

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

INVESTIGATIONS IN THE RETENE FIELD. I. THE SYNTHESIS OF SOME NEW RETENE DERIVATIVES

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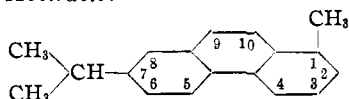
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Researches in the phenanthrene field within recent years have received their stimulus and direction mainly from the endeavor to solve the problem of the constitution of those alkaloids, notably the morphine group, which appear to contain a phenanthrene nucleus.

From the standpoint of terpene chemistry, however, it is retene which is the most interesting of all phenanthrene derivatives, for it occurs in tars of highly resinous pines, and in some mineral resins. Further, it is formed when abietic acid is distilled with sulfur.¹ Retenes or hydroretenes seem to be the basis of many resins and resin acids, and various other lines of connection have been established already between terpene and phenanthrene derivatives, especially by the recent work of Ruzicka and his collaborators. The synthesis and study of new retene derivatives hence seems opportune in the development of the chemistry of the terpenes and of related compounds.

The system of numbering the retene nucleus used in this paper is that adopted by *Chemical Abstracts*.



The appearance of an article by Komppa and Wahlforss² leads us to publish our own results in this same field.

These investigators attempted to prepare an acetylretene by the ordinary Friedel-Crafts reaction using acetyl chloride upon a carbon disulfide solution of the hydrocarbon, but were unsuccessful. We have been more fortunate with this reaction and have obtained the acetylretene in excellent yield. It is possible that this derivative escaped detection by Komppa and Wahlforss because of the fact that its melting point is almost identical with that of retene itself.

It was purified through its picrate and further characterized by the preparation of its oxide, phenylhydrazone and semicarbazone. The acetyl group was not in the 9 or 10 position, since on oxidation an acetylretenequinone was obtained, which condensed with *o*-phenylenediamine to the corresponding phenazine.

Like acetophenone,³ the terminal methyl group of this acetylretene was

¹ Vesterberg, *Ber.*, **36**, 4200 (1903).

² Komppa and Wahlforss, *THIS JOURNAL*, **52**, 5009 (1930).

³ (a) Claisen and Claparède, *Ber.*, **14**, 2463 (1881); (b) Claisen, *ibid.*, **20**, 657 (1887); (c) Claisen and Ponder, *Ann.*, **223**, 148 (1884); (d) v. Kostanecki and Rossbach, *Ber.*, **29**, 1493 (1896).

very reactive and condensed smoothly with various aldehydes to chalcone types, some of which possessed tinctorial properties.

Another noteworthy observation is that, while retene itself yields mainly decomposition products on attempted nitration,^{2,4} this acetylretene nitrates smoothly in acetic acid solution.

By the method of Wolff,⁵ acetylretene semicarbazone was easily reduced to a crystalline ethylretene, the location of whose ethyl group has not yet been determined. It formed a crystalline picrate and on oxidation gave an ethylretenequinone.

A way has thus been opened for the preparation of many new retene derivatives which are likely to be of considerable interest and significance.

Most of the acylretenes and retenequinones gave characteristic color reactions with cold concentrated sulfuric acid, the color vanishing upon dilution. The carbonyl groups are probably responsible for these color changes, since similar changes have been reported before in the case of keto derivatives, and since neither retene nor ethylretene gives this reaction.

The work is being continued and other papers will appear shortly.

Experimental Part

Retene.—Some of the retene (m. p. 98.5–99°, corr.) used in this research was presented by Mr. Eero O. Erkkö, of Helsingfors, Finland, to whom we wish to express our grateful thanks. The rest (m. p., 94.5–96.5°, corr.) was purchased from the Eastman Kodak Company.

Acetylretene (Methyl Retyl Ketone), $\text{CH}_3\text{COC}_{18}\text{H}_{17}$.—To a mixture of 25 g. of retene, 35 g. of acetyl chloride and 150 cc. of carbon disulfide, in a round-bottomed flask with condenser and calcium chloride tube, there was added, in the course of ten minutes, 28 g. of finely pulverized aluminum chloride. A vigorous evolution of hydrogen chloride occurred. The reaction mixture was allowed to stand at room temperature until the evolution of hydrogen chloride had practically ceased. This took about one hour. The carbon disulfide and the excess of acetyl chloride were distilled, and the residue, while still warm, was poured into a beaker containing 300 cc. of ice water. Concentrated hydrochloric acid (10 cc.) was added and the reaction mixture extracted with ether. Some tarry material remained undissolved. The ethereal extract was washed several times with dilute hydrochloric acid, then with sodium carbonate solution and finally with water. It was dried with calcium chloride and the ether evaporated. The residual dark colored oil, when kept for a week in a refrigerator at about 0°, deposited some crystals, which showed the same melting point as retene. However, the mixed melting point test with pure retene gave a considerable depression.

The dark oil was therefore dissolved in 45 cc. of boiling alcohol, a hot solution of 25 g. of picric acid in 120 cc. of alcohol was added and the mixture was boiled for five minutes. As the solution cooled, an acetylretene picrate crystallized in yellow needles. It was recrystallized from alcohol, then suspended in 150 cc. of 10% sodium carbonate solution and the mixture heated for fifteen minutes at about 80°. A resinous material

⁴ (a) Ekstrand, *Ann.*, 185, 79 (1877); (b) Bamberger and Hooker, *ibid.*, 229, 116 (1885).

⁵ Wolff, *ibid.*, 394, 86 (1912).

was obtained. This was washed repeatedly on the filter with a warm sodium carbonate solution and then with water until the wash waters were pale yellow. After drying at room temperature, the resin was dissolved in boiling alcohol. On cooling, acetylretene crystallized in pale brownish needles; yield, 13.5 g. Recrystallized from alcohol, it formed colorless lustrous scales, m. p. 99–99.5° (corr.).

Anal. Calcd. for $C_{20}H_{20}O$: C, 86.9; H, 7.2. Found: C, 86.74; H, 7.48.

In cold concentrated sulfuric acid, it dissolved to an orange solution, the color of which was discharged by dilution.

Picrate.—Short bright yellow needles, m. p. 142–143° (corr.), after two recrystallizations from alcohol.

Oxime.—An alcoholic solution of 2 g. of acetylretene was mixed with an aqueous solution of 1.5 g. of hydroxylamine hydrochloride. A few drops of concentrated hydrochloric acid was added and the mixture was boiled for half an hour. As the solution cooled, the oxime crystallized in colorless lustrous flakes which, after crystallization from dilute alcohol, melted at 167–168° (corr.); yield, nearly that calculated.

Anal. Calcd. for $C_{20}H_{21}ON$: C, 82.5; H, 7.2. Found: C, 82.5; H, 7.39.

Phenylhydrazone.—To an alcoholic solution of 0.5 g. of acetylretene there was added 1 g. of phenylhydrazine dissolved in 4 cc. of 50% acetic acid. The mixture was boiled for ten minutes and then left overnight at room temperature. The phenylhydrazone precipitated in fine colorless lustrous flakes and good yield. Recrystallized from dilute acetic acid, it melted at 202° (corr.). On keeping it gradually turned brownish in color.

Anal. Calcd. for $C_{25}H_{25}N_2$: C, 85.2; H, 7.1. Found: C, 85.16; H, 7.2.

Semicarbazone.—To 0.5 g. of acetylretene dissolved in a small quantity of alcohol, there was added an aqueous solution of 0.5 g. of semicarbazide hydrochloride and 0.5 g. of anhydrous sodium acetate. After standing for a few hours at room temperature, the semicarbazone separated in minute colorless needles; yield, nearly that calculated. Recrystallized first from alcohol and then from acetic acid, it melted at 248.5–249.5° (corr.) with decomposition.

Anal. Calcd. for $C_{21}H_{23}ON_3$: C, 75.6; H, 6.9. Found: C, 75.4; H, 6.64.

Acetylretenequinone, $CH_3COC_{18}H_{16}O_2$.—To a hot solution of 2 g. of acetylretene in 30 cc. of glacial acetic acid there was added 4 g. of chromium trioxide in small portions. After boiling the mixture under a reflux for ten minutes, it was diluted with water and allowed to cool. The quinone separated in dark orange needles; yield, 1.3–1.8 g. Recrystallized from alcohol, it melted at 213–214° (corr.), with decomposition.

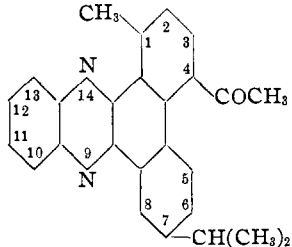
Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.4; H, 5.9. Found: C, 77.92; H, 6.14.

In cold concentrated sulfuric acid it dissolved to a bluish-green solution, whose color disappeared upon dilution.

Acetylretophenazine, (4?)—**Acetyl-1-methyl-7-isopropyl- α,γ -dibenzophenazine.**—

The quinone (0.5 g.) was dissolved in a small amount of acetic acid, *o*-phenylenediamine hydrochloride (0.7 g.) was added, followed by a solution of anhydrous sodium acetate (0.5 g.) in dilute alcohol. The mixture was boiled for ten minutes and then allowed to cool. The phenazine crystallized in fine yellowish needles; yield, 0.5 g. Recrystallized from acetic acid, it melted at 196–197° (corr.).

Anal. Calcd. for $C_{26}H_{22}ON_2$: C, 82.5; H, 5.8. Found: C, 82.25; H, 5.78.



Its solution in cold concentrated sulfuric acid was cherry-red, which color disappeared upon dilution.

Dinitroacetylretene, $\text{CH}_3\text{COC}_{18}\text{H}_{18}(\text{NO}_2)_2$.—Acetylretene (2 g.) was nitrated with a mixture of fuming nitric (3 cc.) and glacial acetic (3 cc.) acids, at low (0–5°) temperature. The yield of crude dinitro derivative was 1.7 g. It crystallized from glacial acetic acid in microscopic yellow crystals which melted at 215–216° (corr.).

Anal. Calcd. for $\text{C}_{20}\text{H}_{18}\text{O}_5\text{N}_2$: N, 7.9; found, 7.9.

Recrystallization from acetic acid gradually lowered the melting point, presumably because of slow decomposition. Heated above its melting point, it decomposed violently with evolution of oxides of nitrogen.

Cinnamylretene (Styryl Retyl Ketone), $\text{C}_6\text{H}_5\text{CH}=\text{CHCOC}_{18}\text{H}_{17}$.—A solution of 1 g. of acetylretene and 1 g. of benzaldehyde in 35 cc. of absolute alcohol was prepared, and to this, at room temperature, there was added 5–8 drops of a strong solution of sodium ethylate in absolute alcohol. On standing overnight, the chalcone separated in yellow glistening flakes; yield, practically that calculated. Recrystallized from acetic acid (about 80%), it melted at 154.5–155.5° (corr.).

Anal. Calcd. for $\text{C}_{27}\text{H}_{24}\text{O}$: C, 89.0; H, 6.7. Found: C, 88.9; H, 6.84.

Its burgundy-red solution in cold concentrated sulfuric acid lost its color when diluted.

***p*-Nitrocinnamylretene**, $\text{O}_2\text{NC}_6\text{H}_4\text{CH}=\text{CHCOC}_{18}\text{H}_{17}$, prepared in similar manner, using *p*-nitrobenzaldehyde in place of benzaldehyde, crystallized from about 80% acetic acid in pale yellow crystals like fine sand, m. p. 188–189° (corr.); yield, nearly that calculated.

Anal. Calcd. for $\text{C}_{27}\text{H}_{23}\text{O}_3\text{N}$: C, 79.2; H, 5.6. Found: C, 78.68; H, 5.71.

In cold concentrated sulfuric acid, the color of the solution was bluish-red, which vanished on dilution.

Ethylretene, $\text{C}_2\text{H}_5\text{C}_{18}\text{H}_{17}$.—A mixture of 4 g. of acetylretene semicarbazone and sodium ethylate (from 1.5 g. of sodium and 18 cc. of absolute alcohol) was heated in a sealed tube for twenty-four hours at 190–200°. When cold, the contents of the tube was removed, acidified with acetic acid and extracted with petroleum ether. Evaporation of the solvent from these extracts left an oil which crystallized on standing; yield over 50%. Recrystallized from petroleum ether, it melted at 54–55° (corr.). By slow crystallization (10 days) at 0°, it was obtained in beautiful transparent colorless glassy prisms.

Anal. Calcd. for $\text{C}_{20}\text{H}_{22}$: C, 91.6; H, 8.4. Found: C, 91.23; H, 8.45.

Picrate.—Recrystallized twice from alcohol, it formed deep orange short needles, m. p. 145–146° (corr.).

Ethylretenequinone, $\text{C}_2\text{H}_5\text{C}_{18}\text{H}_{17}\text{O}_2$.—Ethylretene (0.5 g.) was oxidized by chromium trioxide (1 g.) in glacial acetic acid (15 cc.) solution. It formed dark orange needles, melting with decomposition at 205.5–206.5° (corr.); yield, 0.2 g.

Anal. Calcd. for $\text{C}_{20}\text{H}_{20}\text{O}_2$: C, 82.2; H, 6.8. Found: C, 81.82; H, 6.79.

In cold concentrated sulfuric acid, the solution was green. On dilution, the color was lost.

Summary

1. Acylretenes have been obtained by the application of the Friedel-Crafts reaction to retene.
2. These acylretenes have been further characterized by the preparation therefrom of various derivatives.

3. The acyl group does not enter in either the 9 or 10 position.
4. Whereas it has been impossible to nitrate retene itself, these acyl derivatives nitrate easily.
5. By reduction of acetylretene semicarbazone, ethylretene has been secured.
6. The work has considerable significance for the chemistry of the terpenes and resins.

NEW YORK, N. Y.

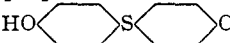
[CONTRIBUTION FROM THE CHEMICAL AND BACTERIOLOGICAL RESEARCH LABORATORIES OF HYNSON, WESTCOTT & DUNNING, INC.]

PREPARATION AND BACTERIOLOGICAL STUDY OF SOME SYMMETRICAL ORGANIC SULFIDES¹

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In the course of a study of the influence of the structure of compounds containing two hydroxyphenyl groups upon the bacteriological properties, we have prepared some derivatives and analogs of 4,4'-dihydroxydiphenylsulfide, HO  OH, where the phenol residue may be substituted by CH₃, OH, Cl, Br, etc. Johnson and his co-workers have published² results dealing with the preparation and study of the bactericidal properties of a number of unsymmetrical organic sulfides. Due to differences in methods of testing, comparisons with values found by these investigators are not in order.

According to Tassinari³ symmetrical organic sulfides are formed when a cold carbon disulfide solution of a phenol is treated with sulfur dichloride.

Table I lists the sulfides which have been prepared by a modification of this method, the details of which appear below.

TABLE I
DATA ON SULFIDES

Phenol used	Empirical formula of sulfide	Sulfur, %		Melting point, °C.	Solubility		
		Calcd.	Found		NaOH	Alcohol	Benzene
Phenol	C ₁₂ H ₁₀ O ₂ S	14.68	14.73	151	Soluble	Soluble	Soluble hot
Resorcin	C ₁₂ H ₁₀ O ₄ S	12.80	13.00	165-167	Soluble	Soluble	Soluble hot
<i>m</i> -Cresol	C ₁₄ H ₁₄ O ₂ S	13.07	12.98	142.5	Soluble	Soluble	Soluble hot
<i>p</i> -Chlorophenol	C ₁₂ H ₉ O ₂ Cl ₂ S	11.15	10.95	173	Soluble	Soluble	Soluble hot
<i>p</i> -Bromophenol	C ₁₂ H ₉ O ₂ Br ₂ S	8.51	8.66	180	Soluble	Soluble	Soluble hot
Thymol	C ₂₀ H ₂₆ O ₂ S	9.70	9.80	152.5- 153.5	Soluble hot	Soluble hot	Slightly hot

¹ Paper read before the Section on Medicinal Chemistry, at the Indianapolis Meeting of the American Chemical Society, April, 1931.

² Hilbert and Johnson, *THIS JOURNAL*, **51**, 1526 (1929); Bass and Johnson, *ibid.*, **52**, 1146 (1930).

³ Tassinari, *Gazz. chim. ital.*, **17**, 83 (1887); **19**, 343 (1889); **20**, 362 (1890).