one hour and then heated up to 45° for 10 minutes. When the acetone was removed *in vacuo* at room temperature, fine white needles precipitated (1.0 g., 36%). After recrystallization from ligroin the needles had a melting point of 132–133°. A mixed melting point with an authentic sample of trimethyl cyanurate (X) was without depression.

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[CONTRIBUTION FROM THE RADIOISOTOPE SERVICE, VETERANS ADMINISTRATION HOSPITAL, MINNEAPOLIS, AND THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, UNIVERSITY OF MINNESOTA]

Protein Binding of Model Quinone Imides. I. The Synthesis of Some Fluorenoquinone Imides[1]

BY H. R. GUTMANN, J. G. BURTLE AND H. T. NAGASAWA

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The *o*-quinone monoimides, 1,2-fluorenoquinone-2-acetimide and 1,2-fluorenoquinone-2-benzimide, were prepared by lead tetraacetate oxidation of N-(1-hydroxy-2-fluorenyl)-acetamide and of N-(1-hydroxy-2-fluorenyl)-benzamide, respectively. These compounds were desired for a study of their interaction with proteins. The preparation of 4,4'-diphenoquinone-4-*p*-tolylsulfonimide and of 2,7-fluorenoquinone-2-*p*-tolylsulfonimide by lead tetraacetate oxidation of the respective amidophenols was attempted in order to explore the possibility of synthesizing quinone monoimides with conjugation extending through two adjacent aromatic rings. The former compound was obtained in pure form, while the latter was unstable and polymerized extensively upon attempted purification. In contrast, the quinone diimide, 2,7-fluorenoquinone-dibenzenesulfonimide, was prepared readily by lead tetraacetate oxidation of 2,7-bis-(benzenesulfonamido)-fluorene. The oxidation products were characterized by infrared and electronic spectra, by reduction to starting material and/or addition of hydrogen chloride.

The binding of a variety of carcinogenic compounds or of metabolites thereof to tissue proteins is currently considered a causative factor in the induction of neoplasms by chemical agents.[2,3] In the majority of instances the identity of these reactive metabolites remains to be determined. In the case of the carcinogen N-(2-fluorenyl)-acetamide the suggestion has been made that the reactive species which interact with cellular protein are quinone imides or quinone imines.[4] These compounds were thought to arise from the intracellular oxidation of hydroxylated intermediates. The latter compounds have been recognized as metabolites of N-(2-fluorenyl)-acetamide.[5] Recent work has provided experimental evidence that enzymatic oxidation of 2-amino-1-fluorenol yielded in fact a product which required the intermediate formation of the corresponding *o*-quinone imine.[6] For an unequivocal proof of the interaction of *o*-fluorenoquinone imines with proteins as well as for a systematic investigation of the mechanism of this reaction it became necessary to synthesize these compounds in quantities sufficient to carry out these studies.

Preliminary experiments showed that 2-amino-1-fluorenol was oxidized by lead tetraacetate, as indicated by appearance of a red color with maximum absorption at 450 mμ; however, attempts to isolate the oxidation product were unsuccessful. Isolation of the *o*-quinone imides derived from N-(1-hydroxy-2-fluorenyl)-benzamide or N-(1-hydroxy-2-fluorenyl)-acetamide appeared more promising in view of the work of Adams and Stewart.[7] These investigators described the preparation of *o*-quinone imides by oxidation of several *o*-amidophenols with lead tetraacetate and showed that successful oxidation required stabilization of the quinonoid system by substitution *para* to the amido group. The aforementioned amidofluorenols may be looked upon as *o*-amidophenols in which this position is occupied by the phenyl group and which therefore satisfy the above requirement. As expected, the respective *o*-quinone imides were obtained readily as bright-red crystalline solids which proved to be indefinitely stable and which interacted rapidly and irreversibly with crystalline bovine serum albumin.[8] The compounds were quite soluble in a number of organic solvents such as chloroform or dioxane to give bright red solutions; however, their stability in solution at room temperature was limited, as evidenced by brownish discoloration after short periods of standing. Since Adams and Stewart[7] were unable to isolate the oxidation product of 6-acetamido-*m*-cresol while 1,2-fluorenoquinone-2-acetimide proved to be a stable compound, it would appear that the phenyl group lends greater stability to the *o*-quinonoid system than the methyl group. The stability of *o*-fluorenoquinone imides in which the quinonoid structure was confined to one aromatic ring prompted the question whether equally stable oxidation products could be prepared when the conjugation was extended to involve two adjacent phenyl rings as in diphenoquinone dibenzenesulfonimide.[9] Accordingly, the oxidation of 2,7-bis-(benzenesulfonamido)-fluorene and of N-(7-hydroxy-2-fluorenyl)-*p*-tolylsulfonamide was attempted. In the case of the former compound, a stable diimide was obtained which exhibited physical properties closely resembling those of diphenoquinone dibenzenesulfonimide.[9] Oxidation of the latter compound yielded an unstable quinone mono-

(1) Supported by grants from the National Cancer Institute, U. S. Public Health Service (C-2571), and the Minnesota Division of the American Cancer Society.

(2) J. A. Miller and E. C. Miller, *Adv. Cancer Research*, **1**, 340 (1953).

(3) E. C. Miller and J. A. Miller, *J. Natl. Cancer Inst.*, **15**, 1571 (1955).

(4) H. R. Gutmann, J. H. Peters and J. G. Burtle, *J. Biol. Chem.*, **222**, 373 (1956).

(5) J. H. Weisburger, E. K. Weisburger and H. P. Morris, *J. Natl. Cancer Inst.*, **17**, 345 (1956).

(6) H. T. Nagasawa, M. A. Morgan and H. R. Gutmann, *Biochim. et Biophys. Acta*, **28**, 665 (1958).

(7) R. Adams and J. M. Stewart, THIS JOURNAL, **74**, 5876 (1952).

(8) C. C. Irving and H. R. Gutmann, unpublished experiments.

(9) R. Adams and R. R. Holmes, THIS JOURNAL, **74**, 3033 (1952).

imide which tended to polymerize in solution and therefore could not be obtained in a state of ultimate purity. These results suggested that replacement of one of the imido groups of the fluorenoquinone diimide by the carbonyl group increased the lability of the molecule. In addition, it is probable that the methylene group of the fluorenoquinone monoimide contributed to its instability since 4,4′-diphenoquinone-4-*p*-tolylsulfonimide could be prepared and readily purified by crystallization. Because of the reactivity of those quinone monoimides in which conjugation was extended through adjacent aromatic rings, the method of oxidation of 2,7-bis-(benzenesulfonamido)-fluorene or of *o*-amidofluorenols (rapid mixing with lead tetraacetate) gave rise to extensive polymerization when it was applied to the preparation of 2,7-fluorenoquinone-2-*p*-tolylsulfonimide or of 4,4′-diphenoquinone-4-*p*-tolylsulfonimide. Polymerization was minimized in these cases when the concentration of amidophenol in the reaction mixture was kept low by the cautious, dropwise addition of the amidophenol to an efficiently stirred solution of excess oxidant.

The oxidation products in this work were characterized (a) by their electronic and infrared spectra and (b) by chemical reduction to the starting materials or formation of adducts with hydrogen chloride or both. Since the quinone imides did not have definite melting points but decomposed on heating, the identity of different preparations and the estimate of their purity were based on their spectral properties. The structural assignments were made by comparing the infrared spectrum of the starting material with that of the respective oxidation product. The absorption characteristics expected of quinone imides were invariably found in the infrared spectra of the oxidized products. Accompanying the oxidation of the amidophenols to the quinone imides the following changes of the infrared spectrum were noted: The —NH— stretching vibrations in the 3μ region were uniformly absent. The quinone monoimides showed no evidence for phenolic —OH deformations which appeared in the parent amidophenols near 7.10 and 8.3 μ.[10] In the *o*-fluorenoquinone imides the amide II band near 6.40–6.50 μ had disappeared. The carbonyl absorption found near 5.90 μ in the *o*-quinone monoimides was shifted toward longer wave lengths (6.10–6.15 μ) in the extended *p*-quinone monoimides. The carbonyl absorption of quinones is similarly affected depending upon whether or not the quinonoid carbonyls are located in the same ring or in different rings.[11] As a rule, the absorption due to —C=N— stretching vibrations of a given quinone monoimide was as intense or more intense than the carbonyl absorption.

Since the reduction of quinone imides to starting material provides the most unequivocal proof of structure, this was attempted with a variety of reagents which have been described for the reduction of quinone mono- and diimides.[9,12] However, with the exception of 2,7-fluorenoquinone dibenzenesulfonimide, the reduction products required extensive purification and the yields were low. The use of lithium aluminum hydride did not improve the purity or yields appreciably, although this reagent has been reported to give nearly quantitative yields in the reduction of certain quinone mono- and diimides.[13,14] These results indicated that the reduction of the compounds under study was complicated by numerous side reactions since hydrogen chloride adducts were obtained in good yields.

The most satisfactory chemical evidence that the oxidation products of amidofluorenols were *monomeric* quinone monoimides was furnished by the ready formation of hydrogen chloride adducts of the correct elementary composition. The precise location of the chlorine remains undetermined. However, the available evidence clearly indicates that hydrogen chloride adds to quinone mono- and diimides by 1,4- addition with respect to the imido group.[2,12,15] Consequently, the hydrogen chloride adducts of 1,2-fluorenoquinone-2-acetimide and of 1,2-fluorenoquinone-2-benzimide prepared in this work are most probably N-(1-hydroxy-4-chloro-2-fluorenyl)-acetamide and N-(1-hydroxy-4-chloro-2-fluorenyl)-benzamide, respectively. The possibility of 1,2-addition to the imido group by hydrogen chloride was excluded by the fact that the infrared spectra of the adducts showed no evidence of ketonic carbonyl absorption. In the case of the hydrogen chloride adduct of 2,7-fluorenoquinone-2-*p*-tolylsulfonimide, the numerous possibilities for position isomerism did not permit conjecture as to the position of the chlorine in the adduct. The chlorine content, the constant melting point upon extensive purification and the constant R_f values on paper chromatography of repeatedly crystallized samples indicated that the isolated compound was homogeneous and represented one of the possible isomers.

Experimental

All melting points were taken on a Fisher–Johns melting point apparatus and are uncorrected. The infrared spectra were taken with a Beckman IR-4 infrared spectrophotometer and the electronic spectra with a Beckman DR recording spectrophotometer. Owing to the insolubility of the quinone imides in ethanol, methanol or ether, chloroform or ethyl acetate were used as spectral solvents and the cutoff of the electronic spectra was at 320 mμ.

N-(1-Hydroxy-2-fluorenyl)-acetamide (I) was prepared essentially by published methods[16,17] with the following modifications. 1-Fluorenol was purified by chromatography on acid-washed, activated alumina with ethyl acetate as eluent which facilitated the final purification of the material by recrystallization from hot distilled water. In the subsequent nitration of 1-fluorenol the purity of the nitration product was improved when addition of distilled water to the reaction mixture[17] was omitted. The product which precipitated during the reaction proved to be mainly 2-nitro-1-fluorenol. Acetylation of 2-amino-1-fluorenol by the method used by Weisburger and Weisburger[17] gave frequently low-melting material which was difficult to purify. Compound I was obtained consistently in satisfactory yield

(10) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 84.
(11) D. Hadži and N. Sheppard, THIS JOURNAL, **73**, 5460 (1951).
(12) R. Adams and J. H. Looker, *ibid.*, **73**, 1145 (1951).
(13) A. Mustafa and M. Kamel, *ibid.*, **75**, 2939 (1953).
(14) A. Mustafa and M. Kamel, *ibid.*, **76**, 124 (1954).
(15) R. Adams and A. S. Nagarkatti, *ibid.*, **72**, 4601 (1950).
(16) E. K. Weisburger and J. H. Weisburger, *J. Org. Chem.*, **18**, 864 (1953).
(17) E. K. Weisburger and J. H. Weisburger, *ibid.*, **19**, 964 (1954).

and purity when acetylation was carried out by the conventional procedure.[18]

1,2-Fluorenoquinone-2-acetimide (II).—A solution of 50 mg. (0.21 mmole) of I in 35 ml. of nitromethane was added rapidly with stirring to 140 mg. (0.32 mmole) of lead tetraacetate in 6 ml. of dry chloroform. Stirring of the bright-red solution was continued for 10 minutes after which time 3 drops of ethylene glycol was added and stirring continued until the excess lead tetraacetate had been destroyed (negative potassium iodide–starch test). After extraction of the reaction mixture with two 25-ml. portions of distilled water the filtrate was concentrated under reduced pressure to approximately 5 ml. at a temperature not exceeding 35–40°. The solution was then cooled in a bath of Dry Ice and acetone to give 31 mg. of bright-red material, 62% yield. Compound II was recrystallized by dissolving the compound in chloroform, cooling the solution in a bath of Dry Ice and acetone and gradually adding petroleum ether to incipient precipitation of the product. After 10 to 15 minutes the bright-red, crystalline material was collected, washed with petroleum ether and dried for 5 hours at 78° over phosphoric anhydride. The compound started to decompose above 130° and gave a black melt from 200–210°. Prolonged drying at 78° *in vacuo* or drying for short periods at higher temperatures resulted in decomposition; $\lambda_{max}^{CHCl_3}$ 463; 330 mμ (ε 2,550; 8,850).

Anal. Calcd. for $C_{15}H_{11}NO_2 \cdot 0.5H_2O$: C, 73.2; H, 4.91; N, 5.69. Found: C, 74.0; H, 4.71; N, 5.63.

The infrared spectrum of II showed no –NH– stretching vibrations in the 3 μ region. Two strong bands, not present in I, appeared at 5.90 and 6.20 μ. The first was due to the carbonyl absorption and the second presumably to —C=N— stretching vibrations. Disappearance of the amide II band at 6.42 μ and of a prominent phenolic –OH band at 7.50 μ after conversion of I to II was in agreement with the assigned structure of II.

Reduction of II to I.—Attempts to reduce II to I with stannous chloride dihydrate[9] or with lithium aluminum hydride[13,14] were unsuccessful.

Addition of Hydrogen Chloride to II.—Dry hydrogen chloride was passed through a solution of 130 mg. (0.54 mmole) of II in 100 ml. of purified dioxane.[19] The bright-red solution was decolorized instantly. The colorless reaction mixture was concentrated to 10 ml. under reduced pressure and 100 ml. of distilled water was added. The precipitate was collected, washed with distilled water and dried *in vacuo* over calcium chloride to give 130 mg. of adduct, m.p. 208–10°; 87% yield. The mixed melting point with authentic I, m.p. 210–212° dec., was depressed (184–198°). Recrystallization of the compound from dilute ethanol gave colorless needles, m.p. 208–210°.

Anal. Calcd. for $C_{15}H_{12}ClNO_2$: C, 65.8; H, 4.42; Cl, 13.0. Found: C, 65.8; H, 4.45; Cl, 12.8.

N-(1-Hydroxy-2-fluorenyl)-benzamide (III).—To a solution of 250 mg. (1.26 mmoles) of 2-amino-1-fluorenol,[17] m.p. 192–195°, in 15 ml. of pyridine was added with stirring 270 mg. (1.95 mmoles) of freshly distilled benzoyl chloride in 1.25 ml. of pyridine. After 0.5 hour the solution was poured into ice-cold dilute hydrochloric acid. The crude product was purified by solution in warm 5% sodium hydroxide and reprecipitation with concentrated hydrochloric acid to give 325 mg. of material, m.p. 234–236°, after drying in air; 86% yield. Recrystallization of the compound from dilute methanol or dilute methyl Cellosolve gave colorless needles, m.p. 234–236°.

Anal. Calcd. for $C_{26}H_{15}NO_2$: C, 79.7; H, 5.02; N, 4.65. Found: C, 79.7; H, 5.09; N, 4.70.

1,2-Fluorenoquinone-2-benzimide (IV).—A solution of 50 mg. (0.17 mmole) of III in 40 ml. of nitromethane was added rapidly with stirring to 233 mg. (0.50 mmole) of lead tetraacetate in 5 ml. of dry chloroform. After 10 minutes 3 drops of ethylene glycol was added and stirring continued until the excess oxidant had been destroyed. The mixture was filtered and the filtrate cooled in Dry Ice. The precipitate was collected, washed with petroleum ether and dried in air to give 20 mg. of red, crystalline material; 39% yield. The compound decomposed gradually above 200° In later experiments it was found more convenient to extract the reaction mixture twice with distilled water and to concentrate the organic phase under reduced pressure to incipient precipitation of the quinone imide as described for II. This method also improved the yields (45–67%). It was also observed that nitromethane could be replaced by nitroethane or by 1- or 2-nitropropane as solvent for III; $\lambda_{max}^{CHCl_3}$ 465; 338 mμ (ε 2,630; 9,110).

Anal. Calcd. for $C_{20}H_{13}NO_2$: C, 80.2; H, 4.39; mol. wt., 299. Found: C, 79.8; H, 4.47 mol. wt. (cryoscopic, benzene), 315.

The infrared spectrum of IV showed no —NH— stretching vibrations in the 3 μ region and a strong carbonyl band associated with the quinone appeared at 5.95 μ. A prominent band at 6.20 μ was probably due to —C=N— stretching vibrations. The amide II band, which was located in III at 6.48 μ, was absent in IV.

Reduction of IV to III.—Twenty-seven milligrams (0.09 mmole) of IV was intimately mixed with 192 mg. (0.85 mmole) of stannous chloride dihydrate. After addition of 5 ml. of glacial acetic acid the mixture was boiled for 2 minutes, cooled and diluted with 10 ml. of distilled water. The precipitate was collected by centrifugation and recrystallized three times from 95% ethanol to yield 3.4 mg. of III, m.p. 233–235°, 12% yield. A mixed melting point with an authentic sample of III, m.p. 234–236°, was not depressed.

Addition of Hydrogen Chloride to IV.—Dry hydrogen chloride was passed through a solution of 71 mg. (0.24 mmole) of IV in 50 ml. of purified dioxane.[19] The bright-red reaction mixture was decolorized instantly. The colorless solution was taken to dryness under reduced pressure, the residue dissolved in 7 ml. of dioxane and the adduct precipitated by the addition of 70 ml. of distilled water. The precipitate was collected, washed with distilled water, dried over calcium chloride and recrystallized from benzene to yield 54 mg. of crystalline material, m.p. 245–247°, 67% yield. For analysis, the compound was crystallized three times from benzene to give colorless needles, m.p. 245–247°. Less pure material was obtained when hydrogen chloride was passed directly into the reaction flask immediately following the oxidation of III, *i.e.*, when the isolation of IV was omitted.

Anal. Calcd. for $C_{20}H_{14}ClNO_2$: C, 71.5; H, 4.20; Cl, 10.6. Found: C, 71.7; H, 4.20; Cl, 10.7.

2,7-Bis-(benzenesulfonamido)-fluorene (V).—To a stirred solution of 16.2 g. (0.06 mole) of 2,7-diaminofluorene hydrochloride[20] in 175 ml. of pyridine at 100° was added dropwise 22.7 g. (0.13 mole) of benzenesulfonyl chloride. After the addition was completed, heating and stirring were continued for 3.5 hours. The mixture was then poured into a large volume of distilled water which caused separation of an oil. The oil solidified when the mixture was acidified with concentrated hydrochloric acid and heated with stirring. The solid was collected, washed with distilled water and dried in air. There was obtained 24.5 g. of material melting at 218–220° dec., 85% yield. For analysis, the product was recrystallized twice from dilute methyl Cellosolve yielding needles, m.p. 219–221° dec.

Anal. Calcd. for $C_{25}H_{18}N_2O_4S_2$: C, 63.0; H, 4.23; N, 5.88. Found: C, 63.0; H, 4.25; N, 6.06.

2,7-Fluorenoquinone Dibenzenesulfonimide (VI).—One gram (0.21 mmole) of V and 1.02 g. (0.23 mmole) of lead tetraacetate were suspended in 20 ml. of glacial acetic acid and 30 ml. of petroleum ether (b.p. 65–67°) and the mixture was stirred at room temperature for 13 hours. The purplish-red precipitate was collected and washed by suspending it in a mixture of 10 ml. of glacial acetic acid, 20 ml. of petroleum ether (b.p. 65–70°) and 2 ml. of ethylene glycol and stirring for one hour followed by an additional wash in 25 ml. of distilled water. The compound was then collected and dried *in vacuo* over calcium chloride to give 0.94 g. of crystalline material which decomposed above 200°. The compound was recrystallized by dissolving 150 mg. in 40 ml. of warm benzene and filtering the solution rapidly; 10 ml. of petroleum ether was added to the filtrate and the mixture was kept at 4° for several hours. The dark-red precipitate was collected and dried *in vacuo* over phosphoric anhydride at 78°, λ_{max}^{EtOAc} 478 mμ (ε 72,400).

(18) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 164.

(19) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 285.

(20) S. Schulman, *J. Org. Chem.*, **14**, 382 (1949).

Anal. Calcd. for $C_{25}H_{18}N_2O_4S_2$: C, 63.3; H, 3.83; N, 5.90. Found: C, 63.7; H, 3.95; N, 5.83.

The corresponding diphenoquinone dibenzenesulfonimide, prepared according to Adams and Holmes,[9] had λ_{max}^{EtOAc} 475 mμ (ε 78,200). The infrared spectrum of VI showed no —NH— stretching vibrations in the 3 μ region and a strong band associated with —C=N— stretching vibrations appeared at 6.65 μ. A strong band at 6.69 μ due to the —C=N— grouping also has been reported for diphenoquinone dibenzenesulfonimide.[9] A band at 6.2–6.3 μ probably due to —C=C— stretching vibrations and found in fluorene compounds, which was present in V, was not observed in VI.

Reduction of VI to V. (a) **With Stannous Chloride.**—One hundred milligrams (0.21 mmole) of VI was mixed with 500 mg. (2.2 mmoles) of stannous chloride dihydrate and 6 ml. of glacial acetic acid. The mixture was decolorized instantly upon boiling. The white precipitate was collected, washed with distilled water and dried for 12 hours *in vacuo* at 65°. There was obtained 66 mg. of V, m.p. 218–220°, 66% yield. A mixed melting point with an authentic sample of V, m.p. 219–221°, was not depressed.

(b) **With Lithium Aluminum Hydride.**—These reductions were carried out under conditions similar to those employed by Mustafa and Kamel.[13,14] Compound VI (190 mg., 0.40 mmole) in 80 ml. of purified dioxane[19] was added dropwise with stirring to 2.0 g. of lithium aluminum hydride in 100 ml. of diethyl ether. The mixture was heated under reflux for 3 hours and allowed to stand overnight. Excess lithium aluminum hydride was then decomposed with aqueous ammonium chloride. The precipitate was collected, washed with diethyl ether and hot acetone and the washings were added to the filtrate. No reduction product could be isolated from the filtrate. The precipitate was triturated with 50-ml. portions of dilute hydrochloric acid, collected, washed with distilled water and recrystallized from dilute methyl Cellosolve (activated charcoal added) to give impure V. The purity of this material was not improved by one further recrystallization. The compound was therefore purified by chromatography on acid-washed, activated alumina using ethyl acetate as eluent and then recrystallized from dilute ethanol to give 26 mg. of V, m.p. 218–220°, 14% yield. The mixed melting point with authentic V was not depressed. When the reaction time was shortened to 2 hours and the reaction mixture worked up immediately, V was obtained in a state of purity such that one crystallization from dilute methyl Cellosolve gave pure material in yields up to 35%.

N-(7-Hydroxy-2-fluorenyl)-*p*-tolylsulfonamide (VII).—A solution of 500 mg. (2.24 mmoles) of the hydrochloride of 2-amino-7-fluorenol[21] and 410 mg. (2.14 mmoles) of *p*-tolylsulfonyl chloride in 15 ml. of pyridine was heated under reflux for 1 hour. The reaction mixture was then poured into cold dilute hydrochloric acid to give an oil which solidified upon boiling. The solid was collected, washed with distilled water and recrystallized from dilute methyl Cellosolve to give 440 mg. of short, colorless needles, m.p. 192–193°, 56% yield. For analysis, the compound was twice recrystallized from dilute methyl Cellosolve (Norit A added) and dried *in vacuo* over phosphoric anhydride, m.p. 192–193°. In larger runs, where the yields approached 70%, more extensive purification of the crude product by chromatography on acid-washed, activated alumina with ethyl acetate as eluent was required.

Anal. Calcd. for $C_{20}H_{17}NO_3S$: C, 68.4; H, 4.88; N, 3.99. Found: C, 68.5; H, 4.92; N, 4.07.

2,7-Fluorenoquinone-2-*p*-tolylsulfonimide (VIII).—A solution of 160 mg. (0.44 mmole) of VII in 12 ml. of 2-nitropropane was added dropwise with stirring to 350 mg. (0.77 mmole) of lead tetraacetate in 25 ml. of dry chloroform. After 10 minutes 3 drops of ethylene glycol was added to destroy the excess lead tetraacetate (negative test with potassium iodide–starch) and stirring was continued for an additional 10 minutes after which time the dark-red reaction mixture was extracted with 25 ml. of distilled water. The organic phase was then cooled in a bath of Dry Ice and acetone and 125 ml. of petroleum ether added gradually. The purplish-red solid which precipitated during 0.5 hour was collected, washed with petroleum ether and dried in air to yield 105 mg. of material which darkened above 200° but did not melt up to 300°, λ_{max} 438 mμ ($E_{1cm.}^{1\%}$ 1,000). In another run, using only chloroform as solvent, the reaction mixture was percolated through a 1.7 × 24 cm. cellulose (Whatman cellulose powder) column. The clear eluate was concentrated under reduced pressure and the product precipitated by addition of petroleum ether. This procedure gave a slightly purer product, λ_{max} 438 mμ ($E_{1cm.}^{1\%}$ 1,250). The infrared spectrum of VIII showed no —NH— stretching vibrations in the 3 μ region. A strong band which appeared in VIII at 6.1 μ, but was not observed in VII, was assigned the —C=O group of the quinone imide. A prominent band located in VIII at 6.55 μ, but not found in VII, was presumably associated with the —C=N— grouping of the quinone imide. Strong bands at 7.50 and 8.15 μ noted in VII and presumably due to the phenolic —OH group of VII were not observed in VIII.

Attempts to purify the crude quinone imide by the procedure used for the *o*-fluorenoquinone monoimides (solution in chloroform and reprecipitation with petroleum ether) resulted in extensive polymerization as evidenced by partial insolubility of the material in chloroform or other organic solvents and a progressive bathochromic shift of the absorption maximum.

Addition of Hydrogen Chloride to VIII.—Dry hydrogen chloride was passed through a solution of 85 mg. of VIII in 60 ml. of purified dioxane[19] whereupon the bright-red color of the reaction mixture was discharged instantly. The colorless solution was concentrated under reduced pressure to 5 ml. and 40 ml. of distilled water was added. The precipitate was collected, washed with distilled water, dried over calcium chloride and the dry material chromatographed on acid-washed, activated alumina using ethyl acetate as eluent. The semi-solid obtained after solvent evaporation was crystallized from dilute ethanol with thorough chilling to yield 39 mg. of short needles, m.p. 151–153°, 41% yield. Additional recrystallization from dilute ethanol did not change the melting point.

Anal. Calcd. for $C_{20}H_{16}ClNO_3$: Cl, 9.18. Found: Cl, 8.79.

The once and twice crystallized materials were subjected simultaneously to ascending chromatography on Whatman #1 paper using the lower phase of 1-butanol–6% ammonium hydroxide (1:1) as the solvent. Only a single, blue spot (R_f 0.76) was obtained for each compound with the Folin spray reagent.[22,23]

Reduction of VIII to VII.—Crude VIII (138 mg.) was partially dissolved in 150 ml. of hot, anhydrous benzene and the dark-red mixture added dropwise with stirring to 600 mg. of lithium aluminum hydride in 600 ml. of anhydrous ether. After heating under reflux for 2 hours, the excess lithium aluminum hydride was decomposed by addition of saturated ammonium chloride solution and the mixture poured into 50 ml. of *N* sulfuric acid. The aqueous layer was extracted with 100 ml. of ethyl acetate in which VII was soluble. The ethyl acetate extract was combined with the organic phase of the reaction mixture and the solution taken to dryness under reduced pressure. The residue was crystallized twice from 95% ethanol (activated charcoal added) to yield 12 mg. of VII, m.p. 186–188°, 9% yield. The mixed melting point with an authentic sample of VII, m.p. 191–192°, was 190°. One additional crystallization from dilute acetic acid afforded material melting at 189–191°.

4'-Hydroxy-4-*p*-tolylsulfonamidobiphenyl (IX).—A solution of 9.63 g. (0.044 mole) of the hydrochloride of 4'-hydroxy-4-aminobiphenyl[24] and of 8.20 g. (0.044 mole) of *p*-tolylsulfonyl chloride in 100 ml. of pyridine was heated under reflux for 2 hours, allowed to stand at room temperature overnight and then poured into a large volume of cold dilute hydrochloric acid. After the solid had been coagulated by brief heating, the precipitate was collected, washed with water and dried over calcium chloride. The dry material was purified by solution in 5% sodium hydroxide (Norit A added) and reprecipitation with concentrated hydrochloric acid. The precipitate was collected, washed with distilled water and dried *in vacuo* at 65° to yield 12.3 g. of

(21) J. H. Weisburger and E. K. Weisburger, *J. Chem. Soc.*, 758 (1954).

(22) H. G. Bray and W. V. Thorpe, "Methods of Biochemical Analysis," D. Glick, ed., Vol. I, Interscience Publishers, Inc., New York, N. Y., 1954, p. 45.

(23) J. H. Weisburger, E. K. Weisburger, H. P. Morris and H. A. Sober, *J. Natl. Cancer Inst.*, **17**, 363 (1956).

(24) E. Täuber, *Ber.*, **27**, 2627 (1894).

material, m.p. 172–174°, 83% yield. Recrystallization from dilute ethanol or dilute methyl Cellosolve gave glistening plates melting at 173–174°.

Anal. Calcd. for $C_{19}H_{17}NO_3S$: C, 67.2; H, 5.05; N, 4.13. Found: C, 66.9; H, 4.89; N, 4.22.

4,4′-Diphenoquinone-4-*p*-tolylsulfonimide (X).—A solution of 150 mg. (0.44 mmole) of IX in 10 ml. of 2-nitropropane was added dropwise with stirring to 252 mg. (0.57 mmole) of lead tetraacetate in 50 ml. of dry chloroform. After stirring for one hour the dark-red mixture was filtered and the filtrate added slowly to 250 ml. of petroleum ether. After cooling in an ice-bath for several hours, the reddish-brown precipitate was collected, washed with petroleum ether and redissolved in 35 ml. of chloroform. The solution was filtered, the filtrate cooled in an ice-bath and the quinone monoimide precipitated by the gradual addition of petroleum ether. After standing at 4° for several hours, 50 mg. of brown, crystalline material, which melted from 195–200° with loss of color above 175°, was obtained. The compound could also be purified by recrystallization from benzene–petroleum ether; $\lambda_{max}^{CHCl_3}$ 433 mμ (ε 67,000).

Anal. Calcd. for $C_{19}H_{15}NO_3S$: C, 67.6; H, 4.48. Found: C, 67.2; H, 4.48.

The infrared spectrum of X showed no —NH— stretching vibrations in the 3 μ region. Strong bands at 6.15 and 6.50 μ, which were not present in IX, were assigned to the carbonyl absorption and the —C=N— grouping of the quinone imide, respectively. Strong bands observed in IX at 7.45 and 8.15 μ and presumably associated with the phenolic —OH group of IX were not noted in X.

Reduction of X to IX.—A solution of 109 mg. (0.32 mmole) of X in 130 ml. of anhydrous benzene was added dropwise with stirring to 350 mg. of lithium aluminum hydride in 30 ml. of anhydrous diethyl ether. The mixture was then heated under reflux for 2.75 hours after which time excess lithium aluminum hydride was decomposed with a saturated solution of ammonium chloride. The organic phase was taken to dryness under reduced pressure and the residual solid recrystallized from dilute ethanol to yield 19 mg. of IX, m.p. 170°, 18% yield. The mixed melting point with an authentic sample of IX, m.p. 172–174°, was 171–173°.

Acknowledgment.—The authors are indebted to Dr. S. W. Fenton for assistance in the interpretation of the infrared spectra and for valuable suggestions.

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[CONTRIBUTION FROM THE GEORGE M. MOFFETT RESEARCH LABORATORIES, CORN PRODUCTS REFINING CO., AND THE RESEARCH AND DEVELOPMENT LABORATORIES, UNIVERSAL OIL PRODUCTS CO.]

The Catalyzed Condensation of Aromatic Compounds with Carbohydrates. 1-Deoxy-1,1-bis-(3,4-dimethylphenyl)-D-glucitol[1]

BY J. HEEREMA, G. N. BOLLENBACK AND C. B. LINN

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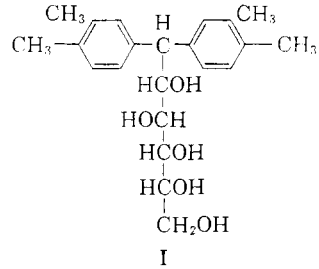
The product of the reaction of starch with *o*-xylene in liquid hydrogen fluoride, 1-deoxy-1,1-bis-(3,4-dimethylphenyl)-D-glucitol, was examined with regard to physical and chemical properties. In addition to behaving in a manner normal for polyhydroxy compounds, this glucitol (1) forms stable gels with bases and certain hydrocarbons, (2) forms a monoanhydro compound by spontaneous decomposition of a mono-*p*-toluenesulfonate, (3) forms a second monoanhydro compound by reaction of its 2,3,4,5-tetrabenzoate 6-*p*-toluenesulfonate with methanolic sodium hydroxide, and (4) dehydrates in the presence of acids to form the second monoanhydro compound, a dianhydro compound and 3,3′,4,4′-tetramethylstilbene.

A practical method has been described recently for the synthesis of 1,1-diaryl-1-deoxy-D-glucitols in which carbohydrates such as starch, cellulose and glucose are condensed with aromatic compounds in the presence of liquid hydrogen fluoride.[2] With this development it became of interest to study some of the properties and reactions of these glucitols. Most of the work reported here describes the compound 1-deoxy-1,1-bis-(3,4-dimethylphenyl)-D-glucitol (I), which was isolated from the reaction of starch with *o*-xylene in liquid hydrogen fluoride. Occasional reference is made to 1-deoxy-1,1-bis-(4-methylphenyl)-D-glucitol.

Two oxidation methods were used to help establish the structure of I. Permanganate oxidation gave excellent yields of the known,[3] crystalline 3,3′,4,4′-tetramethylbenzophenone (II), which was further characterized as the known, crystalline oxime. Isolation of this ketone showed that in the original glucitol both aryl groups are attached to the same carbon atom. Periodate oxidation resulted in the consumption of four moles of periodate with formation of three moles of formic acid and one mole of formaldehyde per mole of glucitol. Such results show the presence of five vicinal hydroxyl groups, one of which is primary. Further evidence on these points was obtained by analysis for hydroxyl groups and the formation of a trityl ether.



I

Periodate oxidations of I originally were made in aqueous ethanol. In such a solvent the appearance of an iodine color indicated overoxidation had occurred.[4] Analytically, periodate consumption was very close to theoretical (four moles per mole of I). However, when attempts were made to isolate the expected diarylacetaldehyde, Ar_2CHCHO (III), only the crystalline ketone, Ar_2CO (II), could be found. Compound III was eventually isolated as a sirup by oxidation of either a very dilute aqueous solution (0.05%) or an aqueous

(1) Presented in part before the Division of Petroleum Chemistry at the 132nd Meeting of the American Chemical Society, New York, N. Y., September, 1957.

(2) (a) C. B. Linn, Abstr. 132nd Meeting of the American Chemical Society, New York, p. 5R (1957); (b) C. B. Linn, U. S. Patent 2,798,098, July 2, 1957.

(3) A. Bistrzycki and E. Reintke, *Ber.*, **38**, 839 (1905).

(4) J. M. Bobbitt, *Adv. in Carbohydrate Chem.*, **11**, 1 (1956).