[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY OF CORNELL UNIVERSITY]

Intramolecular Reactions. III. Reactions of Diazotized *cis*- and *trans*-2-Aminostilbene[1]

BY DELOS F. DETAR[2] AND YUN-WEN CHU[3]

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The thermal decomposition of *cis*-2-stilbenediazonium fluoborate in dilute aqueous acid leads to the formation of 15–40% yields of phenanthrene and 60–70% yields of a cleavage product, indazole, depending upon the reaction temperature. In contrast to the fluorenone ring closure reaction, the phenanthrene ring closure process is markedly influenced by added copper powder, the phenanthrene yield being 60–80% with copper present. *trans*-2-Stilbenediazonium fluoborate gives as predominant products *trans*-2-hydroxystilbene and indazole. The rates of the reactions have been briefly investigated.

The ring closure of diazotized *cis*-2-aminostilbenes to substituted phenanthrenes has been used extensively by many workers for the preparation of phenanthrene derivatives in which the location of the substituents is unequivocal. The first example to be carried out was the synthesis of phenanthrene-9-carboxylic acid,[4] and a great many other examples of the reaction were reported by Pschorr in numerous later papers. In general, the yields of the cyclization process are good. Ruggli and Staub[5] have reported that *cis*-2-stilbenediazonium bisulfate gives phenanthrene in 60–80% yield in the presence of copper powder, and that ring closure even takes precedence over deamination, phenanthrene rather than stilbene being formed with hypophosphorous acid and other deaminating reagents. The fact that copper powder has been used in almost all reported examples of the Pschorr reaction makes the mechanism of the process uncertain at present, since the effect of copper powder on diazonium compounds has yet to be worked out.

Because of our interest in the diazonium cyclization reactions, we have carried out a detailed study of the thermal decomposition of *cis*-2-stilbenediazonium fluoborate in dilute aqueous acids, and a more abbreviated study on the *trans* isomer. The mechanism operating under these conditions is expected to be an ionic one[1]; the elucidation of the mechanism of the copper-catalyzed reaction is an entirely separate problem not dealt with here.

Preliminary experiments showed that the reaction follows a somewhat surprising course in the absence of copper powder. Phenanthrene was formed, but the yields were low. The yield of nitrogen was also low, thus indicating that nitrogen-containing products had been formed. Similar results were obtained with the *trans* isomer. Sterically this isomer cannot give phenanthrene, but the yields of *trans*-2-hydroxystilbene and of nitrogen were only moderate. It seemed possible that one of the nitrogen-containing products might be the unknown 3-phenylcinnoline, and a search was made for basic products. A colorless crystalline nitrogen-containing material was obtained, but the analysis was completely wrong for the cinnoline: the product proved to be indazole, a cleavage product. The other cleavage product, benzaldehyde, was also detected in the reaction, since benzaldehyde infrared peaks were present in the spectra of crude indazole specimens. Previous workers[5a,b] have reported the isolation of benzaldehyde from decomposition of the *trans*-diazonium salt, but no previous mention has been made of the indazole formation. The formation of indazole can be rationalized readily by postulating an electrophilic attack of the terminal nitrogen atom at the ethylenic bond followed by addition of water to give the protonated 3-[α-hydroxybenzyl]-indazole. After transfer of the proton to the 1-nitrogen atom this can undergo a sort of reverse aldol cleavage to indazole and protonated benzaldehyde. A search of the literature revealed that this reaction of diazonium salts and olefins has been previously observed in several reactions, a typical example being the formation of anisaldehyde *p*-nitrophenylhydrazone by reaction of *p*-nitrobenzenediazonium bisulfate and anethole.[6] At the higher reaction temperatures the *cis*-2-stilbenediazonium fluoborate gave moderate amounts of *trans*-2-hydroxystilbene. Although a search was made for the as yet unreported *cis*-2-hydroxystilbene, none could be found.

The quantitative product analyses are summarized in Tables I and II. The analyses were accomplished by chromatographic separation of the products, which were then identified by melting point or by spectra, and weighed. Copper sulfate had no detectable effect on the product ratios, but copper powder greatly increased the phenanthrene yield. The fact that increasing the temperature results in an increase in the phenanthrene yield and a decrease in the indazole yield indicates that the phenanthrene reaction has the higher activation energy.

TABLE I

SUMMARY OF PRODUCTS OF THE THERMAL DECOMPOSITION OF *cis*-2-STILBENEDIAZONIUM FLUOBORATE IN 0.1 *N* SULFURIC ACID

Temp., °C.	Phenanthrene,[c] %	Indazole,[c] %	*trans*-2-Hydroxystilbene, %	N_2,[c] %
25[a]	16	62	..	21
35[a]	24	..	..	28
45[a]	30	53	..	37
100[a]	42	22	20	72
25[b]	60	11	..	..
45[b]	83	..	..	..

[a] Runs with and without $CuSO_4$ averaged. [b] Runs with Cu powder present. [c] Standard deviation of the phenanthrene averages is about 3% relative, of the indazole about 15% relative, and of the nitrogen about 7% relative.

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[1] Previous paper, D. F. DeTar and D. I. Relyea, THIS JOURNAL, **76**, 1680 (1954).

[2] Department of Chemistry, University of South Carolina, Columbia, S. C.

[3] National Science Foundation research assistant.

[4] R. Pschorr, *Ber.*, **29**, 496 (1896).

[5] (a) P. Ruggli and A. Staub, *Helv. Chim. Acta*, **20**, 37 (1937); (b) F. Sachs and S. Hilpert, *Ber.*, **39**, 899 (1906).

[6] A. Quilico and M. Freri, *Gazz. chim. ital.*, **58**, 380 (1928).

TABLE II

PRODUCTS OF THE THERMAL DECOMPOSITION OF *trans*-2-STILBENEDIAZONIUM FLUOBORATE IN 0.1 *N* SULFURIC ACID

Diazonium salt, mmoles	Concn., m*M*	Temp., °C.	Isolation[a] procedure	*trans*-2-Hydroxystilbene, %	Indazole, %	N_2, %
2.052	68.4	Room	C	40	..	..
2.187	72.8	Room	C	40	45	..
0.878[b]	8.8	25	A	49	..	56
.933[b]	9.3	35	A	55	..	51
.749[b]	7.5	45	A	..	..	60
1.759	17.6	Reflux	A	..	..	88

[a] See Experimental. [b] Kinetic run. See Table III.

The rates of the reactions are given in Table III. The reactions were followed by manometrically measuring the nitrogen evolution. The rates were determined both by the slope of the curve obtained by plotting log $(p_\infty - p)$ against time and from the Roseveare[7] method. The reactions were accurately of the first order, the data of the *cis*-2-stilbenediazonium fluoborate at 35°, for example, are summarized by the expression p (in mm. of *p*-xylene) $= 154.19 - 167.09 \exp(-104 \times 10^{-5}\, t)$ from 17% to 98% reaction with a standard deviation of p of 0.4 mm. Thus even though only 28% of the nitrogen was evolved, the fact that its rate of evolution is accurately represented by a first-order expression indicates that all of the reactions by which the diazonium salt disappears are first order within the accuracy of the determination.

TABLE III

RATE OF THERMAL DECOMPOSITION OF *cis*- AND OF *trans*-2-STILBENEDIAZONIUM FLUOBORATES IN 0.1 *N* SULFURIC ACID

Temp., °C.	k, sec.$^{-1}$ × 10^5[a]	
	cis-Salt[b]	*trans*-Salt[c]
25.0	31.6	7.0
35.0	104	24.6
45.0	350	93.5
25.0	34.5[c]	

[a] Precision of the rate constants is about 2%; the accuracy is expected to be about 5% except for the 45° rates which are less certain. [b] For concentration and product data see Tables II and V. [c] 1 *N* sulfuric acid.

TABLE IV

ACTIVATION ENERGIES (ARRHENIUS *E*) FOR THE THERMAL DECOMPOSITION OF *cis*- AND *trans*-2-STILBENEDIAZONIUM FLUOBORATES

Over-all E for *cis*-salt	21,700[a]	
Over-all E for *trans*-salt	23,000[a]	
E for phenanthrene formation only	29,000[b]	$s = 300$
$E_{\text{Phen}} - E_{\text{Indazole}}$	6,000[b]	$s = 600$

[a] Calculated from 25° and 35° k values only since 45° values are less reliable. The standard deviation is 800 cal. for 5% standard deviation of k. [b] For derivation see text.

The activation energies for the reactions are given in Table IV. The over-all activation energies were obtained by applying the Arrhenius equation to the data of Table III. That for the phenanthrene formation reaction was obtained from a series of rate constants derived by multiplying the rate constant of Table III by the fractional yield of phenanthrene at that temperature from Table I. The difference in activation energies of the phenanthrene and the indazole reactions was obtained from k_P/k_I values (the ratio of the rates of formation), the ratio being taken as equal to the ratio of the phenanthrene and indazole yields. The Arrhenius equation was applied to these six ratios using a least squares adjustment based on the assumption of constant random errors in $\ln(k_P/k_I)$.

The reactions of the stilbenediazonium salts appear to fit in readily with the pattern established for the benzophenonediazonium salts. The products and the simplicity of the kinetics are both consistent with the results expected for the operation of ionic mechanisms.

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Experimental[8,9]

trans-o-**Nitro-α-phenylcinnamic Acid.**—In a 500-ml. erlenmeyer flask were placed 30.2 g. (0.2 mole) of *o*-nitrobenzaldehyde, 40 g. (0.3 mole) of phenylacetic acid, 100 ml. of acetic anhydride and 20 g. (0.2 mole) of triethylamine. The mixture was refluxed for 15 minutes, cooled to 90° and 100 ml. of cold water added gradually over a period of five minutes at such a rate as to maintain the temperature above 90°. The solution was heated to 95°, filtered and cooled; 39.5 g. (72%) of light orange crystals of the acid was obtained, m.p. 195–198°. Recrystallization from 500 ml. of toluene gave 37.6 g. of yellow prisms, m.p. 197.8–198.3°.

cis-**2-Aminostilbene Hydrochloride.**—The *trans-o*-nitro-α-phenylcinnamic acid was converted to *cis*-2-aminostilbene hydrochloride by the method of Ruggli and Staub.[5] It was advantageous to distil the crude *cis*-2-nitrostilbene obtained on decarboxylation before recrystallizing it from methanol. The pure nitro compound, bright yellow needles, m.p. 63.0–63.5°, was obtained in 50–54% yield. The nitro group was reduced with an ammonia–ferrous sulfate mixture, and the ether solution of the amine was saturated with hydrogen chloride to precipitate the *cis*-2-aminostilbene hydrochloride. Recrystallization from ethanol gave colorless needles, m.p. 202–203°, in 60% yield (from the nitro compound).

trans-**2-Aminostilbene.**—Residues from the recrystallization of the *cis*-2-nitrostilbene consisted of the eutectic mixture of the *cis* and the *trans* isomers, further separation being difficult. The mixture was isomerized to the *trans* form by the Ruggli and Staub method, which involves heating a nitrobenzene solution containing a little iodine. The *trans*-2-nitrostilbene was obtained as pale yellow prisms, m.p. 70.5–71°. Reduction gave the colorless free amine, after recrystallization from methanol, in 60% yield, m.p. 101.5–102.5°.

Diazonium Fluoborates.—The amine hydrochloride (2 g.) was dissolved in a small amount of hot water, the solution cooled and 7 ml. of 12 *N* hydrochloric acid added. This was followed by the dropwise addition of 5 ml. of water containing 0.7 g. of sodium nitrite. The reaction mixture was allowed to remain at 0–5° for 15 minutes. It was then filtered, and 8 ml. of chilled 40% fluoboric acid was added. After two hours at 0° the yellow precipitate was collected. The material could be purified by solution in a mixture of 80 ml. of methanol and 20 ml. of dimethylformamide followed by precipitation with about 300 ml. of anhydrous ether. The yield of reprecipitated fluoborate was about 65%. The *trans*-salt precipitated in an orange form and in a yellow form; these seemed to be polymorphic forms.

Anal. Calcd. for $C_{14}H_{11}N_2BF_4$: C, 57.16; H, 3.77; N, 9.53. Found: for *cis*-diazonium salt: C, 57.0; H, 3.74; N, 9.55. Found for *trans*-diazonium salt, yellow form: C, 57.1; H, 3.72; N, 9.50. Found for *trans*-diazonium salt, orange form: C, 56.9; H, 3.71; N, 9.64.

Product Separation and Identification.—The results are summarized in Table V.

Procedure A.—The aqueous reaction mixture was filtered and the solid residue chromatographed on alumina by a

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(7) W. E. Roseveare, THIS JOURNAL, **53**, 1651 (1931).

(8) All melting points are corrected.

(9) Microanalyses were done by Mrs. M. Libowitz.

TABLE V

PRODUCTS OF THE THERMAL DECOMPOSITION OF *cis*-2-STILBENEDIAZONIUM FLUOBORATE IN 0.1 *N* SULFURIC ACID

Diazonium salt Mmoles	Concn. m*M*	Copper	Temp., °C.	Isolation[a] procedure	Phenanthrene,[b] %	Indazole,[c] %	N_2[b] %
0.921	36.8	None	Room	B	13	59	..
.682	6.8	None	45		..	..	36
.813	8.1	None	45		..	..	38
.714[e]	7.1	None	45	A	41	..	38
1.023[e]	10.2	None	35	A	24	..	28
1.290[d,e]	12.9	None	25	A	10	..	21
1.594[e]	15.9	None	25	A	12	..	20
1.592	15	None	Reflux	B	>30	..	71
1.386	14	None	Reflux	B	40	..	75
3.404	68	2 g. Cu	45–50	B	64	..	..
1.553	77	1 g. Cu	25	C	60	11	..
1.242	12.4	None	45	C	31	44	36
0.674	6.7	1 g. Cu	45	C	83	..	..
0.682	6.8	2 g. $CuSO_4$	45	C	30	62	34
1.205	40	None	25	C	15	61	..
0.929	31	1 g. $CuSO_4$	25	C	16	65	..
1.280[f]	43	None	Reflux	C	43	23	..
1.729[f]	17	1 g. $CuSO_4$	Reflux	C	40	20	70

[a] See text. [b] Standard deviation is about 10% relative for N_2 and about 5% relative for phenanthrene by procedure C; procedures A and B are less accurate. [c] Standard deviation 15% relative. [d] *N* sulfuric acid. [e] Kinetic run, Table III. [f] *trans*-2-Hydroxystilbene formed in yields of 20% and 21%, respectively.

variety of procedures. The phenanthrene was identified in each case by its melting point, 97–98°, and in one or two examples by comparison of the ultraviolet and infrared spectra with the spectra of a highly purified sample furnished by Dr. D. D. Phillips. The indazole was identified on the basis of its melting point, 145–146°, its elementary analysis, and the fact that such a product is a reasonable cleavage fragment. The *trans*-2-hydroxystilbene was identified by its melting point, 146–147° (depressed by admixture with the indazole). Infrared spectra were run on purified samples of the indazole and of the hydroxystilbene, and as a check on the chromatographic separation, the infrared curves of the presumed fractions were compared with the above reference curves.

Procedure B.—The reaction mixture was extracted with several portions of ether, the ether evaporated, and the residue chromatographed. The fractions were identified as above.

Procedure C.—A systematic isolation procedure was developed involving continuous ether extraction followed by a chromatographic separation using Grade 4 alumina[10] (100 g. of F-20 alumina[11] with 12 g. of water added) and a benzene–heptane solvent followed by a benzene–methanol elution. The weights of the products were obtained after evaporation of the solvent, and the products were identified as above.

Nitrogen was determined with the apparatus used for the rate experiments[12] at 25°, 35° and 45°, and with a nitrometer apparatus at 100°.

Rate Experiments.—Reaction rates were determined by manometric measurement of the rate of nitrogen evolution.[12]

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(10) H. Brockman and H. Schodder, *Ber.*, **74**, 73 (1941).

(11) Chromatographic grade alumina from the Aluminum Ore Company.

(12) D. F. DeTar and M. Turetzky, in preparation.

ITHACA, NEW YORK
COLUMBIA, SOUTH CAROLINA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, INDIANA UNIVERSITY]

Cyclization Studies in the Syntheses of Monomethoxy-1-phenyl-4-hydroxy-2-naphthoic Acids[1]

BY L. H. KLEMM[2] AND THEODORE LARGMAN

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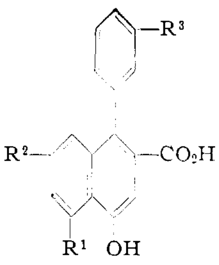
m-Methoxybenzophenone, synthesized by a new procedure, underwent Stobbe condensation to give a mixture of half esters which was cyclized (*via* sodium acetate and acetic anhydride) to two (of the possible three) isolable monomethoxy-1-phenyl-4-hydroxy-2-naphthoic acids, for which tentative structures have been assigned on the basis of chemical and physical properties. The Stobbe product has been hydrolyzed and subsequently reduced to yield two new acids.

1-Phenyl-4-hydroxy-2-naphthoic acid (I) and its derivatives are of interest as possible intermediates in synthetic and structural work on podophyllotoxin and other lignanes,[3] a group of phenolic constituents of some natural resins. Borsche[4] first synthesized I from benzophenone by the successive steps of Stobbe condensation, cyclization by means of sodium acetate and acetic anhydride, and hydrolysis. Only one substituted naphthol was possible as a product in this simplest case. Inasmuch as sodium acetate is a base in either acetic acid or acetic anhydride its function in the cyclization, a process readily visualized as occurring *via* acylation of the aromatic ring (normally an acid-catalyzed reaction) and subsequent enolization of the carbonyl group, seemed highly questionable. But typically acidic conditions give cyclization of Stobbe half-esters preponderantly to indones instead of naphthols.[5–7] It may have been for this



I, $R^1 = R^2 = R^3 = H$
II, $R^1 = OCH_3$, $R^2 = R^3 = H$
III, $R^2 = OCH_3$, $R^1 = R^3 = H$
IV, $R^3 = OCH_3$, $R^1 = R^2 = H$

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(2) Dept. of Chemistry, University of Oregon, Eugene, Oregon, where inquiries should be directed.

(3) R. D. Haworth, *Ann. Reports*, **33**, 270 (1936); R. D. Haworth, *J. Chem. Soc.*, 448 (1942); J. L. Hartwell, *et al.*, THIS JOURNAL, **72**, 246 (1950); **73**, 2909 (1951); **75**, 1308, 2138 (1953).

(4) W. Borsche, *Ann.*, **526**, 1 (1936).

(5) W. S. Johnson and G. H. Daub, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, Chap. 1.

(6) W. S. Johnson and A. Goldman, THIS JOURNAL, **66**, 1030 (1944).

(7) W. S. Johnson and A. Goldman, *ibid.*, **67**, 430 (1945).