude product to hot, rather than to cold, acetic acid, and to allow the hot solution to stand overnight. Unless all but the last traces of the acetic acid were removed in the air, the product decomposed in an oven at 110°.

One-tenth mole of retene proved to be the most satisfactory quantity for these runs, larger amounts being more difficult to handle. The accumulation of sufficient of the pure acid for the further experiments therefore was rather laborious.

Oxime.—A mixture of 10 g. of the above acid, 20 g. of hydroxylamine hydrochloride, 15 g. of barium carbonate, and 200 cc. of absolute methanol, was refluxed for four hours, and filtered hot. The filtrate was cooled, and diluted with water. The sticky yellow precipitate was removed, dried, pulverized, and crystallized twice from toluene. It then appeared in white plates, m. p. 165–166° (cor.); yield, 86% (9 g.).

Anal. Calcd. for $C_{22}H_{23}O_3N$: C, 75.6; H, 6.6. Found: C, 75.7; H, 6.7.

All attempts to rearrange this oxime by the action of acetic anhydride, glacial acetic acid, and dry hydrogen chloride, as carried out so successfully by Mosettig and Krueger[8] in their research, proved futile.

Ethyl β-3-Retoylpropionate (III).—A solution of 10 g. of the retoylpropionic acid (m. p. 193–195° cor.) in 200 cc. of 95% ethanol, containing 10 cc. of concentrated sulfuric acid, was refluxed for five hours. As the solution cooled, a brown oil precipitated. After the addition of 20 cc. of acetone, the mixture was left overnight in the refrigerator, and the ester separated in pale yellow crystals. Recrystallized twice from ethanol, the first time in the presence of Norit, it was obtained in white plates, m. p. 92.5–93° (cor.); yield, 7 g. (65%).

Anal. Calcd. for $C_{24}H_{26}O_3$: C, 79.55; H, 7.2. Found: C, 79.5; H, 7.4.

When the reaction was run in absolute, instead of 95% ethanol, and upon its completion, cooled in ice water for a short time and seeded, the crystals of the ester separated.

Oxime of the Ester (IV).—A mixture of 3 g. of the ester, 6 g. of hydroxylamine hydrochloride, and 4.5 g. of barium carbonate, in 100 cc. of absolute methanol, after being refluxed for eight hours, was filtered and the filtrate diluted with water. The oxime precipitated as a sticky yellow oil, which congealed on standing. Recrystallized first from an ethanol–water mixture and then from 95% ethanol, it was obtained in white plates, m. p. 105–106° (cor.); yield, 2.4 g., or 77%.

Anal. Calcd. for $C_{24}H_{27}O_3N$: C, 76.4; H, 7.2; N, 3.7. Found: C, 76.55; H, 7.3; N, 3.7.

Ethyl 3-Retylsuccinamate (V).—A solution of 5 g. of the above oxime in 100 cc. of anhydrous ether, in a flask protected from ingress of moisture, was treated gradually with 6 g. of pulverized phosphorus pentachloride. After standing for an hour, during which the initial pale yellow of the solution changed to a deep orange, the ether was distilled and to the residual oil cracked ice was added. The oil congealed to a pale yellow solid, which was removed, washed with 10% sodium carbonate solution, then with water, and crystallized from an ethanol–water mixture. Three such recrystallizations, using Norit with the final one, followed by a crystallization from "Skellysolve D," gave white plates, m. p. 168–169° (cor.); yield, 4.3 g., or 86%.

Anal. Calcd. for $C_{24}H_{27}O_3N$: C, 76.4; H, 7.2. Found: C, 76.6; H, 7.4.

3-Aminoretene (VI) **from Ethyl 3-Retylsuccinamate** (V).—One gram of the succinamate was suspended in a solution of 4 g. of potassium hydroxide in 50 cc. of normal propanol, the mixture refluxed for four hours, filtered hot, and the cooled filtrate diluted with water. The flocculent precipitate of crude amine was collected, air-dried, crystallized thrice from ethanol, using Norit in the first crystallization, and then appeared in white plates, m. p. 139–140° (cor.); yield, 0.3 g., or 45%. Mixed with a sample of 3-aminoretene, prepared from 3-acetylretene by the Adelson and Bogert[14] method, the m. p. remained unaltered.

In another experiment, 1 g. of (V) was dissolved in 50 cc. of glacial acetic acid and 15 cc. of hydrochloric acid and 45 cc. of water added. The solution which had a milky appearance in the cold was heated to boiling in an oil-bath for twelve hours, during which time it turned to a light yellow and then a deep orange color. On standing overnight in the refrigerator, the amine hydrochloride precipitated in the form of silky needles. A crystallization from water containing a few drops of hydrochloric acid gave the amine hydrochloride as long, colorless needles. These were converted to the free amine by treatment with dilute ammonium hydroxide. One crystallization from ethanol gave the amine in shining white plates, m. p. 139–140° (cor.); yield, 0.3 g. The amine thus obtained showed no depression of the melting point when mixed with an authentic sample of 3-aminoretene.

This latter is the method of Werner and Kunz,[20] but the alkaline hydrolysis was preferable in being shorter and giving the amine directly instead of its hydrochloride.

Hydrochloride.—A suspension of 0.2 g. of the amine in dilute hydrochloric acid (50 cc. of water + 3 cc. of concen-

(20) Werner and Kunz, *Ann.*, **321**, 314 (1902).

trated acid) was boiled and filtered hot. As the hot filtrate cooled, the amine hydrochloride precipitated in white shining needles, which softened at 255° and melted with decomposition at 267–273° (cor.), in an evacuated melting point tube; yield, 0.2 g.

Anal. Calcd. for $C_{18}H_{20}NCl$: C, 75.7; H, 7.0. Found: C, 75.5; H, 7.1.

3-Acetylretene was prepared as described by Adelson and Bogert,[14] with a few modifications. The m. p. was 99.5–100° (cor.), as given by them, and the yield 34%.

The purity of the aluminum chloride is very important in obtaining a crude product which can be fractioned satisfactorily under diminished pressure. It was found also that stirring the reaction mixture decreased the yield. The average yield of distillate from 50 g. of retene was 45 g. Its ethanol solution, on standing in the refrigerator for two weeks, deposited 5–6 g. of acetylretene, which was purified through its picrate. The acetylretene was freed from the picric acid by chromatographic adsorption on alumina, a method which proved far superior to that involving the decomposition of the picrate by dilute alkali.

Oxime.—Prepared as reported by Bogert and Hasselstrom,[21] this oxime crystallized from 95% ethanol in lustrous needles, m. p. 165–166° (cor.), in agreement with the literature.[21]

Larger amounts were readily prepared by dissolving the acetylretene in methanol, mixing with hydroxylamine hydrochloride and barium carbonate, and refluxing the mixture for four hours. The yield of pure oxime (m. p. 165–166° cor.) was 85%.

3-Acetaminoretene.—The procedure of Adelson and Bogert[14] for the rearrangement of the oxime was modified in a few respects. A solution of 10 g. of the oxime in 200 cc. of anhydrous ether was treated gradually with 15 g. of phosphorus pentachloride, in a 3-necked flask, equipped with reflux condenser and calcium chloride tube. Occasional cooling of the reaction flask was found advisable. After the initial reaction was over, the mixture was allowed to stand for three hours, and its color changed to a deep orange. Crystallized twice from toluene, white crystals were obtained, m. p. 240–241° (cor.) (lit. 240–240.5° cor.); yield, 35%.

3-Aminoretene from 3-Acetaminoretene.—In general, the directions of Adelson and Bogert[14] were followed, except that the hydrolysis was carried out in an 8% solution of potassium hydroxide in *n*-propanol and the refluxing was continued for three hours. It was found inadvisable to run the reaction with more than 6 g. of the acetaminoretene at a time. The product melted at 139–140° (cor.), in agreement with the literature,[14] and the yield was 90%.

When the reaction was conducted in a lower-boiling solvent and for a shorter time, there resulted a mixture of the amine and its acetyl derivative, from which the hydrochloride of the amine could be extracted by hot water containing a small quantity of hydrochloric acid.

7 - Methyl - 3 - isopropylnaphtho[2,1 - g]quinoline (VIIa), or 6-Methyl-10-isopropylnaphtho[1,2-f]quinoline (VIIb).—The procedure followed in this synthesis was in the main similar to that used by Mosettig and Krueger[8] in the case of the naphthoquinolines prepared by them.

A mixture of 6 g. of the aminoretene, 4.8 cc. of freshly distilled nitrobenzene, 9.6 g. of freshly distilled glycerol, and 1 g. of anhydrous ferrous sulfate, was treated with 4.8 cc. of concentrated sulfuric acid. The yellowish-gray paste which resulted from this exothermic reaction was heated, under an efficient air condenser, for an hour at 140–145°, followed by two hours at 160–170°. From the resultant thick black sirup, excess of nitrobenzene was eliminated by steam distillation, and the residue was extracted with three 300-cc. portions of boiling water. These extracts were poured into a liter of water, and the deep yellow solution was cooled and saturated with sodium chloride. A small quantity of black tar separated at first, followed by a pale brownish precipitate of the crude naphthoquinoline hydrochloride. After standing for an hour, the hydrochloride was filtered out, suspended in 200 cc. of warm water and the base liberated by the addition of dilute (10%) ammonium hydroxide solution. The amorphous dark brown crude base (5 g.) was extracted five times with 30-cc. portions of ether, the extracts combined, dried over soda-lime, and the ether distilled off. There remained a dark red oil which, when treated with a small amount of anhydrous ether, congealed to a pale orange solid. Recrystallized thrice from petroleum ether, using Norit as the decolorizing agent, 3.7 g. of white plates, m. p. 87.5–88.5° (cor.), was secured, soluble in alcohol, ether, acetone, or benzene, practically insoluble in water. The crude product could be purified also by distillation under reduced pressure.

Anal. Calcd. for $C_{21}H_{19}N$: C, 88.4; H, 6.7; N, 4.9. Found: C, 88.1; H, 6.7; N, 5.1.

For the success of this synthesis, a prime requisite was that all of the reactants should be dry. The crude product was always contaminated with large amounts of tar and iron salts. Although the yield was less when the purification was accomplished by distillation, due to decomposition, colored impurities were more satisfactorily removed in this way than by recrystallization.

Picrate.—Fine bright yellow needles (from *n*-butanol), which melted with decomposition at 277–279° (cor.) in an evacuated tube; difficultly soluble in most ordinary organic solvents.

Anal. Calcd. for $C_{27}H_{22}O_7N_4$: C, 63.0; H, 4.3. Found: C, 63.0; H, 4.7.

Hydrochloride.—When a suspension of 0.5 g. of the naphthoquinoline in 50 cc. of water containing 2 cc. of concentrated hydrochloric acid was boiled, the clear yellow solution which resulted was filtered hot and, as the filtrate cooled, a yellow curdy precipitate separated, which was subjected to a repetition of the same treatment. The hydrochloride so obtained formed a pale yellow powder which, after drying in a vacuum desiccator, melted at 96–101° (cor.); yield, 0.5 g.

Anal. Calcd. for $C_{21}H_{20}NCl \cdot 3H_2O$: C, 67.1; H, 6.9; N, 3.7; Cl, 9.5. Found: C, 66.8; H, 6.7; N, 3.8; Cl, 9.7.

All attempts to remove water from this compound resulted only in decomposition.

The naphthoquinoline hydrochlorides prepared by Mosettig and Krueger[8] from the 2- and 3-aminophenanthrenes, crystallized from ethanol anhydrous and melted,

(21) Bogert and Hasselstrom, THIS JOURNAL, 53, 3462 (1931).

respectively, at 296–300° (evac. tube) and 239–243°. The former of these was described as being sparingly soluble in alcohol, from which it separated in tiny bright yellow needles, whereas our own hydrated salt dissolved freely in alcohol under similar conditions.

Heated for three hours at 100° under reduced pressure, the compound melted and slowly resolidified to an unidentified deep yellow product, which melted with decomposition at 228–238°, with evolution of hydrogen chloride.

Attempted Hydrogenation of the Naphthoquinoline (VII).—Two attempts were made to obtain a tetrahydro derivative, similar to those secured by Mosettig and Krueger[8] by the hydrogenation of their naphthoquinolines, but both were unsuccessful.

In acetic acid solution, with a platinum oxide catalyst, 1 g. of the base (VII) took ten days to absorb the calculated quantity of hydrogen, and no pure compound could be isolated from the product. This slow absorption of hydrogen coincides with the experience of Mosettig and Krueger[8] in their hydrogenation experiments with naphtho-[1,2-f]quinoline.

When the reduction was essayed in absolute ethanol solution, with a copper chromite catalyst, for three hours at 2100 lb. pressure, some decomposition occurred, and the only compound isolated was unchanged initial material (VII). Mosettig and Krueger were unable to hydrogenate naphtho[1,2-f]quinoline in alcoholic solution, with a platinum oxide catalyst.

Mosettig and Krueger[8b] were able to hydrogenate their naphthoquinolines by either of these methods, the second one being preferred, although in one case they reported an unstable tetrahydro derivative, and in several cases mixtures of products.

7,10 - Dimethyl - 3 - isopropylnaphtho[2,1 - g]quinoline, or 3,6-dimethyl-10-isopropylnaphtho[1,2-f]quinoline.—An intimate mixture of 4 g. of 3-aminoretene, 6 cc. of concentrated hydrochloric acid, and 4 cc. of paraldehyde was refluxed for two hours at 100°. The resultant brown liquid was extracted with small quantities of hot water (1 liter in all), leaving a considerable amount of undissolved tarry material.

A portion of this brown aqueous extract was made alkaline by the addition of dilute ammonium hydroxide solution, the red resinous precipitate filtered out, dissolved in ether, the ether solution dried with soda-lime, and the solvent removed. There remained a heavy red oil, which could not be induced to crystallize.

The rest of the original brown aqueous extract, therefore, was boiled with Norit, filtered, and to the cooled filtrate there was added 30 cc. of concentrated hydrochloric acid. The crude naphthoquinaldine hydrochloride separated in pale brown needles, which were recrystallized from water containing a few drops of hydrochloric acid. Treatment of this salt with dilute ammonium hydroxide solution liberated the base as an amorphous solid which proved very difficult to purify. The hydrochloride, therefore, was digested with excess of picric acid in 95% ethanol. The yellow picrate which separated as the solution cooled was recrystallized from 95% ethanol, air-dried, dissolved in benzene, and the solution passed through a column of aluminum oxide to adsorb the picric acid. The colorless benzene solution so obtained, after removal of the solvent, left a viscous yellow oil which crystallized almost immediately. One recrystallization from dilute ethanol, followed by one from petroleum ether, yielded 1 g. of white plates, m. p. 110–111° (cor.).

Anal. Calcd. for $C_{22}H_{21}N$: C, 88.3; H, 7.0; N, 4.7. Found: C, 87.9; H, 7.1; N, 4.8.

Hydrochloride.—Prepared in similar manner to the preparation of the hydrochloride of the naphthoquinoline (VII), by dissolving 0.1 g. of the naphthoquinaldine in 300 cc. of hot water containing three drops of concentrated hydrochloric acid, this salt formed fine hair-like pale yellow needles, m. p. 258–261° (cor.); yield, 0.1 g.

Anal. Calcd. for $C_{22}H_{22}NCl + 3H_2O$: C, 67.8; H, 7.2. Found: C, 67.7; H, 7.4.

All attempts at removing water from this compound yielded only decomposition products.

Picrate.—Prepared in 95% ethanol and recrystallized from the same solvent. Silky yellow needles, m. p. 221–226° (cor.), with decomposition; yield, about 0.15 g. from 0.1 g. of the base.

Anal. Calcd. for $C_{28}H_{24}N_4O_7$: C, 63.6; H, 4.5. Found: C, 63.6; H, 4.7.

1 - (3′ - Reto) - 2 - phenyl - 4,5 - diketopyrrolidine - 4-(3′-retoanil) (X).—A solution of 2.5 g. of 3-aminoretene in 50 cc. of absolute ethanol, to which 2 cc. of freshly distilled benzaldehyde and some clay chips had been added, was refluxed for a few minutes, and then 2 cc. of freshly distilled pyruvic acid in 10 cc. of absolute ethanol was run in. The mixture was refluxed on a steam-bath, and after about fifteen minutes white crystals began to separate. Refluxing was continued for an hour and a quarter, the solution cooled and filtered, and the material on the filter washed with a few cc. of cold ethanol and air-dried. This yielded 1.3 g. of crude material. Two recrystallizations from normal butyl alcohol gave 1 g. of white plates, insoluble in either acid or alkali, m. p. 218–219° (cor.).

Anal. Calcd. for $C_{46}H_{42}N_2O$: C, 86.5; H, 6.6; N, 4.4. Found: C, 86.9; H, 6.9; N, 4.7.

A small quantity of alkali-soluble yellow solid was isolated as a by-product in this reaction, but not enough was obtained for identification.

Picrate.—This was prepared as described for the picrate of the naphthoquinoline (VII), but in anhydrous benzene solution: dark red powder, from benzene, m. p. 234.5–235.5° (cor.), with decomposition; yield about 0.15 g. from 0.1 g. of the anil.

Anal. Calcd. for $C_{52}H_{45}N_5O_8$: C, 72.0; H, 5.2. Found: C, 72.2; H, 5.2.

1 - (3′ - Reto) - 2 - phenyl - 4,5 - diketopyrrolidine - 4-oxime (XI) was obtained from the anil (X) by the procedure described for the preparation of the oxime (IV) from ethyl β-retoylpropionate, but using a *n*-propanol solution and refluxing for four hours. On dilution of the reaction mixture with water, a small portion of a brown tar separated, followed by a flocculent yellow precipitate. The solid residue in the reaction flask was extracted twice with hot 95% ethanol, and the extract joined to a solution of the crude oxime in ethanol. Cooling liberated the oxime, which was once more recrystallized from ethanol, using Norit. The oxime was thus obtained in white

needles, m. p. 208–209° (cor.); yield, 0.8 g., from 1 g. of the anil.

Anal. Calcd. for $C_{28}H_{26}N_2O_2$: C, 79.6; H, 6.1; N, 6.6. Found: C, 79.2; H, 6.4; N, 6.4.

The oxime group is placed on carbon no. 4, because it is believed that the reaction proceeds through a displacement of the anil group by the hydroxylamine, rather than by a condensation with the free carbonyl group in position no. 5, the latter being sterically hindered.

3-Benzalaminoretene (VIII).—A solution of 1 g. of 3-aminoretene in 30 cc. of absolute ethanol was refluxed for three hours with 2 cc. of freshly distilled benzaldehyde. The mixture slowly turned red during the course of the reaction. The solution was cooled and allowed to stand overnight in the refrigerator. This precipitated the benzalamine as clumps of yellow crystals, which were dissolved in hot absolute methanol, cooled slowly to room temperature, and again allowed to stand overnight in the refrigerator. The benzalaminoretene came down as clusters of shining yellow blades, which were dried for a week in a vacuum desiccator. The compound was unstable, and even on short contact with moist air, the odor of benzaldehyde became apparent, m. p. 88–89° (cor.); yield, 0.6 g.

Anal. Calcd. for $C_{25}H_{23}N$: C, 89.0; H, 6.8. Found: C, 88.5; H, 6.9.

Summary

1. 3-Aminoretene is more conveniently prepared from β-3-retoylpropionic acid than from 3-acetylretene.

2. From this amine, a retopyridine (naphthoquinoline) has been synthesized by the Skraup reaction, and a retopicoline (naphthoquinaldine) by the Doebner–von Miller reaction.

3. The classical Doebner reaction, for the production of cinchoninic acids, converts the aminoretene into a diketopyrrolidine anil, without the formation of appreciable quantities of either benzalaminoretene or the expected cinchoninic acid derivative.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The High-Temperature Photolysis of Acetone and the Action of Free Methyl Radicals on Propane

BY AUGUSTINE O. ALLEN

Acetone illuminated by light of wave lengths between 2000 and 3200 Å. is known to break up cleanly to free methyl and acetyl radicals.[1] This reaction provides a convenient source of free methyl radicals for the study of reactions induced by them over the temperature range 150–400°. For inducing oxidation reactions especially, acetone has a great advantage over such sources as methyl iodide and dimethylmercury, in that no reactive oxidation inhibitors are simultaneously produced from the source to complicate the reaction. It is well known, however, that at these temperatures a complicating reaction occurs in the acetone photolysis, leading to the formation of methane.[2] In the present work, studies on the products and mechanism of this reaction are described. Also, the use of acetone as a source of free methyl radicals is illustrated by some data on the products obtained by illumination of mixtures of acetone and propane.

(1) (a) Gorin, *J. Chem. Phys.*, **7**, 256 (1939); (b) Herr and Noyes, THIS JOURNAL, **62**, 2052 (1940).

(2) (a) Leermakers, *ibid.*, **56**, 1879 (1934); (b) Winkler, *Trans. Faraday Soc.*, **31**, 761 (1935); (c) Akeroyd and Norrish, *J. Chem. Soc.*, 890 (1936); (d) Taylor and Rosenblum, *J. Chem. Phys.*, **6**, 119 (1938).

Experimental

A 500-watt high-pressure Hanovia mercury arc lamp was used for the light source; a starting switch provided with the lamp allowed some variation of the intensity. The cylindrical fused quartz reaction vessel (capacity about 200 cc.) was placed in a hand-regulated aluminum block furnace. In a slit in the side of the furnace, between light source and reaction vessel, was placed a quartz cell through which flowed a 0.02 *N* solution of acetic acid to filter out wave lengths below 2000 Å. Acetone vapor and C. P. propane (warranted 99.9% pure) were introduced into a 2-liter storage bulb, then drawn into the reaction vessel as needed. No stopcocks were used in the filling and reaction systems, their place being taken by Hoke packless diaphragm-type valves of brass, sealed into the glass system by picein wax.

The reaction products were withdrawn by means of a hand-operated Toepler type pump, consisting simply of a vertical glass cylinder connected to a mercury leveling bulb, with a three-way stopcock at the top. For runs in which only the permanent gas fraction was analyzed, a liquid-air trap was inserted next to the reaction vessel, and the uncondensed gas (which would contain substantially no ethane) was pumped by the hand Toepler into an Orsat apparatus. To obtain a more complete analysis, recourse was had to a fractionation apparatus patterned after that of Ward.[3] Through a series of five small traps, which

(3) Ward, *Ind. Eng. Chem., Anal. Ed.*, **10**, 169 (1938).