or acetic acid, sparingly soluble in xylene, and moderately soluble in ethyl benzoate (boiling). It crystallizes from either of the last two solvents in golden-yellow plates, m. p. 360–362°, dec.

4′,8′-Diacetoxy-1,2,5,6-dibenzanthraquinone (VI).—A suspension of 350 mg. of the above diacetate in 35 cc. of glacial acetic acid was refluxed for three hours with 420 mg. of anhydrous sodium dichromate and, after cooling, the orange quinone was collected and recrystallized from ethyl benzoate. It formed delicate orange needles, m. p. 340–345°, dec.; yield 320 mg. (85%). A sample for analysis was recrystallized from ethyl benzoate and then sublimed in high vacuum; the melting point was unchanged.

Anal. Calcd. for $C_{26}H_{16}O_6$: C, 73.58; H, 3.79. Found: C, 74.02; H, 4.04.

This quinone gives no color with aqueous alkali but forms a pale orange vat after boiling for a few minutes. On reoxidation by air the violet color characteristic of the free dihydroxy compound is produced.

Degradation of VI.—A mixture of 100 mg. of the diacetoxy dibenzanthraquinone and 1 g. of potassium hydroxide was placed in a platinum crucible and heated in a nitrite-bath at 260° for ten minutes and then at 280° for ten minutes. Other conditions of time and temperature were less satisfactory. The cooled melt was dissolved in 4 cc. of warm water and heated in a boiling water-bath for ten minutes. After filtering with Super-cel the acidic product was precipitated and collected, and it was then reprecipitated from a similarly treated bicarbonate solution. The brown product so obtained was sublimed at 1 mm. and 180–190° and crystallized once from water. This gave 40 mg. (45%) of nearly colorless needles of 5-hydroxy-2-naphthoic acid, m. p. 213–214.5°. This gave no depression with a sample of pure synthetic acid (known), m. p. 214.5–215.5,° prepared by a modified procedure which will be described in a future paper, and the color reaction with ferric chloride was the same (dirty red precipitate). The fusion was carried out successfully with 50 mg. of the quinone and 0.5 g. of potassium hydroxide, the yield being 10 mg. (22.5%).

4′,8′-Dihydroxy-1,2,5,6-dibenzanthraquinone.—The diacetoxy quinone (50 mg.) was boiled with 5 cc. of 1 *N* alcoholic potassium hydroxide for five minutes and after dilution with 50 cc. of water the opaque purple solution was neutralized at the boiling point with carbon dioxide as described for IV. The orange-red precipitate on sublimation in high vacuum afforded 35 mg. (87%) of crystalline, deep maroon colored dihydroxy quinone. This decomposes without melting at 370–375°.

Anal. Calcd. for $C_{22}H_{12}O_4$: C, 77.64; H, 3.55. Found: C, 77.35; H, 3.81.

The quinone gives a brilliant violet color in dilute alkali and a pale orange vat, reoxidation restoring the violet color. In common with the dihydroxydibenzanthracene, it dissolves with decomposition in boiling ethyl benzoate and only amorphous material separates on cooling.

Summary

4′,8′-Dihydroxy-1,2,5,6-dibenzanthracene has been synthesized by disulfonation of dibenzanthraquinone, reduction, and fusion with alkali. The structure was established by a degradative method applicable on a micro scale.

The synthetic dihydroxydibenzanthracene differs from the isomer isolated by Levi and Boyland as a product of the metabolism of the hydrocarbon by rabbits but very probably is identical with the substance excreted by hydrocarbon-injected mice and rats (Dobriner, Rhoads and Lavin).

Certain theoretical considerations are presented concerning the nature and significance of the reactions involved in the metabolism of carcinogenic hydrocarbons.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 20, 1940

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

The Synthesis of 2-, 4- and 9-Fluoreneacetic Acid

BY W. E. BACHMANN AND JOHN CLARK SHEEHAN[1]

Of the five possible isomeric fluoreneacetic acids only the 2- and 9-isomers have been prepared. What appears to be another fluoreneacetic acid has been prepared by heating fluorene and chloroacetic acid[2] but its structure does not seem to have been established. Its melting point (148°) does not correspond with either the 2- or 9-isomer. This fluoreneacetic acid has been found to possess plant hormone properties.[3] It appeared of interest to prepare the entire series of fluoreneacetic acids, and in this paper is reported the synthesis of the new 4-fluoreneacetic acid, as well as new procedures for obtaining the 2- and 9-isomers.

Von Braun and Engel[4] prepared 2-fluoreneacetic acid from fluorene by an eight-step process. We

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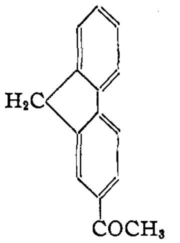
[1] From the Ph.D. dissertation of John Clark Sheehan.

[2] Wolfram, Schörnig, and Hausdörfer, U. S. Patent 1,951,686 (1934).

[3] Zimmerman and Wilcoxon, *Contrib. Boyce Thompson Inst.*, **7**, 209 (1935); *C. A.*, **30**, 1431 (1936); Killeffer, *Ind. Eng. Chem.*, *News Ed.*, **18**, 395 (1940).

[4] Von Braun and Engel, *Ber.*, **57B**, 191 (1924).

have prepared the acid by two different methods. In one, 2-cyanofluorene was hydrolyzed to 2-fluorenecarboxylic acid and the latter was converted to 2-fluoreneacetic acid through the Arndt–Eistert reaction. A more convenient method for obtaining the compound is the Willgerodt reaction. In this reaction, 2-acetylfluorene (I), readily available by acetylation of fluorene, was converted to 2-fluoreneacetamide (II) in good yield with ammonium polysulfide. Hydrolysis of the acid amide yielded the desired 2-fluoreneacetic acid.



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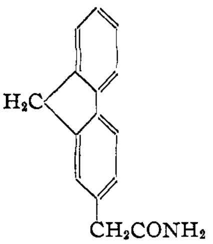

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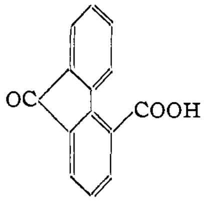

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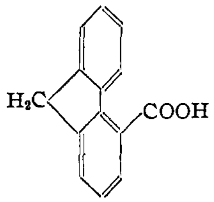
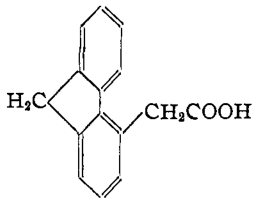
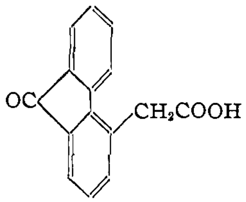


IV



V



VI

In order to prepare the 4-isomer, 4-fluorenonecarboxylic acid (III) was reduced to 4-fluorenecarboxylic acid (IV) in two steps. In the first step, III was reduced by zinc and sodium hydroxide to the intermediate 4-fluorenolcarboxylic acid, which was then reduced by hydriodic acid to 4-fluorenecarboxylic acid. From the latter, 4-fluoreneacetic acid (V) was prepared in excellent yield through the Arndt–Eistert reaction. Similarly, 4-fluorenonecarboxylic acid (III) was converted to 4-fluorenoneacetic acid (VI). Reduction of the latter compound likewise yielded 4-fluoreneacetic acid.

4-Fluoreneacetic acid is of interest in view of the possibility of cyclizing it to a derivative of 4,5-methylenephenanthrene. However, both V and VI have failed to cyclize under the conditions which suffice to convert 2-biphenylacetic acid to a phenanthrene derivative.[5] Other methods are being investigated.

9-Fluoreneacetic acid has been prepared previously from ethyl 9-fluorylglyoxalate by various procedures[6] and from fluorenone through the Reformatsky reaction.[7] We have now prepared it from 9-bromofluorene through the malonic ester synthesis.

The three fluoreneacetic acids are being tested for plant hormone properties.

Experimental

2-Acetylfluorene (I).—This compound has been prepared by Dziewoński and Schnayder[8] from fluorene and acetyl chloride but the details were not available to us. We employed the following procedure. To a solution of 34.6 g. of aluminum chloride in 150 cc. of nitrobenzene was added 14.6 cc. of acetic anhydride. The solution was cooled to −5° and 20 g. of finely powdered fluorene was added in portions while the solution was stirred mechanically. The mixture was stirred at 0° for three hours and then for the same length of time at room temperature. After hydrolysis with ice and dilute hydrochloric acid, the mixture was steam distilled. The residue was distilled under reduced pressure (1.0 mm.) and the product recrystallized from acetone, from which 18.9 g. of colorless leaflets was obtained; m. p. 128–129° (reported, 132°[8]). From the filtrate 2 g. of only slightly less pure ketone was isolated, making a total yield of 83%.

2-Fluoreneacetamide (II).—Following the recent directions of Fieser and Kilmer,[9] 4 g. of 2-acetylfluorene, 16 cc. of dioxane and 20 cc. of ammonium polysulfide reagent were heated in a sealed tube at 160° for ten hours. On cooling, the mixture deposited the product in gleaming, nearly colorless prisms. The amide was filtered and washed with a mixture of ammonium sulfide solution and dioxane; yield, 3.02 g. (70%); m. p. 260–262.5°. A sample recrystallized from acetic acid formed colorless leaflets; m. p. 264–266° with slight decomposition.

Anal. Calcd. for $C_{15}H_{13}ON$: N, 6.2. Found: N, 6.1.

2-Fluoreneacetic Acid. (a) From 2-Fluoreneacetamide.—A mixture of 1 g. of the amide in 10 cc. of acetic acid and 3 cc. of hydrochloric acid was refluxed for three and one-half hours. The addition of 3 cc. of hydrochloric acid at the end of this time precipitated a mass of colorless crystals of the product; m. p. 185–186°; yield, 0.94 g. An additional 0.04 g. of the acid, obtained by diluting the filtrate with water, brought the yield to 98%. A sample, after sublimation at 170° at 0.01 mm., crystallized from benzene in colorless, nacreous plates; m. p. 186–187° (reported, 178°[4]).

(b) From 2-Fluorenecarboxylic Acid.—By means of the Arndt–Eistert reaction on 0.5 g. of 2-fluorenecarboxylic

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[5] Schönberg and Warren, *J. Chem. Soc.*, 1838 (1939).

[6] Mayer, *Ber.*, **46**, 2586 (1913); Wislicenus and Eble, *ibid.*, **50**, 261 (1917); Sieglitz and Jassoy, *ibid.*, **54**, 2133 (1921).

[7] Von Braun and Anton, *ibid.*, **62**, 145 (1929).

[8] Dziewoński and Schnayder, *Bull. intern. acad. polon. sci.*, 529 (1930A); *Roczniki Chem.*, **11**, 407 (1931).

[9] Fieser and Kilmer, This Journal, **62**, 1354 (1940).

acid, using the procedure described for the 4-isomer, 0.16 g. (32%) of 2-fluoreneacetic acid was obtained. The acid melted at 185–186° alone and at 186–187° when mixed with the acid obtained in (a).

4-Fluorenolcarboxylic Acid.—A mixture of 6 g. of 4-fluorenonecarboxylic acid (III),[10] 6 g. of powdered zinc, 60 cc. of water, 7.05 g. of sodium hydroxide (95%) and 1 cc. of toluene (to reduce frothing) was refluxed for two hours. After removal of the toluene by boiling, the mixture was acidified. The precipitated acid was filtered off, dissolved in sodium carbonate solution and reprecipitated. The dry acid (5.42 g., m. p. 195–196.5°) was dissolved in hot acetone, the solution filtered and evaporated. Recrystallization from benzene, in which the acid is sparingly soluble, gave 5.12 g. (85%) of the acid melting at 202–203° (reported, 203° by Graebe and Aubin[11]).

4-Fluorenecarboxylic acid (V).—A mixture of 10 g. of 4-fluorenolcarboxylic acid, 10 g. of iodine, 10 g. of red phosphorus, 20 cc. of water, and 200 cc. of acetic acid was refluxed for one hour. The cooled mixture was treated with Filter-Cel and filtered, and the filtrate was poured into a liter of water containing 8 g. of sodium bisulfite. The acid was recrystallized from benzene, from which it was obtained as fine colorless needles; m. p. 189–190°; yield, 8.5 g. (92%). A sample after sublimation at 180° at 0.01 mm. and recrystallization from benzene melted at 191–191.8°. Graebe and Aubin,[11] who prepared this acid by reduction of the acid chloride of 9,9-dichloro-4-fluorenecarboxylic acid, report 175°. The melting point of the methyl ester of our acid (63.5–64.5°) is in agreement with the value (64°) reported by them.

4-Fluoreneacetic Acid (V).—To a suspension of 1.96 g. of 4-fluorenecarboxylic acid in 10 cc. of anhydrous ether and 1 drop of pyridine was added 0.9 cc. of thionyl chloride. After the mixture had stood at room temperature for three hours with occasional swirling, the solvent and excess of reagent were removed under reduced pressure, 3 cc. of benzene was added and the latter removed under reduced pressure, finally at 40°. A solution of the acid chloride in 15 cc. of anhydrous ether was added dropwise with swirling to a solution of diazomethane in 150 cc. of ether, prepared from 6 cc. of nitrosomethylurethan. After three hours, the ether was evaporated under reduced pressure, and the diazo ketone dissolved in 20 cc. of anhydrous methanol. After addition of 0.2 g. of silver oxide (Mallinckrodt U. S. P.), the mixture was refluxed for twenty minutes, then an additional 0.2 g. of silver oxide was added and refluxing continued for forty minutes more. Norit and Filter-Cel were added and the hot solution was filtered. Two cc. of 40% sodium hydroxide was added and the solution was refluxed for one hour. After removal of the methanol, the salt of the acid was dissolved in water, the solution boiled with Norit, filtered and acidified. The acid (2 g., m. p. 174.5–175.5°) on recrystallization from benzene was obtained as fine, colorless needles; m. p. 178.5–179°; yield, 1.48 g. Additional acid from the filtrate only slightly less pure brought the yield to 1.86 g. (89%).

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.4; H, 5.4. Found: C, 80.6; H, 5.4.

Methyl 4-Fluorenoneacetate.—The Arndt–Eistert reaction was carried out on 1 g. of 4-fluorenonecarboxylic acid (III) in the manner just described. The diazo ketone crystallized in yellow leaflets upon removal of the solvent under reduced pressure. It was found advisable to digest the crystalline mass with 8 cc. of a cold mixture of equal volumes of ether and 30–60° petroleum ether, after which the diazo ketone was filtered off and allowed to dry. A mixture of 10 cc. of anhydrous methanol and 0.15 g. of silver oxide was heated until a mirror formed (about three minutes). The solid diazo ketone was then added and the mixture refluxed for thirty minutes. At the end of this time and also fifteen minutes later 0.08-g. portions of silver oxide were added to the boiling mixture. After a total time of one hour, the solution was clarified with Norit and Filter-Cel and filtered. From the cooled solution 0.55 g. of the ester crystallized in fine, yellow needles; m. p. 134.5–135.5°. Additional slightly lower melting ester obtained by subliming the product in the filtrate at 0.1 mm. brought the yield to 0.95 g. (84%). A sample sublimed at 0.01 mm. and recrystallized from methanol melted at 135.5–136°.

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.2; H, 4.8. Found: C, 75.8; H, 4.5.

4-Fluorenoneacetic Acid (VI).—A solution of 0.5 g. of the aforementioned ester in methanol was refluxed with 5 cc. of *N* sodium hydroxide for one hour. After removal of the methanol, a solution of the sodium salt of the acid in water was boiled with Norit, filtered and acidified, yielding 0.445 g. (94%) of the acid as fine, yellow needles melting at 204–206°. A sample sublimed at 180° at 0.01 mm. and recrystallized from alcohol melted at 206.0–207° with slight previous softening.

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.7; H, 4.2. Found: C, 75.5; H, 4.2.

A 0.1-g. portion of the acid was reduced by zinc and sodium hydroxide, then by hydriodic acid in the same manner as III. The product (0.035 g., 37%) crystallized from benzene in colorless needles, which melted at 178–179° alone and when mixed with 4-fluoreneacetic acid (V).

9-Fluoreneacetic Acid.—A 91% yield of 9-bromofluorene was obtained by adding 4 g. of acetyl bromide to 4 g. of fluorenol. A vigorous reaction took place and in a short time the bromofluorene solidified. After the mixture had been warmed on a steam-bath for a few minutes, the acetic acid and excess of reagent were removed by evaporation under reduced pressure and the product digested with petroleum ether; yield 4.91 g.; m. p. 102–103°.

A solution of 4.5 g. of 9-bromofluorene in 15 cc. of dry benzene was added to a chilled solution of sodio-malonic ester prepared from 0.75 cc. of sodium, 6.7 cc. of diethyl malonate and 30 cc. of absolute alcohol in an atmosphere of nitrogen. When the reaction was carried out in an atmosphere of air, the product was slightly yellow. After the mixture had been refluxed for one hour, the solvents were distilled from the mixture and the residual ester was hydrolyzed with 40% aqueous potassium hydroxide solution. The dicarboxylic acid was heated at 200° for twenty minutes, the product was dissolved in hot acetone and the solution was boiled with Norit and Filter-Cel. The acid obtained from the solution by evaporation was recrystallized from dilute acetic acid, from which it

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[10] Bischoff and Adkins, THIS JOURNAL, **45**, 1030 (1923).

[11] Graebe and Aubin, *Ann.*, **247**, 283 (1888).

was obtained as colorless needles; m. p. 129.5–130.5°; yield, 3.67 g. (89%). Distillation at 170° at 0.01 mm. followed by two recrystallizations from benzene–petroleum ether and one from dilute acetic acid, raised the melting point to 131.5–132.5°. There appears to be a lack of agreement in regard to the melting point of this acid. Values of 128–129° (Mayer[6]), 137° (Sieglitz and Jassoy[6]), and 138–139° (Wislicenus and Eble[6]) have been reported.

Summary

Methods are described whereby 2- and 9-fluoreneacetic acid can be obtained readily and in good yields.

The synthesis of the new 4-fluoreneacetic acid is described.

ANN ARBOR, MICHIGAN RECEIVED JULY 15, 1940

[CONTRIBUTION FROM RESEARCH LABORATORIES, SHAWINIGAN CHEMICALS LTD.]

Macropolymerization; the Mechanism of Activation

BY ERNEST P. IRANY

The formal definition of macropolymerization as a chain reaction[1]

$$\begin{array}{lll} M \longrightarrow M^* & & \text{(Activation)} \\ M^* + M \longrightarrow M_2^* & \multirow{2}{*}{} & \text{(Chain propagation)} \\ M_r^* + M \longrightarrow M_{r+1}^* & & \\ M_r^* + M_s^* \longrightarrow M_{r+s} & & \text{(Termination)} \end{array}$$

does not attempt a specific description of the state of activation which is presumed to be transmitted through the reaction sequence. That this state is distinguished by a higher energy content than that possessed by the average molecule is obvious and, for general considerations of kinetics, sufficient. However, our understanding of the chemical mechanism of the process remains incomplete unless it be possible to interpret the enhanced energy content of the activated molecule in terms of chemical reactivity and, hence, in some distinctive concept of structure.

The usual assumption with respect to activation is that of the "opening double bond"[2]

$$M = CH_2{=}CHX \qquad M^* = {-}CH_2{-}CHX{-}$$

which is preferred because the moderate energy increase attributed to this transformation seems to be in accord with the energy of activation observed for the whole polymerization process. A small number of monomeric molecules are supposed to attain the state M* and, thereupon, to initiate chain propagation in two directions

$$\begin{array}{ccc} {-}CH_2{-}CHX{-} & {-}(CH_2{-}CHX)^*{-} & {-}CH_2{-}CHX{-} \\ \text{Addend molecule} & \text{Initially activated} & \text{Addend molecule} \\ \longleftarrow \text{Propagation} & & \text{Propagation} \longrightarrow \end{array}$$

This conception of macropolymerization encounters various difficulties, several of which are discussed in the following.

(a) Termination cannot be explained satisfactorily.—The state of activation resides in two separate portions of the growing macromolecule which, with increasing length of the interposed chain, must become entirely independent of each other, so that they may be regarded as two disconnected monovalent radicals

$${-}(CH_2 \ldots\ldots CHX){-}$$

Such a structure cannot come to rest as a stable molecule[3] except through the saturation of both terminal valences. How this is to occur in the absence of independent monovalent radicals cannot be explained; the free end valences are definitely paired and, though it may be possible to account for the eventual stabilization of individual molecules through "transfer" of their state of activation to new monomeric centers,[4] it is impossible to explain the termination of the process as such. For this reason, some subsidiary mechanism must be assumed which can only be based on dissociation into monovalent radicals, disproportionation, internal stabilization through "mesomerization," or cyclization. The first two possibilities are excluded by excessive energy requirements, and the latter by their statistical improbability. Resonance between the terminal groups as well as their union becomes practically inconceivable once the saturated main structure of the chain has achieved a certain length; if these possibilities existed, low polymer products would predominate, but they are usually entirely absent.[5]

(b) The opening double bond mechanism is

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[1] Chalmers, *Can. J. Research*, **7**, 113, 472 (1932); H. Mark, "IX Congr. Chim.," Madrid, 1934; Dostal and Mark, *Z. physik. Chem.*, **B29**, 299 (1935); Staudinger, *Trans. Faraday Soc.*, **32**, 97 (1936), etc.

[2] Staudinger, *Ber.*, **59**, 3035 (1926); Flory, THIS JOURNAL, **59**, 241 (1937).

[3] Staudinger, *Ber.*, **59**, 3035 (1926); Taylor and Vernon, THIS JOURNAL, **53**, 2527 (1931).

[4] Flory, *ibid.*, **59**, 241 (1937).

[5] Chalmers, *ibid.*, **56**, 912 (1934).