[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

Fluoradene

BY HENRY RAPOPORT AND GERALD SMOLINSKY[1]

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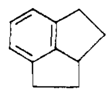
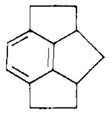
In contrast to 9-*o*-aminophenyl-9-fluorenol, which on deamination gave the rearranged product tribenzotropone,[4] 9-*o*-aminophenylfluorene underwent deamination normally, giving the expected indeno[1,2,3-jk]fluorene, fluoradene. Fluoradene is another example of the strained cyclopentindene ring system and exhibits the properties characteristic of a strained and warped benzene ring, *viz.*, ease of catalytic hydrogenation and oxidation by perbenzoic acid. In addition, fluoradene is the most acidic hydrocarbon known, having a pK_a' of 11 ± 0.5. By the action of oxygen on an alkaline solution of fluoradene, the dimeric substance 12,12′-bifluoradenyl is formed.

Introduction.—The effect of strain on the planarity of a benzene ring, and the consequent effect on resonance stabilization has been the object of considerable study. We have approached this question through an examination of the cyclopentindenes, two of which, I[2] and II,[3] already have been reported. In addition, attention has been directed toward the cyclopentindenes with further fused benzene rings, III and IV, since these compounds were anticipated to exhibit an appreciable increase in strain over that found in I.


I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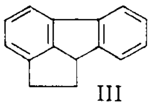
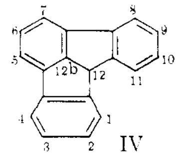
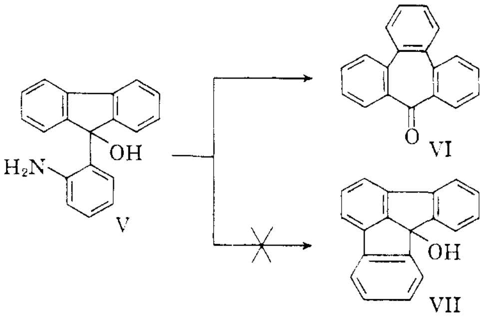

III

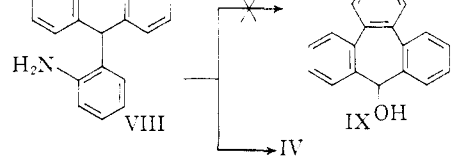


IV

In particular, our interest was focused on IV by the recently reported[4] isolation of tribenzotropone (VI) from the deamination of 9-*o*-aminophenyl-9-fluorenol (V). None of the hydroxyindenofluorene VII was found. It did not appear likely that failure to form VII was due to prohibitive strain in this indenofluorene ring system, since the cyclopentindene I has shown only a very slight degree of strain. The additional fused benzene rings definitely should increase this strain, but not to the point of excluding the existence of such a ring system. Rather, the rearrangement observed could have been promoted by the hydroxyl group on C_9 and the stabilization it might afford for the developing positive charge at this carbon.[5]



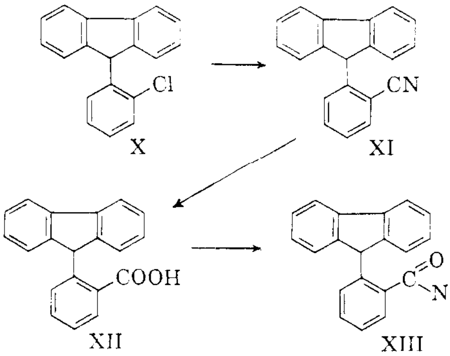
If this hypothesis is correct, deamination in the absence of this hydroxyl group, *i.e.*, deamination of 9-*o*-aminophenylfluorene (VIII), should lead not to the rearranged product tribenzotropyl alcohol (IX), but to the indenofluorene fluoradene (IV).



To test this hypothesis and to ascertain the effect of the two additional fused benzene rings on the properties of the cyclopentindene ring system (I), the synthesis of IV was undertaken.[6]

Synthesis of Fluoradene (Indeno [1,2,3-jk]-fluorene)(IV).—The necessary intermediate VIII was potentially available from the fluorenol V by hydrogenolysis of the hydroxyl group. However, the difficulties and poor yield encountered in the reported[4] preparation of V dissuaded us from attempting to repeat this synthesis. Instead, the synthesis of 9-*o*-carboxyphenylfluorene (XII) was undertaken, since the amine VIII then might be prepared from the acid in any of several ways.

A satisfactory synthesis of 9-*o*-carboxyphenylfluorene has been reported[7] by the sequence below, using cuprous cyanide and pyridine in a sealed tube at 250° to convert the chloride X to the nitrile XI. By substituting quinoline for pyridine, this



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[1] National Science Foundation Predoctoral Fellow, 1956–1958.

[2] H. Rapoport and J. Z. Pasky, THIS JOURNAL, **78**, 3788 (1956).

[3] H. Rapoport and G. Smolinsky, *ibid.*, **82**, March 5 (1960).

[4] M. Stiles and A. J. Libby, *J. Org. Chem.*, **22**, 1243 (1957).

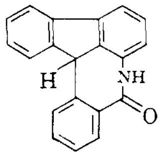
[5] A somewhat similar rearrangement has been observed by D. H. Hey and T. M. Moyneham, *J. Chem. Soc.*, 1563 (1959). They found biphenyl-2-carboxyanilides as one of the products of the catalytic decomposition of diazotized N-*o*-aminobenzoyldiphenylamines.

[6] A preliminary account of this work has been reported; H. Rapoport and G. Smolinsky, THIS JOURNAL, **80**, 2910 (1958).

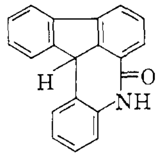
[7] N. Campbell and A. Marks, *J. Chem. Soc.*, 2941 (1951).

step could be performed at reflux at atmospheric pressure on a large scale, and alkaline hydrolysis of the nitrile led to the acid XII in quantity and in good yield.

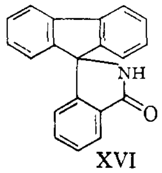
The azide XIII then was prepared from the acid chloride of XII and was decomposed by warming with absolute ethanol. Boiling this solution with potassium hydroxide resulted in the formation of two nitrogen-containing compounds, one of which proved to be the desired amine VIII (21% yield), while the other was identified as a lactam (33% yield). The molecular formula of the lactam was established as $C_{20}H_{13}NO$, and its ultraviolet spectrum indicated that the 9-phenylfluorene nucleus of the original acid was still present. On this basis, one can write four possible lactam structures



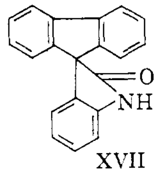
XIV



XV



XVI

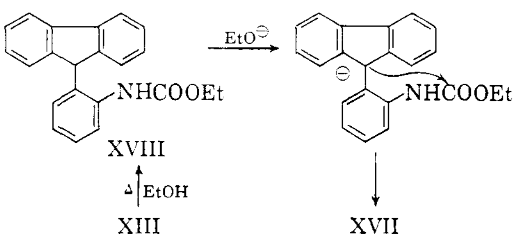


XVII

Advantage first was taken of the fact that structures XIV and XV both have an acidic, benzylic hydrogen atom while structures XVI and XVII do not. By subjecting the lactam to conditions which would allow such a benzylic hydrogen to be replaced by deuterium, it should be possible to determine whether the lactam belonged to the five- or seven-membered ring group. It was necessary to establish conditions under which this exchange could occur, and for this purpose 9-*o*-chlorophenylfluorene (X) was used as a model. Hydrogen–deuterium exchange was readily effected when a solution of X in deuterium ethoxide containing a trace of dissolved sodium was boiled for several hours. The deuterium was removed from X just as easily with sodium ethoxide in ethanol, but could not be removed with boiling ethanol alone. The introduction of deuterium had a profound effect on the infrared spectrum of X in the 7 to 12 μ region, and thus the infrared spectrum afforded a means for detecting the presence of deuterium.

When the lactam was subjected to the conditions capable of producing exchange, only the hydrogen on the nitrogen was replaced. Recrystallization of this N-deuterated lactam from alcohol removed the deuterium. Clearly this result showed that the lactam belonged to the five-membered ring series and had structure XVI or XVII. Hydrolysis of the lactam in boiling alkaline ethylene glycol was accompanied by decarboxylation and gave as the sole product (93% yield) 9-*o*-aminophenylfluorene (VIII). This behavior, typical of 9-fluorenecarboxylic acids,[8] constitutes definitive evidence that the lactam has structure XVII.

The question as to how spiro[oxindole-3,9-fluorene] (XVII) was formed was answered by a stepwise conversion of the azide XIII to the amine VIII. Rearrangement of the azide in ethanol produced the carbamate XVIII in 93% yield. Boiling this carbamate with aqueous alcoholic potassium hydroxide gave a mixture of compounds which was separated into the amine VIII (29%) and the lactam XVII (27%); however, boiling the carbamate with sodium ethoxide in abs. ethanol led in 96% conversion to the lactam XVII. Undoubtedly the formation of lactam XVII results *via* a displacement of ethoxide by the fluorenyl anion. The acidity of this benzylic hydrogen and the proximity of the carbonyl group provide an ideal situation for consummating this interesting cyclization.



Attempted deamination of 9-*o*-aminophenylfluorene (VIII), using the previous procedure,[4] was found to be unsatisfactory due to the fact that the amine and its diazonium salt both were insoluble in the 3 *N* sulfuric acid. This resulted in incomplete diazotization and complicated the product isolation. Complete diazotization was accomplished using glacial acetic acid as the reaction medium in which both the amine and its diazotized product are highly soluble. Addition of 3 *N* sulfuric acid precipitated the diazonium salt, and this mixture was warmed on the steam-bath, resulting in vigorous evolution of nitrogen and formation of a dark amorphous material which was extracted with benzene. Initial attempts at removing the by-product 9-*o*-hydroxyphenylfluorene (XIX) with aqueous alkali proved futile, and it also was recognized that one component of the product mixture (later shown to be fluoradene) suffered an irreversible change in alkali. Cognizance of this alkaline sensitivity resulted in modifying the isolation procedure so the *p*H was maintained at all times below 7 and acid-washed alumina was used. Thus it was possible to isolate fluoradene (IV) in 23% yield along with a 69% yield of 9-*o*-hydroxyphenylfluorene (XIX). A small quantity of a rather insoluble, high melting hydrocarbon of molecular formula $C_{38}H_{22}$ was also obtained in approximately 5% yield—this hydrocarbon is bifluoradenyl and will be discussed in detail below.

No evidence of the presence of the tropyl alcohol IX was found even though the deamination was carried out six times under various conditions. It appears, as originally suspected, that the rearrangement of 9-*o*-aminophenyl-9-fluorenol (V) to tribenzotropone (VI) during deamination is dependent upon the presence of the C_9-hydroxyl group.

Properties of Fluoradene.—Proof of the structure of fluoradene as well as an insight into some of its unusual properties was provided by an examination

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(8) W. Wislicenus and A. Ruthing, *Ber.*, **46**, 2770 (1913).

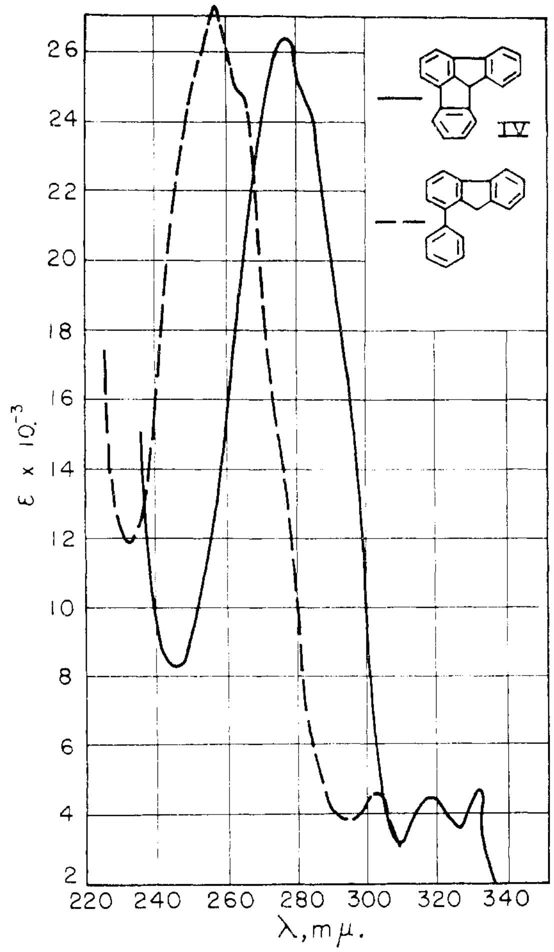


Fig. 1.—Ultraviolet absorption spectra in cyclohexane of fluoradene (IV) ———, and 1-phenylfluorene – – – –.

of its ultraviolet spectrum, catalytic hydrogenation, reaction with perbenzoic acid and acidity.

Table I reveals that 9-phenylfluorene has an ultraviolet spectrum similar to the spectra of simple alkyl substituted fluorenes such as 1-methyl- and 9-methylfluorene. On the other hand, 1-phenylfluorene (Fig. 1) has a spectrum quite different from that of the fluorene derivatives listed, as would be expected from the additional conjugation. The ultraviolet spectrum of fluoradene (Fig. 1) has some elements of similarity with both 1- and 9-phenylfluorene; however there are sufficient differences in peak ratios and positions of maxima to indicate the presence of a modified absorbing system. Undoubtedly the bathochromic shifts are due to strain[3] in the fluoradene molecule.

TABLE I

ULTRAVIOLET ABSORPTION MAXIMA OF SOME FLUORENE DERIVATIVES[a]

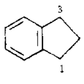
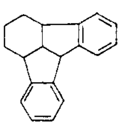
Compound	λ, mμ	ε	λ, mμ	ε	λ, mμ	ε
Fluoradene (IV)	276	26,600	317	4500	331	4,630
1-Phenylfluorene	256	27,400	302	4570		
9-Phenylfluorene	265	20,300	293	6320	304	10,300
1-Methylfluorene	266	20,950	289	6040	301	8,760
9-Methylfluorene	264[b]	17,130	290	4090	301	7,900

[a] All spectra taken in hexane or cyclohexane. [b] Center of doublet.

Fluoradene was found to hydrogenate rapidly in ethanolic solutions at room temperature and atmospheric pressure with 5% palladized charcoal as catalyst. Hydrogen absorption ceased at 300 mole %, and the resulting hexahydrofluoradene (XX) exhibited an ultraviolet spectrum consistent with that of other dialkyl substituted indanes (Table II). This facile hydrogenation of the benzene ring of the cyclopentindene ring system in fluoradene and the nature of the hydrogenation product constitute direct evidence for the structural assignment for fluoradene as indeno[1,2,3-jk]fluorene (IV). There is no reason why either of the other benzene rings should be hydrogenated and, had they been, the product would have been a fluorene rather than the indane actually found. This hydrogenation is consistent with that observed in the other two cyclopentindenes,[2,3] and again indicates strain in this benzene ring.

TABLE II

ULTRAVIOLET ABSORPTION MAXIMA OF SOME SUBSTITUTED INDANES[a]

Compound	Structure	λ, mμ	ε	λ, mμ	ε	λ, mμ	ε
Indane[b]		260	860	268	1300	273	2400
1,2-dimethyl-indane[b]		258	790	265	1230	273	1440
1,3-Dimethyl-indane[b]		258	790	265	1230	273	1440
4b,5,6,7,7a,12b-Hexahydro-fluoradene (XX)		263	1880	269	3080	275	3320

[a] Spectra taken in isoöctane or hexane solution. [b] J. Entel, C. H. Ruof and H. C. Howard, *Anal. Chem.*, **25**, 1303 (1953).

Further evidence of the strained nature of the cyclopentindene benzene ring in fluoradene was obtained from perbenzoic acid oxidation experiments. At room temperature in chloroform solution fluoradene consumed 400 mole % of perbenzoic acid to give an epoxyhydroxybenzoate while 9-phenylfluorene, subjected to identical conditions, consumed only 50 mole %, indicating oxidation only at the 9-position. Of the other two cyclopentindenes, compound II also reacts rapidly with perbenzoic acid (300 mole % consumption) under these conditions[3] while I is essentially unreactive.[2] From this we conclude that the strained benzene ring of fluoradene possesses considerable olefinic character, much more than I, but less than II, since fluoradene is stable toward air oxidation while II reacts rapidly.[3]

Evidence of the unusual acidity of fluoradene was first observed during its isolation from the deamination reaction, as exhibited by its extreme alkali sensitivity and irreversible ultraviolet spectral shift in alkaline media. Acid and neutral solutions are colorless, while alkaline solutions have a color similar to that of alkaline phenolphthalein solutions. In addition, fluoradene readily undergoes deuterium exchange by merely boiling in deuterium ethoxide. This ease of exchange should be contrasted with the conditions necessary to effect exchange with 9-*o*-chlorophenylfluorene, which requires a strong alkaline catalyst.

Obtaining an estimate of the pK_a of fluoradene presented several difficulties. Of the various methods available for determining the pK_a of an acid, one had to be used which did not necessitate exposing the hydrocarbon to strong base in the presence of oxygen for more than a few seconds due to the facile oxidation of this molecule at high pH. The low solubility of fluoradene in alcohols was another limitation.

A spectrophotometric procedure in abs. ethanol with ethoxide ion as the base[9,10] appeared very attractive. However, even when oxygen- and carbon dioxide-free solutions were used and the operation was conducted in an argon atmosphere, the initially pink alkaline solutions of fluoradene faded in a few seconds, indicating destruction of the fluoradenyl anion. Values for the pK_a obtained from such determinations were quite erratic. It appears that the inability to exclude all traces of oxygen and the extremely rapid oxidation of fluoradene in alkaline media rendered this spectrophotometric procedure inapplicable.

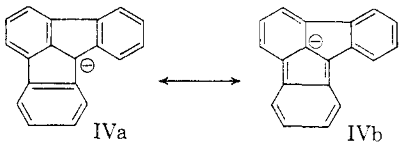
Finally, consistent results were obtained by determining the distribution coefficient for fluoradene in a suitable solvent system as a function of the pH. From the relationship[11] where P is the true

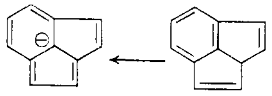
$$pK_a' = pH - \log \frac{P - P'}{P'}$$

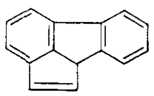
distribution coefficient and P' is the apparent distribution coefficient, both of which could be determined, the pK_a' may be calculated. The solvent system used was hexane *vs.* 97% aqueous methanol in which P is 1.62. Various buffers were added to the aqueous methanol, the pH was determined, and fluoradene was added and distributed between the aqueous methanol and hexane. From the optical density at 330 mμ, the amount of fluoradene remaining in the hexane could be calculated, and from this P' was obtained. In this way, four determinations of the pK_a' were made, and the value 13.6 ± 0.2 was found.

In order to relate the pK_a' determined in this solvent (97% aqueous methanol) to the pK_a' in a more aqueous solvent, a similar determination was made for 9-*o*-hydroxyphenylfluorene (XIX), since this was considered a reasonable model compound. By distribution between hexane and 97% methanol at various pH's, the pK_a' in this solvent was found to be 12.1. Spectrophotometrically,[10] in 20% aqueous methanol, 9-*o*-hydroxyphenylfluorene was found to have a pK_a' of 9.7. Applying this correction, 2.4 pK units, to fluoradene, an extrapolated value of 11 ± 0.5 is obtained for the pK_a' of fluoradene in 20% aqueous methanol.[12]

The remarkable acidity of fluoradene is comparable to that of a phenol and far greater than that of the most acidic hydrocarbons heretofore known—9-phenylfluorene, phenylacetylene and indene—for which pK_a''s of 21 or greater have been reported.[13,14] This acidity must reside in the very high resonance stabilization of the anion (IVa, IVb) as compared to the parent hydrocarbon, and the anion actually constitutes a new aromatic system. It is interesting that molecular orbital calculations for the recently discovered cyclazines[15] were based on the isoelectronic cyclopentindene anion XXIa, and a high order of stability was predicted. This has been confirmed in the high acidity of fluoradene,[16] which is the dibenzo analog of XXI. Acidity should increase as benzo groups are removed in the order XXI > XXII > IV, since the added resonance contribution of the fused rings decreases the difference in resonance energy between the hydrocarbon and its anion. The synthesis of XXI and XXII is under investigation to test this prediction.

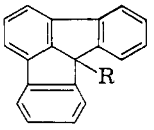

IVa IVb


XXIa XXI


XXII

Derivatives of Fluoradene; Bifluoradenyl.—With the objective of learning more of the chemistry of fluoradene and of better characterizing bifluoradenyl, the $C_{38}H_{22}$ hydrocarbon isolated as a minor product from the deamination reaction, a number of fluoradene derivatives were examined.

Fluoradene when treated with N-bromosuccinimide gave a good yield of the bright yellow 12-bromofluoradene (XXIIIa). In methanol, this was converted to 12-methoxyfluoradene (XXIIIb), and in aqueous tetrahydrofuran it gave 12-hydroxyfluoradene (XXIIIc), both of which are colorless. The 12-position was assigned on the basis of the ready displacement of bromide, and the



XXIIIa, R = Br
b, R = OCH_3
c, R = OH

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[9] R. S. Stearns and G. W. Wheland, This Journal, **69**, 2025 (1947).

[10] D. H. Rosenblatt, *J. Phys. Chem.*, **58**, 40 (1954).

[11] J. Cymerman-Craig and A. A. Diamantis, *J. Chem. Soc.*, 1619 (1953).

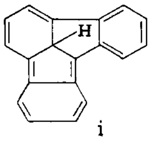
[12] Considerable effort was made to carry out a direct potentiometric titration of fluoradene, but it proved futile since no suitable solvent could be found.

[13] J. B. Conant and G. W. Wheland, This Journal, **54**, 1212 (1932)

[14] W. K. McEwen, *ibid.*, **58**, 1124 (1936).

[15] R. J. Windgassen, W. H. Saunders and V. Boekelheide, *ibid.*, **81**, 1459 (1959).

[16] The tautomeric structure i was considered briefly for fluoradene, but was rejected on the basis of the hydrogenation data and the perbenzoic acid oxidation results cited above. Fluoradene recovered from an alkaline solution was unchanged, and we could find no evidence for the existence of tautomer i.



i

TABLE III

ULTRAVIOLET ABSORPTION MAXIMA OF FLUORADENE DERIVATIVES[a]

Compound	λ, mμ	ε	λ, mμ	ε	λ, mμ	ε	λ, mμ	ε
Fluoradene	276	26,600	317	4,500	331	4,630		
12-Bromo-	228	30,700			263	22,400	294	13,200
12-Methoxy-	230	36,000	254	13,800	263	16,400	291	19,000
12-Hydroxy-	232	35,100	255	10,700	264	15,200	292	17,800

[a] Spectra taken in hexane solution.

fact that neither the 12-hydroxy nor 12-methoxy compound showed a spectral shift with alkali. This indicates the absence of the 12-hydrogen in both and the non-phenolic character of 12-hydroxyfluoradene.

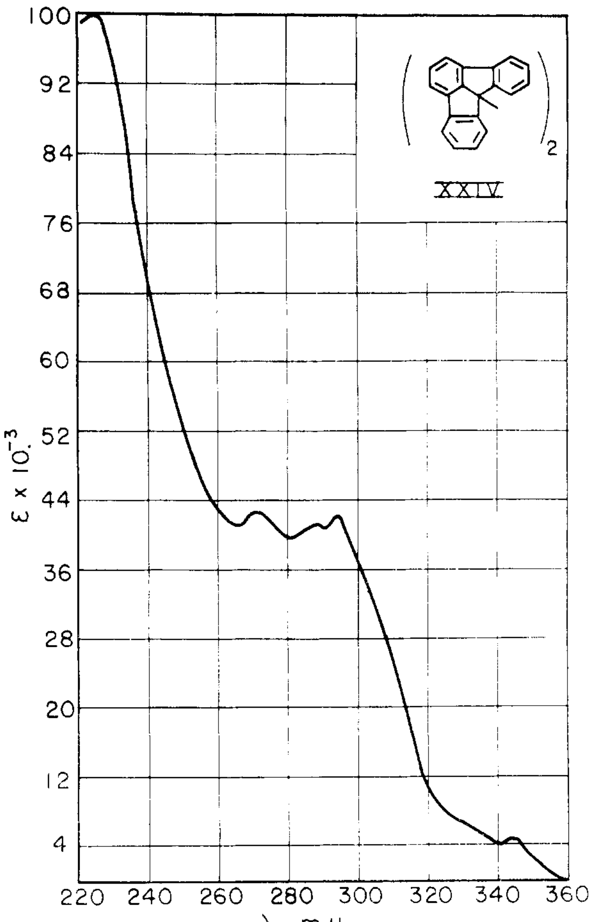


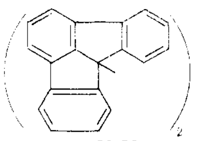
Fig. 2.—Ultraviolet absorption spectrum in cyclohexane of 12,12′-bifluoradenyl (XXIV).

In the ultraviolet, the 12-substituted fluoradenes show close similarities, but they are quite different from fluoradene itself (see Table III). This spectral difference is puzzling, but an analogy is found in the behavior of 9-substituted fluorenes. While 9-alkyl and 9-aryl substituents cause little change in absorption, electronegative substituents cause marked changes in the spectrum.[17] Apparently the π-system of fluorene can interact in the excited state with substituents on the benzylic carbon, and this appears to be true for fluoradene as well.

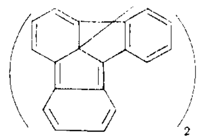
By far the most interesting derivative was bifluoradenyl. This hydrocarbon, as has been mentioned, was obtained as a minor product from the deamination of VIII, as well as by oxidation of the colored fluoradene anion IVa. In addition, when a solution of 12-bromofluoradene (XXIIIa) in benzene was shaken with mercury, a 50% yield of bifluoradenyl was obtained.

Analytical data established bifluoradenyl as consisting, empirically, of two fluoradene nuclei coupled with elimination of hydrogen, and a structural assignment was made on the basis of hydrogenation and tritium exchange studies. At room temperature and atmospheric pressure with a 5% palladized carbon catalyst, 700 mole % of hydrogen was absorbed and the hexahydrofluoradene XX was isolated in quantitative yield. Six moles of hydrogen was consumed in reducing the cyclopentindene benzene rings (as was true with fluoradene itself), and the seventh mole was used for hydrogenolysis of the carbon–carbon bond.[18] This establishes the presence of two intact fluoradene nuclei in the bis compound.

To determine at which position the two fluoradene nuclei were joined, evidence was sought for the presence or absence of any acidic hydrogens. Fluoradene readily exchanged its hydrogen at C_{12} for tritium when boiled in a mixture of ethanol and toluene containing tritium oxide. Even extending the reflux period fourfold gave no exchange with bifluoradenyl under these conditions. Thus the acidic C_{12}-hydrogens are absent, and XXIV appears to be the most reasonable structure for bifluoradenyl. Structure XXV would also be consistent with bifluoradenyl's lack of acidic hydrogens. However, the exclusive reduction of the cyclopentindene benzene ring on catalytic hydrogenation appears to favor structure XXIV. The ultraviolet absorption of bifluoradenyl (Fig. 2) is different from that of fluoradene and its other derivatives, but this difference probably is due to overlap of the two π-systems present in bifluoradenyl.



XXIV



XXV

Evidence was sought for the possible dissociation of 12, 12′-bifluoradenyl into fluoradenyl radicals. However, electron spin resonance measurements in benzene solutions did not detect the presence of any radicals, and the ultraviolet absorption of bifluoradenyl did not change with

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(17) C. Eaborn and R. A. Shaw, *J. Chem. Soc.*, 2027 (1954).

(18) Similar hydrogenolyses have been observed with completely phenylated ethanes by H. F. Bent and J. E. Cuthbertson, THIS JOURNAL, **58**, 170 (1936), and L. A. Pinck, *ibid.*, **55**, 1711 (1933).

concentration in the range 10^{-4} to 10^{-6} *M*. Thus there is no indication of any stability for the fluoradenyl radical. Similarly, attempts to prepare the cation of fluoradene (as the perchlorate) failed.

Experimental[19]

9-*o*-Carboxyphenylfluorene (XII).—A mixture of 28 g. (0.1 mole) of 9-(*o*-chlorophenyl)-fluorene (X),[7] 12 g. (0.15 mole) of cuprous cyanide, 50 ml. of quinoline and 5 ml. of acetonitrile was heated under reflux in an atmosphere of nitrogen with efficient stirring. The bath temperature, originally at 250–260°, was slowly raised to 280–290° over a period of 12 hours and maintained there for an additional 12 hours, during which complete solubility was obtained. The contents of the cooled reaction solution was distributed between 100 ml. of concd. ammonium hydroxide and 100 ml. of benzene, the mixture was filtered, and the benzene layer was separated and washed successively with ammonium hydroxide, water, 2 *N* sulfuric acid and water.

To the dark residue obtained on evaporation of the benzene at reduced pressure was added 100 ml. of ethylene glycol and a solution of 40 g. of potassium hydroxide in 25 ml. of water. This mixture was boiled in a nitrogen atmosphere for 21 hours, and the solution was then cooled, diluted with 250 ml. of water and washed with benzene. The aqueous phase was acidified with concd. hydrochloric acid, and the precipitated acid was extracted into ether. The dried ether solution was evaporated and the residue was recrystallized three times from acetic acid to give 16.9 g. (59%) of acid, m.p. 240–241° (reported[7] m.p. 241–242°).

9-*o*-Ethoxycarbonylaminophenylfluorene (XVIII).—Thionyl chloride (120 ml.) and 32.3 g. (0.11 mole) of 9-*o*-carboxyphenylfluorene (XII) were maintained at 40–50° until the mixture became homogeneous and gas evolution ceased. Excess thionyl chloride was removed at reduced pressure, 50 ml. of dry benzene was added, the benzene was removed at reduced pressure, and the addition and removal of benzene was repeated twice more. To a stirred, cooled (0–5°) solution of the acid chloride in 1500 ml. of dry acetone was added 11 g. (0.17 mole) of activated sodium azide[20] in 40 ml. of water. This mixture was stirred for 15 minutes and then sufficient ice-water was added to effect complete solution. Stirring was continued for 1.5 hours, not allowing the temperature to rise above 5°, after which ice-water was added in small portions to a total volume of 5 l. The precipitate (XIII) was collected, washed with ice-water, and dried over magnesium perchlorate overnight *in vacuo*.

A portion of the azide XIII (10.0 g., 0.032 mole) was suspended in 200 ml. of dry ethanol and gently warmed on the steam-bath until the initial vigorous evolution of nitrogen abated, after which the solution was boiled for 1.5 hours. The ethanol was removed at reduced pressure, the residue was taken up in 100 ml. of benzene, and the benzene solution was washed with *N* carbonate solution, dried, and evaporated to give an oil (10.2 g., 93%) which slowly crystallized on standing. The carbamate was found to be soluble in hot benzene–methylcyclohexane (1:10) solution from which crystals slowly separated, m.p. 110–111°.

Anal. Calcd. for $C_{22}H_{19}NO_2$: C, 80.2; H, 5.8; N, 4.3; OC_2H_5, 13.7. Found: C, 79.8; H, 5.8; N, 4.6; OC_2H_5, 13.4.

Spiro[oxindole-3,9-fluorene] (XVII).—A solution of 1.93 g. (5.9 mmoles) of the carbamate XVIII in 30 ml. of dry ethanol in which 340 mg. (15 mmoles) of sodium had been dissolved was boiled in a nitrogen atmosphere for 17 hours. After the ethanol was evaporated at reduced pressure, the residue was suspended in 75 ml. of water and this mixture was extracted with three 20-ml. portions of methylene chloride. The combined extracts were dried and evaporated and the residue was digested with 10 ml. of benzene. Cooling, then filtering, gave the benzene-insoluble lactam XVII, 1.6 g. (96%), m.p. 251–253°. Recrystallization from isopropyl alcohol raised the m.p. to 259–260°; $\lambda_{\max}^{\mathrm{EtOH}}$ 260 mμ (ε 20,000), 293 (5,580), 305 (5,790).

Anal. Calcd. for $C_{20}H_{13}NO$: C, 84.8; H, 4.6; N, 5.0; mol. wt., 283. Found: C, 84.8; H, 4.6; N, 5.2; mol. wt. (Rast), 300.

9-*o*-Aminophenylfluorene (VIII).—Lactam XVII (936 mg., 3.3 mmoles) was boiled with 40 ml. of ethylene glycol, 10 ml. of water and 13 g. of potassium hydroxide in a nitrogen atmosphere for 15 hours. The mixture became homogeneous after several minutes and remained so for about 45 minutes after which a precipitate formed which collected on the cooler surfaces of the flask and condenser. The cooled reaction mixture was diluted with 200 ml. of water and extracted with methylene chloride, and the residue obtained on evaporation of the dried methylene chloride extracts was sublimed. Crystallization of the sublimate from benzene–hexane and resublimation (100° (0.03 mm.)) gave amine (790 mg., 93%) of m.p. 161–162°; $\lambda_{\max}^{\mathrm{EtOH}}$ 264 mμ (ε 18,040), 293 (7,840), 303 (8,090); upon addition of acid $\lambda_{\max}$ 268 mμ (ε 17,830), 293 (5,210), 304 (7,310).

Anal. Calcd. for $C_{19}H_{15}N$: C, 88.7; H, 5.9; N, 5.4. Found: C, 88.5; H, 5.9; N, 5.8.

This amine was found to be very slightly soluble in 1 *N* mineral acid and impossible to extract from an organic solvent with aqueous acid.

Deamination of 9-*o*-Aminophenylfluorene (VIII).—Finely divided amine VIII (11 g., 0.041 mole) was stirred with 160 ml. of glacial acetic acid and 2.75 ml. of concd. sulfuric acid with external cooling (*ca.* 13°). The amine dissolved but after a few minutes the salt separated as very small crystals and a slow addition (over the course of one-half hour) of 3.24 g. (0.047 mole) of sodium nitrite in 30 ml. of water was begun, resulting finally in a yellow homogeneous solution. Cold (3°) 3 *N* sulfuric acid (550 ml.) was added to this solution causing the formation of a precipitate, and excess nitrous acid was destroyed by addition of sulfamic acid. Heating the aqueous mixture on the steam-bath for 0.5 hour with efficient stirring caused a vigorous evolution of nitrogen and the formation of brown viscous material. After the reaction mixture had cooled somewhat, it was extracted with 150 ml. of benzene, and the benzene phase was washed with seven 100-ml. portions of water to remove any acetic acid, dried, concentrated to about 20 ml. and allowed to stand overnight. The crystals which separated were recrystallized from toluene and sublimed (200° (5 μ)) giving 456 mg. (4.6%) of 12,12′-bifluoradenyl (XXIV), m.p. 300–301° dec.

Anal. Calcd. for $C_{38}H_{22}$: C, 95.4; H, 4.6. Found: C, 95.1; H, 4.9.

The material remaining in the benzene solution was adsorbed on 300 g. of acid-washed alumina. From the column, 2.29 g. (23%) of fluoradene (IV) was eluted with hexane, 7.6 g. (69%) of the phenol XIX was removed with benzene and 0.4 g. (3.6%) of an uncharacterized deep red material was removed with chloroform–isopropyl alcohol.

Fluoradene (IV) was recrystallized from hexane and sublimed (80° (0.05 mm.)) to give material of m.p. 129.8–130.3°; $\lambda_{\max}^{\mathrm{hexane}}$ 276 mμ (ε 26,600), 317 (4,500), 331 (4,630); in methanol the extinction coefficients were lowered slightly to 26,000, 4,400 and 4,400.

Anal. Calcd. for $C_{19}H_{12}$: C, 95.0; H, 5.0; mol. wt., 240. Found: C, 94.8; H, 4.9; mol. wt. (Rast), 235.

The phenol XIX was recrystallized from benzene–hexane and sublimed (120° (0.05 mm.)) to give material of m.p. 142–143°; $\lambda_{\max}^{\mathrm{EtOH}}$ 265, 268 mμ (doublet) (ε 16,300), 292 (5,590), 304 (8,890); in ethanolic potassium hydroxide, $\lambda_{\max}$ 262 mμ (ε 16,000), 298 (8,800).

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.3; H, 5.5. Found: C, 88.1; H, 5.6.

12-Bromofluoradene (XXIIIa).—To a solution of 302 mg. (1.26 moles) of fluoradene (IV) in 6 ml. of carbon tetrachloride was added 294 mg. (1.26 mmoles) of N-bromosuccinimide.[21] The mixture was boiled in a dry nitrogen at-

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[19] Boiling points are not corrected. All melting points are corrected and those above 150° were taken in evacuated capillaries. Infrared spectra were taken on a Baird Associates recording spectrophotometer, and ultraviolet spectra were taken on a Cary recording spectrophotometer, model 11 or 14. Anhydrous sodium sulfate was employed as the drying agent for solutions unless otherwise stated. Microanalyses were performed by the Microchemical Laboratory, University of California, Berkeley.

[20] P. A. S. Smith in "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 382.

[21] The N-bromosuccinimide was recrystallized from hot water, dried over magnesium perchlorate and used immediately. It was added to the reaction solution as large crystals since in one experiment in which the N-bromosuccinimide had been ground to a powder it was consumed much more rapidly (within 3 hours) and no bromofluoradene was formed.

mosphere until the N-bromosuccinimide had been consumed (about 12 hours) as evidenced by the disappearance of insoluble material at the bottom of the solution and the formation of a new precipitate on the surface of the reaction solution. The hot, yellow reaction mixture was filtered, and the filtrate was evaporated leaving a bright yellow residue which was heated in a sublimation apparatus for 24 hours at 75° (0.1 mm.) to remove succinimide. Crystallization of the residue from carbon tetrachloride and sublimation (135° (0.02 mm.)) gave 300 mg. (75%) of 12-bromofluoradene, m.p. 193–194° dec.; $\lambda_{\max}^{\text{cyclohexane}}$ 228 mμ (ϵ 30,700), 263 (22,400), 294 (13,200).

Anal. Calcd. for $C_{19}H_{11}Br$: C, 71.5; H, 3.5; Br, 25.0. Found: C, 71.3; H, 3.5; Br, 25.2.

12-Methoxyfluoradene (XXIIIb).—The bromide XXIIIa (36 mg., 0.11 mmole) was boiled with 10 ml. of dry methanol for 12 hours, and the colorless solution then was diluted with 30 ml. of water and extracted with three 10-ml. portions of benzene. The residue obtained on evaporation of the dried benzene extracts was chromatographed on 2 g. of alumina. Elution with hexane gave 12-methoxyfluoradene in fractions 7–17, and after sublimation (90°/0.3 mm.)) it melted at 149–150°; $\lambda_{\max}^{\text{cyclohexane}}$ 230 mμ (ϵ 36,000), 254 (13,800), 263 (16,400), 291 (19,000).

Anal. Calcd. for $C_{20}H_{14}O$: C, 88.9; H, 5.2; OCH_3, 11.5. Found: C, 88.6; H, 5.5; OCH_3, 11.7.

12-Hydroxyfluoradene (XXIIIc).—A solution of 140 mg. (0.44 mmole) of 12-bromofluoradene (XXIIIa), 1 ml. of water and 9 ml. of tetrahydrofuran was boiled for 18 hours. The colorless solution was diluted with 30 ml. of water and extracted with three 15-ml. portions of benzene, and the benzene extracts were washed with carbonate, dried, and evaporated. The residue was chromatographed on 4 g. of acid-washed alumina and the 12-hydroxy compound was eluted with 1:1 hexane–benzene (25-ml. fractions) in fractions 3–15. Sublimation (110° (0.1 mm.)) gave material which softened at 140–144° and decomposed at 160° (in a nitrogen atmosphere); $\lambda_{\max}^{\text{cyclohexane}}$ 232 mμ (ϵ 35,100), 255 (10,700), 264 (15,200), 292 (17,800); the spectrum in methanol was identical and unchanged on addition of alkali.

Anal. Calcd. for $C_{19}H_{12}O$: C, 89.0; H, 4.7. Found: C, 88.8; H, 4.9.

4b,5,6,7,7a,12b-Hexahydrofluoradene (XX).—A mixture of 102 mg. (0.425 mmole) of fluoradene (IV) in 10 ml. of abs. ethanol was hydrogenated at room temperature and atmospheric pressure using 24 mg. of 5% palladized carbon as catalyst. After 4.5 hours and a hydrogen consumption of 280 mol. %, hydrogen absorption ceased and the mixture was filtered. The crystals obtained on evaporation of the filtrate were recrystallized from ethanol–water and sublimed (90° (0.1 mm.)) to give material of m.p. 118–119°; $\lambda_{\max}^{\text{cyclohexane}}$ 262 mμ (ϵ 1,880), 269 (3,080), 275 (3,320).

Anal. Calcd. for $C_{19}H_{18}$: C, 92.6; H, 7.4. Found: C, 92.5; H, 7.2.

Perbenzoic Acid Oxidation of Fluoradene (IV).—A 9:1 chloroform–benzene solution of perbenzoic acid was prepared according to Braun[22] using the modification of Kolthoff.[23] This solution was diluted to the desired concentration and standardized against a standard 0.00288 *M* sodium thiosulfate solution.

Fluoradene (335 mg., 1.4 mmoles) was weighed into a 50-ml. volumetric flask and filled to the mark with standard 0.185 *M* perbenzoic acid solution. In a similar manner a 5-ml. solution of 9-phenylfluorene (33.5 mg., 0.138 mmole) was prepared. At various times 100 λ aliquots from each reaction solution were removed and titrated with the standard thiosulfate solution. After 24 hours at room temperature it was found that fluoradene had consumed 422 mole % perbenzoic acid, 9-phenylfluorene had consumed 49 mole %, while a blank run was found to have changed by only 4%.

12,12′-Bifluoradenyl (XXIV). A. From Fluoradene (IV).—Nitrogen was bubbled through a solution of 105 mg. (0.43 mmole) of fluoradene in 6.6 ml. of 1:1 methanol–benzene for 0.5 hour, then 0.5 ml. of 1.04 *N* sodium hydroxide was added, and the solution immediately took on the color of an alkaline phenolphthalein solution. The solution was maintained in a nitrogen atmosphere for 90 hours, during which time the color slowly faded and crystals separated from solution. Recrystallization from toluene and sublimation (200° (0.01 mm.)) gave bifluoradenyl, m.p. 306–307° dec., $\lambda_{\max}^{\text{cyclohexane}}$ 226 mμ (ϵ 100,000), 271 (42,800), 288 (41,600), 294 (42,300), 330 (6,650), 344 (4,780).

Anal. Calcd. for $C_{38}H_{22}$: C, 95.4; H, 4.6. Found: C, 95.4; H, 4.7.

When a solution of fluoradene at the same concentration as above but open to the air was made alkaline, the color was observed to fade within one hour. The colored species shows a broad band in the visible absorption spectrum, $\lambda_{\max}$ 420–590 mμ, ϵ ~200–400. Reacidification of an alkaline solution of 52 mg. of fluoradene in 4 ml. of 1:1 methanol–benzene in a nitrogen atmosphere, after 0.5 hour, resulted in recovery of 49 mg. of unchanged hydrocarbon.

B. From 12-Bromofluoradene (XXIIIa).—Nitrogen was bubbled through a solution of 99 mg. (0.31 mmole) of 12-bromofluoradene (XXIIIa) in 100 ml. of dry benzene, and to this pale yellow solution was added 740 mg. (2.7 mmoles) of mercury and a few particles of granulated lead. This mixture was stirred vigorously for 5 hours and then filtered. The filtrate was concentrated to about 10 ml., cooled, filtered, and the precipitate was recrystallized from toluene to give 29 mg. (49%) of 12,12′-bifluoradenyl, m.p. 304–305°. The mixed melting point of this compound with the hydrocarbon obtained above from the alkaline oxidation of fluoradene was also 304–305°.

Hydrogenation of 12,12′-Bifluoradenyl (XXIV).—A mixture of 104 mg. (0.217 mmole) of bifluoradenyl in 50 ml. of toluene was hydrogenated at room temperature and atmospheric pressure using 90 mg. of 5% palladized charcoal as catalyst. After 6 hours and a hydrogen consumption of 700 mole %, hydrogen absorption ceased and the mixture was filtered. The crystals obtained on evaporation of the filtrate had a m.p. of 110–113°, and a mixed melting point with the hexahydrofluoradene (XX) was found to be 110–114°. The infrared spectra of the two compounds in chloroform were identical.

Deuterium Exchange Reactions.—Deuterium ethoxide of better than 95% deuterium content was prepared as follows: A 4:1 mixture of ethyl orthosilicate and deuterium oxide was boiled at 130° for 24 hours, after which the volatile material was distilled. The distillate was boiled with 10% its weight of sodium for 8 hours and then fractionated through an efficient column. Throughout the preparation care was taken that all equipment be dry, and the reaction was protected from atmospheric moisture.

A. 9-*o*-Chlorophenylfluorene-9-*d* (Xd).—A solution of 118 mg. (0.43 mmole) of the chlorophenyl derivative X and 5 ml. of deuterium ethoxide containing a small amount of dissolved sodium was boiled for 12 hours after which the alcohol was removed at reduced pressure and 3 ml. of deuterium oxide was added to the residue. This mixture was extracted with ether and the ether was dried and evaporated. The infrared spectrum of the sublimed residue was quite different from that of the starting chloride, and the original protonated compound could be regenerated (as shown by its infrared spectrum) by boiling a solution of the deuterated material in ethanol containing a small quantity of dissolved sodium, but the deuterium could not be exchanged by boiling in ethanol alone.

B. Fluoradene-12-*d* (IVd).—Fluoradene (67 mg.) was boiled with 5 ml. of deuterium ethoxide in a dry nitrogen atmosphere for 15 hours (complete solubility was never attained). After removal of the alcohol at reduced pressure, the residue was taken up in benzene, filtered and evaporated. A comparison of the infrared spectrum in chloroform of the sublimed residue with that of the original hydrocarbon showed major differences in the 7–12.4 μ region. The deuterium was completely removed by boiling this compound with ethanol for 11 hours as shown by the fact that its infrared spectrum was now identical with that of fluoradene.

Tritium Exchange Reactions.—A solution consisting of 15 ml. of ethanol, 15 ml. of toluene and 100 λ of water containing tritium oxide (200 μc.) was prepared for use in the following two experiments.

A. Fluoradene-12-*t* (IVt).—Fluoradene (56 mg.) was boiled with 10 ml. of the above stock solution in a nitrogen atmosphere for 16 hours, after which the solvent was evaporated and the residue sublimed. The activity of the sub-

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[22] G. Braun, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1944 p. 431.

[23] I. Kolthoff, T. Lee and M. Maier, *J. Polymer Sci.*, **2**, 199 (1947).

limate was determined in a scintillation counter[24] and had an average value of 520 d.p.m./mg.

B. **12,12'-Bifluoradenyl** (XXIV) (55 mg.) was boiled with 10 ml. of the stock solution in a nitrogen atmosphere for 65 hours. (The concentration of hydrocarbon in the cold solution was determined by means of its ultraviolet absorption to be 2.6×10^{-4} *M*. The solubility of the dimer in the boiling solvent is estimated to be at least 10^{-3} *M* since on cooling considerable quantities of crystals separate from solution). The cold solution was filtered and the crystals washed with benzene and sublimed to give material of m.p. 307° dec. A 1-mg. sample of this material showed no activity as measured by the scintillation counter.

9-Phenylfluorene.—A solution of 218 mg. (0.79 mmole) of 9-*o*-chlorophenylfluorene (X) and 72 mg. (0.88 mmole) of sodium acetate in 50 ml. of alcohol was hydrogenated at room temperature and atmospheric pressure using 65 mg. of 5% palladized carbon as catalyst. The hydrogen absorption was rapid and ceased at 100 mole %. The catalyst was removed by filtration, and the filtrate was evaporated to give material which recrystallized readily from ethanol and after sublimation (80° (0.05 mm.)) had a m.p. of 147–148° (reported[25] m.p. 146°); $\lambda_{\max}^{\text{cyclohexane}}$ 265 mμ (ε 20,300), 293 (6,320), 304 (10,300).

1-Phenylfluorene.—A solution of 1-phenylfluorenone[26] (354 mg., 1.38 mmoles) in 25 ml. of benzene–10 ml. ethanol, was hydrogenated at room temperature and atmospheric pressure using 73 mg. of 5% palladized carbon as catalyst. The total hydrogen uptake ceased at 180 mole %, after which the reaction mixture was filtered and the filtrate was evaporated. Chromatography of the oily residue (331 mg.) on 8 g. of neutral alumina using hexane as the eluent resulted in an oil which on sublimation (80° (0.1 mm.)) crystallized on the cold finger; m.p. 38–41°; $\lambda_{\max}^{\text{cyclohexane}}$ 256 mμ (ε 27,400), 302 (4,570).

Anal. Calcd. for $C_{19}H_{14}$: C, 94.2; H, 5.8. Found: C, 93.9; H, 5.9.

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(24) We wish to express our appreciation to Mr. I. M. Whittemore of the Donner Laboratories, University of California, Berkeley, for his assistance with the radioactivity analyses in these experiments.

(25) A. Kliegl, *Ber.*, **38**, 288 (1905).

(26) We wish to thank B. L. Smolinsky for preparing this compound according to the directions of Stiles and Libby[4] by heating the peroxide of 1-carboxyfluorenone in benzene.

BERKELEY 4, CALIF.

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

The Anomeric 2,3,4-Tri-*O*-benzoyl-D-ribopyranosyl Fluorides and 2,3,5-Tri-*O*-benzoyl D-ribofuranosyl Fluorides. A Novel Transformation from the D-Ribopyranose to the D-Ribofuranose Series

BY CHRISTIAN PEDERSEN[1] AND HEWITT G. FLETCHER, JR.

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Brief treatment of β-D-ribopyranose tetrabenzoate with liquid hydrogen fluoride gives both anomeric 2,3,4-tri-*O*-benzoyl-D-ribopyranosyl fluorides, the *cis* or α-anomer being sufficiently stable to debenzoylate to α-D-ribopyranosyl fluoride. Longer treatment of β-D-ribopyranose tetrabenzoate or 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosyl fluoride with hydrogen fluoride affords 3,4-di-*O*-benzoyl-β-D-ribopyranosyl fluoride, a topic of the succeeding paper. From this long treatment of β-D-ribopyranose tetrabenzoate with hydrogen fluoride a second di-*O*-benzoylpentosyl fluoride was obtained. Benzoylation of the substance led to the isolation of a third tri-*O*-benzoylpentosyl fluoride which was converted to the known β-D-ribofuranose tetrabenzoate. The third tri-*O*-benzoylpentosyl fluoride was also synthesized from 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose. From 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose a fourth tri-*O*-benzoylpentosyl fluoride, convertible to β-D-ribofuranose tetrabenzoate and to methyl β-D-ribofuranoside, was obtained. It is tentatively concluded that the third and fourth tri-*O*-benzoyl-D-pentosyl fluorides are, respectively, the α- and β-anomers of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl fluoride.

Through a number of earlier researches in this Laboratory, extending over a period of some twelve years, the preparation and properties of a number of benzoylated aldopyranosyl and aldofuranosyl bromides and chlorides have been investigated.[2] We have recently turned our attention to some of the benzoylated glycosyl fluorides of the ribose and arabinose series. The present paper will deal with results obtained in the D-ribose series; the paper immediately following will describe work in the L-ribose and L-arabinose series.

When β-D-ribopyranose tetrabenzoate[3] (I) was treated with liquid hydrogen fluoride at room temperature for ten minutes, two crystalline tri-*O*-benzoylpentosyl fluorides were obtained, a levorotatory isomer in 59% yield and a dextrorotatory isomer in 12% yield. On fusion with a mixture of benzoic acid and anhydrous calcium benzoate both isomers gave β-D-ribopyranose tetrabenzoate (I); with barium methoxide they were both converted to methyl β-D-ribopyranoside (V). These facts demonstrate that the two fluorides are D-ribopyranose derivatives. That they are anomers (II and III) is evidenced through comparison (Tables I and II) of their rotations with those of the corresponding 2,3,4-tri-*O*-benzoyl-α-D-ribopyranosyl and 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosyl halides reported in earlier work.[4] As expected[5–8] the α-anomer is more weakly dextrorotatory than the corresponding α-chloride while the β-anomer is more weakly levorotatory than the corresponding β-chloride. In the transformations mentioned above the α-(*cis*)-fluoride reacts with simple inversion while the displacement of the halogen in the β-(*trans*)-fluoride involves neighboring group participation, the products in both cases having the substituents at C_1 and C_2 in a *trans* relationship.

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(1) Chemical Foundation Fellow 1958–1960.

(2) For reviews and specific references see: H. G. Fletcher, Jr., *Record Chem. Progr. Kresge-Hooker Sci. Lib.*, **19**, 147 (1958), and L. J. Haynes and F. J. Newth, *Advances in Carbohydrate Chem.*, **10**, 207 (1955).

(3) R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **70**, 4052 (1948).

(4) R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **73**, 959 (1951).

(5) D. H. Brauns, *ibid.*, **45**, 2381 (1923).

(6) D. H. Brauns, *ibid.*, **46**, 1484 (1924).

(7) C. S. Hudson, *ibid.*, **46**, 462 (1924).

(8) A. K. Bose and B. G. Chatterjee, *J. Org. Chem.*, **23**, 1425 (1958).