acid. Carbon dioxide was evolved immediately and a temperature rise was observed. After 45 min. all the isocyanate had been added. The temperature of the reaction mixture was then raised from 45° to 85° and held at 85° for one hr. The reaction mixture was then concentrated to dryness *in vacuo* leaving 468 g. (98.5%) of white solid. Recrystallization from methanol-ether gave white crystals, m.p. 220–230° (dec.).

From methyl N-(3,3-dinitrobutyl)carbamate. A mixture of 160 g. (0.72 mole) of methyl *N*-(3,3-dinitrobutyl)carbamate and 480 ml. of concentrated hydrochloric acid was heated on the steam bath overnight. Then 480 ml. of water was added and the mixture cooled to 10°. A portion of unchanged starting material crystallized and was collected. The mother liquor was evaporated to yield the desired amine hydrochloride. The recovered starting material was hydrolyzed again with 200 ml. of concentrated hydrochloric acid for 10 hr. and worked up as before. A total of 127 g. (88.0%) of product was obtained, m.p. 220–230° (dec.).

Ureas (VII). The preparation of bis(5-carbomethoxy-3,3-dinitropentyl)-urea is given as typical. To 60 g. (0.23 mole) of 5-carbomethoxy-3,3-dinitropentyl isocyanate was added a solution of 180 ml. of acetone and 60 ml. of water. The mixture warmed up immediately and was refluxed until crystals precipitated. Upon cooling the whole mass solidified. The product was collected and recrystallized from ethylene dichloride to give 60.0 g. (93.4%), of white solid, m.p. 159–160°.

Acknowledgment. We are indebted to the Office of Naval Research for the financial support of this work.

CONTRIBUTION NO. 202
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Preparation of 2-Fluoro-9,10-phenanthrenequinone[1,2]

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Received September 12, 1961

Takizawa[5] has demonstrated that *p*-benzoquinone and α-naphthoquinone are carcinogenic and that phenanthrenequinone will produce papillomas of the skin, on mice. Frequently, the addition of a fluorine atom to a molecule that is already physiologically active will enhance its activity. For example, it is known that fluorination increases the tumor-producing effects of *N*,*N*-dimethylaminoazobenzene.[6] Also the 6-α-fluoro substituted steroids[7] show increased progestational, androgenic, and corticoid activity. Further, 7-fluoro-2-acetamidofluorene[8] is more carcinogenic in the liver of the rat than 2-acetamidofluorene.[9] Therefore, in selecting a project for an undergraduate research problem, it was deemed of interest to prepare the 2- and 4-fluoro derivatives of phenanthrenequinone, since these compounds are not listed in the literature, to see if their potency would be thereby increased. The preparation of the 2-isomer is herewith described. Work is in progress on the preparation of the 4-fluoro compound.

Starting with phenanthrene, the synthesis involved first, oxidation to phenanthrenequinone, then nitration of the quinone and separation of the resulting 2- and 4-nitro isomers. Reduction of the 2-nitro compound to the 2-amino compound was immediately followed by diazotization and addition of fluoboric acid to give the fluoborate. Finally, the fluoroborate was decomposed by heating at reduced pressure and the fluoro compound separated from the resulting tarry mixture by sublimation at reduced pressure. This method of introducing a fluorine atom into an aromatic nucleus was first described by Balz and Schiemann.[10] The general method has been reviewed by Roe.[11]

The reduction of the 2-nitro compound was effected by tin and hydrochloric acid as described by Schmidt and Spoun.[12] In our hands the method of Brass and Ferber[13] using sodium hydrosulfite did not give consistent results, so the former method was used even though it was longer and involved decomposing the resulting tin double salt with hydrogen sulfide.

Because of the poor solubility of the 2-amino compound for diazotization, it was decided to carry out the reduction of the 2-nitro compound in such a manner as to keep the resulting amine in solution and proceed to the diazotization directly. It was noticed by Goldberg *et al.*,[14] in the preparation of 9-fluorophenanthrene, that the presence of dioxane was essential to the formation of the diazonium salt and the subsequent fluoborate. Therefore when the amine salt was found to be soluble in dioxane, it was decided to precipitate the tin sulfide in a water-dioxane mixture, leaving the amine salt in solution. After the tin sulfide was removed, the solution was cooled and diazotized and fluoboric acid added to

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[1] Part of this work was first presented at the 7th Meeting-in-Miniature of the New York Association of ACS Student Affiliate Societies at Adelphi College, May 1959.

[2] Part of this work was done with the aid of a grant from the New York City Cancer Committee of the American Cancer Society, Inc

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[10] G. Balz and G. Schiemann, *Ber.*, **60**, 1186 (1927).

[11] A. Roe, *Org. Reactions*, p. 193 (1949).

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form the fluoborate. Here it was found necessary to refrigerate the reactants for twenty-four hours to allow the reaction to be complete and the fluoborate to precipitate.

The proper condition for controlling the decomposition of the fluoborate was found by following a suggestion in Roe's[15] review that "carrying out the decomposition at a reduced pressure often helps control the reaction." An arrangement was devised to carry out a vacuum sublimation of the tar resulting from the initial decomposition. This method gave a good separation of a crude product which could be purified in the usual manner.

Although the average yield on the decomposition of a fluoborate is around 65%, Roe noted that if nitro groups were present the decomposition was unruly and gave low yields. It was anticipated that the ortho quinone grouping would give trouble also, so the low yield in the present instance, 0.5 g. of pure 2-fluoro compound from 6.0 g. of fluoborate (8.3%) was not unexpected.

A sample of the 2-fluorophenanthrenequinone has been given to Sloan-Kettering Institute for testing for carcinogenic activity. These results will be reported elsewhere.

EXPERIMENTAL[16]

Phenanthrenequinone II. The preparation of compound II was carried out according to the procedure of Anschutz and Schultz[17] as modified by Oyster and Adkins.[18] Phenanthrene, I, (Eastman Kodak) in 100-g. lots was oxidized by chromic acid and purified by means of the bisulfite addition compound and subsequent crystallization from glacial acetic acid.

2-Nitrophenanthrenequinone, III. The nitration was carried out in 30-g. lots using the method described by Schmidt and Spoun,[12] which is a modification of the method used by Werner.[19] This method yields a mixture of the 2- and 4-nitro isomers which have to be separated by fractional crystallization from ethanol. In as much as the next compound in the synthesis IV cannot be characterized by a melting point, efforts were made to prepare very pure 2-nitro compound. By repeated recrystallizations from glacial acetic acid, 80 g. of III were obtained which melted 265–268°. This compound, 0.5 g., was sublimed twice at 3 mm. in apparatus described below; it melted at 270–272° with partial sublimation. This value differs from values reported in the literature; 257°,[17] 258–260°,[12] 274.8–275.3°.[20]

Anal. Calcd. for $C_{14}H_7O_4N$: C, 66.41; H, 2.79; N, 5.53. Found: C, 66.33; H, 2.85; N, 5.50.

2-Diazonium fluoborate-9,10-phenanthrenequinone. Compound III (10 g.) was reduced according to the method of Schmidt and Spoun[12] except instead of suspending the resulting tin double salt in a liter of water, a mixture of 200 ml. of dioxane and 800 ml. of water was used. After the tin sulfide precipitate was filtered off, the precipitate was washed with four 25-ml. portions of dioxane and these washings added to the solution of the amine salt, IV. Then air was blown through the solution for 2 hr. This solution was cooled to −10° with stirring and 3.5 g. of sodium nitrite in 20 ml. of water was added until a positive test with starch iodide paper was obtained. Urea was not added to destroy excess nitrous acid.

Fluoboric acid was made simultaneously with the diazotization by the addition of 3.5 g. of boric acid to 9 g. of hydrofluoric acid (48%) cooled in an ice-salt bath. The cold fluoboric acid was then poured into the diazonium solution which was below 0°. Stirring was continued for 2 hr. The suspension of diazonium fluoborate was allowed to stand on ice in a refrigerator for 24 hr. The precipitated fluoborate was filtered with suction, washed with ice water and dried in a vacuum desiccator, first over conc. sulfuric acid (sp. gr. 1.84), then over phosphorus pentoxide. Washing with alcohol and ether as recommended by Schiemann and Winkelmüller[21] in the preparation of *p*-fluorobenzoic acid was harmful to the product. The yield of the yellow brown dry solid (VI) was 5 to 6 g. (39 to 47% based on III). The product is hygroscopic and decomposes at 115°.

2-Fluoro-9,10-phenanthrenequinone, (VII). Compound VI (6 g.) was placed in the bottom of a large Pyrex test tube (45 × 150 mm.), fitted with a 2-holed rubber stopper, in one hole of which was a small test tube (15 × 75 mm.) filled with Dry Ice, to serve as a cold finger. In the other hole was a wide delivery tube (dia. 10 mm.) leading to the vacuum system. A safety shield of asbestos covered the beaker used for the oil bath and was cut to allow passage of the large test tube and a thermometer. This prevented any Dry Ice from dropping into the oil bath.

At first a vacuum of 130 mm. was applied by a water pump and the fluoborate decomposed by gentle heating with a free flame.[22] When the reaction was complete an oil pump was attached. At a pressure of 3 mm. the tarry residue in the large test tube was heated gradually using an oil (Crisco) bath. The 2-fluoro compound started to sublime at 135° (oil bath) and at 230° the sublimation was practically complete. The 2-fluoro compound so obtained weighed 2.0 grams. After recrystallization from benzene and resublimation using the same procedure, the yield of VII was 0.5 g. (8.3%) of orange-yellow needles m.p. 246–248°.

Anal. Calcd. for $C_{14}H_7O_2F$: C, 74.30; H, 3.12; F, 8.41. Found: C, 4.50; H, 3.13; F, 8.16.

Phenazine of 2-fluoro-9,10-phenanthrenequinone.[23] A well-ground mixture of 100 mg. of VII and 50 mg. of freshly sublimed *o*-phenylenediamine was heated slowly in a small flask in an oil bath to 110° and kept at this temperature for one hour. The resulting phenazine was recrystallized twice from ethanol, vacuum-sublimed at 2 mm. pressure in the apparatus described above and then recrystallized from ethanol to obtain 32 mg. of white silky needles of phenazine, m.p. 226–228°.

Anal. Calcd. for $C_{20}H_{11}N_2F$:N, 9.39. Found: N, 9.09.

Properties. Compound VII is soluble in conc. sulfuric acid forming a dark green solution from which it may be recovered with unchanged m.p. on dilution with water. It is slightly

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(15) Roe, *Org. Reactions*, p. 210 (1949).

(16) All analyses were made by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Melting points were taken using an aluminum block as described by L. Fieser, *Experiments in Organic Chemistry*, p. 251, Fig. 44.5, 3rd Ed., D. C. Heath and Co., Boston 1955, and are uncorrected.

(17) R. Anschutz and G. Schultz, *Ann.*, **196**, p. 37 (1879).

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(19) A. Werner, *Ber.*, **37**, 3086 (1904).

(20) S. Kato, M. Maezawa, S. Hirano, and S. Ishigaki, *Yûki Gôsei Kagaku Kyôkai Shi*, **15**, 29 (1957); *Chem. Abstr.*, **51**, 10462 (1957).

(21) G. Schiemann and W. Winkelmüller, *Org. Syntheses*, **Coll. Vol. II**, 299 (1943).

(22) Use of a higher vacuum at this point caused sublimation of the 2-fluoro compound simultaneously with the evolution of boron trifluoride.

(23) This derivative was prepared by Arthur A. Gresen—present address, Albert Einstein Medical College.

soluble in ether and moderately soluble in benzene, toluene, ethanol, and dioxane. One ml. of boiling glacial acetic acid dissolves 23 mg. of VII from which solution 20 mg crystallizes on cooling. With 2,4-dinitrophenylhydrazine a bright scarlet product is formed which after repeated (4 times) recrystallizations from acetone melts at 340–345°. The analysis for nitrogen for this product was 2% low in spite of repeated attempts to obtain a pure product.

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3,3'-Sulfonylbis(phenyl Isocyanates)

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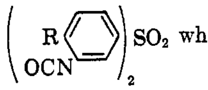
Received August 25, 1961

In recent years diisocyanates have become of considerable industrial importance. With the object of preparing less reactive diisocyanates, the reaction rate of which might be more easily controlled, attention was directed to the diisocyanato derivatives of diaryl sulfones. One such compound, 4,4'-sulfonylbis(phenyl isocyanate), has been described by Heymann and Fieser.[2] The reactivity of this compound has been studied by Bailey, Kirss, and Spaunburgh,[3] who found that its reaction with 2-ethylhexanol, using infrared spectroscopy to follow the reaction, was too rapid to permit calculation of the reaction rate constant.

The diisocyanates prepared for study were 3,3'-diisocyanato diphenyl sulfones, having the general formula



where R = H(I), Cl(II), CH_3(III), and $(CH_3)_3C$(IV)

They were prepared from the parent diaryl sulfones by nitration, reduction to the diamino sulfones using alcoholic stannous chloride, and phosgenation in chlorobenzene solution. The four diisocyanates and the intermediates bis(*tert*-butylphenyl) sulfone, bis(3-nitro-4-*tert*-butylphenyl) sulfone, and bis(3-amino-4-*tert*-butylphenyl) sulfone have not previously been described.

The relative reactivities of the four diisocyanates were semiquantitatively determined by following the reaction with a hindered alcohol, 2-ethylhexanol, in an infrared spectrophotometer using the technique of Bailey and co-workers.[3] Compounds I and II reacted quite rapidly and at almost exactly the same rates. In both cases the reaction was 50% completed in five minutes and was practically completed in thirty minutes. Compounds III and IV reacted relatively much more slowly. The reaction of III was 50% completed in forty minutes and practically completed in six hours. Compound IV, because of the greater steric hindrance of the *tert*-butyl groups, required two and one-half hours for 50% completion and twenty-two hours for practical completion of the reaction.

Comparison of these results with those of Bailey and coworkers[3] would lead to the conclusion that a sulfone group meta to the isocyanate group has less effect on increasing the reactivity of an isocyanate group than a sulfone group para to the isocyanate group, and confirms the observation of these workers that alkyl groups ortho to the isocyanate group exert a strong inhibiting effect due to steric hindrance.

EXPERIMENTAL[4]

Bis(4-chlorophenyl) sulfone. This compound was kindly contributed by the Stauffer Chemical Company and and the Diamond Alkali Company. The material obtained from the latter company contained about 20% water, which was removed by drying at 120°. The compound, m.p. 148–149°, was used for nitration without further purification.

Bis(p-tolyl) sulfone. This sulfone was prepared by a modification of the procedure of Meyer.[5] In a 6-l. three necked flask equipped with heating mantle, stirrer, water trap, and reflux condenser was placed 16 moles (1702 ml.) of toluene. To this was added 8 moles (436 ml.) of 98% sulfuric acid and 22 ml. of water, making the acid concentration 93% to prevent charring. This mixture was heated with stirring at the reflux temperature of toluene over a period of several days until the separation of water had practically ceased. At this point 183 ml. of water had been collected. A calculated amount of phosphorus pentoxide (357 g.) to react with the remainder of water to be removed to complete the reaction was added to the hot solution in portions with vigorous stirring to disperse the solid. The resultant mixture was refluxed for 5 hr. and then poured while hot into a large excess of ice and water.

The crude product was removed by filtration, washed several times with water, once with sufficient 5% sodium carbonate solution to neutralize residual acid, and then twice with water. The washed air-dried product weighed 1637 g., an 83% yield. Two recrystallizations from alcohol, using Darco on the first, gave a white crystalline product melting at 154°, lit.[5] 158°. The melting point can be raised to 160° by further recrystallization from glacial acetic acid or ethyl acetate.

tert-Butylbenzene. This intermediate, b.p. 167–70°, was prepared by the method of Nightingale and co-workers[6] by the reaction of *tert*-butyl chloride, benzene, and anhydrous ferric chloride catalyst.

p-tert-Butylbenzenesulfonyl chloride. This compound was made from *tert*-butylbenzene and chlorosulfonic acid by the method of Huntress and co-workers.[7] The product, m.p. 83–84°, was obtained in 70% yield.

Bis(4-tert-butylphenyl) sulfone. This sulfone was prepared

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(4) Melting points and boiling points are uncorrected.

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(7) (a) E. H. Huntress and F. H. Carten, *J. Am. Chem. Soc.*, **62**, 511 (1940); (b) E. H. Huntress and J. S. Autenrieth, *J. Am. Chem. Soc.*, **63**, 3446 (1941).