[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE]

Further Observations on the Mechanism of Chlorinolysis of Sulfur–Carbon Bonds; the Chlorinolysis of 4-Benzylthio-7-chloroquinoline

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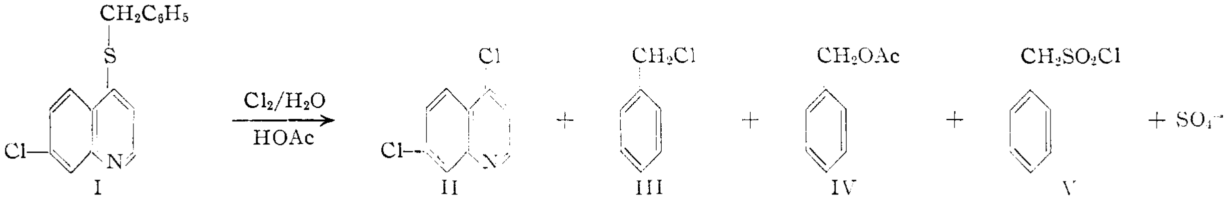
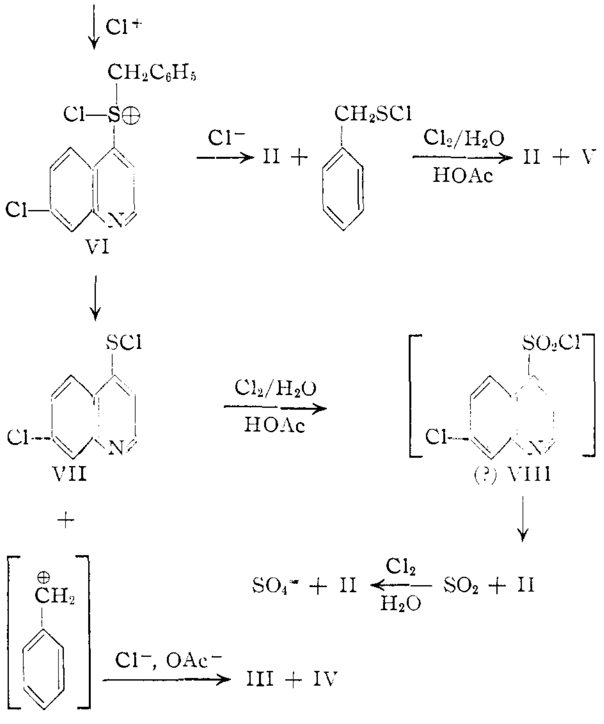
A re-examination of the cleavage of the title[7] compound by chlorine in aqueous acetic acid solution yielded the products previously reported, as well as others which were not anticipated on the basis of the earlier[3] postulation of the reaction mechanism. These results and those obtained from studies of the reaction in chloroform solution are in accord with ideas recently suggested[2] and logically can be extended to some of the remaining anomalies that have been reported on this subject in the literature.[7]

Introduction

The chlorinolysis of aryl alkyl sulfides in aqueous acetic acid has been demonstrated to be a satisfactory diagnostic test[2] for determining the nature and position of substituents on sulfur–carbon bonds. In each of the cases studied the products obtained were the aryl sulfonyl chloride, the alkyl chloride and the alkyl acetate. The mechanism which was proposed[2] to account for these and other results in the literature involved the formation of a chlorosulfonium ion[3] followed by the unimolecular cleavage of the bond between sulfur and the alkyl carbon. This cleavage was aided by both the electron-attracting power of the aryl group and the ability of the alkyl group to stabilize positive charge. The sulfenyl chloride, which was assumed to be the initial product of the cleavage, was oxidized to sulfonyl chloride in a succeeding reaction with aqueous chlorine.[4] The S_N2 displacement of the sulfonium ion by chloride ion was shown to be extremely unlikely in the cases observed.





Several reports[5–7] seemed, however, to contradict this mechanism. We chose to reinvestigate the chlorinolysis of 4-benzylthio-7-chloroquinoline[7] (I) in the attempt to ascertain the source of the anomaly. The products that had been reported were 4,7-dichloroquinoline (II) and benzyl chloride (III), although the latter product had not been isolated. Since none of the expected 7-chloro-4-quinolinesulfonyl chloride (VIII) had been obtained, the inference existed that a nucleophilic displacement by chloride ion had occurred at C_4 on the quinoline moiety. It is doubtful that the sulfur–quinolyl bond in the sulfide would cleave quantitatively in a unimolecular fashion. Nevertheless, since no sulfur-containing products had been detected, the manner of cleavage was entirely uncertain.

Results and Discussion

The chlorinolysis was carried out in an acetic acid solution containing approximately twice the theoretical amount of water. Since the reaction was accompanied by the evolution of heat, the reaction mixture was cooled in an ice-bath to maintain room temperature, or below, and thereby to minimize substitution by chlorine.

The previously reported products[7] of the reaction, II and III, were obtained in 90.8 and 47.0%

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[1] Part of the material in this paper was taken from the dissertation of L. J. Miller, submitted in partial fulfillment of the requirements for the Degree of Master of Science at the University of Delaware, June, 1957.

[2] (a) H. Kwart and R. K. Miller, THIS JOURNAL, **78**, 5008 (1956); (b) **78**, 5678 (1956).

[3] D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 17 (1951).

[4] N. Kharasch, S. J. Potempa and H. L. Wehrmeister, *ibid.*, **39**, 291 (1946), and references cited therein.

[5] J. M. Sprague and T. B. Johnson, THIS JOURNAL, **57**, 2252 (1935).

[6] T. B. Johnson and J. M. Sprague, *ibid.*, **58**, 1348 (1936).

[7] R. H. Baker, R. M. Dodson and B. Riegel, *ibid.*, **68**, 2636 (1946).

yield, respectively. In addition, phenylmethanesulfonyl chloride (V, 8.5–12%) and sulfate ions (83.7–75.7%) were obtained. The remainder of the liquid products gave a positive hydroxamic acid test[8] for esters and boiled in the right range for benzyl acetate (IV), thereby accounting for a fair material balance in each case.

The formation of the major products of this reaction could be interpreted in either of two ways: (1) "normal cleavage"[2] had occurred, namely, cleavage of the sulfur–benzyl bond followed by decomposition of the resulting quinolinesulfonyl chloride (VIII) or one of the intermediates on the path to VIII; (2) "abnormal cleavage" had occurred, namely, cleavage of the sulfur–quinolyl bond followed by decomposition of the resulting phenylmethanesulfonyl chloride (V) or one of its precursors. The "abnormal cleavage" course was considered, at first, as a distinct possibility because dibenzyl disulfide was desulfurized on chlorinolysis,[9] while various other dialkyl disulfides were cleaved to the alkyl sulfur trichlorides.[9] The oxidation of benzyl mercaptan by chlorine in aqueous acetic acid was, therefore, carried out, since this reaction in all likelihood involves the same intermediates as the formation of V from I.[4] However, a 90% yield of V was obtained, showing that extensive decomposition of an intermediate had not occurred. The stability of V itself was checked by treating it with chlorine in aqueous acetic acid solution for 1 hour both at room temperature and at 45–50°. The material was recovered unchanged.

Normal cleavage (1), on the other hand, would stipulate the unusual decomposition of a sulfonyl chloride VIII or one of the intermediates in its formation under the reaction conditions. While most sulfonyl chlorides are stable, a few have been described as decomposing to the corresponding chloride and sulfur dioxide under various conditions.[10]

It was decided to determine the products of a chlorinolysis of I in dry chloroform. Chlorinolysis in anhydrous solvents cannot result in oxidation to the sulfonyl chloride; in many cases[4,11] such reactions lead to sulfenyl chlorides or sulfur trichlorides. It was hoped that without changing its essential course, the reaction might thus be arrested after cleavage had occurred but before any decomposition of the sulfur-containing compound could take place.

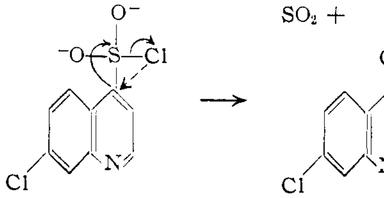
The chlorinolysis in anhydrous chloroform yielded the hydrochloride of 4-quinolinesulfenyl chloride (VII) as a yellow precipitate which reacted readily upon exposure to moist air to give an almost white mixture from which no pure compounds could be isolated. The mixture contained 61.7% of the total sulfur initially charged. Chlorinolysis of the mixture in aqueous acetic acid gave II and sulfate ions.

When the yellow precipitate was treated at once with *cis*-2-butene in fresh dry chloroform, it dissolved completely within a few seconds. From this solution was isolated a product which gave an analysis approximating that of the hydrochloride of 3-chloro-2-butyl 7′-chloro-4′-quinolyl sulfide. The free sulfide could be obtained by removing the hydrogen chloride with dilute ammonia solution. Hydrogen chloride must have been generated by chlorination of the chloroform solvent.

The sulfenyl chloride VII also was allowed to react with cyclohexene to give the expected adduct; with potassium iodide in acetic acid solution to liberate iodine; and with nitric acid to produce II and sulfate ions. Nitric acid previously had been used to effect the oxidation of sulfenyl chlorides to sulfonyl chlorides.[4]

The chloroform solution yielded 67% of the theoretical amount of benzyl chloride. Earlier investigators reported[12] that benzal chloride was one of the major cleavage products of the chlorinolysis of aryl benzyl sulfides in inert solvents. This side reaction would account for the reduction in yield of II in chloroform.

Clearly, the major products have resulted from a reaction step involving rupture of the sulfur–benzyl bond in the chlorosulfonium ion VI and this deduction is entirely in agreement with the mechanism of the chlorinolysis reaction previously proposed.[2] It is not yet well understood how the sulfur–quinolyl bond is broken. An SNi reaction similar to that written for the decomposition of chlorosulfite esters is one possibility to be considered, taking place in the sulfonyl chloride VIII as



However, the mechanistic details provided by Cram[13a] and by Lewis and Boozer[13b] for the chlorosulfite ester decomposition do not directly fit the sulfonyl chloride reaction since ionization to an ion pair (equilibrium) is required in the rate-determining step of the former. The development of positive charge at C_4 on the quinoline ring seems somewhat unlikely.

Another sidelight of these experiments is the rather facile decomposition of the sulfenyl chloride VII. Perhaps this was not unexpected in view of a number of other sulfenyl halides, *e.g.*, *p*-nitrobenzenesulfenyl chloride[14a] and β-naphthalenesulfenyl

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[8] D. Davidson and D. Perlman, "A Guide to Qualitative Organic Analysis," Rev. Ed., Brooklyn College Book Store Press, Brooklyn, N. Y., 1954, p. 28.

[9] I. B. Douglass, K. R. Brower and F. T. Martin, THIS JOURNAL, **74**, 5770 (1952).

[10] (a) C. M. Suter, "The Organic Chemistry of Sulfur–Tetracovalent Sulfur Compounds," John Wiley & Sons, Inc., New York, N. Y., 1944, p. 497; (b) F. Ullmann and P. Kertész, *Ber.*, **52**, 545 (1919); (c) R. Otto, *Ann.*, **141**, 93 (1867); (d) R. Schiller and R. Otto, *Ber.*, **9**, 1634 (1876); (e) C. S. Rondestvedt and P. K. Chang, THIS JOURNAL, **77**, 6532 (1955).

[11] I. B. Douglass and F. T. Martin, *J. Org. Chem.*, **15**, 795 (1950); see also reference 3, p. 37, and compare references 5 and 9.

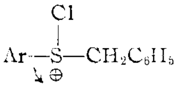
[12] (a) T. Zincke, *Ber.*, **44**, 769 (1911); (b) T. Zincke and A. Dahm, *ibid.*, **45**, 3457 (1912); (c) T. Zincke and O. Krüger, *ibid.*, **45**, 3470 (1912); (d) T. Zincke and K. Arnold, *ibid.*, **50**, 116 (1917).

[13] (a) D. J. Cram, THIS JOURNAL, **75**, 332 (1953); (b) E. S. Lewis and C. E. Boozer, *ibid.*, **74**, 308 (1952); C. E. Boozer and E. S. Lewis, *ibid.*, **75**, 3182 (1953).

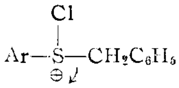
[14] (a) T. Zincke and S. Lenhardt, *Ann.*, **400**, 2 (1913); (b) T. Zincke and K. Eismayer, *Ber.*, **51**, 751 (1918).

chloride[14b] which are reported as very unstable in moist air and showing a strong tendency to disproportionation of the hydrolysis products. A ready explanation of these facts is not yet at hand.

Apparently a minor proportion of I does undergo "abnormal" cleavage to produce phenylmethanesulfonyl chloride (V). This type of cleavage could be due to a partial change in mechanism with some nucleophilic displacement at C_4 on the quinoline nucleus. As a remote possibility, it could also be due to the electron-attracting power inherent in the benzyl radical which would allow it to compete successfully with the quinolyl radical for electrons in the unimolecular decomposition of the chlorosulfonium ion (VI). In either case, an increase in the electron-attracting power of the benzyl ring would be expected to increase the amount of phenylmethanesulfonyl chloride formed. This effect was investigated by subjecting 4-(2,4-dichlorobenzylthio)-7-chloroquinoline to chlorinolysis in aqueous acetic acid. The yield of the corresponding substituted phenylmethanesulfonyl chloride was increased to 17%. This represented a relative increase of at least 40% in the amount of phenylmethanesulfonyl chloride formed. In addition only 63% of the initially charged sulfur appeared as sulfate ion which might be accepted as confirming the changed direction of bond cleavage in the chlorosulfonium ion. Discounting errors which could have been caused by slight, unavoidable variation in temperature and difficulties in recovery of all the sulfur-containing products in this experiment, the results nevertheless indicate a correlation between the amount of cleavage of the sulfur–quinolyl bond and the electron-withdrawal effect of the benzyl radical.



$$Ar\text{—}\overset{\displaystyle Cl}{\underset{\searrow\ \oplus}{S}}\text{—}CH_2C_6H_5$$



$$Ar\text{—}\overset{\displaystyle Cl}{\underset{\oplus\ \swarrow}{S}}\text{—}CH_2C_6H_5$$

The observations made on the chlorinolysis of I logically can be extended to the chlorinolysis of 4-benzylthio-8-nitroquinoline, from which 4-chloro-8-nitroquinoline was obtained.[7] The reasons for other apparently anomalous cases[5,6] are as yet obscure.

Experimental[15]

4-Benzylthio-7-chloroquinoline (I), prepared according to the method of Baker, Dodson and Riegel,[7] melted at 140–141°.

Chlorinolysis of I in Acetic Acid.—Chlorine was passed into a solution of I (50.0 g.) in glacial acetic acid (250 ml.) and water (12.5 ml., about twice the amount theoretically needed). The solution was stirred mechanically, and an ice-bath was used to keep the temperature near room temperature or below. After 15 minutes no more heat seemed to be produced. The passage of chlorine was discontinued after 0.5 hour. The mixture was allowed to stand for 15 minutes, then poured into 5 times its volume of ice-water. A yellow oil as well as a crystalline precipitate formed. The mixture was extracted 10 times with a total of 2 l. of petroleum ether. After the third extraction the crystalline phenylmethanesulfonyl chloride, which remained insoluble in either medium, was filtered off and washed with water. The sulfonyl chloride weighed 4.1 g. (12%) m.p. 91–93° (lit.[16] m.p. 92°), and yielded an anilide, m.p. 102.5–1035° (lit.[16] m.p. 102°).

As the first petroleum ether extracts were diluted with successive extracts, 4,7-dichloroquinoline hydrochloride precipitated. After it was washed with ether the crude product weighed 12.5 g. (30.5%) and sublimed between 130–155°. The analytical sample was purified by two sublimations at 2 mm. pressure. Recrystallization from aqueous ethanol gave 4,7-dichloroquinoline, m.p. 84–85.5° (lit.[17] m.p. 83.5–84.5°, 86°, 85–86°). A mixed melting point with an authentic sample showed no depression.

Anal. Calcd. for $C_9H_6Cl_3N$: inorganic Cl, 15.12; total Cl, 45.36. Found: inorganic Cl, 15.27; total Cl, 45.20.

The aqueous acid solution was neutralized approximately to a *p*H of 5, and the 4,7-dichloroquinoline (20.9 g., 60.3%) which precipitated was collected and washed with water. The melting point,[17] 85.5–86.5°, was not depressed by mixture with an authentic sample.

The addition of more base to the aqueous solution precipitated only 1.2 g. of a light brown impure material. The solution was re-acidified with hydrochloric acid, and 5% barium chloride solution was added. The barium sulfate which precipitated was ignited at 800°; weight 30.9 g. (75.7%).

The petroleum ether extracts were concentrated by distilling off the solvent. A tan solid material (0.8 g.) separated from the residue. The liquid residue was distilled under reduced pressure; 10.4 g. (47.0%) of benzyl chloride was obtained, plus some higher boiling material which gave a positive hydroxamic acid test[8] for esters. The benzyl chloride fraction was redistilled; b.p. 764 mm. (micro method) 178.5° (lit.[18] b.p. 179°), $n^{20}D$ 1.5354 (lit.[19] value $n^{17.4}D$ 1.5391). The infrared spectrum was very similar to that of an authentic sample. The β-naphthyl ether[20] was prepared; m.p. and mixed m.p. 99–100°.

More light tan solid was obtained from the residue of the liquid extracts and was added to the small amount previously obtained (total weight 2.0 g.). The material sublimed between 199–227°, m.p. (sealed tube) 198–205°. It contained nitrogen, no inorganic chlorine and corresponded approximately in chlorine content to a pentachloroquinoline.

Anal. Calcd. for $C_9H_2Cl_5N$: Cl, 58.85. Found: Cl, 58.36.

A second run, using 50.0 g. of I, gave 2.83 g. (8.5%) of phenylmethanesulfonyl chloride, and one-tenth of the aqueous solution yielded 3.417 g. (83.7%) of barium sulfate.

Oxidation of Benzyl Mercaptan with Chlorine.—Benzyl mercaptan (1.3 g.) was dissolved in acetic acid (60 ml.) and water (1.1 ml., about 3 times the amount theoretically needed). The solution was treated with a stream of chlorine for 1 hour. On pouring the reaction mixture into 500 ml. of ice-water, phenylmethanesulfonyl chloride precipitated. The dried material weighed 1.8 g. (90%), m.p.[16] 92.0–92.5°, m.p. of anilide[16] 102.5–103.0°.

Attempted Desulfurization of Phenylmethanesulfonyl Chloride.—Phenylmethanesulfonyl chloride (2.0 g.) was dissolved in acetic acid (40 ml.) and water (1 ml.). The solution was treated at room temperature with a slow stream of chlorine for 35 min. and then allowed to stand for 40 minutes. The total mixture was poured into 5 times its volume of ice-water and filtered. The recovered phenylmethanesulfonyl chloride weighed 1.8 g. The experiment was repeated at 45–50° for a period of 1 hr.; a maximum of only 7.3% of the starting material was lost.

Chlorinolysis of I in Dry Chloroform.—Twenty grams of I was dissolved in dry chloroform (200 ml.) and chlorine was passed in through a sulfuric acid-bath. After 7 min. a yellow precipitate (A) formed. After 15 min. no more precipitate appeared to be forming, and after a total of 0.5 hour, the passage of chlorine was discontinued. The pre-

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(15) Melting and boiling points are uncorrected. The melting point apparatus was similar to that described by A. May, *Anal. Chem.*, **21**, 1427 (1949), except that it was heated electrically.

(16) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 277.

(17) (a) A. R. Surrey and H. F. Hammer, THIS JOURNAL, **68**, 113 (1946); (b) C. C. Price and R. M. Roberts, *ibid.*, **68**, 1204 (1946); (c) see ref. 6.

(18) Reference 16, p. 255.

(19) N. A. Lange, "Handbook of Chemistry," 8th Ed., Handbook Publishers, Inc., Sandusky, Ohio, 1952, p. 1312.

(20) Reference 16, p. 193.

cipitate (A) was filtered off and treated in one of several ways.

In one run, starting with 50.0 g. of I, the mother liquor was diluted with petroleum ether to precipitate more solid material (5.1 g.), concentrated on a steam-bath, diluted with petroleum ether again to remove a small amount (0.3 g.) of solid product, and distilled. Most of the liquid product distilled between 66–71° at 15 mm. A portion was redistilled at atmospheric pressure. The properties (b.p.[18] 176–183°, $n^{17.4}$D 1.5375,[19] m.p. and mixed m.p. of β-naphthyl ether[20] 99–100°) identified the product as benzyl chloride (14.9 g., 67.3% yield of crude material).

When (A) was allowed to react with the moisture in the air, it turned almost white. From 50.0 g. of I, 32.9 g. of this material was obtained. The product did not react with cyclohexene or potassium iodide. Two grams of the product was suspended (the material was insoluble) in acetic acid (50 ml.) and water (2 ml.) and chlorine was passed into the mixture for 0.5 hour. The material gradually went into solution. The solution was poured into ice-water (200 ml.). Besides some unidentified products, 4,7-dichloroquinoline, m.p.[17] 84.5–86.0°, and sulfate ions were found by the methods mentioned above.

When (A) was used immediately upon filtration, it was soluble in glacial acetic acid. When potassium iodide was added, the solution turned red and a yellow precipitate formed. The solution was diluted with carbon tetrachloride and the characteristic purple color of iodine appeared. (A) reacted vigorously with concentrated nitric acid. The resulting solution was diluted; one portion gave a precipitate with barium chloride, while another portion yielded 4,7-dichloroquinoline upon neutralization. The melting point,[17] 85–86°, showed no depression when mixed with an authentic sample.

***cis*-2-Butene Adduct of 7-Chloro-4-quinolinesulfenyl Chloride.**—The material (A) (obtained from 25.0 g. of I) was immediately suspended in fresh dry chloroform (175 ml.) and treated with approximately 0.11 mole of *cis*-2-butene. The solid material went into solution almost as fast as the butene could be supplied. The solution was poured into petroleum ether (2 l.) to precipitate the hydrochloride of the butene adduct. The petroleum ether solution was saturated with hydrogen chloride, and more of the hydrochloride was collected. The hydrochloride, after recrystallization from benzene, melted over a wide range (117–125°); further recrystallization from benzene or from ethyl acetate did not improve its melting behavior. Melting point ranges between 85–130° were obtained, and they seemed to be very strongly dependent on the rate of heating and the particle size.

Anal. Calcd. for $C_{13}H_{14}Cl_3NS$: total Cl, 32.96; inorganic Cl, 10.99; S, 9.94; N, 4.34. Found: total Cl, 32.15; inorganic Cl, 12.41; S, 9.54; N, 4.3.

The hydrochloride was dissolved in a small amount of chloroform, and the solution was washed repeatedly with dilute ammonium hydroxide until the wash was free of chloride ions. The chloroform solution was washed with water and evaporated. The solid residue was recrystallized from aqueous ethanol; cooling in Dry Ice–acetone was necessary to avoid greater losses. The 3-chloro-2-butyl 7′-chloro-4′-quinolyl sulfide thus obtained weighed 5.0 g. (20%) and melted at 61–62°. The analytical sample was recrystallized once more without any significant change in the melting point.

Anal. Calcd. for $C_{13}H_{13}Cl_2NS$: Cl, 24.78; S, 11.20. Found: Cl, 24.60; S, 11.14.

Cyclohexene Adduct of 7-Chloro-4-quinolinesulfenyl Chloride.—A portion of (A) obtained from 15.0 g. of I was immediately added to 100 ml. of dry chloroform and about 20 ml. of cyclohexene. A vigorous reaction took place and the material quickly dissolved. The solution was washed with dilute ammonium hydroxide followed by water. The chloroform solution was evaporated to an oil and diluted with petroleum ether. A precipitate (6.8 g.) formed which could be recrystallized from petroleum ether. The cyclohexene adduct (5.2 g., 32% yield) thus obtained was light yellow and melted at 98–100°. After two treatments with decolorizing charcoal and three recrystallizations from hexane the material was white and melted at 100–101°.

Anal. Calcd. for $C_{15}H_{15}Cl_2NS$: C, 57.69; H, 4.84. Found: C, 57.94; H, 4.85.

4-(2,4-Dichlorobenzylthio)-7-chloroquinoline.—The general procedure of Baker, Dodson, and Riegel[1] was followed, except that the reaction mixture was refluxed only 10 minutes. The product after one recrystallization from ethanol was obtained in a 68.4% yield. The analytical sample was recrystallized a second time and melted at 151–152°.

Anal. Calcd. for $C_{16}H_{10}Cl_3NS$: Cl, 29.99; N, 3.95; S, 9.04. Found: Cl, 30.19; N, 3.79; S, 8.84.

Chlorinolysis of 4-(2,4-Dichlorobenzylthio)-7-chloroquinoline.—The procedure was similar to that given for the chlorinolysis of I. The 2,4-dichlorophenylmethanesulfonyl chloride obtained from 40.0 g. of sulfide weighed 5.0 g. (17%) after one recrystallization from hexane. The long colorless needles melted at 80.5–82.5° (lit.[21] m.p. 79–81°). The aqueous solution was diluted to 1 l. A 100-ml. aliquot yielded 1.746 g. (66.3%) of barium sulfate.

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[21] C. Ziegler and J. M. Sprague, *J. Org. Chem.*, **16**, 621 (1951).

NEWARK, DELAWARE

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

Stereoelectronic Factors in the Addition of Sulfenyl Halides to Norbornene

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The reactions of *o*-nitrobenzenesulfenyl chloride and *p*-nitrobenzenesulfenyl chloride with norbornene give only one product in each case. These products were identified by known degradative processes. A stereoelectronic interpretation has been advanced to explain these observations. Dipole moment studies have been made on the adducts, and an explanation or the deviation of these moments from the calculated result is suggested.

Introduction

We have reported[2] that when 2,4-dinitrobenzenesulfenyl chloride was added to norbornene in non-polar solvents, the normal 1:1 adduct and a smaller amount of nortricyclyl 2,4-dinitrophenyl sulfide resulted. An increase in the amount of the nortricyclyl sulfide was evident when a polar solvent, such as acetic acid, was used. When *p*-toluenesulfenyl chloride was added to norbornene, only the normal 1:1 adduct was obtained.

It has been suggested by Kharasch and coworkers[3] that a three-membered cyclic cationic intermediate is formed by addition of 2,4-dinitrobenzenesulfenyl cation to the double bond. By keeping this in mind, two explanations can be advanced to account for the effect of the structure of the sulfenyl chlorides on the addition reaction:

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[1] National Science Foundation predoctoral fellow, 1954–1955.

[2] H. Kwart and R. K. Miller, THIS JOURNAL, **78**, 5678 (1956).

[3] N. Kharasch and C. M. Buess, *ibid.*, **71**, 2724 (1949).