conditions. Benzophenone does not react. Straight-chain aldehydes undergo self-condensation.

Acetone could not be condensed with methylene chloride or 1,1,1,2,2,3,3-heptachloropropane.

LONDON, S. W. 1, ENGLAND RECEIVED APRIL 29, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Orienting Effect of Negatively Substituted Vinyl Groups in Aromatic Substitution

BY F. G. BORDWELL AND KENNETH ROHDE[1]

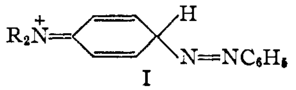
The orienting influence of groups on the course of aromatic substitution reactions was one of the first problems attacked in the development of the "English theory."[2] The directive properties of negatively substituted vinyl groups attracted attention during the early growth of the theory,[3,4] but groups of this nature have since been largely ignored in discussions and reviews. Baker and Wilson in their study of the nitration of ω-nitrostyrene found that the *p*- and *o*-isomers were formed almost exclusively. At that time they believed that the electron attracting effect of the nitro group was "damped out" by the electrons available in the olefinic bond, and that the substituted vinyl group was analogous to a methyl group in its directive properties. Since this early study, additional data concerning the orienting effect of substituted vinyl groups have become available, and the theory has also progressed.

The literature contains no mention of *m*-isomers from the nitration of such negatively substituted vinylbenzenes as α-methoxystyrene,[3] β-bromostyrene,[5] ω-nitrostyrene,[4] cinnamic acid,[6] α-chlorocinnamic acid,[7] α,β-dibromocinnamic acid[7] or 2-phenylethenesulfonyl chloride.[8,9] By careful analysis Baker and Wilson[4] found that the amount of *m*-isomer formed in the nitration of ω-nitrostyrene was less than 2%. Using a similar procedure, we have found that nitration in the *m*-positions of 2-phenylethenesulfonyl chloride also occurs to the extent of less than 2%. These data clearly illustrate the powerful *o*-*p*-directing effect of substituted vinyl groups.

In order to describe completely the orienting effect of a substituent on the course of aromatic substitution, it is necessary to know not only the positions taken by incoming groups under its direction, but also whether the substituent activates or deactivates the benzene nucleus. To determine the latter property for substituted vinyl groups, competitive nitration experiments were carried out by the method developed by Ingold, *et al.*[10] The competitive nitration of 2-phenylethenesulfonyl chloride and benzene was first studied, but the results obtained were not precise. Much better data were obtained from a study of the competitive nitration of cinnamic acid and benzene. The rates of nitration of 2-phenylethenesulfonyl chloride and of cinnamic acid were found to be appreciably lower than that of benzene, and of the same order as that of chlorobenzene. Negatively substituted vinyl groups, therefore, appear to belong with the halogen atoms in the class of strong *o*-*p*-directing groups which deactivate the benzene nucleus toward electrophilic substitution reactions.

Discussion

According to the most recent concepts of the role of orienting groups in aromatic substitution, the ability of a group to produce a more rapid reaction at *o*-*p*- than at *m*-positions is accounted for by assuming a resonance stabilization of the transition state for *o*-*p*- but not *m*-substitution.[11] Thus in the coupling of the benzenediazonium ion with dialkylaminobenzenes, Hughes and Ingold[11] attribute the *o*-*p*-directing influence of the dialkylamino groups to its ability to enhance the stability of the transition state by virtue of the contribution of structure I.



I

This concept of the role of orienting groups can be applied to all common *o*-*p*-directing groups, assuming a hyperconjugation effect for alkyl groups.[11] It is useful in explaining the fact that halogen atoms are strong *o*-*p*-directing groups despite their deactivating effect on the benzene nucleus. Al-

---

[1] Abstracted from the M. S. thesis of Kenneth Rohde, August' 1947.

[2] See, for example, Allan, Oxford, Robinson and Smith, *J. Chem. Soc.*, 401 (1926); Ingold and Ingold, *ibid.*, 1310 (1926); and subsequent papers by Robinson and Ingold and their collaborators.

[3] Ingold and Ingold, *J. Chem. Soc.*, **127**, 870 (1925).

[4] Baker and Wilson, *ibid.*, 842 (1926).

[5] Flürscheim, *J. prakt. Chem.*, **66**, 19 (1902).

[6] Müller, *Ann.*, **212**, 124 (1882); Underwood and Kochman, THIS JOURNAL, **48**, 254 (1926).

[7] Pfeiffer, *Ber.*, **47B**, 1755 (1914).

[8] Bordwell, Colbert and Alan, THIS JOURNAL, **68**, 1778 (1946).

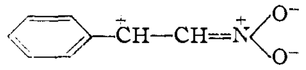
[9] However, nitration of 1-phenyl-1-nitro-2-(*p*-nitrophenyl)-ethene gave 21% of the *meta* isomer,[4] and Moore and Tucker, THIS JOURNAL, **49**, 258 (1927), isolated about 17% of *m*-sulfocinnamic acid from the sulfonation of cinnamic acid.

[10] Bird and Ingold, *J. Chem. Soc.*, 918 (1938), and previous papers.

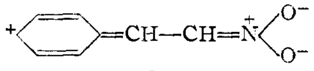
[11] (a) Hughes and Ingold, *ibid.*, 608 (1941); (b) Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, p. 470; (c) Wheland, THIS JOURNAL, **64**, 900 (1942); Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 256.

though the withdrawal of electrons from the benzene ring by the halogen atoms lowers the over-all rate of substitution in halobenzenes as compared to benzene itself, the rate of substitution at *o*-*p*-positions is greater than that at *m*-positions by virtue of resonance stabilization in the transition state.[12]

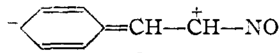
The transition state theory is particularly helpful in accounting for the orienting effects of negatively substituted vinyl groups, since predictions made on the basis of resonance possibilities in the initial states of these molecules are misleading. In the initial state the contribution of structures, such as II and III for ω-nitrostyrene, would be expected to be appreciable and to lead to *m*-substitution. The inductive effect of the nitro group transmitted through a vinyl group should also favor *m*-substitution. These effects are manifested by a lower rate of substitution for negatively substituted vinyl benzenes as compared to benzene. Structures of the type of IV probably would be relatively unimportant. However, in an electrophilic substitution reaction such as nitration of ω-nitrostyrene, which probably involves reaction with the NO_2^+ ion,[13] the energy of the transition state may be lowered appreciably when reaction occurs at the *o*-*p*-positions by the contribution of structures illustrated by V. No such resonance stabilization of the transition state can occur for reaction at the *m*-positions.



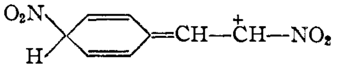
II



III



IV



V

Experimental[14]

Percentage of Isomers Formed in the Nitration of 2-Phenylethenesulfonyl Chloride.—In earlier work[8] approximately 50% of the *p*-isomer and 20% of the *o*-isomer have been isolated from a 95% yield of crude nitration mixture. Repetition of the experiment gave a 94% yield of crude nitration product from which fractional crystallization gave 53.4% of *p*-isomer, 19.7% of *o*-isomer, and 10.7% of a mixture. A study was made of the reaction of 2-(*o*- and *p*-nitrophenyl)-ethenesulfonhydrazides with 90% aqueous hydrazine to see whether this reaction could be used to further resolve the mixture. This method has been used[15] to separate isomeric nitrobenzenesulfonhydrazides. The 2-(*o*- and *p*-nitrophenyl)-ethenesulfonhydrazides were readily prepared but not easily purified. The acetone derivatives were prepared for identification purposes. Crude 2-(*p*-nitrophenyl)-ethenesulfonhydrazide, m. p. 142–144°, was converted to the 2-(*p*-nitrophenyl)-ethenesulfonhydrazone of acetone, m. p. 201–202°.

Anal. Calcd. for $C_{11}H_{13}N_3O_4S$: C, 46.60; H, 4.62. Found: C, 46.75; H, 4.64.

Crude 2-(*o*-nitrophenyl)ethenesulfonhydrazide, m. p. 116–119°, was converted to the 2-(*o*-nitrophenyl)-ethenesulfonhydrazone of acetone, m. p. 157–159°.

Anal. Calcd. for $C_{11}H_{13}N_3O_4S$: C, 46.60; H, 4.62. Found: C, 46.58; H, 4.50.

Nitrogen was evolved in the reaction of the 2-(*o*- and *p*-nitrophenyl)-ethenesulfonhydrazides with 90% aqueous hydrazine, but no pure products could be isolated from the reaction.

The amount of *m*-isomer in the unresolved 10.7% of nitration product was determined by hydrolysis of the 2-(nitrophenyl)-ethenesulfonyl chlorides followed by oxidation with aqueous potassium permanganate to a mixture of nitrobenzoic acids. The nitrobenzoic acids, obtained in 84% yield, were converted to their barium salts. Fractional crystallization yielded only very small quantities of slightly soluble barium salts, and mixed melting points taken with the acid produced from these salts indicated that the *m*-nitrobenzoic acid thus produced was very impure. The oxidation product was almost exclusively *o*-nitrobenzoic acid, m. p. 128–132°, which gave mixed melting points of 90–95° and 132–134° with *m*- and *o*-nitrobenzoic acids, respectively.

Competitive Nitration of 2-Phenylethenesulfonyl Chloride and Benzene.—The nitrations were run by a method similar to that described by Bird and Ingold.[10] The "R values"[10] in ten determinations ranged from 0.04 to 0.2. The source of error was apparently in the method of separation of the nitration products.

Competitive Nitration of Cinnamic Acid and Benzene.—The nitrations were carried out by keeping a solution consisting of 0.015 mole of benzene, 0.015 mole of cinnamic acid, 0.012 mole of nitric acid and 30 ml. of acetic anhydride at a thermostatically controlled temperature of 25° for eighteen to twenty hours. The reaction mixture was then stirred with about 200 g. of ice and water for one hour, the temperature being kept below 20°. The resulting mixture was extracted with four portions of a 10% solution of benzene in ether, and the cinnamic and nitrocinnamic acids were removed from the combined ethereal solutions by four extractions with aqueous sodium carbonate. The quantity of nitrobenzene and nitrocinnamic acids formed in the reaction was determined by titration of separate solutions containing these substances with titanium trichloride according to the method developed by Francis and Hill.[16] In four determinations the moles of nitrobenzene produced were 0.0034, 0.0028, 0.0039 and 0.0041, respectively, and the moles of nitrocinnamic acids were 0.00043, 0.00034, 0.00048 and 0.00053, respectively. Using the correction formula developed by Ingold and his co-workers,[10] the mean value for the ratio of the rate constants, *k*(cinnamic acid)/*k*(benzene) was found to be 0.111. For the competitive nitration of 2-phenylethene-1-sulfonyl chloride and benzene the ratio of rate constants is approximately 0.07. Bird and Ingold[10] reported a ratio of rate constants of 0.0353 for the competitive nitration of chlorobenzene and benzene at 25°.

Summary

1. Nitration of 2-phenylethenesulfonyl chlo-

---

[12] The calculations of Ri and Eyring, *J. Chem. Phys.*, **8**, 433 (1940), indicate that even in the initial state the charge distribution in chlorobenzene is such as to make the *p*- and *o*-positions more negative than the *m*-positions.

[13] Westheimer and Kharasch, THIS JOURNAL, **68**, 1871 (1946); Bennett, Brand and Williams, *J. Chem. Soc.*, 869 (1946); Goddard, Hughes and Ingold, *Nature*, **158**, 480 (1946).

[14] Microanalyses were by Miss Patricia Craig.

[15] Dann and Davies, *J. Chem. Soc.*, 1050 (1929); Davies, Storries and Tucker, *ibid.*, 624 (1931).

[16] Francis and Hill, THIS JOURNAL, **46**, 2498 (1924).

ride was found to give less than 2% of *m*-isomer, further illustrating the strong *o*-*p*-directing effect of negatively substituted vinyl groups.

2. The mean value for the ratio of rate constants, *k*(cinnamic acid)/*k*(benzene), determined by the competitive nitration of cinnamic acid and benzene was found to be 0.111. This ratio is of the same order as that obtained by Bird and Ingold[10] for the competitive nitration of chlorobenzene and benzene.

3. The *o*-*p*-orienting effect of negatively substituted vinyl groups has been accounted for by the assumption that resonance stabilization in the transition state, involving the electrons of the olefinic bond, is the determining factor.

EVANSTON, ILLINOIS RECEIVED OCTOBER 17, 1947

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT, ABBOTT RESEARCH LABORATORIES]

Polysaccharide Acid Esters as Cation Exchange Media

BY FLOYD C. MCINTIRE AND JAY R. SCHENCK

In the development of a method for the purification of histamine[1] there arose a need for a cation exchange medium with properties not possessed by the commercially available cation exchangers. It was found that if cotton were *partially esterified* with succinic acid the acid ester so produced would function very nicely as a cation exchanger. The preparation of acid esters by the partial esterification of cellulose and other polysaccharides was then studied further with a view toward a more general use of these materials as cation exchange media.

To this end we have partially esterified cotton with glutaric, maleic, phthalic, and succinic acids and wood cellulose and starch with succinic acid.

Experimental

Esterification of Polysaccharides.—Two methods of esterification were used: (1) The acid anhydride, 0.2 mole, was dissolved in 300 ml. of pyridine. Ten grams of polysaccharide was suspended in this solution and the temperature was maintained at 60° for eighteen to twenty-four hours. The insoluble product was washed successively with water, dilute hydrochloric acid, water and alcohol and then dried *in vacuo*; (2) the acid anhydride, 0.2 to 0.4 mole, and 10 g. of anhydrous sodium acetate were dissolved in 300 ml. of glacial acetic acid. Ten grams of polysaccharide was introduced and the temperature was maintained at 100° for forty-eight hours. The product was washed with dilute hydrochloric acid, water and alcohol and then dried. The latter method is preferable for most purposes as it produces little or no obvious changes in the gross structure of the materials esterified. Satisfactory preparations of cotton acid maleate could be made only by this method. Starch was esterified in this way. During the esterification of wood cellulose and starch the reaction mixture was stirred continuously.

Determination of Cation Binding Capacity and Degree of Esterification.—Free carboxyl groups were determined by shaking a given amount of polysaccharide acid ester with an excess of 0.05 *M* sodium carbonate for fifteen to twenty minutes and titrating an aliquot of the solution for either total sodium or carbonate sodium. In this determination the original concentration of the second sodium ion of sodium carbonate should exceed the sodium ion binding capacity of the acid ester. The values so obtained agreed closely with the values for free carboxyl groups obtained by electrometric titrations. Direct titration with sodium hydroxide in the presence of an indicator was less reliable.

The degree of esterification was calculated from the determination of free carboxyl groups on the assumption that the number of ester linkages was equal to the number of free carboxyls.

Results and Discussion

The esterification of polysaccharides with dicarboxy acids is not new. This was perhaps first claimed by Levy,[2] and since then such esters have been covered in numerous patents.

In nearly all previous reports the polysaccharides were almost completely esterified and the products were soluble in organic solvents as the free acids or in water as the sodium salts. To our knowledge there is no previous report of the partial esterification of polysaccharides with dicarboxy acids for the preparation of cation exchange media. By effecting only partial esterification of the polysaccharides under conditions which minimize changes in mechanical structure, one can obtain products with physical properties which are very desirable for many cation exchange procedures. These partially esterified products do not jel in organic solvents as the free acids or in water as the sodium salts. In appearance they resemble the original polysaccharides very closely. The fibers of cotton acid esters seem more wiry and more brittle than cotton. The starch acid esters have less affinity for water than does the original starch.

Table I shows some representative values for the degree of esterification and the sodium ion binding capacity of the polysaccharide acid esters. The degree of esterification has a rather wide range. As many as one-fourth of the available hydroxyls of cotton have been esterified without noticeable breakdown of the fibers; with starch nearly half of the available hydroxyls were esterified and the product did not jel in water or alcohol either as the sodium salt or as the free acid. The degree of esterification can be controlled within reasonable limits.

The polysaccharide acid esters participate

---

[1] F. C. McIntire, L. W. Roth and J. L. Shaw, *J. Biol. Chem.*, **170**, 537 (1947).

[2] H. A. Levy, *Ind. Eng. Chem.*, **12**, 743 (1920).