volume yielded five further fractions weighing 2.0, 1.7, 0.9, 1.4 and 0.9 g. Systematic recrystallization of these fractions afforded eight fractions. Their weights and specific rotations in acetone are given in Table I.

TABLE I

RESOLUTION OF 2′-IODO-9,9′-SPIROBIFLUORENE-2-CARBOXYLIC ACID WITH STRYCHNINE

Fract. of salt	Salt, g.	Spec. rot.	Acid, g.	M. p., °C.	Rotation Actual	Rotation Specific
1	0.4	−26.6	0.25	318	−0.06	− 7.1
2	1.3	−26.7	0.8	328	− .05	− 5.1
3	0.6	−28.1	0.4	336	− .03	− 3.2
4	0.8	−31.6	0.5	341	+ .15	+15.5
5	0.6	−18.6	0.35	350	+ .28	+25.5
6	0.3	−39.8	0.2	336	− .02	− 2.0
7	0.8	−27.2	0.5	347	+ .12	+15.0
8	2.1	−51.9	1.0	344	− .18	−16.8

The various fractions of salt were decomposed by solution in a small volume of acetone, acidification and dilution with hot water. The resulting precipitates were filtered, washed with hot water and air-dried. The results are shown in Table I. The fractions of maximum positive and negative rotations were recrystallized from acetic acid. Fraction 5 yielded 0.1 g. (m. p. 350–351°; α +0.10°, $[\alpha]^{28}\text{D}$ +16.9°) from 20 ml. of solvent. The filtrate diluted with 5 ml. of water at the boiling point gave 0.2 g. (m. p. 350–351°, α +0.19°, $[\alpha]^{28}\text{D}$ +37.9°). Fraction 8 from 55 ml. of solvent yielded 0.5 g. (m. p. 344–345°, α −0.09°, $[\alpha]^{28}\text{D}$ −14.3°). The filtrate diluted with 18 ml. of water produced 0.4 g. (m. p. 341–342°, α −0.11°, $[\alpha]^{28}\text{D}$ −16.8°).

2′-Nitro-9,9′-spirobifluorene-2-carboxylic Acid (VII).—Fourteen and seven-tenths grams of V was dissolved in 1300 ml. of hot acetic acid. With mechanical stirring 370 ml. of concentrated nitric acid (d. 1.42) was run into the boiling solution over a period of 25 minutes. Toward the end a precipitate started forming. The mixture was refluxed with stirring for another 70 minutes and allowed to stand for four hours. The yellow microcrystals were filtered off, washed with acetic acid and alcohol, and oven-dried. They weighed 10.3 g. After recrystallization from 220 ml. of nitrobenzene, 9.3 g. of small granules, m. p. 360°, was obtained. *Anal.* Calcd. for $C_{26}H_{15}O_4N$: N, 3.46. Found: N, 3.41. From the acetic acid filtrate a further 5.8 g. of crude material was recovered by dilution with water.

Summary

On the basis of theoretical considerations fluorene was shown to be planar. This finding was corroborated experimentally by a study of the stereochemistry of mono- and disubstituted 9,9′-spirobifluorenes.

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[CONTRIBUTION FROM THE LABORATORY OF RADIOCHEMISTRY, UNIVERSITY OF CINCINNATI]

Some Derivatives of 9,9′-Spirobifluorene[1]

BY JOHN H. WEISBURGER,[2] ELIZABETH K. WEISBURGER[2] AND FRANCIS E. RAY[3]

The chemistry of 9,9′-spirobifluorene, first synthesized by Clarkson and Gomberg,[4] was investigated in connection with a study of the structure of fluorene.[5]

With concentrated sulfuric acid sulfonation of 9,9′-spirobifluorene did not occur below 100° while above this temperature disulfonation resulted. When one equivalent of chlorosulfonic acid in chloroform was employed about one-half of the spirane disulfonated; the remainder was recovered unchanged.

This tendency for disubstitution was also observed in the nitration of 9,9′-spirobifluorene. However, by rather careful control of the concentration of nitric acid and the reaction time, it was eventually possible to isolate a small amount of the pure monosubstituted derivative.

It is not surprising that the spirane disubstitutes readily if its structure is considered in detail. The absorption spectrum shown in Fig. 1 closely resembles the sum of the spectra of fluorene and biphenyl.[6] This indicates negligible resonance coupling[6,7] between the two moieties of 9,9′-spirobifluorene with the result that each spirane molecule acts as if it consisted of two nearly independent fluorene molecules. The isolation of a monosubstituted spirobifluorene appears possible only if there is an appreciable difference in the energy of activation of the mono- and disubstitution reactions.

Considering the close relationship of 9,9′-spirobifluorene to fluorene, it seemed likely that electrophilic substituents would attack the 2 position. This was confirmed by degrading the known 9,9′-spirobifluorene-2-carboxylic acid[5] to the amine by a Curtius reaction. This amine was identical with the amine obtained by nitration of the hydrocarbon and reduction of the nitro derivative. In disubstitution one group would be expected to enter into each moiety of the hydrocarbon. This indeed takes place since the 2-iodo-9,9′-spirobifluorene-2′-carboxylic acid[5] and the 9,9′-spirobifluorene-2,2′-disulfonic acid[8] were found to be resolvable. If both groups were located in the same moiety of the spirane, these compounds would not be resolvable. The 9,9′-spirobifluorene derivatives prepared during this investigation are shown in Table I.

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(4) Clarkson and Gomberg, THIS JOURNAL, **52**, 2881 (1930).

(5) Weisburger, Weisburger and Ray, *ibid.*, **72**, 4250 (1950).

(6) Jones, *ibid.*, **67**, 2021, 2127 (1945).

(7) Branch and Calvin, "Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, pp. 168 ff.

(8) J. H. Weisburger, Ph.D. Thesis, University of Cincinnati, 1949, p. 61.

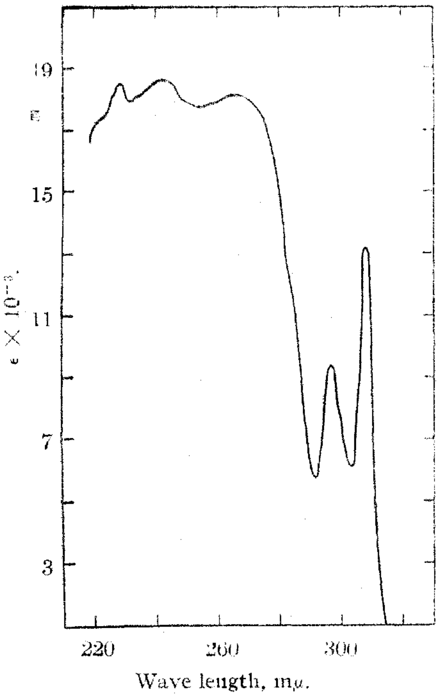
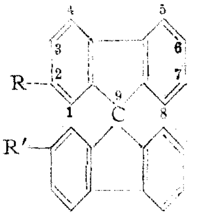


Fig. 1.—Absorption spectrum of 9,9′-spirobifluorene.

TABLE I

9,9′-SPIROBIFLUORENE DERIVATIVES



	R	R′
II[4]	H	H
III	SO_3H	SO_3H
IV	NCO	H
V	NO_2	H
VI	$NHCOCH_3$	H
VII	NH_2	H
VIII	NO_2	NO_2
IX	NH_2	NH_2
X	$NHCOCH_3$	$NHCOCH_3$

Experimental

9-(2-Biphenyl)-9-fluorenol (I).—The original procedure of Clarkson and Gomberg[4] was modified as follows: The fluorenone was dissolved in a 1:2 mixture of benzene and ether instead of ether alone. This decreased the volume of solution to be added to the Grignard reagent. The reaction time was shortened from overnight to three hours.

9,9′-Spirobifluorene (II).—Sixty-five and four-tenths grams of this compound (m.p. 200–202°) crystallized directly from the reaction mixture when a few drops of concentrated hydrochloric acid were added to a refluxing solution of 72.5 g. of I in 300 ml. of acetic acid. Only 1.7 g. (m. p. 195–197°) was recovered upon addition of water to the filtrate. Clarkson and Gomberg isolated the compound (m. p. 198–199°) by diluting the entire reaction mixture with water.

The ultraviolet absorption spectrum was determined[9] in a Beckman DU spectrophotometer. A solution of 3.5 mg. of the spirane in 100 ml. of 95% ethanol was used. Readings were taken at 10 Å. intervals, with 5 Å. intervals at the peaks. The maxima of absorption ($\epsilon_m \times 10^{-3}$) and corresponding wave lengths (in mμ) were as follows: 18.50, 228; 18.65, 242; 18.15, 265; 9.39, 297; 13.18, 308.

9,9′-Spirobifluorene-2,2′-disulfonic Acid (III).—Over a period of one and one-quarter hours 5.4 ml. of distilled chlorosulfonic acid in 20 ml. of chloroform was dropped into a refluxing solution of 12.8 g. of 9,9′-spirobifluorene in 80 ml. of chloroform. A white precipitate formed after one hour. The mixture was refluxed on a steam-bath for a total of three hours and cooled. The product was filtered, washed with chloroform and dried *in vacuo* over potassium hydroxide. The light grayish-white powder weighed 17.9 g. and melted at 225° with slight effervescence. The acid crystallized from dioxane (1 ml. of solvent per gram of material) with two molecules of solvent of crystallization. The white needles melted with decomposition (turning black) at 250° after discoloring somewhat from 230° upward. On a copper block decomposition occurred at 155° (removal of solvent of crystallization). *Anal.* Calcd. for $C_{25}H_{16}O_6S_2 \cdot 2C_4H_8O_2$: S, 9.81; equiv. wt., 326.1. Found: S, 10.10; equiv. wt., 326.6.

The dipotassium salt was prepared by addition of sufficient solid potassium chloride to a concentrated aqueous solution of the disulfonic acid to make it 20% in potassium chloride. The salt precipitated as a white powder upon cooling in an ice-bath and stirring for several hours. It was crystallized from water in the ratio of 15 g. of solid per 20 ml. of water. *Anal.* Calcd. for $C_{25}H_{14}O_6S_2K_2$: K, 14.15. Found: K, 14.13.

The ditoluidine salt was prepared from equivalent amounts of the disulfonic acid and *p*-toluidine in boiling water. Long, slender, light yellow needles were obtained. In a capillary, the material sintered somewhat from 250° upward, but had no definite melting point; it decomposed around 300°. On a copper block the substance melted around 290°, blackened at 300°. *Anal.* Calcd. for $C_{25}H_{14}O_6S_2 \cdot 2C_7H_9N$: N, 4.05. Found: N, 4.19.

9,9′-Spirobifluorene-2-isocyanate (IV).—One gram of 9,9′-spirobifluorene-2-carboxylic acid[5] was treated with 25 ml. of thionyl chloride for forty-five minutes. After removal of the excess reagent *in vacuo* 20 ml. of petroleum ether (b. p. 30–60°) was added and distilled off. The crystalline residue was dissolved in 25 ml. of dry acetone. To the ice cold solution 0.37 g. of sodium azide in 1 ml. of water was added and the mixture stirred for thirty minutes. Dilution with 100 ml. of water precipitated 1.0 g. of the light yellow 9,9′-spirobifluorene-2-azide (dec. 100° with gas evolution, the residue melting at 170–179°). The product was heated in 25 ml. of benzene for four hours at the end of which period the gas evolution was negligible. After removal of the benzene 0.9 g. of light yellow clusters, m. p. 173–178°, was obtained. Two-tenths gram recrystallized four times from 1 ml. of benzene and 2 ml. of petroleum ether left 0.05 g. of small white needles assembled in spherical globules, m. p. 182–184°. *Anal.*[10] Calcd. for $C_{25}H_{15}ON$: N, 3.92. Found: N, 4.02.

2-Nitro-9,9′-spirobifluorene (V).—At 90°, 37.8 ml. of concentrated nitric acid was added dropwise with mechanical stirring over a period of three hours to a solution of 6.3 g. of 9,9′-spirobifluorene (II) in 300 ml. of acetic acid. After standing overnight the mixture was refluxed for exactly thirty minutes and cooled. Two hours later 2.7 g. of light yellow granules (A), m. p. 205–210°, was collected. The filtrate diluted dropwise with 500 ml. of water yielded 3.7 g. of yellow powder (B), m. p. 207–218°. Product (A) was recrystallized from 60 ml. of acetic acid to give 0.8 g. of pale yellow needles, m. p. 235–236°. *Anal.*[10] Calcd. for $C_{25}H_{15}O_3N$: C, 83.08; H, 4.18; N, 3.89. Found: C, 83.33; H, 4.31; N, 3.92. Product B was dissolved in the mother liquor from the crystallization of A and after standing overnight 3.5 g. of lemon yellow granules, m. p. 227–228° resulted.

2-Acetylamino-9,9′-spirobifluorene (VI).—A mixture of 9.6 g. of V, 10 g. of tin foil and 80 ml. of acetic acid was refluxed for two hours and filtered hot. Upon standing overnight a white powder (6.4 g.), m. p. 250–259°, crystallized out. It was recrystallized from 30 ml. of dioxane to give 5.1 g. of small needles, m. p. 266–269°. *Anal.*[10] Calcd. for $C_{27}H_{19}ON$: C, 86.84; H, 5.13; N, 3.75. Found: C, 86.86; H, 5.46; N, 3.73.

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(9) It is a pleasure to acknowledge the coöperation of Dr. Mary E. Maver of the National Cancer Institute.

(10) We are indebted to J. Williams and R. Koegel of the National Cancer Institute for this analysis.

2-Amino-9,9′-spirobifluorene (VII). Method A.—Six and four-tenths grams of VI was suspended in 150 ml. of 10% ethanolic potassium hydroxide and refluxed gently on a steam-bath. After three and one-half hours the mixture was cooled. Nearly colorless plates (3.2 g.), m. p. 230–232°, were collected. Crystallization from benzene–petroleum ether lowered the melting point to 227–229°. *Anal.*[10] Calcd. for $C_{25}H_{17}N$: C, 90.60; H, 5.16; N, 4.24. Found: C, 90.14; H, 5.42; N, 4.35.

Method B.—To a refluxing suspension of finely ground V (3.6 g.) and iron powder (4.0 g.) in 75 ml. of ethanol 13 ml. of concentrated hydrochloric acid was added over a period of one hour. After filtering off the excess iron the volume was reduced by one-half. Dilution of the solution with 200 ml. of water yielded a precipitate which was washed with a small amount of dilute hydrochloric acid and water. Stirring this material with dilute ammonia for two hours afforded a white powder (2.8 g.) melting at 210–215°. The material (1.8 g.) recrystallized from 18 ml. of benzene yielded 1.0 g. of transparent microcrystals possessing a greenish sheen, melting at 218–224° to a red liquid. The melting point could not be raised by further recrystallizations. However, when a small sample was acetylated it yielded VI, m. p. 266°, after recrystallization from dioxane.

Method C.—A mixture of 700 mg. of IV and 40 ml. of 30% ethanolic potassium hydroxide was refluxed on a steam-bath for nine hours. After cooling 330 mg. of the amine, pale yellow prisms assembled in clusters, m. p. 227–228°, was filtered off. A further 200 mg. of impure compound was precipitated from the filtrate by addition of water. A mixture with the amine prepared by method A melted at 228–230°. *Anal.*[11] Calcd. for $C_{25}H_{17}N$: N, 4.24. Found: N, 4.23.

Fifty mg. of the compound refluxed with 0.2 ml. of acetic anhydride and 2 ml. of benzene for one-quarter hour deposited 25 mg. of the acetyl derivative, m. p. 263–265°, after standing for four hours. A mixture with VI melted at 264–266°.

2,2′-Dinitro-9,9′-spirobifluorene (VIII).—A mixture of 150 ml. of concentrated nitric acid (d. 1.42) and 150 ml. of acetic acid was added to a boiling solution of 15.1 g. of 9,9′-spirobifluorene in 500 ml. of acetic acid over a period of one-half hour and refluxed for an additional one and one-quarter hours. After standing for one hour an equal volume of water was added precipitating 18.5 g. of a yellow crystalline powder (m. p. 220–224°). This was recrystallized from 250 ml. of acetic acid to yield 12.7 g. of light yellow needles, m. p. 245–249.5°. The analytical sample melted at 249–250.5°. *Anal.* Calcd. for $C_{25}H_{14}O_4N_2$: N, 6.89. Found: N, 6.93.

2,2′-Diamino-9,9′-spirobifluorene (IX). Method A.—Over a period of one-half hour 35 ml. of concentrated hydrochloric acid was dropped into a boiling suspension of 12.0 g. of finely ground VIII and 12.0 g. of iron powder in 350 ml. of ethanol. After refluxing for another one-half hour the excess iron was filtered off. With mechanical stirring 35 ml. of 50% sodium hydroxide was added to the hot ethanolic solution precipitating iron hydroxide which was filtered off rapidly on a preheated funnel. The precipitate was dissolved in a small amount of hydrochloric acid, 250 ml. of hot ethanol added and the precipitation repeated. The combined alcoholic filtrates were diluted with 1 l. of water yielding 9.7 g. of a white powder. This was dissolved in 200 ml. of water containing 6 ml. of concentrated hydrochloric acid and treated with Darco. Addition of 8 ml. of concentrated ammonia afforded 7.9 g. of a white powder melting at 244–248°, with some sintering occurring at 155°. *Anal.* Calcd. for $C_{25}H_{18}N_2$: N, 8.10. Found: N, 8.06. The diamine crystallized from benzene in colorless rectangular prisms with one mole of solvent of crystallization. The melting point was 246.5–248.5° with pronounced effervescence at 130° (removal of solvent of crystallization) and resolidification around 160–180°. *Anal.* Calcd. for $C_{25}H_{18}N_2 \cdot C_6H_6$: N, 6.62. Found: N, 6.57.

Method B.—A mixture of 4.0 g. of finely ground VIII and 4.0 g. of iron powder in 100 ml. of ethanol was refluxed while 15 ml. of concentrated hydrochloric acid was dropped in over a period of thirty minutes. Refluxing was continued for another thirty minutes and the excess iron filtered off. The green filtrate was added to 400 ml. of water containing 15 ml. of concentrated ammonium hydroxide and 20 g. of potassium sodium tartrate. The white diamine was filtered from the dark green solution of the iron complex, redissolved in dilute hydrochloric acid, and stirred at room temperature with Darco. After filtration the mechanically stirred solution was neutralized dropwise with ammonium hydroxide. The resulting white powder weighed 3.5 g. Recrystallization from benzene afforded a material identical with that obtained by the first method.

2,2′-Diacetylamino-9,9′-spirobifluorene (X).—Acetylation of 1.7 g. of IX yielded 1.3 g. of material. After recrystallization from 100 ml. acetic acid 0.7 g. of brilliant white needles, melting above 360° (presumably below 400°), was obtained. *Anal.* Calcd. for $C_{29}H_{32}O_2N_2$: N, 6.52. Found: N, 6.32.

Summary

9,9′-Spirobifluorene disubstitutes very readily in the 2 and 2′ positions. In certain cases monosubstitution can be secured. This behavior is related to the structure of the hydrocarbon.

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[11] We are indebted to M. Jensen and R. Koegel of the National Cancer Institute for this analysis.