[CONTRIBUTION FROM THE LABORATORY OF BIOCHEMISTRY, NATIONAL CANCER INSTITUTE[1]]

A New Route to 3- and 2,6-Substituted Fluorenes[2]

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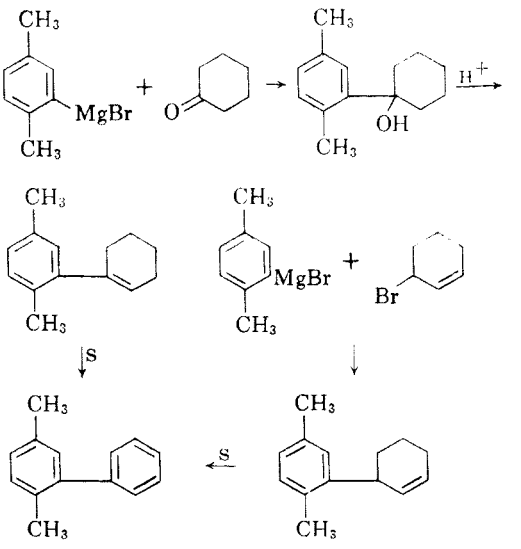
The isomeric 1- and 3-(2,5-xylyl)cyclohexene were prepared from 2,5-xylylmagnesium bromide and cyclohexanone, or 3-bromocyclohexene, respectively. Comparative ultraviolet absorption data on these and the related saturated molecule suggest a steric inhibition of resonance in the first compound owing to the 2-methyl group. Dehydrogenation of the cyclohexene derivatives led to 2,5-dimethylbiphenyl which was oxidized to 2,5-biphenyldicarboxylic acid. Ring closure gave 9-oxo-3-fluorenecarboxylic acid which was the starting material for the preparation of a number of 3- and 2,6-substituted fluorene derivatives. The ultraviolet absorption spectra of these compounds are discussed in relation to the resonance interaction of a substituent at the 3- and as compared to the 2-position of fluorene.

Direct substitution by electrophilic reagents in the polynuclear hydrocarbon fluorene usually involves the 2-position.[cf.3] Further reaction affects the 7-, and also to some extent the 5-position, when the group in the 2-position is electron-attracting. On the other hand, the second substituent enters the 7-, 3-, and 1-positions, in order of decreasing quantitative importance, if the 2-positions contain an electron-donating substituent. Therefore, only the 2-monosubstituted and the 2,7-and the 2,3-disubstituted derivatives of fluorene are readily available using the hydrocarbon itself as starting material. Compounds with substituents at the other carbon atoms are in general prepared by degrading a larger ring system or by building up the fluorene skeleton. Fluorenes or fluorenones with a substituent in the 3-position have been synthesized from properly substituted 2-aminobenzophenones *via* a Pschorr reaction,[4] from biphenyl derivatives by ring closure,[5] by elimination of a substituent at the 2-position in 2,3-disubstituted fluorenes,[5b,6] or by building up the fluorene ring system from indane derivatives.[7] The problem of the synthesis of 3-substituted fluorenes thus hinges on the development of satisfactory methods for the preparation of the crucial intermediates. This paper presents a simple procedure leading to 2,5-biphenyldicarboxylic acid, which can be converted readily into 9-oxo-3-fluorenecarboxylic acid. This compound and the corresponding fluorene derivative have been found useful for the further preparation of 3-fluorenamine and of a number of 2,6-disubstituted fluorenes.

The reaction of 2,5-xylylmagnesium bromide with cyclohexanone furnished the readily dehydrated 1-(2,5-xylyl)cyclohexanol. Hydrolysis of the Grignard reaction mixture had to be performed by saturated ammonium chloride rather than by an acid solution if dehydration of some of the tertiary alcohol were to be avoided. However, the ease with which loss of water occurred under the influence of hydrogen ion facilitated the preparation of the desired 1-(2,5-xylyl)cyclohexene in a single step without isolating the intermediate cyclohexanol.



The isomeric 3-(2,5-xylyl)cyclohexene was prepared by an adaptation of the method used by

(1) National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare.

(2) Presented in part before the Division of Organic Chemistry, at the 131st meeting of the American Chemical Society, Miami, Florida, April, 1957; abstracts of papers, p. 69-0.

(3) (a) G. Rieveschl, Jr., and F. E. Ray, *Chem. Revs.*, **23**, 287 (1938); (b) E. Sawicki, B. Chastain, and H. Bryant, *J. Org. Chem.*, **21**, 754 (1956).

(4) An excellent review on this topic has recently appeared: DeLos F. DeTar, *Org. Reactions*, **9**, 409 (1957); E. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **80**, 33 (1946) has also described the use of this method.

(5) (a) F. E. Ray and J. G. Barrick, *J. Am. Chem. Soc.*, **70**, 1492 (1948); (b) N. Campbell and W. H. Stafford, *J. Chem. Soc.*, 299 (1952); (c) K. Alder, K. Heimbach, and K. Neufang, *Ann.*, **586**, 138 (1954); (d) E. K. Weisburger, *J. Am. Chem. Soc.*, **77**, 1914 (1955).

(6) (a) A. Eckert and E. Langecker, *J. prakt. Chem.*, **118**, 263 (1928); (b) F. E. Bardout, *Anales asoc. quím. arg.*, **19**, 117 (1931); (c) M. Hayashi and A. Nakayama, *J. Soc. Chem. Ind., Japan*, Suppl. binding, **36**, 127B (1933); (d) A. Barker and C. C. Barker, *J. Chem. Soc.*, 870 (1954); (e) N. Campbell and N. H. Keir, *J. Chem. Soc.*, 1233 (1955); (f) N. Ishikawa and M. Hayashi, *Yûki Gôsei Kagaku Kyôkai Shi*, **14**, 80 (1956), **15**, 202 (1957); (g) N. Ishikawa, M. Okazaki, and M. Hayashi, *Yûki Gôsei Kagaku Kyôkai Shi*, **16**, 34 (1958).

(7) *cf.* H. Bryant and E. Sawicki, *J. Org. Chem.*, **21**, 1322 (1956) for pertinent references.

Biggerstaff *et al.*,[8] namely reaction of 2,5-xylylmagnesium bromide with 3-bromocyclohexene. For the purpose of comparative studies of the spectra in this series of compounds the corresponding saturated (2,5-xylyl)cyclohexane was also synthesized by the alkylation of cyclohexene with *p*-xylene. Curiously, both the wave lengths of maxima of absorption in the ultraviolet and the molar extinction coefficients at the maxima are very similar for all three compounds (Fig. 1). This is not the case

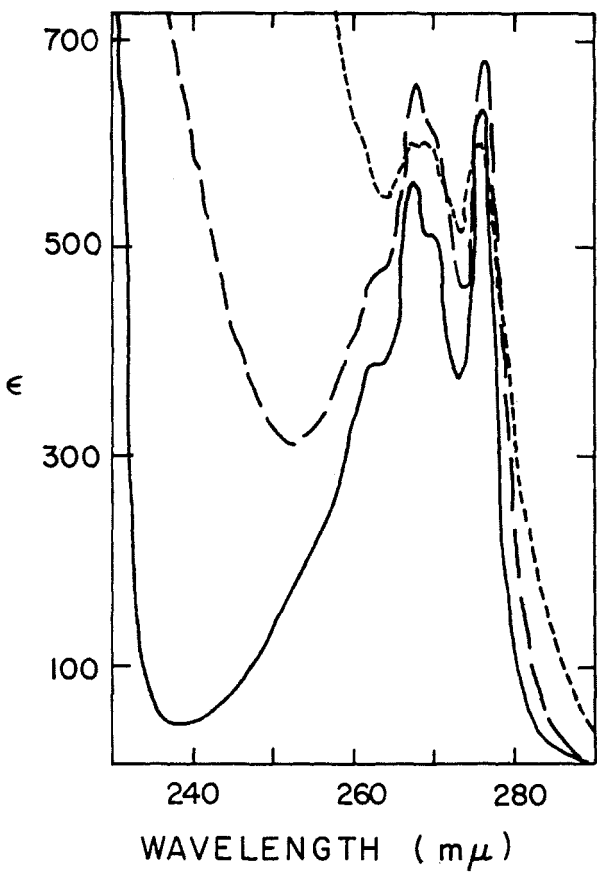


Fig. 1. Ultraviolet absorption spectra of; ——— 2-cyclohexyl-1,4-dimethylbenzene, - - - - 1-(2,5-xylyl)cyclohexene, and — — — 3-(2,5-xylyl)cycohexene

with the corresponding phenylcyclohexane and cyclohexenes[9a] which suggests that the methyl group in the 2-position interferes with the planarity of the exocyclic (to the aromatic ring) double bond in 1-(2,5-xylyl)cyclohexene. Molecular models show that the methyl group at the 2-position prevents a planar configuration of the double bond in relation to the aromatic ring. Carlin and Landerl[9b] and Carlin and Constantine[9c] have also concluded that a methyl group in the 2-position can interfere with the planarity of the molecules; this is reflected in their physical properties. A comparison of the refractive indices in this series of compounds (*cf.* Experimental section and reference 9a) supports this concept.

Dehydrogenation of either the 1- or 3-cyclohexene derivative to give 2,5-dimethylbiphenyl proceeded readily with sulfur at 220–240° as an exothermic reaction. In two cases the reaction was followed by collecting the evolved hydrogen sulfide, which was obtained in a quantitative yield. However, the recovery of 2,5-dimethylbiphenyl was only 50–60%, and the balance of the material was a non-distillable, somewhat viscous residue. Further study of this reaction might be of some interest. Johnson[10] noted recently that dehydrogenations performed with a mixture of sulfur and palladium-on-charcoal facilitated the reaction and gave somewhat higher yields than with sulfur alone. Another method, dehydrogenation with chloranil, was considerably more cumbersome and did not lead to improved yields.

The permanganate oxidation of 2,5-dimethylbiphenyl was a slow process owing to the relative insolubility of the hydrocarbon in the aqueous oxidation system. A fair proportion of the compound was recovered unchanged even after a long reaction period (10 hours). Attempts to obviate the difficulty by addition of a solvent, pyridine, were only moderately successful. The oxidation was more rapid and all of the added hydrocarbon was oxidized. However, a considerable excess of permanganate was required, since pyridine itself was attacked under the conditions of the reaction. In addition, the resulting 2,5-biphenyldicarboxylic acid was not as pure as that obtained by oxidation without the added solvent.

Ring closure of 2,5-biphenyldicarboxylic acid to yield 9-oxo-3-fluorenecarboxylic acid was performed with polyphosphoric acid. The Wolff-Kishner reduction of the fluorenone derivative proceeded at an unusually low temperature. Gas evolution started at 120°, and was substantial at 140°. This might be the result of a strong electron-attracting group, the carboxyl ion, in a *para* position to the ketone function.

3-Fluorenecarboxylic acid was readily converted to 3-fluorenamine *via* the diacetyl derivative in a modified Curtius reaction, which had been successfully used with another fluorenecarboxylic acid under analogous conditions,[11] and where the normal Curtius procedure failed owing to the difficulty in securing hydrolysis of the intermediary urethan. The more direct Schmidt reaction likewise was unsuitable, probably owing to concomitant sulfonation. The sequence of reactions described thus furnishes another approach leading to 3-fluoren-

(8) W. R. Biggerstaff, A. P. Menditto, and I. Yokoyama, *J. Org. Chem.*, **19**, 934 (1954).

(9) (a) E. L. Eliel, J. W. McCoy, and C. C. Price, *J. Org. Chem.*, **22**, 1533 (1957); (b) R. B. Carlin and H. P. Landerl, *J. Am. Chem. Soc.*, **75**, 3969 (1953); (c) R. B. Carlin and D. A. Constantine, *J. Am. Chem. Soc.*, **69**, 50 (1947). We are indebted to the reviewers of this paper for drawing our attention to references 9b and 9c.

(10) E. A. Johnson, *J. Chem. Soc.*, 4155 (1957).

(11) E. K. Weisburger and J. H. Weisburger, *J. Org. Chem.*, **18**, 864 (1953).

amine, a compound of some interest in cancer research.[12] In addition, certain 2,3-disubstituted fluorenes can be derived from this amine, since the amino group facilitates further substitution in the same ring.

3-Fluorenecarboxylic acid, on the other hand, could be made the starting point for some 2,6-disubstituted fluorenes, since the carboxyl function hinders substitution in the same ring, and thereby directs the entering group into the unsubstituted ring. In concordance with the expected reactivity of the fluorene molecule, nitration occurred mainly at the 7-position, yielding 3,7-(or 2,6-)disubstituted derivatives. Proof that the substitution had occurred at the 7-position was adduced from the fact that 2-nitrofluorene was obtained from the deamination of 7-nitro-3-fluorenamine, itself derived from 7-nitro-3-fluorenecarboxylic acid. These methods have permitted the synthesis of a number of 2,6-disubstituted fluorenes (I) bearing a variety of functional groups. Heretofore, only 2-nitro-6-bromofluorene[6e] and the corresponding fluorenone,[5b] and 2,6-diaminofluorenone[6f] had been available.

The ultraviolet spectra of 3-substituted fluorenes exhibit a characteristic arrangement of triple peaks, which also persists in 2,6-disubstituted derivatives (Figs. 2 and 3). This can be tentatively

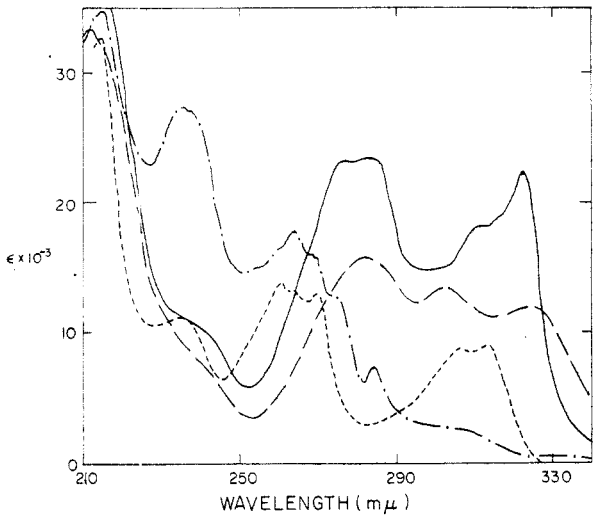


Fig. 2. Ultraviolet absorption spectra of: ——— *N*-(6-hydroxy-2-fluorenyl)acetamide, - - - - 3-fluorenol, — — — 7-amino-3-fluorenol, and — • — 3-fluorenecarboxylic acid

ascribed to the fact that the 3-position of fluorene is somewhat independent of the main resonance interactions in this hydrocarbon which involve the extended biphenyl system, *i.e.* the 2- and 7-positions. Therefore, a substituent (carboxyl, amino, hydroxyl, amido) which can participate in electron exchanges located in the 3-position might give rise to a supplementary disturbance of the

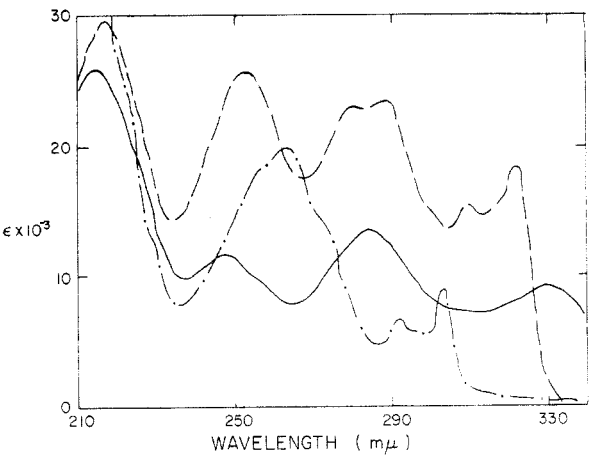
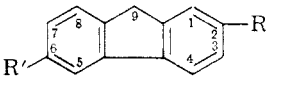


Fig. 3. Ultraviolet absorption spectra of; ——— 2,6-fluorenediamine, — — — *N*,*N*′-2,6-fluorenylenebisacetamide, and — • — *N*-3-fluorenyldiacetamide

electron field which would be reflected in the ultraviolet spectra as an additional maximum.



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R	R′	R	R′
NO_2	COOH	NH_2	$NHCOCH_3$
NO_2	COCl	NH_2	NH_2
NO_2	CON_3	$NHCOCH_3$	$NHCOCH_3$
NO_2	$N(COCH_3)_2$	NO_2	OH
NO_2	NH_2	NH_2	OH
NO_2	$NHCOCH_3$	$NHCOCH_3$	OH

Where the substituent does not provide a sizable electron interchange, as is the case with the diacetamide (Fig. 3), the spectrum does not show a triple peak, and indeed, is quite similar to that of fluorene.[13] Parallel correlations exist in the case of *N*-2-fluorenyldiacetamide, which also has a spectrum not unlike that of fluorene. A general lack of resonance interactions of the functional group in diacetamides is also evidenced by their relatively low melting points and high solubilities in organic solvents.

EXPERIMENTAL

The melting points were determined in a capillary tube and are uncorrected. The ultraviolet spectra were recorded by Mr. P. H. Grantham on a Cary recording spectrophotometer as 0.05-millimolar solutions in ethanol, and the infrared spectra on a Perkin-Elmer spectrophotometer, Model 21, as solids in potassium bromide disks. We are indebted to Dr. W. C. Alford, and Mr. R. Koegel, and their staffs, for the microanalyses.

1-(2,5-Xylyl)cyclohexanol. A Grignard reagent was prepared in 1.5 hr. in a nitrogen atmosphere from 25 g. of magnesium and 185 g. (1 mole) of 2-bromo-1,4-dimethylbenzene

(12) E. K. Weisburger and J. H. Weisburger, *Advances in Cancer Research*, **5**, 331 (1958).

(13) R. A. Friedel and M. Orchin, *Ultraviolet Spectra of Aromatic Compounds*, John Wiley and Sons, New York, 1951, spectrum Number 311.

(Eastman Kodak Organic Chemical No. 4670) in 500 ml. of distilled anhydrous ether. A few crystals of iodine were required to initiate the reaction, which was vigorous. A solution of 98.1 g. of redistilled cyclohexanone in 300 ml. of ether was added, with stirring, to the Grignard reagent at the boiling point over a period of 40 min., and refluxing was continued for 4 hr. longer. After hydrolysis with saturated ammonium chloride solution, the solvent was distilled off. The residue was fractionated at 0.5 mm. pressure using a 30-cm. long Widmer column. The fraction boiling at 85 to 120°, n_D^{25} 1.5370, was a light yellow viscous liquid weighing 110 g. Redistillation of a sample through a 15-cm. Vigreux column gave a constant boiling fraction, b.p. 119–120° (0.5 mm.), n_D^{25} 1.5410, d^{28} 1.0030. Ultraviolet spectrum: λ_{max} 263.5 (ϵ = 381) inflection point, 269 (ϵ = 511), and 277 mμ (ϵ = 492); λ_{min} 243.5 (ϵ = 167), and 274 mμ (ϵ = 381).

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.16; H, 9.91.

1-(2,5-Xylyl)cyclohexene. A. Concentrated hydrochloric acid (0.5 ml.) was added to a boiling solution of 50 g. of the cyclohexanol derivative in 100 ml. of acetic acid. A slightly exothermic reaction was accompanied by some darkening. The mixture was refluxed 15 min. longer, then subjected to vacuum distillation through a 30-cm. Vigreux column. The fraction (40 g.) boiling between 70 and 95° (0.5 mm.) was 1-(2,5-xylyl)cyclohexene, n_D^{28} 1.5355. Refractionation of a sample gave a colorless mobile liquid, b.p. 84° (0.5 mm.), n_D^{28} 1.5362, d^{28} 0.9241. Ultraviolet spectrum: max. 269 (ϵ = 600), and 276 mμ (ϵ = 600); min. 264 (ϵ = 550), and 273.5 mμ (ϵ = 514).

Anal. Calcd. for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.15; H, 9.95.

B. This compound was obtained directly from the Grignard reaction without isolation of the intermediate cyclohexanol as follows: The Grignard reaction mixture was hydrolyzed with dilute hydrochloric acid. After removal of the ether by distillation, the residue was fractionated at 0.5 mm. pressure through a 30-cm. Widmer column. However, the distillation was stopped when the vapor at the top of the column reached 45°. The pot contents from a 1-mole scale reaction were diluted with 150 ml. of acetic acid, the solution heated to the boiling point, and 1 ml. of concentrated hydrochloric acid was added. After the initial vigorous reaction subsided, the mixture was refluxed for 0.5 hr., cooled, and then subjected to fractional vacuum distillation in the same equipment. The fraction (109 g.), with a boiling point of 80–90° (0.5 mm.), n_D^{28} 1.5340, was allowed to stand overnight over solid potassium hydroxide pellets. Refractionation through the 30-cm. Widmer column gave 94 g. (0.5 mole) of a colorless liquid, b.p. 80–86° (0.5 mm.), n_D^{28} 1.5358, identical to the material obtained above.

3-(2,5-Xylyl)cyclohexene. Over a period of 3 hr., a Grignard reagent (17 g. of magnesium, 119 g. of 2-bromo-1,4-dimethylbenzene, 500 ml. of ether) was dropped into a stirred refluxing solution of 102 g. of 3-bromocyclohexene in 140 ml. of ether and refluxing was continued for another 4 hr. After hydrolysis by the slow addition of 550 ml. of 1.6*N* hydrochloric acid, the ether layer was separated and washed. The solution was fractionated at 0.5 mm. pressure. A forerun weighing 42 g., b.p. to 65°, was composed of *p*-xylene and unchanged 3-bromocyclohexene. The main fraction, b.p. 65–120° (0.5 mm.), wt. 60.1 g., was redistilled to give 49.5 g. or 51% (based on the 85% yield of Grignard reagent) of a colorless oily product, b.p. 90–110° (0.5 mm.), n_D^{22} 1.5435, d^{27} 0.930. Ultraviolet spectrum: max. 263 (ϵ = 480), 267.5 (ϵ = 654), and 276.5 mμ (ϵ = 680); min. 253 (ϵ = 313), 264 (ϵ = 476), and 274 mμ (ϵ = 465).

Anal. Calcd. for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.55; H, 9.16.

2-Cyclohexyl-1,4-dimethylbenzene. To a stirred and ice-cooled mixture of 25 ml. of concentrated sulfuric acid and 370 ml. of *p*-xylene, 102 ml. of cyclohexene was added dropwise over a period of 75 min. Stirring was continued for another 75 min. The sulfuric acid was decanted and the organic layer washed rapidly with 25 ml. of cold sulfuric acid, water, 3% sodium hydroxide solution, and water. Upon distillation *p*-xylene (194 g.), b.p. 134–135.5° was recovered. Further distillation at 1 mm. pressure gave 84 g. of a colorless liquid, b.p. 80–120° and a solid residue in the still. Redistillation of the liquid gave 25 g. of a forerun, b.p. 77–98° (1 mm.), n_D^{22} 1.5253, and 55 g. of pure 2-cyclohexyl-1,4-dimethylbenzene, b.p. 98–100° (1 mm.), n_D^{22} 1.5262, d^{27} 0.926. Ultraviolet spectrum: max. 262 (ϵ = 385,) 268 (ϵ = 564), 270 (ϵ = 511), and 276 mμ (ϵ = 632); min. 237 (ϵ = 34), 263.5 (ϵ = 380), 270 (ϵ = 506), and 274 mμ (ϵ = 367). Bodroux[14] reported the following physical constants for this compound: b.p. 261–263° (759 mm.), n_D^{18} 1.529, d^{18} 0.936.

This compound could not be aromatized with sulfur under the condition where the cyclohexene derivatives were smoothly converted to biphenyls.

Anal. Calcd. for $C_{14}H_{22}$: C, 89.29; H, 10.71. Found: C, 89.70; H, 10.98.

The still residue was dissolved in 220 ml. of hot acetic acid. On cooling 20 g. of material, m.p. 145–150°, crystallized. Two recrystallizations from 150 ml. of acetic acid gave 13.5 g. of 1,4-dicyclohexyl-2,5-dimethylbenzene, m.p. 157° (lit.[14] m.p. 156–157°).

Anal. Calcd. for $C_{20}H_{30}$: C, 88.82; H, 11.18. Found: C, 88.62; H, 10.92.

2,5-Dimethylbiphenyl. A. By dehydrogenation of 3-(2,5-xylyl)cyclohexene with sulfur. A mixture of 14.5 g. (78 mM.) of 3-(2,5-xylyl)cyclohexene and 5.9 g. of sulfur was heated in a slow stream of nitrogen. The gas was scrubbed in traps containing an acidified solution of copper sulfate. Evolution of hydrogen sulfide commenced when the reaction mixture reached a temperature of 180° and was rapid at 210°. The temperature rose spontaneously to 245° and was then maintained near the boiling point of 270° for 20 min. longer. A quantitative yield of copper sulfide (14.7 g.) was obtained in the traps. Upon vacuum distillation of the pot contents, 8.3 g. (45 mM.) of 2,5-dimethylbiphenyl distilled at 106–115° (2 mm.) as a colorless liquid, n_D^{22} 1.5785. Upon refractionation a sample had a b.p. 107–109° (2 mm.), n_D^{22} 1.5800, and d^{27} 0.9814. The ultraviolet spectrum had a maximum at 238 mμ (ϵ = 9,180), an inflection point at 275 mμ (ϵ = 1,080), and a minimum at 231 mμ (ϵ = 8,400).

Anal. Calcd. for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 92.03; H, 7.89.

B. By dehydrogenation of 1-(2,5-xylyl)cyclohexene with sulfur. A mixture of 94 g. (0.5 mole) of 1-(2,5-xylyl)cyclohexene and 35 g. of sulfur was slowly heated and maintained at the boiling point for 0.5 hr. The cooled mixture was distilled *in vacuo* through a Claisen head giving 72 g. of a colorless liquid, b.p. 80–110° (0.5 mm.), n_D^{28} 1.5795. Redistillation through a 30-cm. Vigreux column yielded 50 g. (0.27 mole) of 2,5-dimethylbiphenyl, b.p. 88° (0.5 mm.), n_D^{28} 1.5758.

C. By dehydrogenation of 1-(2,5-xylyl)cyclohexene with chloranil. A solution of 63 g. of chloranil and 19.2 g. (103 mM.) of 1-(2,5-xylyl)cyclohexene in 200 ml. of xylene was refluxed for 5.5 hr. The precipitate obtained on cooling to 4° was filtered off and washed twice with xylene. The combined filtrate and washings were diluted with 250 ml. of ether and extracted repeatedly with 5% potassium hydroxide solution and water. The dried ether solution was distilled and the residue was fractionated to give 10.2 g. of a slightly yellowish liquid, b.p. 88–90° (0.5 mm.), n_D^{28} 1.5718. This material, diluted with 50 ml. of petroleum ether, was percolated through a 2 × 15 cm. column of alumina. The column was washed with petroleum ether and 250 ml. of eluate was collected. Upon distillation 8.2 g. (45%)

(14) D. Bodroux, *Ann. chim. (Paris)*, [10], 11, 511 (1929).

of colorless 2,5-dimethylbiphenyl, b.p. 78–80° (0.4 mm.), n_D^{28} 1.5725 was obtained.

2,5-Biphenyldicarboxylic acid. A. Without solvent. The procedure was patterned after that described for *o*-chlorobenzoic acid.[15] A well stirred suspension of 45.1 g. of 2,5-dimethylbiphenyl in a solution of 158 g. of potassium permanganate in 4 l. of water was kept under gentle reflux for 10 hr. at which time the permanganate was exhausted. The mixture was allowed to cool to 70°, then was extracted 3 times with 100 ml. of benzene which removed 16 g. of unoxidized material (35%). Steam distillation was impractical owing to the slow rate of distillation of 2,5-dimethylbiphenyl. The aqueous phase was filtered by suction, and the precipitate of manganese dioxide was washed 3 times with a total of 1 l. of hot water. Acidification of the filtrate and cooling to 4° gave 29 g. of white 2,5-biphenyldicarboxylic acid (74% yield based on the amount of material oxidized), m.p. 278°. Recrystallization of 134 mg. by solution in 3.5 ml. of ethanol and addition of 15 ml. of hot water gave 96 mg. of white crystals, m.p. 280°. Ultraviolet spectrum: max. 230 (ϵ = 24,000), and 295 mμ (ϵ = 2,400); min. 217 (ϵ = 19,500), and 280 mμ (ϵ = 2,100).

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16. Found: C, 69.78; H, 4.30.

B. With solvent. To a stirred and boiling solution of 56 g. of 2,5-dimethylbiphenyl in 610 ml. of pyridine a hot solution of 325 g. of potassium permanganate in 3.2 l. of water was added over a period of 105 min. The permanganate solution was kept hot in order to prevent crystallization of the material. After 75 min. of gentle refluxing 1 l. of hot water was added and the mixture was filtered by suction. The precipitate was reextracted twice with a total of 2 l. of boiling 0.3% potassium hydroxide solution. The combined colorless filtrates were reduced in volume to about 2 l. Acidification and cooling afforded 57 g. (75%) of powdery white material, m.p. 267–269°.

3-Fluorenecarboxylic acid. A mechanically stirred suspension of 20.4 g. of 2,5-biphenyldicarboxylic acid in 630 g. of polyphosphoric acid was heated to 200° over a period of 0.5 hr. Upon cooling to 100° ice was added to a volume of 2 l. The filtered yellow precipitate was dissolved in a warm solution of 7 g. of sodium hydroxide in 1.8 l. of water and treated with 1 g. of Norit for 1 hr. Acidification of the filtered solution gave 17.3 g. (97%) of 9-oxo-3-fluorenecarboxylic acid, m.p. 299° (lit.[5b] 304°).

A solution of 14 g. of this compound, 5 g. of sodium hydroxide, and 19 ml. of 85% hydrazine hydrate in 120 ml. of diethylene glycol was refluxed for 1.5 hr. A considerable evolution of gas occurred between 120 and 140° (the liquid temperature at the boiling point was 150°). The reaction mixture was diluted with 1 l. of water and neutralized with 75 ml. of 6*N* hydrochloric acid. The precipitate and 1.2 g. of Norit in 800 ml. of 1.4% sodium bicarbonate solution was refluxed 0.5 hr. The filtered solution was neutralized with 100 ml. of 3*N* hydrochloric acid to give a white powder (11.5 g., 88%), m.p. 224°. Recrystallization of 450 mg. from 4.5 ml. of acetic acid yielded 340 mg. of 3-fluorenecarboxylic acid m.p. 227–228° (lit.[5b] 230°).

3-Fluorenamine. The acid chloride, m.p. 121–122°, was prepared from 2 g. of 3-fluorenecarboxylic acid by refluxing with thionyl chloride. A solution of 0.75 g. of sodium azide in 5 ml. of water was added to an ice-cold solution of the acid chloride in 75 ml. of acetone and stirred for 3 hr. Dilution with water gave 2.16 g. of 3-fluorenecarbonyl azide, m.p. 94° (dec.). The azide was refluxed in 25 ml. of acetic anhydride, yielding 2.3 g. of *N-3-fluorenyldiacetamide*, m.p. 143–144°, after crystallization from benzene–petroleum ether. Ultraviolet spectrum: max. 262 (ϵ = 19,800), 292 (ϵ = 6,400), and 303 mμ (ϵ = 8,800); min. 236 (ϵ = 7,800), 287 (ϵ = 4,800), and 297 mμ (ϵ = 5,400).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.95; H, 5.70. Found: C, 76.79; H, 5.69.

Hydrolysis of the diacetamide in 1:1 ethanol-6*N* hydrochloric acid afforded 3-fluorenamine, m.p. 149–151° (lit.[5d] 152–153°). The over-all yield of amine from the acid was 90%. Acetylation of the amine in benzene yielded *N*-3-fluorenylacetamide, m.p. 189–190° (lit.[5d] 189–190°). Conversion of the amine to 3-fluorenol by standard procedures gave a product, m.p. 138° (lit.[6g,7] m.p. 137–138°).

2-Nitro-3-fluorenamine. *N*-3-Fluorenylacetamide (1 g.) in 20 ml. of acetic acid was nitrated by the addition of 2.2 ml. of concentrated nitric acid (d = 1.42) and heating to 65°. On cooling 1 g. of bright lemon yellow needles, m.p. 210°, crystallized. Recrystallization from ethanol gave *N-(2-nitro-3-fluorenyl)acetamide*, m.p. 210–210.5°. Ultraviolet spectrum: max. 218 (ϵ = 21,200), 238 (ϵ = 15,300), 266 (ϵ = 11,800), and 338 mμ (ϵ = 12,000); min. 232 (ϵ = 14,800), 255 (ϵ = 10,600), and 284 mμ (ϵ = 5,300).

Anal. Calcd. for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51. Found: C, 67.41; H, 4.65.

Hydrolysis in ethanol–hydrochloric acid yielded *2-nitro-3-fluorenamine*, light orange needles, m.p. 195°. Ultraviolet spectrum: max. 227 (ϵ = 16,600), 243 (ϵ = 14,500) (inflection point), 330 (ϵ = 14,600), and 425 mμ (ϵ = 7,400); min. 223 (ϵ = 16,500), 285 (ϵ = 4,100), and 378 mμ (ϵ = 4,200).

Anal. Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.01; H, 4.46. Found: C, 68.91; H, 4.43.

Low pressure catalytic reduction of 2-nitro-3-fluorenamine in ethanol over platinum oxide gave 2,3-fluorenediamine, m.p. 192°, identical in melting point and infrared spectrum with an authentic sample prepared by the reduction of 3-nitro-2-fluorenamine.[6a]

7-Nitro-3-fluorenecarboxylic acid. A solution of 75 ml. of yellow fuming nitric acid (d = 1.50) and 18 g. of 3-fluorenecarboxylic acid in 360 ml. of acetic acid was warmed to 85° whereupon the reaction occurred. Upon cooling 15.5 g. of yellow fluffy needles, m.p. 285°, crystallized. Recrystallization from acetic acid (60 ml./g.) and from ethanol gave pale yellow needles, m.p. 305°. Ultraviolet spectrum: max. 245 (ϵ = 11,400), and 324 mμ (ϵ = 14,500); min. 268 mμ (ϵ = 3,100).

Anal. Calcd. for $C_{14}H_9NO_4$: C, 65.88; H, 3.55; N, 5.49. Found: C, 65.57; H, 3.99; N, 5.38.

7-Nitro-3-fluorenamine. Fourteen grams of 7-nitro-3-fluorenecarboxylic acid was converted to the acid chloride, m.p. 163–167°, with thionyl chloride. Reaction of the acid chloride in 950 ml. of acetone with 5 g. of sodium azide in 25 ml. of water yielded 15 g. of the azide, m.p. 143–145°. The azide was refluxed for 3 hr. in 250 ml. of acetic anhydride to give 15 g. of *N-(7-nitro-3-fluorenyl)diacetamide*, m.p. 198–198.5° after crystallization from benzene-ethanol. Ultraviolet spectrum: max. 324 mμ (ϵ = 21,200); min. 263 mμ (ϵ = 3,400).

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: C, 65.79; H, 4.55; N, 9.03. Found: C, 65.66; H, 4.86; N, 9.06.

Hydrolysis of 14 g. of the diacetamide by refluxing for 4 hours in 1:1 ethanol and 6*N* hydrochloric acid gave 11 g. of reddish-orange 7-nitro-3-fluorenamine,[16] m.p. 192–195°. Repeated recrystallizations from benzene, or percolation of a benzene solution through a column of alumina followed by crystallization, raised the melting point to 210°. Ultraviolet spectrum: max. 327 (ϵ = 10,200), and 290 mμ (ϵ = 6,200) (inflection point); min. 260 mμ (ϵ = 4,600). After reaching the peak at 327 mμ the spectrum exhibits a long shallow curve (minor inflection point about 358 mμ) and shows appreciable absorption even beyond 400 mμ.

Anal. Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.01; H, 4.46; N, 12.39. Found: C, 69.07; H, 4.77; N, 11.98.

(15) H. T. Clarke and E. R. Taylor, *Org. Syntheses*, **Coll. Vol. II**, 135 (1943).

(16) Removal of the amino group (diazotization followed by hypophosphorous acid) yielded 2-nitrofluorene, m.p. 150°, with an infrared spectrum identical to that of authentic 2-nitrofluorene.

The acetyl derivative, N-(7-nitro-3-fluorenyl)acetamide, prepared by the action of acetic anhydride in benzene, melted at 260–260.5° after recrystallization from 60% aqueous acetic acid. Ultraviolet spectrum: max. 230 (ϵ = 22,000), 260–265 (ϵ = 11,200) (inflection point), and 340 mμ (ϵ = 13,600); min. 219 (ϵ = 18,000), and 281 mμ (ϵ = 4,600).

Anal. Calcd. for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51. Found: C, 66.74; H, 4.69.

N-(7-Amino-3-fluorenyl)acetamide. Low pressure (40–50 p.s.i.) hydrogenation in ethanol over platinum oxide of 0.2 g. of the nitro derivative gave 0.12 g. of white crystals, m.p. 212.5–213.5°, after crystallization from 50% ethanol and from benzene. Ultraviolet spectrum: max. 219 (ϵ = 27,800), 251 (ϵ = 24,200), 290 (ϵ = 19,900), and 323 mμ (ϵ = 10,900) (inflection point); min. 236 (ϵ = 16,300), and 269 mμ (ϵ = 12,500).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92. Found: C, 75.42; H, 6.02.

2,6-Fluorenediamine. Catalytic reduction (ethanol, platinum oxide) of 0.35 g. of 7-nitro-3-fluorenamine afforded 0.17 g. of an almost white product, m.p. 153–154.5°, after 2 crystallizations from 50% ethanol and one from benzene. Ultraviolet spectrum: max. 214 (ϵ = 25,800), 247 (ϵ = 11,800), 284 (ϵ = 13,500), and 300 mμ (ϵ = 9,400); min. 237 (ϵ = 9,800), 264 (ϵ = 7,800), and 316 mμ (ϵ = 7,200).

Anal. Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.17. Found: C, 79.36; H, 6.40.

The *diacetyl derivative, N,N'-2,6-fluorenylenebisacetamide,* prepared with acetic anhydride in benzene, melted at 277–278°, after crystallization from ethanol. Ultraviolet spectrum: max. 217 (ϵ = 29,600), 253 (ϵ = 25,600), 280 (ϵ = 23,000), 289 (ϵ = 23,400), 309.5 (ϵ = 15,500), and 322 mμ (ϵ = 18,400); min. 234 (ϵ = 14,400), 267 (ϵ = 17,600), 283 (ϵ = 22,800), 304.5 (ϵ = 13,600), and 313 mμ (ϵ = 14,600).

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: N, 10.00. Found: N, 9.62.

7-Nitro-3-fluorenol. The outcome of the reaction described below is materially affected by the experimental conditions. The best procedure was found to be as follows: 7-Nitro-3-fluorenamine (1 g.) was dissolved by warming in a mixture of 25 ml. of acetic acid and 10 ml. of water. A thick mush formed upon cooling in an ice bath and adding 25 ml. of concentrated sulfuric acid. A solution of 0.4 g. of sodium nitrite in 10 ml. of water was stirred in, causing most of the precipitate to dissolve. After another 1.25 hr., the diazonium solution was dropped over a period of 15 min. into a refluxing solution of 100 ml. of water, 10 ml. of sulfuric acid, and 20 ml. of acetic acid. The mixture was poured on ice after an additional 15 min. The crude yellow material, 0.95 g., m.p. 247°, was twice recrystallized from 65% ethanol (Norit) to give 0.59 g. of fine yellow needles, m.p. 257°. Ultraviolet spectrum: max. 271 (ϵ = 8,500), and 349 mμ (ϵ = 18,600); min. 251 (ϵ = 6,500), and 281 mμ (ϵ = 5,600).

Anal. Calcd. for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.17. Found: C, 68.45; H, 4.12; N, 6.39.

7-Amino-3-fluorenol. Catalytic reduction (platinum oxide) of 0.48 g. of 7-nitro-3-fluorenol in ethanol gave 0.41 g. of amine, m.p. 248° (dec.). Recrystallization of 65 mg. of product from 30 ml. of 50% aqueous ethanol yielded 60 mg. of small white needles, m.p. 255° (dec.). Ultraviolet spectrum: max. 212 (ϵ = 32,700), 243 (ϵ = 7,100) (inflection point), 281 (ϵ = 15,700), 302 (ϵ = 13,200), and 324 mμ (ϵ = 11,800); min. 253 (ϵ = 3,600), 295 (ϵ = 12,200), and 316 mμ (ϵ = 11,000).

Anal. Calcd. for $C_{13}H_{11}NO$: C, 79.16; H, 5.62. Found: C, 78.69; H, 5.60.

N-(6-Hydroxy-2-fluorenyl)acetamide. A hot solution of 0.4 g. of 7-amino-3-fluorenol in 50 ml. of 0.1*N* hydrochloric acid was filtered and cooled. After the addition of 3 g. of sodium acetate and 4 ml. of acetic anhydride the mixture was stirred in an ice bath for 5 hr. The white precipitate, 0.46 g., m.p. 238°, was recrystallized twice from 30% aqueous ethanol giving 0.34 g. of fine needles, m.p. 241°. Further crystallization from aqueous ethanol and xylene raised the melting point to 246°. Ultraviolet spectrum: max. 240 (ϵ = 10,500) (inflection point), 277 (ϵ = 23,100), 284 (ϵ = 23,400), 310 (ϵ = 18,000) (inflection point); and 322 mμ (ϵ = 22,200); min. 252 (ϵ = 5,600), 279 (ϵ = 22,900), and 295 mμ (ϵ = 14,800).

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.29; H, 5.48. Found: C, 75.31; H, 5.55.

BETHESDA 14, MD.

[CONTRIBUTION FROM THE FOREST PRODUCTS LABORATORY, UNIVERSITY OF CALIFORNIA]

Extractive Components from Incense Cedar Heartwood (*Libocedrus decurrens* Torrey). VI. On the Occurrence of 3-Libocedroxythymoquinone

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A new quinoid pigment has been isolated from the heartwood of incense cedar and its structure deduced on the basis of the presented spectroscopic, degradative, and synthetic experimental evidence. It has been demonstrated that the isolated quinone occurs *in situ* as well as forming through air oxidation of the other incense cedar extractives.

During our investigation of the extractive components of incense cedar heartwood, *Libocedrus decurrens* Torrey,[1] the petroleum ether extract of the sawdust was found to have a reddish color. This could not be caused by the formation of the quinquidrone type compounds between the various phenols present and thymoquinone[2] since it persisted upon removal of the latter either by distillation or by conversion to its semicarbazone followed by extraction with alkali. This indicated the presence of an unknown coloring matter which prompted us to investigate this component.

On extracting incense cedar heartwood sawdust with petroleum ether, a 1.5% yield (dry wood basis) of a mixture of various components was obtained. Chromatography on alumina yielded a red fraction

(1) E. Zavarin and A. B. Anderson, *J. Org. Chem.*, **20**, 788 (1955).

(2) E. Zavarin and A. B. Anderson, *J. Org. Chem.*, **20**, 82 (1955).