[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY, THE STATE UNIVERSITY OF NEW JERSEY]

The Antifungal Agent from Osage Orange Wood[1]

BY RODERICK A. BARNES AND NANCY NICHOLS GERBER

RECEIVED JANUARY 5, 1955

The wood of the Osage orange, *Toxylon pomiferum*, has been found to contain approximately 1% of 2,3′,4,5′-tetrahydroxystilbene. This substance was toxic to five of thirteen microörganisms which were tested and its presence is believed to be the main reason for the remarkable resistance of Osage orange wood to decay.

It has been suggested[2] that the unusual resistance of certain woods to decay results from the presence of substances which are toxic to the fungi that normally initiate the decomposition processes. This theory has been substantiated to some extent by the isolation of 3,5-dihydroxystilbene from *Pinus silvestris*[3] and isopropyltropolones from *Thuja plicata don*[4]; both of these substances have been shown to be toxic to fungi.

The wood of the Osage orange, *Toxylon pomiferum*[5] is noted for its great durability and resistance to decay. It was the purpose of this research to ascertain whether or not there was a naturally occurring protective substance which could be responsible for this characteristic of the wood.

The organism chosen for determining the toxicity of the wood extracts and for following the fractionation procedure was *Myrothecium verrucaria*, a fast growing cellulolytic fungus. Preliminary extractions with isoöctane, chloroform, acetone and water indicated that water and to a lesser extent acetone, extracted from the wood appreciable amounts of a toxic material. Further processing of the water extract to remove inactive materials finally produced a yellow-brown glass which was chromatographed on silicic acid to yield the toxic principle as a pale yellow, amorphous solid. The yield of this substance based on the weight of wood extracted was 0.5–1.0% depending on the purification procedure used

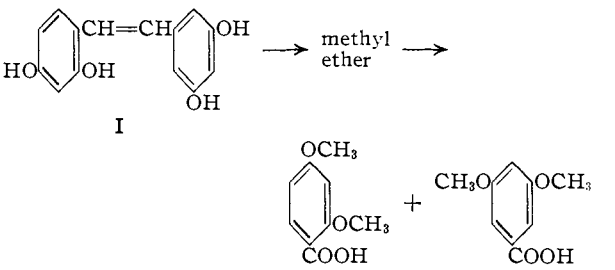
In Table I are listed the results of the preliminary microbiological tests carried out with the crude amorphous solid using a concentration of 0.2 mg. per milliliter.[6]

TABLE I

	Microörganism	Inhibition of growth
1.	*Myrothecium verrucaria*	Complete
2.	*Pullularia pullulans*	Complete
3.	*Aspergillus fumigatus*	None
4.	*Aspergillus niger*	None
5.	*Candida albicans*	None
6.	*Microsporum audouini*	None
7.	*Penicillium notatum*	None
8.	*Rhodotorula glutinis*	None
9.	*Saccharomyces cerevisiae*	None
10.	*Ceratostomella ulmi*	None
11.	*Fusarium bulbigenum*	Partial
12.	*Microsporum canis*	Complete
13.	*Trichophyton mentagrophytes*	Complete

The antifungal agent was finally proved to be 2,3′,4,5′-tetrahydroxystilbene (I), a substance which had been isolated previously by Takaoka[7] from the phenolic fraction of an extract of the roots of the white hellebore (*Veratrum grandiflorum*). The identification was complicated by the fact that I is usually obtained as an amorphous, partially hydrated material which can be crystallized in an anhydrous form only with difficulty. The molecular formula was not established with certainty until three crystalline derivatives, the acetate, benzoate and methyl ether were prepared.

The melting point of the acetate and benzoate agreed with the values reported; however, our methyl ether was crystalline (m.p. 83–84°) while this compound as obtained by Takaoka was an oil. In order to clear up this discrepancy the crystalline methyl ether was oxidized with potassium permanganate.[8]



I

The identification of the two acids from the oxidation proved that our compounds were definitely the same as those reported by Takaoka.

A projected synthesis for I was carried as far as the methyl ether IV. An attempt to reduce II with sodium borohydride was unsuccessful; however, after methylation of the phenolic hydroxyl groups, lithium aluminum hydride reduction proceeded in quantitative yield.

Attempts to cleave ether IV with a variety of acidic and basic reagents were unsuccessful. The isolation of resorcinol from some of the reactions carried out under acid conditions suggested that the ether groups were cleaved but the resulting hydroxystilbene was immediately degraded further.

(1) This paper is based on work performed under contract Nonr-632(00), Project NR 353-291 of the Office of Naval Research.

(2) L. F. Hawley, L. C. Fleck and C. A. Richards, *Ind. Eng. Chem.*, **16**, 699 (1924).

(3) H. Erdtmann and E. Rennerfelt, *Svensk. Papperstidn.*, **47**, 45 (1944); E. Rennerfelt, *Medd. Skogsförsökanst, Stockholm*, **34**, 391 (1946).

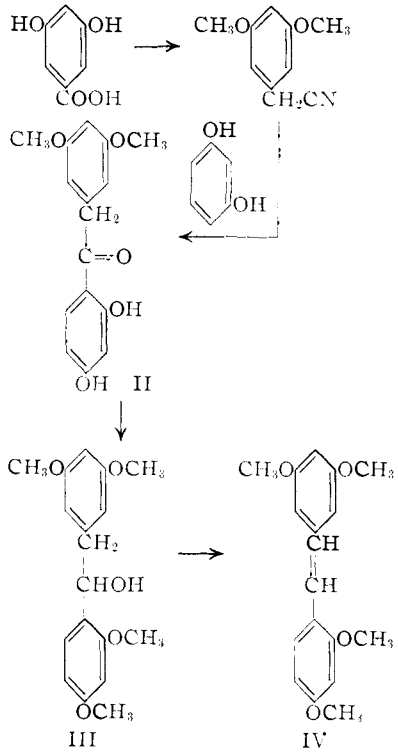
(4) H. Erdtman and J. Grippenberg, *Acta Chem. Scand.*, **2**, 625 (1948); T. Nozoe, *Bull. Chem. Soc. Japan*, **11**, 295 (1936), also isolated isopropyltropolones from the Hinoki tree, a species botanically related to the western red cedar.

(5) This name is usually preferred; however, *Maclura aurantica* and *Maclura pomifera* also have been used.

(6) We wish to thank Mr. F. E. Pansy, Division of Microbiology, Squibb Institute for Medical Research, for carrying out all of these tests except the first two in Table I which were done by N. N. Gerber.

(7) M. Takaoka, *J. Faculty Sci., Hokkaido Imp. Univ. Ser. III*, **3**, 1 (1940); *J. Chem. Soc. Japan*, **60**, 1261 (1939).

(8) Takaoka, ref. 7, carried out a similar oxidation of his acetate and benzoate derivatives with chromic acid.



Although a review article by Mell[9] states that Osage orange wood has been found to contain morin (2′,3,4′,5,7-pentahydroxyflavone) and maclurin (2,-3′,4,4′,6-pentahydroxybenzophenone), we could find no experimental paper in support of this statement. However, the wood of a related species, *Chlorophora tinctoria* does contain these two substances.[10] The confusion apparently resulted because Osage orange wood extract has sometimes been used in dyeing as a substitute for "fustic," the common name for the wood of *Chlorophora tinctoria*.

As might have been expected from the similarity in dyeing properties we did identify the flavone in Osage orange wood as morin but were unable to isolate any maclurin.[11]

Acknowledgment.—The authors wish to express their appreciation to Dr. W. J. Nickerson of the Institute of Microbiology, Rutgers University, for assistance in setting up the microbiological assay procedure; and to Dr. A. Zimmerli and Dr. G. R. Buckwalter for donating considerable quantities of Osage orange wood.

Experimental[12]

Isolation of 2,3′,4,5′-Tetrahydroxystilbene.—Chips of the yellow heartwood of an Osage orange tree (600 g.), cut in November 1951, were boiled for about one hour with distilled water (6 liters). The aqueous extract was decanted and reduced in volume to 600 ml. by vacuum distillation or by evaporation of the warm liquid in a stream of dry air. The concentrated solution was allowed to stand for 48 hours and the solid which separated was filtered off and discarded. The filtrate was extracted with five 100-ml. portions of ether and the ether extracts were evaporated to dryness on a steam-bath. The residual solid was stirred with distilled water (600 ml.) and a yellow precipitate (2.4 g.) of a flavanoid substance was filtered off.

The concentrated aqueous solution thus obtained was originally processed by evaporation to dryness to yield a yellow-brown viscous residue which was taken up in ether and placed on a column of silicic acid. Elution of the column with dry ether removed about two thirds of the material on the column as a light-yellow amorphous solid. Acetone eluted a small amount of a dark-colored, non-toxic solid.

In a simplified procedure the aqueous extract from 600 g. of wood was placed in a liquid–liquid extractor provided with a magnetic stirrer and extracted continuously for 24 hours with ether. The extract was evaporated to yield an oil which was dissolved in 600 ml. of water and allowed to stand for at least one day. During this time most of the flavanoid material precipitated and finally was filtered. The filtrate was concentrated to half its original volume, partially frozen and then stored overnight at −5°. The frozen liquid was warmed until the ice melted, leaving a suspension which was filtered. In this way 0.5–1.2 g. of the crude toxic material was obtained; further concentration and freezing yielded additional product. The total yield of dry, amorphous product from 600 g. of wood varied between 3 and 6 g.; the higher yields were obtained when the opportunity for air oxidation during the isolation were least.

Repeated chromatography of the product obtained in this way always yielded the same amorphous material which melted from 95–200°. Some crystals were finally obtained from an aqueous solution and later from dilute ethanol and dilute acetic acid. These crystals melted at 95–100°; however, under the microscope the melt could be observed to crystallize again as the temperature was raised and then to melt at 190–200°. Some relatively pure crystals (m.p. 203–208°) of the high melting material were obtained by dissolving 5–10 mg. of well-dried amorphous solid in 100 ml. of hot toluene and allowing the solution to cool slowly.

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.84; H, 4.95. Found: C, 68.20; H, 5.98.

Analysis of the amorphous product indicated that it was a partially hydrated form.

Microbiological Assay Procedure.—A malt extract nutrient broth was prepared by a standard method.[13] Erlenmeyer flasks (125 ml.) each containing 25 ml. of broth were sterilized with steam at 15 lb. pressure for 15 minutes. The flasks were inoculated with spores of *Myrothecium verrucaria* taken from potato-dextrose agar slants prepared weekly from a standard culture.[14] The material to be tested was dissolved or suspended in sterile water and added to the flask with a sterile pipet. The test solutions and the controls were allowed to incubate at room temperature (22–32°) until growth in the controls was abundant. This usually required 2–4 days. At least three different concentrations of the test substance were used and the inhibition of growth was estimated by visual comparison with the controls. An attempt was made to filter the mold mycelium and weigh it for a more exact comparison. The weights involved were too small to be measured with reasonable accuracy by a simple process of filtering, drying and weighing the mycelium on a filter paper or in a sintered glass funnel.

These determinations were made at each step of the isolation. According to this assay very little of the activity was lost during the purification process.

Acetylation of I.—Amorphous solid I (6 g.) was dissolved in acetic anhydride (41 g.) containing sodium acetate (1 g.) and allowed to stand for 10 days at room temperature. The reaction mixture was poured into distilled water (1 liter) and the suspension chilled overnight. The very viscous oil was separated by decantation, dissolved in a minimum of hot dioxane and reprecipitated by dropwise addition to cold water (1 liter). The light tan solid was filtered and dried; there was obtained 7.6 g. (76%) of material which melted at 115–130°. Fine white needles which melted at 141–143° (reported[7] m.p. 141–142°) were obtained by re-

(9) C. D. Mell, *Textile Colorist*, **53**, 749 (1931).

(10) R. Wagner, *J. prakt. Chem.*, [1] **51**, 82, 91 (1850).

(11) Three procedures which have been successful for the isolation of maclurin from other plant sources were carried out, all with negative results. These experiments were performed by A. C. Martellock.

(12) All melting points were determined using the Kofler Micro Hot Stage. Analyses were by J. F. Alicino, Metuchen, New Jersey and W. Manser, Zurich, Switzerland.

(13) "Difco Manual," 8th edition, Difco Laboratories, Inc., Detroit, Michigan, p. 164.

(14) No. 9095 from the American Type Culture Collection, Washington, D. C.

crystallization from dioxane–water. The ultraviolet spectrum had $\lambda_{max.}$ at 299 mμ (log ε 4.39).

Anal. Calcd. for $C_{22}H_{20}O_8$: C, 64.06; H, 4.19; mol. wt., 412. Found: C, 63.76, 63.86; H, 4.76, 4.59; mol. wt. (cryoscopic in benzene), 400.

Benzoylation of I.—A mixture of I (1 g.), pyridine (25 ml.) and benzoyl chloride (7 ml.) was allowed to stand at room temperature for 10 days. The mixture was poured into a 5% solution of hydrochloric acid (200 ml.). The product was extracted with ether and the ether solution washed successively with dilute hydrochloric acid, water and sodium bicarbonate solution. The ether extract was concentrated and chilled overnight to yield 1.45 g. (55%) of a yellowish solid which could be recrystallized from dioxane water to produce white needles which melted at 192–194° (reported[7] m.p. 193.5°).

Anal. Calcd. for $C_{42}H_{32}O_8$: C, 76.35; H, 4.27; mol. wt., 661. Found: C, 76.34; H, 4.24; mol. wt. (cryoscopic), 640.

2,3′,4,5′-Tetramethoxystilbene (IV). A. From Methylation of I.—A solution of I (3.8 g.) in methanol (12 ml.) and 50% potassium hydroxide solution (6.4 ml.) was warmed to 50° while dimethyl sulfate (9 g.) and 50% potassium hydroxide solution were added separately, dropwise during 45 minutes so that the solution was always alkaline. The reaction mixture was stirred for 45 minutes after the addition was complete and then the addition of dimethyl sulfate and potassium hydroxide was repeated twice more exactly as at first.

The cold reaction mixture was extracted with 50:50 benzene–ether and the extract dried and concentrated; there was obtained 3.0 g. (63%) of crude liquid product. A portion (1.81 g.) of this material was placed on a column of activated alumina (45 g.) in carbon tetrachloride. Elution with carbon tetrachloride or benzene removed a colorless oil (0.92 g.) which crystallized on standing. Recrystallization from isoöctane yielded needles which melted at 83–84°.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.99; H, 6.71; mol. wt., 300. Found: C, 71.64; H, 6.35; mol. wt. (cryoscopic), 310.

This same product resulted when I (1.0 g.) was allowed to stand for 6 days with a solution of diazomethane (*ca.* 1.4 g.) in ether (50 ml.) and the crude product was purified by chromatography. The melting points and infrared spectra of the two methylation products were identical.

B. From Carbinol III.—2,4-Dimethoxyphenyl-3′,5′-dimethoxybenzylcarbinol (0.1 g.) was dissolved in anhydrous ether (10 ml.) and treated with purified thionyl chloride (0.1 g.) and pyridine (1 drop). The reaction mixture was refluxed for one hour, then dry pyridine (2 ml.) was added and the refluxing continued for another hour. The reaction mixture was washed with water and the solvents distilled; the residue was dissolved in carbon tetrachloride and chromatographed on alumina. Elution with benzene yielded a colorless oil which was crystallized from aqueous ethanol to yield 11 mg. (12%) of white needles which melted at 81–83°.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.99; H, 6.71. Found: C, 71.78; H, 6.85.

A mixture of this product and that obtained in part A also melted at 81–83°.

Oxidation of 2,3′,4,5′-Tetramethoxystilbene (IV).—Compound IV (36.2 mg.) prepared by methylation of I, was suspended in water containing a few drops of 10% sodium hydroxide solution. Dilute potassium permanganate solution was added dropwise with stirring so that no excess of permanganate accumulated in the reaction mixture. After 30 hours the addition was stopped when the pink color of the solution became permanent. A few drops of ethanol were added to decolorize the solution which then was filtered and acidified. The clear solution deposited 9.1 mg. (42%) of white crystals which melted at 173–179°. Recrystallization raised the melting point to 183–184°.

Anal. Calcd. for $C_9H_{10}O_4$: C, 59.33; H, 5.53. Found: C, 59.66; H, 5.21.

The melting point of a mixture of authentic 3,4-dimethoxybenzoic acid (m.p. 179–180°) and this oxidation product was 138–165°. However, a mixture with authentic 3,5-dimethoxybenzoic acid (m.p. 183–184°, prepared from orcinol dimethyl ether) melted at 183–184°. Also, the infrared spectrum of the oxidation product was identical with that of 3,5-dimethoxybenzoic acid.

The solution remaining after filtration of the crystals of the first oxidation product was extracted with ether in a small continuous extractor. From the ether extract there was isolated 16.5 mg. (75%) of product which melted at 102–106°. Recrystallization from water raised the melting point to 106–108°. The melting point of a mixture of this substance with authentic 2,4-dimethoxybenzoic acid (m.p. 109–110°) was 106–109°. The infrared spectra of these two samples were also identical and different from either 3,4- or 3,5-dimethoxybenzoic acid.

2,4-Dihydroxyphenyl 3′,5′-Dimethoxybenzyl Ketone (II).—3,5-Dimethoxybenzyl cyanide was prepared from 3,5-dimethoxybenzoic acid[15] by reduction with lithium aluminum hydride to the alcohol (73%)[16] followed by conversion to the chloride which was treated with sodium cyanide.[17]

The cyanide (2 g.) and freshly fused zinc chloride (2 g.) were added to a solution of resorcinol (3 g.) in anhydrous ether (100 ml.). This solution was saturated with hydrogen chloride at 0° and allowed to stand for 5 days. The solid which separated was filtered and then boiled with water (100 ml.) for 50 minutes. The hot aqueous layer was decanted from an oily residue. The aqueous solution, after long standing, deposited 0.4 g. (20%) of crystalline 3,5-dimethoxyphenylacetic acid. From the oil there was isolated by crystallization from aqueous ethanol 0.55 g. (17%) of ketone II, m.p. 138–140°.

Anal. Calcd. for $C_{16}H_{16}O_5$: C, 66.67; H, 5.59. Found: C, 66.41; H, 5.69.

The 2,4-dinitrophenylhydrazone of II melted at 225–226.5° after recrystallization from ethanol–ethyl acetate.

Anal. Calcd. for $C_{22}H_{20}O_8N_4$: C, 56.40; H, 4.30. Found: C, 56.39; H, 4.24.

2,4-Dimethoxyphenyl 3′,5′-Dimethoxybenzyl Ketone.—Ketone II (0.2 g.) was methylated by refluxing in acetone (20 ml.) with dimethyl sulfate (0.8 ml.) and anhydrous potassium carbonate (4.0 g.). After 20 hours, additional dimethyl sulfate (0.4 ml.) and potassium carbonate (0.4 g.) were added. The crude solid obtained by evaporating the solvent and dissolving the inorganic salts with water, was recrystallized from aqueous ethanol. There was obtained 0.12 g. (53%) of product which melted at 95–104°. Recrystallization raised the melting point to 102–104°.

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.35; H, 6.37. Found: C, 68.11; H, 6.36.

2,4-Dimethoxyphenyl-3′,5′-dimethoxybenzylcarbinol (III).—A solution of 2,4-dimethoxy-3′,5′-dimethoxybenzyl ketone (0.55 g.) in ether (20 ml.) was added to a suspension of lithium aluminum anhydride (0.5 g.) in anhydrous ether (20 ml.). The reaction was stirred for 90 minutes at room temperature, refluxed 40 minutes and then decomposed by dropwise addition of water. The reaction mixture was poured into cold dilute hydrochloric acid, the product extracted with ether and the ether extract concentrated to yield an oil which crystallized from aqueous ethanol to yield 0.6 g. (quant.) of white needles, m.p. 76–79°. Recrystallization from isoöctane yielded pure III which melted at 80–82°.

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.90; H, 6.97. Found: C, 67.78; H, 6.90.

The acetate derivative of III was prepared by reaction with refluxing acetic anhydride for 45 minutes. After several recrystallizations from ethanol–water, this substance melted at 65–73°.

Anal. Calcd. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.38; H, 6.94.

Isolation of Morin.—The crude flavanoid material obtained as a water insoluble precipitate (non-toxic to *Myrothecium verrucaria*) in the isolation of 2,3′,4,5′-tetrahydroxystilbene, was purified by forming the ethanol-insoluble potassium salt which was recrystallized from 60% acetic acid; this process finally yielded pale yellow needles which melted at 285–289° (reported[18] 289–296°).

(15) *Org. Syntheses*, **21**, 27 (1941); C. M. Suter and A. W. Weston, THIS JOURNAL, **61**, 232 (1939).

(16) H. W. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 509.

(17) R. Adams, S. Mackenzie and S. Loewe, THIS JOURNAL, **70**, 664 (1948).

(18) Q. L. Morris, T. B. Gage and S. H. Wender, *ibid.*, **73**, 3340 (1951).

The methylation of this flavone with dimethyl sulfate and potassium carbonate yielded a pentamethyl ether which melted at 158–159° (reported[19] 156–157°).

(19) T. J. Haley and M. Bassin, *J. Am. Pharm. Assoc.*, **40**, 111 (1951).

Anal. Calcd. for $C_{20}H_{20}O_7$: C, 64.50; H, 5.41. Found: C, 64.42; H, 5.49.

The melting point of a mixture of this sample and an authentic sample of morin pentamethyl ether was 158.5–160°.

NEW BRUNSWICK, N. J.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF BOSTON UNIVERSITY]

Friedel–Crafts Reaction of 1-Benzenesulfonyl-2-bromomethylethyleneimine and Benzene[1]

BY WALTER J. GENSLER AND JOHN C. ROCKETT

RECEIVED DECEMBER 9, 1954

1-Benzenesulfonyl-2-bromomethylethyleneimine (I) reacts with benzene in the presence of aluminum chloride to give 3,3-diphenyl-1-benzenesulfonamidopropane (X). Possible reaction paths are considered. The following are shown not to be intermediates: 1-bromo-2-benzenesulfonamido-3-phenylpropane (II), 1,3-diphenyl-2-benzenesulfonamidopropane (III), 1-benzenesulfonyl-2-benzylethyleneimine (IV) and N-(cinnamyl)-benzenesulfonamide (VI).

Interest in the chemistry of 1-benzenesulfonyl-2-bromomethylethyleneimine (I)[2] prompted trial of the Friedel–Crafts reaction of 1-benzenesulfonyl-2-bromomethylethyleneimine (I) with benzene. The present paper is concerned with the structure and the mode of formation of the reaction product, $C_{21}H_{21}NO_2S$, a solid melting at 128–129°. This material was obtained in only moderate yield when benzene was the solvent and when 1.5 moles of aluminum chloride was used. No other pure product could be isolated, nor could the yield be improved by varying conditions. Treatment of the material with sodium and isoamyl alcohol[3] or with lithium aluminum hydride effected removal of a benzenesulfonyl grouping. A better method, however, was hydrolytic cleavage using concentrated hydrochloric acid at 160°. The resulting amine could be handled conveniently as the hydrochloride ($C_{15}H_{17}N\cdot HCl$) or as the ammonium carbamate ($C_{15}H_{16}NCOO^-\cdot \overset{+}{C}_{15}H_{17}NH$).[4] The latter derivative formed readily by simply exposing the oily amine to the air. The original Friedel–Crafts product could be regenerated by treating the amine with benzenesulfonyl chloride.

The coincidence in melting points of our amine hydrochloride with that reported for the hydrochloride of 3,3-diphenyl-1-aminopropane[5,6] was the lead that helped us establish the structures of our products. Preparation of 3,3-diphenyl-1-aminopropane (by lithium aluminum hydride reduction of the amide of β,β-diphenylpropionic acid[7]) and direct comparisons of hydrochlorides, carbamates and benzenesulfonyl derivatives left no doubt that the amine obtained from the Friedel–Crafts product was 3,3-diphenyl-1-aminopropane, and that the Friedel–Crafts product itself was 3,3-diphenyl-1-benzenesulfonamidopropane (X).[8]

The accompanying formulations define several possible sequences for conversion of the ethyleneimine I to the product X. Test of some of these reaction paths was made by exposing intermediates to the action of aluminum chloride in benzene solvent under conditions comparable to those used in the original reaction. No 3,3-diphenyl-1-benzenesulfonamidopropane (X) was obtained when such experiments were carried out with compounds II, III, IV, and VI. The benzenesulfonamido derivative of cinnamylamine (VI)[9] furnished only benzenesulfonamide. 1-Bromo-2-benzenesulfonamido-3-phenylpropane (II)[10] was largely recovered, as was 1,3-diphenyl-2-benzenesulfonamidopropane (III).[11] 1-Benzenesulfonyl-2-benzylethyleneimine (IV)[10] gave rise to an intractable oil. Three reaction paths remain untested, *viz.*, I via compounds VI and VIII to X,[12] I via IX to V and by isomerization to X, and I via XI to X. Intermediate XI is of special interest in that a four membered ring compound is derived from a three membered ring compound in a manner at least formally analogous to the generation of cyclobutyl compounds from the cyclopropylmethyl cation.[13] Further work is planned.

Experimental[14]

3,3-Diphenyl-1-benzenesulfonamidopropane (X) from 1-Benzenesulfonyl-2-bromomethylethyleneimine (I).—A mix-

(1) Abstracted from the thesis submitted by John C. Rockett to the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Master of Arts, 1951.

(2) *Cf.* W. J. Gensler, THIS JOURNAL, **70**, 1843 (1948).

(3) C. C. Howard and W. Marckwald, *Ber.*, **32**, 2031 (1899).

(4) *Cf.* M. Frankel and E. Katchalski, THIS JOURNAL, **65**, 1670 (1943); E. Katchalski, C. Berliner-Klibanski and A. Berger, *ibid.*, **73**, 1829 (1951).

(5) S. K. Freeman, W. F. Ringk and P. E. Spoerri, *ibid.*, **69**, 858 (1947).

(6) D. W. Adamson, *J. Chem. Soc.*, 144S (1949).

(7) D. Vorländer, E. Rack and W. Leister, *Ber.*, **56**, 1131 (1923).

(8) A feature that was misleading in that it indicated absence of the $-SO_2NH-$ grouping in the Friedel–Crafts product was its insolubility in aqueous alkali. However, once the structure was established we were left with no choice but to accept this property as a peculiarity of the molecule. Subsequently we determined that 1,3-diphenyl-2-benzenesulfonamidopropane (III) was likewise insoluble in aqueous alkali. Other alkali-insoluble benzenesulfonyl derivatives of primary amines have been reported (*cf.* W. H. Carothers and G. A. Jones, THIS JOURNAL, **47**, 3051 (1925); W. H. Carothers, C. F. Bickford and G. S. Hurwitz, *ibid.*, **49**, 2908 (1927).

(9) T. Posner, *Ber.*, **26**, 1856 (1893).

(10) W. J. Gensler and J. C. Rockett, THIS JOURNAL, **74**, 4451 (1952).

(11) C. F. Koelsch, *ibid.*, **67**, 1718 (1945).

(12) Several unsuccessful attempts have been made in these laboratories to synthesize N-(bromoallyl)-benzenesulfonamide (VII).

(13) Compare J. D. Roberts and R. H. Mazur, THIS JOURNAL, **73**, 3542 (1951), and references therein.

(14) Melting points are uncorrected. Analyses were carried out by Carol K. Fitz, Ph.D., 115 Lexington Avenue, Needham Heights 94, Mass.