The Lead Tetraacetate Oxidation of 1- and 2-Benzenesulfonamido- and Benzamidonaphthalenes[1]

HENRY J. RICHTER AND ROBERT L. DRESSLER

Department of Chemistry, University of Colorado, Boulder, Colorado

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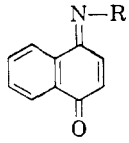
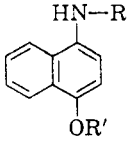
A study of the lead tetraacetate oxidation of 5-benzenesulfonamidoacenaphthene now in progress, produced a number of unknown products.[2]

The oxidation under similar conditions, of selected amides of 1- and 2-naphthylamine where many reference compounds are known,[3] was studied since the results may provide information helpful in elucidating the structures of the products obtained from the amide of 5-aminoacenaphthene. This study has led to a simple method for preparing some 1,4-naphthoquinonemonoimides and 2-substituted 1,4-naphthoquinones.

1-Benzenesulfonamidonaphthalene was oxidized by lead tetraacetate to produce 1-benzenesulfonimido-1,4-naphthoquinone (I). This substance exhibited physical properties similar to the compound previously prepared by Adams and co-workers[4] by the oxidation of 4-benzenesulfonamido-1-naphthol (II). Catalytic reduction of I gave the substituted naphthol II.



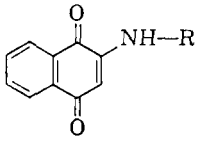
I. R = $SO_2C_6H_5$
III. R = $SO_2C_6H_4$-4-$NHCOCH_3$



II. R = $SO_2C_6H_5$; R′ = H
IV. R = $SO_2C_6H_4$-4-$NHCOCH_3$, R′ = H
V. R = COC_6H_5, R′ = $COCH_3$
VI. R = COC_6H_5; R′ = H

The oxidation of 1-benzamidonaphthalene was found to give somewhat different results. Treatment of this compound with lead tetraacetate gave a white fibrous substance, m.p. 194–195°, for which the infrared spectrum and elemental analysis required the introduction of one acetoxyl group into the original benzamide giving a benzamidonaphthol acetate. Since oxidation had been shown to occur at the 4-position in the sulfonamide I, the oxidation product was compared with a sample of 4-benzamido-1-naphthol acetate (V) prepared from 4-amino-1-naphthol. The samples were identical in all respects. Acid hydrolysis of V gave 4-benzamido-1-napthol (VI), which has been characterized by Witt and Dedichen.[5]

A similar oxidation of 2-benzenesulfonamidonaphthalene failed to give a quinonemonoimide. Yellow needles, m.p. 254–256°, were obtained which showed an absorption at 3220 cm.$^{-1}$ indicating that the N—H group was still intact.[6a] Chemical analysis required the introduction of two atoms of oxygen and chromic acid oxidation of the yellow product gave phthalic acid as shown by a positive fluorescein test.[7a] These facts are accommodated by oxidation at the 1- and 4-positions to give 2-benzenesulfonamido-1,4-naphthoquinone (VII).



VII. R = $SO_2C_6H_5$
VIII. R = H
IX. R = COC_6H_5
X. R = $SO_2C_6H_4$-4-$NHCOCH_3$

Further evidence for structure VII was obtained by acid hydrolysis which formed 2-amino-1,4-naphthoquinone (VIII), previously prepared by F. Kehrmann *via* a five-step synthesis starting from 1-naphthol.[8]

The oxidation of 2-benzamidonaphthalene proceeded in an analogous manner to give IX, which was hydrolyzed to VIII.

The oxidation of 1-(4-acetamidobenzenesulfonamido)naphthalene by lead tetraacetate gave 1-(4-acetamidobenzenesulfonimido)-1,4-naphthoquinone (III), which was reduced to 4-(4-acetamidobenzenesulfonamido)-1-naphthol (IV) identical with the product prepared from 4-amino-1-naphthol and 4-acetamidobenzenesulfonyl chloride. An attempt to obtain the substituted sulfanilamides, 1-(4-aminobenzenesulfonimido)-1,4-naphthoquinone and 2-(4-aminobenzenesulfonamido)-1,4-naphthoquinone through acid hydrolysis of III and X resulted in destruction of the quinoid system and failed to yield an identifiable product.

Experimental[9]

1-Benzenesulfonimido-1,4-naphthoquinone (I).—A suspension of 14.2 g. (0.05 mole) of 1-benzenesulfonamidonaphthalene in 100 ml. of glacial acetic acid was stirred while 46.5 g. of lead tetraacetate was added in small portions over a period of 45 min. The temperature of the mixture was kept under 35° by occasional cooling. After 90 min. 3 ml. of ethylene glycol was added, and stirring was continued for 10 min. The mixture was cooled to 15° in an ice bath. The yellow-green product (6.3 g., 42%)

(1) This work was supported by Research Grant CY-2997 from the National Cancer Institute, National Institute of Health, U. S. Public Health Service.

(2) This is to be the subject of a subsequent paper.

(3) For a review of quinonemonoimides see R. Adams and W. Reifschneider, *Bull. soc. chim. France*, 23 (1958).

(4) R. Adams and R. Wankel, *J. Am. Chem. Soc.*, **73**, 131 (1951); R. Adams and L. Whitaker, *ibid.*, **78**, 658 (1956).

(5) O. N. Witt and J. Dedichen, *Ber.*, **29**, 2954 (1896).

(6) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., John Wiley & Sons, Inc., New York, N. Y., 1958, (a) p. 205, (b) p. 179, (c) p. 136, (d) p. 150.

(7) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., (a) p. 224, (b) p. 238.

(8) F. Kehrmann, *Ber.*, **27**, 3337 (1894).

(9) All melting points are uncorrected.

was collected, washed first with 10 ml. of cold glacial acetic acid and then thoroughly with water. Crystallization from ethanol gave orange plates, m.p. 154–156° (lit.,[4] 152–154°).

4-Benzenesulfonamido-1-naphthol (II).—Two grams (0.0067 mole) of 1-benzenesulfonimido-1,4-naphthoquinone (I) suspended in 100 ml. of absolute ethanol was reduced catalytically with 0.10 g. of 10% palladium on charcoal and hydrogen at 37 p.s.i. Evaporation of the solvent gave 2.0 g. (99%) of crude tan product. Crystallization from glacial acetic acid gave white crystals, m.p. 201–203° (lit.,[4] 193–194°). A mixed melting point determination with an authentic sample showed no depression and the infrared spectra of the two samples were identical.

4-Benzamido-1-naphthol Acetate (V).—A stirred suspension of 6.17 g. (0.025 mole) of 1-benzamidonaphthalene in 100 ml. of dry ether was treated with 23.25 g. of lead tetraacetate. The mixture was stirred at ambient temperature for 4 hr. giving a dark brown solution in which a white solid was suspended. After adding 2 ml. of ethylene glycol, the white solid was collected, dissolved in 50 ml. of chloroform, and the solution washed with several portions of water. Evaporation of the chloroform gave 5.2 g. (68%) of crude product. Crystallization from benzene gave a mass of interlocking white fibrous solid, m.p. 194–194.5°; ν_{max} 3240 cm.$^{-1}$ (N—H^{6a}), 1750 cm.$^{-1}$ (acetate C=O^{6b}), 1640 cm.$^{-1}$ (amide C=O^{6a}).

Anal. Calcd. for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.38; H, 5.07; N, 4.41.

A mixture of 4-benzamido-1-naphthol (VI) (0.35 g., 0.0013 mole), 1g. of sodium acetate, and 3 ml. of acetic anhydride was heated to the boiling point and then cooled. Trituration of the resulting mixture with water left 0.28 g. (69%) of white crude product. A mixed melting point determination with the substance prepared from 1-benzamidonaphthalene showed no depression and the infrared spectra were identical.

One-half gram of the acetate V was heated on the steam bath for 24 hr. with 10 ml. of concentrated hydrochloric acid. On cooling 0.35 g. (81.3%) of crude 4-benzamido-1-naphthol (VI) was obtained. Crystallization from ethanol gave white needles, m.p. 229–231° (lit.,[5] 228–229°) which were identical with the product obtained on treating 4-amino-1-naphthol with benzoyl chloride in the presence of pyridine.

2-Benzenesulfonamido-1,4-naphthoquinone (VII).—2-Benzenesulfonamidonaphthalene (14.15 g., 0.05 mole) was suspended in 45 ml. of glacial acetic acid, and 70.0 g. of lead tetraacetate was added in *ca.* 3-g. portions over a period of 15 min. with continuous stirring. The temperature of the mixture was kept below 30° by occassional cooling in an ice–water bath. The mixture was stirred for 75 min. during which time the product precipitated. One milliliter of ethylene glycol was added and stirring was continued for 5 min. The mixture was cooled at 15° for 45 min., and the crude yellow product (11.4 g., 73%) was collected, washed with cold glacial acetic acid followed by water. Crystallization from acetone with decolorizing carbon gave yellow needles, m.p. 254–256°; ν_{max} 3220 cm.$^{-1}$ (N—H^{6a}), 1670 cm.$^{-1}$ and 1650 cm.$^{-1}$ (quinone C=O^{6d}).

Anal. Calcd. for $C_{16}H_{11}NO_4S$: C, 61.33; H, 3.54; N, 4.47. Found: C, 61.33; H, 3.46; N, 4.48.

Acid hydrolysis of VII according to the procedure described by Fieser[7b] for the acetamido analog gave 2-amino-1,4-naphthoquinone (VIII) in 94.5% yield. A sample crystallized from ethanol, m.p. 206–208° (lit.,[7b] 206°), showed no depression of melting point when mixed with an authentic sample.

2-Benzamido-1,4-naphthoquinone (IX).—To a suspension of 6.17 g. (0.025 mole) of 2-benzamidonaphthalene in 50 ml. of glacial acetic acid was added 35 g. of lead tetraacetate while the mixture was stirred at ambient temperature. After 2 hr. 5 ml. of ethylene glycol was added to the orange solution and stirring was continued for 5 min. The mixture was poured into cold water giving a viscous red tar which subsequently turned green on standing in water. The tar was dissolved in hot ethanol, treated with decolorizing carbon, and on cooling gave 2.72 g. (39%) of yellow-green plates, m.p. 137–138°.

Anal. Calcd. for $C_{17}H_{11}NO_3$: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.71; H, 4.15; N, 5.01.

Acid hydrolysis by the procedure referred to for VII gave 2-amino-1,4-naphthoquinone (VIII) in 97.5% yield.

1-(4-Acetamidobenzenesulfonimido)-1,4-naphthoquinone (III).—To a stirred suspension of 3.49 g. (0.01 mole) of 1-(4-acetamidobenzenesulfonamido)naphthalene[10] in 25 ml. of glacial acetic acid was added 8.95 g. of lead tetraacetate. After 70 min. the excess lead tetraacetate was decomposed with 0.5 ml. of ethylene glycol. The mixture was cooled thoroughly and the crude yellow product (1.61 g., 45%) was collected, washed once with cold glacial acetic acid, and then with water. Crystallization from dry chloroform gave yellow needles, m.p. 207–208°; ν_{max} 3300 cm.$^{-1}$ (N—H^{6a}), 1660 cm.$^{-1}$ (doubly conjugated C=O^{6c}), 1525 cm.$^{-1}$ (doubly conjugated C=N^{11}). Attempts to crystallize the crude product from ethanol, acetone, benzene, or acetic acid led to decomposition.

Anal. Calcd. for $C_{18}H_{14}N_2O_4S$: C, 61.00; H, 3.98; N, 7.90. Found: C, 61.15; H, 4.03; N, 7.89.

An attempt to obtain 1-(4-aminobenzenesulfonimido)-1,4-naphthoquinone by hydrolysis of the acetamido group using 10% hydrochloric acid under reflux resulted in the formation of a red-brown solid, m.p. 150–157°, which could not be crystallized and was not characterized. The infrared spectrum indicated that the quinoid structure had been destroyed.

4-(4-Acetamidobenzenesulfonamido)-1-naphthol (IV).—One-half gram (0.0014 mole) of 1-(4-acetamidobenzenesulfonamido)-1,4-naphthoquinone (III) and 0.4 g. of zinc dust were suspended in 20 ml. of glacial acetic acid. The mixture was heated to 80° and stirred until the orange coloration of the quinonemonoimide was discharged (*ca.* 1 hr.). The white product which separated during the reaction was dissolved by adding additional acetic acid (75 ml. total), and the excess zinc dust was filtered from the mixture. On cooling 0.47 g. (96%) of the white crystalline product was obtained. Recrystallization from ethanol plus several drops of acetic acid gave white plates, m.p. 235–236°.

Anal. Calcd. for $C_{18}H_{16}N_2O_4S$: C, 60.66; H, 4.53; N, 7.86. Found: C, 60.46; H, 4.62; N, 7.85.

The product was identical with that obtained in 74% yield on treating 4-amino-1-naphthol with 4-acetamidobenzenesulfonyl chloride in the presence of pyridine. A mixed melting point determination showed no depression and the infrared spectra were superimposable.

2-(4-Acetamidobenzenesulfonamido)-1,4-naphthoquinone (X).—2-(4-Acetamidobenzenesulfonamido)naphthalene[10] (3.4 g., 0.01 mole) was suspended with stirring in 35 ml. of glacial acetic acid, and 13.5 g. of lead tetraacetate was added. After 20 min. the yellow-orange product started separating, and after 30 min., 1 ml. of ethylene glycol was added and stirring continued for an additional 5 min. The crude product (2.6 g., 70%) was collected and washed thoroughly with water. Attempts to crystallize this material from ethanol, acetone, acetic acid, or chloroform led to decomposition. Crystallization was achieved by suspending the crude product in boiling benzene and adding dimethylformamide dropwise until all solid had dissolved. Upon cooling, the pure substance was obtained as yellow microcrystals, m.p. 256–257°; ν_{max} 3300 cm.$^{-1}$ (N—H^{6a}), 1670 cm.$^{-1}$ and 1640 cm.$^{-1}$ (quinone C=O^{6d}), 1530 cm.$^{-1}$ (amide C=O^{6a}).

Anal. Calcd. for $C_{18}H_{14}N_2O_5S$: C, 58.37; H, 3.81; N, 7.56. Found: C, 58.32; H, 3.69; N, 7.42.

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(11) R. Adams and E. L. De Young, *J. Am. Chem. Soc.*, **79**, 705 (1957).

Attempts to obtain 2-(4-aminobenzenesulfonamido)-1,4-naphthoquinone by hydrolysis of X using (a) refluxing concentrated hydrochloric acid, or (b) refluxing 50% sulfuric acid, gave unchanged starting material as the only isolable material.

When the product X was subjected to acid hydrolysis as described for the quinones VII and IX, 2-amino-1,4-naphthoquinone (VIII) was obtained in 90% yield.

The Formation of 1,5,7,11-Tetrathiaspiro[5.5]-undecane in the Reaction of Cyclic Trimethylene Trithiocarbonate with 2,2′-Iminodiethanol[1]

THOMAS P. JOHNSTON, CARL R. STRINGFELLOW, JR., AND ANNE GALLAGHER

Kettering-Meyer Laboratory, Southern Research Institute, Birmingham 5, Alabama

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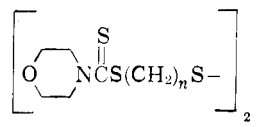
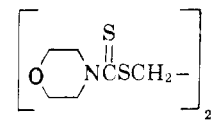
Ammonium dithiocarbamate and certain of its derivatives, including some with *S*-substitution, have been reported[2,3] to be effective in protecting mice from radiation-induced injury; Foye and Mickles[4] recently reported that a number of dithiocarbamates afforded significant protection to mice exposed to sub-lethal radiation dosage. Therefore, the products of the nucleophilic attack by secondary amines on cyclic ethylene trithiocarbonate—2-mercaptoethyl dithiocarbamates[5] and the corresponding disulfides[6]—should be evaluated as antiradiation agents. The corresponding propyl dithiocarbamates, which should be obtainable from cyclic trimethylene trithiocarbonate, are also of potential interest.

Attempting to use the literature procedures[6] described in general terms, we were unable to obtain the reported high yields (about 95%) of the dithiodiethylene *N,N*-disubstituted dithiocarbamates from the reaction of ethylene trithiocarbonate with dimethylamine and morpholine. The only pure product that we isolated from the reaction of equivalent amounts of ethylene trithiocarbonate and morpholine was not the expected dithiodiethylene 4-morpholinecarbodithioate (I) but ethylene 4-morpholinecarbodithioate (II). Ethylene esters such as II were previously identified as by-products of this general reaction and were obtained in increased yields by modifications of the original procedure; for example, by the addition of base.[7] The anomalous formation of these ethylene esters has been rationalized[7] as involving the base-catalyzed elimination of ethylene sulfide from 2-mercaptoethyl dithiocarbamates.[8] Durden, *et al.*,[9] apparently unaware that the products originally described as thiols[6] were later identified as disulfides,[5] recently demonstrated that the product they isolated in 40% yield from the reaction of ethylene trithiocarbonate with morpholine was the disulfide I. These observed variations in products and yields are apparently due in part to differences in isolation procedure. To make the disulfides in high yield we resorted to the alkylation of sodium dithiocarbamates with bis(2-chloroethyl) disulfide, an alternative procedure mentioned by Delaby, *et al.*[5]

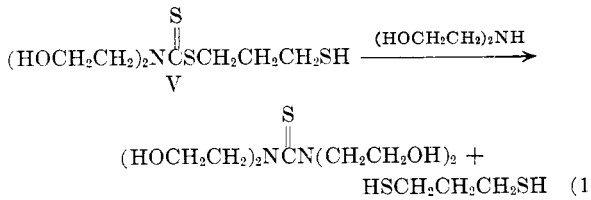


I. $n=2$
IV. $n=3$



II

Cyclic trimethylene trithiocarbonate (III) was opened with morpholine without difficulty to give 3-mercaptopropyl 4-morpholinecarbodithioate (92% pure by iodometric titration), which was subsequently oxidized by iodine to dithiodi(trimethylene) 4-morpholinecarbodithioate (IV). An attempt to prepare 3-mercaptopropyl bis(2-hydroxyethyl)dithiocarbamate (V) from III and 2,2′-iminodiethanol, however, led to the isolation in appreciable yield of a white crystalline compound, which has been identified as 1,5,7,11-tetrathiaspiro[5.5]undecane (VI) on the basis of elemental analysis, molecular weight, and the n.m.r. spectrum shown in Fig. 1. This spectrum, in conjunction with that of the starting material III, confirms the proposed structure as it shows two band systems in the region expected from methylene proton absorption (between 1.5 and 3.5 p.p.m.) whose areas are in a 2:1 ratio. The complex multiplet structure of each band system indicates strong spin coupling among adjacent methylene groups. The following sequence of reactions is proposed to explain the formation of VI:



(1)

(1) This investigation was supported by the U.S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-2028).

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(8) *Cf.* the mercaptoethylation of amines by the use of 2-mercaptoethyl carbamates [D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, **26**, 5116 (1961)].

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