stirrer, thermometer, and wide-bore dropping funnel were added 34.6 ml (0.090 mole) of benzyldimethylsulfonium chloride (99.3% D_2O), 27.0 g (0.27 mole) of formaldehyde (98.6% D_2O–CH_3OD), and 30.0 ml of toluene. To the stirred mixture preheated to 50° was added 27.7 ml (0.36 mole) of 13.0 *N* sodium deuterioxide (99.7% D_2O). The reaction temperature rose immediately to 72°. The temperature was kept between 64 and 70° for 30 min. Then, the dark yellow organic layer was separated from the aqueous layer and was extracted with water. The organic layer was dried over anhydrous $MgSO_4$ and was filtered to yield 41.0 ml of toluene solution. The determination of the oxirane content of the toluene solution by the pyridine-HCl method[17] indicated a 62% yield based on benzyldimethylsulfonium chloride. The distillation of the solution at 59–60° (5 mm) gave 6.5 g (60%) of styrene oxide, and the mass spectrometric analysis is listed in Table I. Proton nmr analysis indicated 88% deuteration in the α position and 5–6% deuteration in the β position. Infrared analysis indicated a C–D absorption at 2230 cm^{-1}. The distillation residue of 1.3 g was analyzed by vpc and mass spectrometry and the results are shown in Table II. The mass spectrometric analysis of the cold trap of the above distillation indicated the presence of toluene and methyl sulfide. The methyl sulfide was deuterated to the extent of 82.4% according to the following distribution: d_0, 4.2%; d_1, 0.6%; d_2 0.95%; d_3, 3.5%; d_4, 13.4%; d_5, 35.1%; and d_6, 42.0%. The ratio of d_6/d_5, 1.3, was calculated by E. B. Baker from deuterium analyses by nmr. Infrared analysis confirmed the presence of deuterium with C–D absorptions at 2300 and 2260 cm^{-1}.

Attempted Deuteration of Methyl Sulfide with D_2O and Sodium Hydroxide. To 1.86 g (0.03 mole) of methyl sulfide in 10 ml of toluene was added a solution of 4.8 g (0.12 mole) of NaOH and 1.75 g (0.03 mole) of NaCl in 25 ml of 99.5% D_2O. The stirred mixture was heated to 70° and refluxed at 60–65° for 30 min. The reaction mixture was separated. The organic layer was extracted three times with water and dried over anhydrous $MgSO_4$. Mass spectrometric and infrared analyses did not detect any deuteration of the methyl sulfide.

Acknowledgment. We wish to express our sincere appreciation to the following persons of The Dow Chemical Company, Midland, Mich., for the spectroscopic analyses: E. B. Baker and J. P. Heeschen, nmr; L. Westover, G. Kallos, and J. C. Tou, mass spectrometry; and R. A. Nyquist, infrared.

A New Reaction of Thionyl Chloride with a Carboxylic Acid in the Presence of a Tertiary Amine. An X-Ray Crystallographic Proof of Structure of α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride

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Abstract: When 4-nitro-2,5-dimethoxyphenylacetic acid was treated with thionyl chloride and a small amount of tertiary amine, a sulfur-containing product, $C_{10}H_8NO_5SCl_3$, was obtained. A single-crystal three-dimensional X-ray crystallographic study showed the structure of this product to be α-chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl chloride. Some chemical and physical properties of this unusual compound are reported and discussed. That this novel reaction may be general is suggested by the fact that phenylacetic acid gives an analogous compound, $C_8H_5OSCl_3$.

Although the use of thionyl chloride with a tertiary amine is a well-known method for the preparation of carboxylic acid chlorides, we wish to report a new reaction arising from attempted application of this method,[2] for which little precedent has been found. When 4-nitro-2,5-dimethoxyphenylacetic acid was treated with excess thionyl chloride and 0.3–0.4 equiv of pyridine (or triethylamine), the expected 4-nitro-2,5-dimethoxyphenacetyl chloride was not obtained. The beautifully crystalline yellow product, isolated in 75% yield, was found to contain sulfur as well as a high percentage of chlorine. The analysis of the product (C, H, N, S, O, Cl, mol wt, OMe) corresponded to the formula $C_{10}H_8NO_5SCl_3$ (2OCH_3). The structure and some chemical reactions of this compound are the subjects of this report.

Physical Evidence for the Structure of the $C_{10}H_8NO_5SCl_3$ Compound

The infrared spectrum (Figures 1 and 2) showed the presence of the nitro group (1346, 1527 cm^{-1}), the methoxyl groups (1224 cm^{-1}) as well as the aromatic ring (1624, 1580, 1495 cm^{-1}), and a relatively complicated pattern in the carbonyl region, with a strong peak at 1766 cm^{-1}, inflections at 1783 and 1800 cm^{-1}, and a medium-strength peak at 1808 cm^{-1} (in carbon tetrachloride). The spectrum taken in KBr was very little different in this region. The presence of an acid chloride was strongly indicated although the material did not appear to be degraded by the water usually present in an ordinary KBr pressing. This stability to water will be discussed further below.

The proton magnetic resonance spectra were clear-cut and readily interpretable. There were only two pairs of singlets, at 3.97 and 4.03 ppm and at 7.47 and 7.57 ppm, in the ratio 3:1. The high-field pair could be assigned to the methoxyl protons, and the low-field pair to two protons on the aromatic ring.

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[1] (a) Polaroid Corp., Cambridge, Mass. (b) Harvard University, Cambridge, Mass.

[2] (a) P. Carré and D. Liebermann, *Compt. Rend.*, **199**, 1422 (1934); *ibid.*, 200, 1215 (1935); (b) J. P. E. Human and J. A. Mills, *Nature*, **158**, 877 (1946); (c) W. Gerrard and A. M. Thrush, *J. Chem. Soc.*, 741, (1952); 2117 (1953); J. A. Cade and W. Gerrard, *Nature*, 172, 29 (1953).

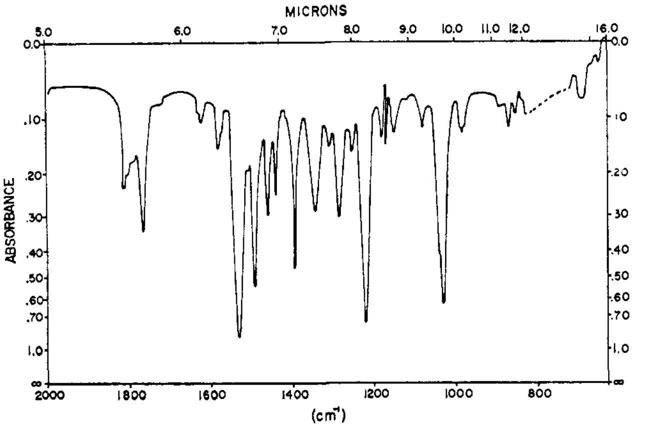


Figure 1.

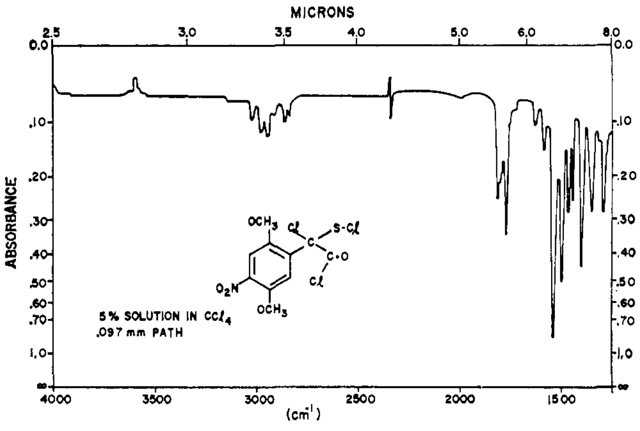
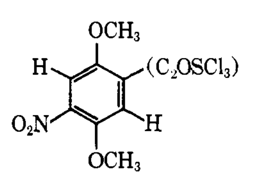
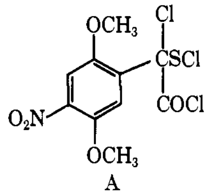


Figure 2.

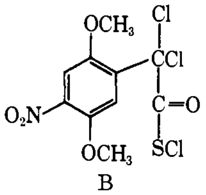
This accounted for all eight protons in the compound, and underlined the unique character of the side chain. A partial structure could be written



The evidence from the carbonyl region of the infrared spectrum favored structure A, although structure B[3] could not be dismissed.



A



B

High-resolution mass spectra were run in an attempt to determine the structure of the side chain.[4] The molecular ion confirmed the earlier analytical data. The most intense peaks in the high mass ($m/e > 200$) region of the spectrum (Table I) fell into three groups which corresponded to the loss of COSCl (peaks at 264,[5] 265, 266, 268), the loss of SCl (peaks at 292,[5] 294), and the loss of COCl (peaks at 296,[5] 298, 300). Less intense, but still prominent, were peaks corresponding to the loss of $COCl_3$ and C_2HOCl_3.

Neither structure A nor B explains all these fragmentations without invoking major rearrangements. For example, if we examine structure B we can readily visualize formation of the m/e 264 (−COSCl) and the m/e 292 (-SCl) peaks. However, the peak at 296 (−COCl) requires some rearrangement which attaches the sulfur atom to the α-carbon or the ring, and the 226 (−$COCl_3$) and 213 (−C_2HOCl_3) peaks also must arise from extensive rearrangements.

If structure I is considered, the 292 (−SCl) and 296 (−COCl) peaks can be explained as simple cleavages, but the 264 peak (−COSCl) requires a rearrangement which attaches a chlorine atom to the fragment, either at the ring or at the side-chain carbon atom. In this case as well, the origin of the 226 and 213 peaks is not clear.

Table I. High-Resolution Mass Spectrum Analysis

Found	Calcd	Formula	Assignment
362.9123	362.9130	$C_{10}H_8NO_5{}^{35}Cl^{37}Cl_2S$	Mol wt
361.9208	361.9237	$^{12}C_9{}^{13}CH_8NO_5{}^{35}Cl_2{}^{37}ClS$	
360.9180	361.9159	$C_{10}H_8NO_5{}^{35}Cl_2{}^{37}ClS$	
358.9196	358.9189	$C_{10}H_8NO_5{}^{35}Cl_3S$	
299.9500	299.9492	$C_9H_8NO_4{}^{37}Cl_2S$	−COCl
297.9523	297.9522	$C_9H_8NO_4{}^{35}Cl^{37}ClS$	
295.9565	295.9551	$C_9H_8NO_4{}^{35}Cl_2S$	
293.9755	293.9750	$C_{10}H_8NO_5{}^{35}Cl^{37}Cl$	−SCl
291.9780	291.9780	$C_{10}H_8NO_5{}^{35}Cl_2$	
267.9764	267.9771	$C_9H_8NO_4{}^{37}Cl_2$	−COClS
265.9779	265.9801	$C_9H_8NO_4{}^{35}Cl^{37}Cl$	
264.9852	264.9842	$^{12}C_8{}^{13}CH_8NO_4{}^{35}Cl_2$	
263.9809	263.9830	$C_9H_8NO_4{}^{35}Cl_2$	
226.0173	226.0174	$C_9H_8NO_4S$	$-COCl_3$
213.0090	213.0096	$C_8H_7NO_4S$	$-C_2HOCl_3$

The ambiguity posed by the mass spectra and other evidence, physical as well as chemical (*vide infra*), suggested that only an X-ray determination could allow for an unequivocal structural assignment. Single crystals of the $C_{10}H_8NO_5SCl_3$ compound suitable for X-ray analysis were obtained by recrystallization of the crude reaction product from hexane.

Single-Crystal X-Ray Analysis[6]

No precautions were taken to prevent exposure of the crystals to atmospheric conditions throughout the data collection. Rotation, precession, and Weissenberg photographs of the approximately cube-shaped crystals (average dimension = 0.15 mm) provided the lattice constants: a = 10.90 ± 0.01, b = 10.35 ± 0.01, c = 14.82 ± 0.02, and β = 121°45′ ± 15′.

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[3] Acylsulfenyl chlorides have previously been reported; see H. Böhme and M. Clement, *Ann. Chem.*, **576**, 61 (1952); H. Böhme, H. W. Goubeaud, and H. D. Stachel, *Chem. Ber.*, **92**, 362 (1959).

[4] We are indebted to Professor K. Biemann of Massachusetts Institute of Technology for determining this spectrum, and for many helpful discussions.

[5] These are the monoisotopic peaks; see K. Biemann, "Mass Spectrometry: Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 59.

[6] J. Z. G. and W. S. are pleased to acknowledge support of the crystallographic research by the U. S. Air Force Office of Scientific Research under Grant No. AF-AFOSR-1059-66.

Table II. Atomic Coordinates from the Final Cycle of Least-Squares Analysis

Atom	x_f	$\sigma(x)$	y_f	$\sigma(y)$	z_f	$\sigma(z)$
1	0.21318	0.00030	0.32434	0.00035	0.10794	0.00021
2	0.10578	0.00037	0.30784	0.00037	0.18197	0.00026
3	0.56018	0.00041	0.08043	0.00048	0.15945	0.00045
4	0.48011	0.00038	0.24790	0.00040	0.31091	0.00026
5	0.21739	0.00092	0.05368	0.00093	−0.00202	0.00065
6	0.16401	0.00125	−0.02433	0.00143	−0.09626	0.00094
7	0.20979	0.00078	−0.14716	0.00080	0.33971	0.00057
8	0.26221	0.00156	−0.06950	0.00154	0.43305	0.00108
9	0.34766	0.00124	0.19645	0.00137	0.17669	0.00094
10	0.43387	0.00175	0.19949	0.00179	0.12164	0.00123
11	0.42290	0.00116	0.28742	0.00121	0.06275	0.00082
12	0.08513	0.00088	−0.29094	0.00101	0.15128	0.00067
13	0.10050	0.00092	−0.37104	0.00094	0.09981	0.00068
14	0.01170	0.00115	−0.30743	0.00123	0.18952	0.00080
15	0.28549	0.00106	0.06698	0.00122	0.17682	0.00080
16	0.21508	0.00112	−0.00396	0.00141	0.08093	0.00087
17	0.15495	0.00114	−0.12102	0.00126	0.07683	0.00084
18	0.15301	0.00088	−0.16484	0.00098	0.16345	0.00064
19	0.21479	0.00103	−0.09769	0.00126	0.25772	0.00076
20	0.28438	0.00116	0.02110	0.00132	0.26286	0.00084

Systematic extinctions for 0*k*0 (*k* odd) and *h*0*l* (*l* odd) indicated, unambiguously, the monoclinic space group $P2_1/c$. The observed density (flotation method) of 1.66 g/cm^3 is in reasonable agreement with the calculated value 1.68 g/cm^3, assuming four molecules of $C_{10}H_8NO_5SCl_3$ per unit cell.

Intensities within the copper sphere from zones *h*0*l*–*h*7*l* were measured on a Supper–Pace automatic diffractometer. A comparison of these intensities with visually estimated intensities from zones 0*k*l–1*k*l indicated that individual scale factors for the *b* axis data were not necessary at this stage. Only the more accurately measured diffractometer data were used in the structure analysis.

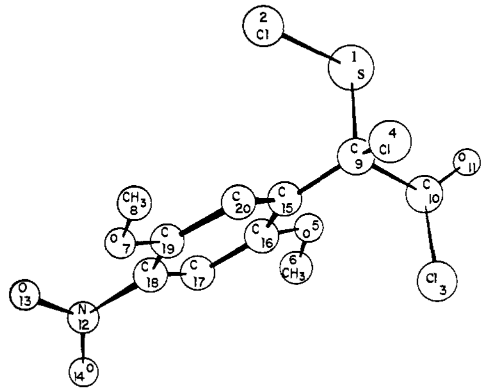

Figure 3.

After correction for the Lorentz–polarization factors, the 2069 independent intensities were placed on an absolute scale using the method of Wilson.[7] A sharpened Patterson function was computed and examined for the Harker-type interactions between symmetry-related heavy atoms. While all self-interactions of four independent heavy atoms were clearly evident, the many ambiguities necessarily introduced in the extension of Patterson vectors to atomic positional vectors $\{X_i(\text{atomic}) = X_i(\text{Patterson}) + S;\ S = 0, 0.5\}$ did not enable us at this point to establish a unique arrangement for all four heavy atoms. However, two of the possible independent heavy atom sites were separated by 2 A and therefore indicative of the fragment S–Cl.

A structure factor calculation based on the coordinates of these two atoms showed the reliability index to be $R = 0.59$. The corresponding electron density synthesis revealed, in addition to the peaks from the fragment S–Cl, two other relatively intense peaks at positions consistent with the previously observed Harker interactions. These four peaks were accepted as corresponding to the sulfur and chlorine atoms; their relative spatial orientation was suggestive of the geometry expected for the four heavy atoms of structure A.

The correctness of this choice was further substantiated by the Patterson function which clearly revealed all symmetry-independent heavy atom interactions corresponding to the vectors between the four chosen atoms. A second structure factor calculation based on these four atoms ($R = 0.51$) followed by electron density synthesis revealed the remainder of structure A.

One cycle of least-squares refinement of the coordinates of all 20 atoms (omitting H) of structure A obtained from the second electron density map reduced the reliability index to $R = 0.27$ for the 2069 independent reflections.

Additional cycles of least-squares refinements in which all coordinates, anisotropic temperature factors assigned to the chlorine and sulfur atoms, isotropic temperature factors assigned to the other atoms, and individual zone scale factors were allowed to vary resulted in $R = 0.10$ for the 1300 most intense reflections. The final reliability index for the 2069 reflection was $R = 0.13$. A difference synthesis revealed well-defined peaks in positions expected for the aromatic hydrogen atoms. No other significant peaks were observed.

The atomic coordinates from the final cycle of least-squares analysis are presented in Table II. A computer-drawn structural formula of the molecular conformation in the crystal lattice is shown in Figure 3.

The reaction between 4-nitro-2,5-dimethoxyphenylacetic acid and thionyl chloride led, therefore, to α-chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl chloride I, structure A.

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(7) A. J. C. Wilson, *Nature*, **150**, 152 (1942).

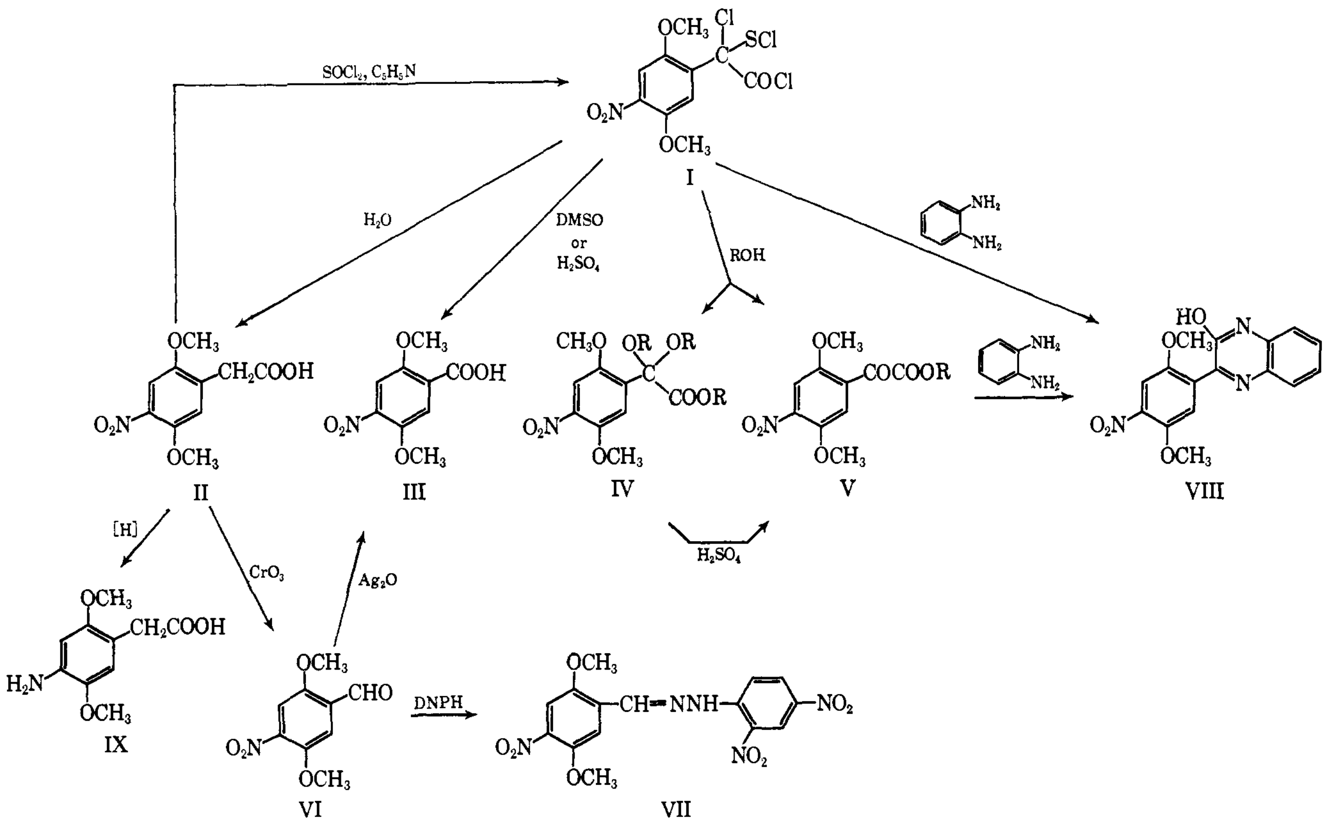


Figure 4.

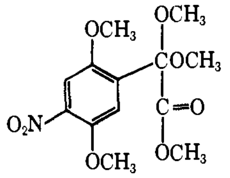
Chemical Behavior of α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride (I)

The chemical reactions described are summarized in Figure 4. The iodometric titration of I by Bohme's method[8] showed the presence of one chlorine on sulfur.

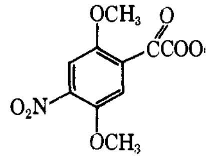
As noted above, the infrared spectrum of this compound in a KBr pressing (in which some water is normally present) was very similar to the spectrum taken in carbon tetrachloride. This suggested that the compound was inert to water, a suspicion which was confirmed by suspending the compound for 12 hr in water at 25° and recovering it unchanged. However, the lack of reactivity proved to be due to the fact that the solid compound was not soluble in and not wetted by water, since treatment of a dioxane solution of the sulfenyl chloride with water led to a quantitative yield of 4-nitro-2,5-dimethoxynitrophenylacetic acid (II). Exposure to acetone–water or tetrahydrofuran–water gave the same product in lower (68–80%) yields, as did solution in 10% aqueous sodium hydroxide followed by acidification (89% yield). Heating the sulfenyl chloride I with 10% hydrochloric acid at 100° for 18 hr led to 70% recovery, and the only other product isolatable was a small amount of the same phenylacetic acid II.

This hydrolysis appears to be an oxidation of the sulfur atom at the expense of the oxidation state of the α-carbon atom[9] since the formation of sulfur dioxide could be demonstrated. The acidic hydrolysis solution was swept with air; the effluent gases were collected, and the sulfur dioxide formed was determined by oxidizing to sulfate and precipitating the barium salt.[10]

Reaction of the acid chloride with alcohols did not take the same course as hydrolysis. Refluxing I in methanol for 18 hr gave a 72% yield of the ketal ester IV, mp 172–173° (ν 1763 cm⁻¹), whose structure was demonstrated by elemental analysis and infrared and proton magnetic resonance spectra. When the reaction was run in a sealed tube reaction at 100° or when I was refluxed in methanol–water (4:1), the keto ester V, mp 158–159° (ν 1739, 1689 cm⁻¹), was isolated as well as IV. Ethanol gave the analogous keto ester, mp 143–145° (ν 1748, 1685 cm⁻¹), and a ketal ester, mp 109–110°, which was difficult to purify and had an unsatisfactory analysis. The keto esters were recovered unchanged when solutions in concentrated sulfuric acid were kept for 1 hr at room temperature and then precipitated with water. Under these conditions IV could be efficiently converted to V.



IV



V

α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl chloride (I) reacted vigorously with dimethyl sulfoxide. Slow addition of the solid acid

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(8) H. Böhme and E. Schneider, *Ber.*, **76**, 483 (1943).

(9) W. A. Waters, "The Chemistry of Free Radicals," Oxford University Press, London, 1946, p 253; L. Birkenbach, K. Kellermann, and W. Stein, *Ber.*, **65**, 1071 (1932); F. F. Rust and W. E. Vaughn, *J. Org. Chem.*, **7**, 491 (1942).

(10) A. A. Noyes and E. H. Swift, "Qualitative Chemical Analysis of Inorganic Substances," The MacMillan Co., New York, N. Y., 1942, p 331.

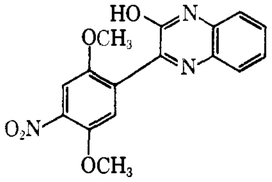
chloride to DMSO, followed by heating at 100° for 15 min, and treatment with water yielded (79%) a bicarbonate-soluble product which was shown to be 2,5-dimethoxy-4-nitrobenzoic acid (III), mp 196–198°. Proof of structure stemmed from elemental analysis, infrared spectrum, and the following series of reactions.

When 4-nitro-2,5-dimethoxyphenylacetic acid was treated with chromium trioxide in acetic acid at 100° for 30 min, then worked up with water, the product, mp 171–173°, ν 1698 cm^{-1}, was found to be insoluble in bicarbonate solution and to analyze correctly for 2,5-dimethoxy-4-nitrobenzaldehyde (VI). This assignment as an aldehyde was confirmed by the proton magnetic resonance spectrum and formation of the 2′,4′-dinitrophenylhydrazone, mp 290–291°, and comparison showed it was neither 2,5-dimethoxy-3-nitrobenzaldehyde nor 2,5-dimethoxy-6-nitrobenzaldehyde.[11] It is noteworthy that under the same reaction conditions *p*-nitrophenylacetic acid was oxidized by CrO_3 all the way to *p*-nitrobenzoic acid.

The 2,5-dimethoxy-4-nitrobenzaldehyde (VI) could be oxidized further with silver oxide in alkaline solution in 74% yield to the corresponding benzoic acid III, mp 195–197.5°. Substance III was identical with the product from the reaction of the acid chloride I with dimethyl sulfoxide.

The possibility that nitration of 2,5-dimethoxyphenylacetic acid gave the 6-nitro product was considered early in this work and was ultimately eliminated by both the nmr studies and the oxidation to 2,5-dimethoxy-4-nitrobenzaldehyde (VI). Less persuasive, but still pertinent, was the following evidence. Reduction of the nitro group gave an amino acid (X) which could be sublimed without change. The 6-aminophenylacetic acid derivative would be expected to cyclize to the lactam under these conditions.

o-Phenylenediamine could be reacted with I to yield a yellow halogen-free, base-soluble product, the hydroxyquinoxaline VIII, mp 332–333°, ν 1670 cm^{-1}. The identical product was obtained from *o*-phenylenediamine and the keto ester V.

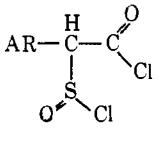


VIII

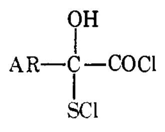
Discussion

The oxidation of a carbon atom adjacent to an aromatic ring by thionyl chloride is the subject of a number of reports. Boon[12] described the oxidation of 2,4-dimethylthiazole-5-carboxylic acid to 4-methylthiazole-2,5-dicarboxylic acid dichloride, and reported sulfur dichloride as a by-product of the reaction. In the presence of pyridine, however, the 2,4-dimethylthiazole-5-carboxylic acid chloride was formed. Earlier reports of the oxidation of toluene derivatives to the corresponding benzoic acid derivatives were the subject of a German patent.[13] Preobrazhenskii and Beer[14] reported conversion of 4-methylnicotinic acid to 4-trichloromethylnicotinic acid by short refluxing in thionyl chloride. We have found no prior reference in the literature to the formation of a sulfenyl chloride by this reagent.

The synthesis of I may involve the formation of the acid chloride, $ARCH_2COCl$, which in a pyridine-catalyzed reaction with another molecule of thionyl chloride could give



The latter might be postulated to undergo an internal oxidation of the α-carbon atom and reduction of the sulfur atom to

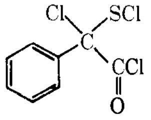


$$AR{-}\overset{\displaystyle OH}{\underset{\displaystyle SCl}{C}}{-}COCl$$

followed by displacement of the hydroxyl substituent by chlorine to yield I.[15]

Alternatively, an α,α-dichloroacetyl intermediate could react with some sulfur-containing fragment arising from an independent reaction[12,16] of the thionyl chloride.[17]

Although the generality of this reaction has not been thoroughly investigated, initial experiments with phenylacetic acid have led to the isolation of a liquid product with an analogous empirical formula, $C_8H_5OSCl_3$. Reaction of $C_8H_5OSCl_3$ with methanol yielded methyl benzoylformate and treatment with *o*-phenylenediamine gave 2-hydroxy-3-phenylquinoxaline. The infrared spectrum showed carbonyl peaks at 1780 and 1811 cm^{-1}. We assign this compound structure XI by analogy.



XI

Experimental Section[18]

4-Nitro-2,5-dimethoxyphenylacetic Acid (II). To a stirred suspension of 2,5-dimethoxyphenylacetic acid (24.0 g, 0.122 mole) in 90 ml of acetic acid at 15° was added, dropwise, a solution of 18 ml of fuming nitric acid (90%) in 18 ml of acetic acid. The temperature

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[11] L. Rubenstein, *J. Chem. Soc.*, 1998 (1925). The sample of 2,5-dimethoxy-3-nitrobenzaldehyde was kindly supplied by Dr. D. Ross.

[12] W. R. Boon, *J. Chem. Soc.*, 602 (1946).

[13] Farbwerke Meister Lucius in Hoechst and Bruening German Patent 282,133 (1913).

[14] N. A. Preobrazhenskii and A. A. Beer, *J. Gen. Chem. USSR*, **15**, 667 (1945); *Chem. Abstr.*, 40, 5724 (1946).

[15] When $ArCH_2COCl$, prepared from the nitrodimethoxyphenylacetic acid and oxalyl chloride, is treated with thionyl chloride and pyridine, the chlorosulfenyl acid chloride I is formed in about 40% yield.

[16] E. Koenigs and H. Greiner, *Ber.*, **64**, 1049 (1931).

[17] In order to test the assumption that the role of pyridine was to cause formation of sulfur dichloride, and that the latter led to the formation of I, the nitrodimethoxyphenylacetic acid was treated with thionyl chloride and sulfur dichloride in the absence of pyridine. The only tractable product appeared on the basis of infrared evidence to be an α-chlorinated phenylacetyl chloride.

[18] Elemental analyses were by Dr. A. Bernhardt, Mülheim, Germany, and Dr. C. Fitz, Needham, Mass. Ultraviolet spectra were taken on a Cary Model 14 recording spectrophotometer, infrared spectra on a Perkin-Elmer Infracord No. 237 spectrophotometer, and nmr spectra on a Varian A-60 instrument with TMS as internal reference. Melting points were taken in a micro aluminum block using a calibrated partial immersion thermometer, and are corrected.

was kept below 25° (ice bath). The resulting heavy yellow precipitate was let stand 20 min, then poured onto 150 g of ice–water. The solid product was filtered, washed with water until free of acid, and crystallized from 500 ml of ethanol to produce an 82% yield (24.5 g, 0.1 mole) of 4-nitro-2,5-dimethoxyphenylacetic acid, mp 203–205°, as heavy yellow rods. Further recrystallization from ethanol gave a sample suitable for analysis, mp 204–205°; $\lambda_{\max}^{\mathrm{EtOH}}$ in mμ (ε): 244 (7200), 274 (5400), 364 (3100).

Anal. Calcd for $C_{10}H_{11}NO_6$: C, 49.79; H, 4.60; N, 5.81; O, 39.80. Found: C, 50.01; H, 4.61; N, 5.99; O, 39.61.

α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride (I). Under rigidly anhydrous conditions a solution of 4-nitro-2,5-dimethoxyphenylacetic acid (4.0 g, 0.0166 mole), 25 ml of redistilled thionyl chloride (Matheson Coleman and Bell, practical grade, distilled through a 12-in. Vigreux column, center cut, bp 76° used), and 0.5 ml of pyridine (Eastman Kodak Company, Karl Fischer reagent grade. dried over KOH pellets) was refluxed 3 hr, evaporated to dryness *in vacuo*, and treated twice with benzene (reagent grade, dried over sodium wire), evaporating to dryness each time to remove all traces of thionyl chloride. The yellow semisolid product was extracted two times with 15-ml portions of anhydrous ether and the clear yellow ether solution allowed to stand overnight. A first crop of heavy crystals (3.2 g, mp 110–111.5°) was filtered off and a second crop separated afterward (1.55 g, mp 109–111.5°). The total yield of stout yellow crystals was 79.5% (4.75 g, 0.0132 mole). The analytical sample was crystallized from hexane, mp 110.5–112°; $\lambda_{\max}^{\mathrm{hexane}}$ in mμ (ε): 260 (3000), 346 (4100). The infrared spectrum showed bands at 1808 (m), 1800 (sh), 1783 (sh), 1766 (s) cm^{-1} in the carbonyl region (5% in CCl_4 solution) (Figure 1).

Anal. Calcd for $C_{10}H_8NO_5SCl_3$: C, 33.31; H, 2.24; N, 3.89; O, 22.29; S, 8.89; Cl, 29.50; mol wt, 360.6; OMe, 17.22. Found: C, 33.4, 33.58; H, 2.1, 2.17; N, 3.9, 3.75; O, 22.02; S, 8.9, 8.43; Cl, 29.5, 29.74; mol wt, 328 (Rast), 355;[19] OMe, 17.30.

Principal mass spectral peaks above 200 are listed in Table I;[4,20] nmr spectrum (TMS as internal reference): δ 3.97 (s) (3 H), 4.03 (s) (3 H), 7.47 (s) (1 H), and 7.57 (s) (1 H) ppm.

Titration for sulfenyl chloride:[6] 0.07818 g of compound, one S–Cl required 2.19 ml of 0.101 *N* I_2 solution; found, 2.21 ml.[21]

4-Amino-2,5-dimethoxyphenylacetic Acid (IX). A solution of 4-nitro-2,5-dimethoxyphenylacetic acid (2.4 g, 0.01 mole) in 240 ml of anhydrous ethanol with 220 mg of platinum oxide was hydrogenated at 25° and atmospheric pressure until 0.03 mole of hydrogen was taken up. The suspension was filtered under nitrogen. The product crystallized out of the ethanol filtrate in yellowish white needle clusters, sintering at 165°, melting at 171.5–174° dec, 1.56 g, 74%. Several recrystallizations from ethanol produced a sample suitable for analysis, mp 174–176°.

Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63; O, 30.30. Found: C, 57.10; H, 6.12; N, 6.58; O, 30.55.

A sample of 4-amino-2,5-dimethoxyphenylacetic acid, mp 170–173°, was sublimed at 190° (1 mm). The sublimate, sintering at 165°, mp 171–173°, had an infrared spectrum identical with the original sample.

4-Nitro-2,5-dimethoxybenzaldehyde (VI). A suspension of 1.2 g (0.005 mole) of 4-nitro-2,5-dimethoxyphenylacetic acid in 25 ml of acetic acid was stirred and heated to 100°. and 2.0 g of chromium trioxide suspended in 10 ml of acetic acid was added. The brown mixture was heated at 100° for 30 min, during which time the color became green and solution was complete. Dilution with 70 ml of water and cooling yielded 0.4 g (40%) of crude aldehyde VI, mp 168–171°. Extraction with aqueous sodium bicarbonate solution gave 0.37 g, mp 169–171°, and recrystallization from methanol produced an analytically pure product, mp 171–173°; $\lambda_{\max}^{\mathrm{hexane}}$ in mμ (ε): 254 (9500), 364 (4300); $\nu_{\max}^{\mathrm{KBr}}$ in cm^{-1}: 1697. Mixture melting point with 6-nitro-2,5-dimethoxybenzaldehyde,[11] mp 163.5–166.5°, showed depression to 137–140°. The infrared spectra were not identical.

Anal. Calcd for $C_9H_9NO_5$: C, 51.19; H, 4.30; N, 6.63; O, 37.88. Found: C, 51.40; H, 4.40; N, 6.64; O, 37.96.

2,4-Dinitrophenylhydrazone (VII), mp 290–291° (acetic acid), gave the following analysis: Calcd for $C_{15}H_{13}N_5O_8$: C, 46.04; H, 3.35; N, 17.90; O, 32.71. Found: C, 46.67, 46.13; H, 3.73, 3.82; N, 17.73, 17.92; O, 32.00, 32.26.

Hydrolysis of α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride. I. Neutral Hydrolysis. a. I (100 mg, mp 107–111°) was finely ground and stirred in 5 ml of water at ambient temperature for 20 hr. The filtered product was dried to yield 100 mg, mp 106–110°, mixture melting point with starting material undepressed.

b. I (0.20 g, mp 110.5–112°) was dissolved in 3 ml of dioxane (peroxide free) and 2 ml of water was added. After 2 hr at room temperature the acidic solution was evaporated to dryness to give a quantitative yield of crude 4-nitro-2,5-dimethoxyphenylacetic acid (II), mp 188–192°, identified by infrared spectrum.

c. A solution of I (2 g) in 35 ml of acetone and 15 ml of water was stirred overnight at 25–35°. Evaporation to dryness and water washing of the residue yielded 1.22 g (81%) of crude 4-nitro-2,5-dimethoxyphenylacetic acid (II), mp 180–185°. Fractionation with aqueous sodium bicarbonate solution and crystallization from ethanol raised the melting point to 197–201°.

The phenylacetic acid was esterified (ethanol–H_2SO_4) to ethyl 4-nitro-2,5-dimethoxyphenylacetate, mp 86.5–88°. Infrared spectra of the acid and ester were identical with spectra of previously prepared samples.

d. Compound I (3.0 g) in 35 ml of tetrahydrofuran (peroxide free) and 35 ml of water was stirred 3 days at room temperature. The deep yellow solid which had separated from the strongly acidic solution (pH 1) weighed 1.45 g, 72% yield of 4-nitro-2,5-dimethoxyphenylacetic acid (II), which was esterified directly to yield ethyl 4-nitro-2,5-dimethoxyphenylacetate, mp 86–87° (acetone–hexane).

II. Alkaline Hydrolysis. Compound I (50 mg, mp 109–111°) slowly dissolved on stirring in 5 ml of 10% sodium hydroxide solution for 1 hr. The dark brown aqueous solution was acidified and extracted with ethyl acetate. and the organic phase was washed neutral with water, dried, and evaporated to yield a dark brown syrup. Treatment of the syrup with benzene yielded yellow crystals, 30 mg, 89%, of the 4-nitro-2,5-dimethoxyphenylacetic acid (II), mp 195–201°.

III. Acidic Hydrolysis. a. Compound I (50 mg, mp 109–111°) was finely ground and suspended in 6 ml of 10% hydrochloric acid. Heating at 100° did not dissolve the material, and after 1 hr 40 mg of starting material, mp and mmp 103–108°, was recovered. Prolonged heating (18 hr) at 100° again led to recovery of the bulk of the starting material, but the aqueous filtrate deposited yellow crystals, mp 180–190°, which were shown (infrared, mixture melting point) to be crude 4-nitro-2,5-dimethoxyphenylacetic acid (II).

b. A spatulaful of the acid chloride (I) in 10 ml of concentrated hydrochloric acid was heated 18 hr at 100°. The bright yellow solution deposited fine yellow needles sintering at 155°, melting at 170–187°, which proved to be crude 4-nitro-2,5-dimethoxyphenylacetic acid (II) (infrared, mixture melting point).

IV. Hydrolysis and Determination of Sulfur Dioxides. A solution of 0.361 g (0.001 mole) of α-chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl chloride (I) in 4 ml of dioxane was treated with 0.4 ml of water and one drop of 70% perchloric acid in a test tube equipped with an air inlet leading to the bottom of the tube and a side-arm outlet leading to the bottom of a second tube. The latter contained barium nitrate, hydrogen peroxide, and ammonium acetate–acetic acid in water.[10] Air was drawn through both tubes at a rapid rate. After a short time a precipitate of barium sulfate began forming in the second tube. After 5.5 hr a total of 66.5 mg (32%) was obtained.

Methyl α,α-Dimethoxy-4-nitro-2,5-dimethoxyphenylacetate (IV, R = CH_3). A solution of 1.8 g (0.005 mole) of α-chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenacetyl chloride in 300 ml of methanol was refluxed 3 days and evaporated to dryness. The gummy yellow crystals which resulted were crystallized from 10 ml of methanol to yield 1.0 g of crude methyl α,α-dimethoxy-4-nitro-2,5-dimethoxyphenylacetate, mp 159–163°. This was contaminated with methyl 4-nitro-2,5-dimethoxybenzoylformate, so five recrystallizations from methanol were required to obtain the analytical sample, mp 171–172°; $\lambda_{\max}^{\mathrm{hexane}}$ in mμ (ε): 263 (2200), 345 (2790); $\nu_{\max}^{\mathrm{KBr}}$ in cm^{-1}: 1763.

Anal. Calcd for $C_{13}H_{17}NO_8$: C, 49.52; H, 5.44; N, 4.44; O, 40.60. Found: C, 49.62; H, 5.57; N, 4.40; O, 40.40.

The nmr spectrum showed singlets at δ 3.22 (6 H), 3.78 and 3.82 (6 H), 4.00 (3 H), 7.45 (1 H), and 7.92 (1 H) ppm ($CDCl_3$).

Methyl 4-Nitro-2,5-dimethoxybenzoylformate (V, R = CH_3). I. A solution of I, 1.0 g (0.0028 mole), in 100 ml of methanol (spectroscopic grade) was heated in a pressure bottle at 100° for 3 days. The resultant solution (stench) was boiled with Norit, filtered through Filter-Cel, and evaporated to dryness to yield a mixture of crystals and oil, 0.95 g. Two crystallizations from methanol

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(19) Determined on a Mechrolab vapor pressure osmometer, Model 301A.

(20) Determined on a CEC 21-110 mass spectrometer.

(21) We thank Dr. L. Rubin of the Polaroid Analytical Laboratory for this analysis.

yielded methyl α,α-dimethoxy-4-nitro-2,5-dimethoxyphenylacetate as light yellow prisms, 0.4 g, mp 171–173°. Evaporation of the mother liquor yielded 0.45 g of yellow oil. Chromatography on Florisil from 1:1 benzene–hexane solution followed by elution with benzene yielded a yellow crystalline product which was recrystallized from acetone–hexane, benzene, and acetone to yield the analytical sample of methyl 4-nitro-2,5-dimethoxybenzoylformate, mp 158–159°; $\lambda_{\max}^{\text{hexane}}$ in mμ (ε): 225 (8400), 259 (6600), 365 (4300); $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1739, 1689.

Anal. Calcd for $C_{11}H_{11}NO_7$: C, 49.07; H, 4.12; N, 5.20; O, 41.60. Found: C, 49.14; H, 4.36; N, 5.32; O, 41.34.

II. A solution of 300 mg of methyl α,α-dimethoxy-4-nitro-2,5-dimethoxyphenylacetate (IV, R = CH_3, mp 172–173°) in 1 ml of concentrated H_2SO_4 was let stand 1 hr at 25° and treated with excess water to yield the theoretical amount of the keto ester V (R = CH_3), mp 152–153°, identical by infrared spectrum with the analytical sample.

Ethyl 4-Nitro-2,5-dimethoxybenzoylformate (V, R = C_2H_5). Compound I (1.0 g, 0.0028 mole) was refluxed in 250 ml of ethanol for 3 days. Concentration of the solution to a dark brown oil and addition of 5 ml of cold ethanol yielded yellow crystals, 350 mg, mp 134–137° (44% yield). Purification was effected by chromatography on Wölhm neutral alumina from benzene, eluting with ethyl acetate, and recrystallization from ethanol to yield stout yellow prisms, mp 142–146°; $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1745, 1690.

Anal. Calcd for $C_{12}H_{13}NO_7$: C, 50.88; H, 4.63; N, 4.95. Found: C, 50.9; H, 4.6; N, 4.9.

4-Nitro-2,5-dimethoxybenzoic Acid (III). a. From α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride with DMSO. One gram of the acetyl chloride I was added gradually to 4 ml of dimethyl sulfoxide (Baker, reagent grade). After the heat and gas evolution ceased the originally red-orange solution, now yellow, was heated at 100° for 15 min. The strongly acidic mixture (pH 1), obtained by adding water (yellow precipitate), was neutralized with 5% sodium bicarbonate solution, whereupon all the precipitate redissolved except for a small amount of tan gum which was discarded. The aqueous solution was acidified to yield crude 4-nitro-2,5-dimethoxybenzoic acid (III), 0.5 g, 79%, mp 192–195°. Two crystallizations from benzene gave stout yellow needles, 0.4 g, mp 196–198°; $\lambda_{\max}^{\text{EtOH}}$ in mμ (ε): 223 (13200), 257 (8900), 273 (9000), 365 (3000); $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1708, 1670.

Anal. Calcd for $C_9H_9NO_6$: C, 47.58; H, 3.99; N, 6.17; O, 42.26. Found: C, 47.80, 47.81; H, 3.90, 3.92; N, 6.40, 6.29; O, 41.51, 42.13.

Ethyl 4-nitro-2,5-dimethoxybenzoate was prepared by ethanol–H_2SO_4 esterification, mp 96–98° (ethyl acetate–hexane); $\lambda_{\max}^{\text{EtOH}}$ in mμ (ε): 359 (3440); $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1734.

Anal. Calcd for $C_{11}H_{13}NO_6$: C, 51.76; H, 5.13; N, 5.49; O, 37.61. Found: C, 51.64; H, 4.94; N, 5.52; O, 37.50.

b. From 4-Nitro-2,5-dimethoxybenzaldehyde (VI). The aldehyde (1.1 g, 0.00475 mole) was refluxed 4 hr with 2.2 g (0.0095 mole) of silver oxide in 45 ml of 50% aqueous ethanol containing 1 g of sodium hydroxide. The hot suspension was diluted with 100 ml of hot water and filtered and the orange filtrate acidified with concentrated HCl. The orange solid which precipitated was crude 4-nitro-2,5-dimethoxybenzoic acid (III), 0.85 g, 75%, mp 192–195°. Recrystallization from benzene yielded fine dark yellow needles, sintering at 190°, mp 193–196°. Further recrystallization from acetone gave bright yellow crystals, mp 195–197.5°, identical in infrared spectrum and mixture melting point with the DMSO product.

c. From α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride (I) with Sulfuric Acid. The acetyl chloride (1.8 g, 0.005 mole) was heated gently in 4 ml of concentrated H_2SO_4 until the foaming evolution of HCl had modified, then heated at 100° until no further action could be seen. The resultant brown solution was cooled, diluted with saturated sodium chloride solution, and extracted with ethyl acetate. The ethyl acetate solution was washed to neutrality, dried, and evaporated to yield 1.14 g of crude product. Crystallization from benzene (Norit) yielded 0.6 g, mp 175–178°, of yellow crystals, further purified by crystallization from acetone–hexane to mp 179–187°. The infrared spectrum of the material at this stage of purification agreed closely with a spectrum of material, mp 198°, from the dimethyl sulfoxide route (mmp 189–195°).

A sample (0.1 g) of the mp 179–187° material was esterified to yield 55 mg of ethyl 4-nitro-2,5-dimethoxybenzoate, mp 94–95°, fine yellow needles (mixture melting point with an earlier sample of mp 96–98° showed mp 93–94°; infrared spectra identical).

2-Hydroxy-3-(4′-nitro-2′,5′-dimethoxyphenyl)quinoxaline (VIII). a. From α-Chloro-α-chlorosulfenyl-4-nitro-2,5-dimethoxyphenylacetyl Chloride. The acetyl chloride I (1.8 g, 0.005 mole) was refluxed with *o*-phenylenediamine (1.5 g, 0.014 mole) in 25 ml of benzene until the original solid material dissolved (H_2S evolved) and an orange solid (3.1 g) precipitated. This was extracted with 5% HCl solution to yield 1.6 g of yellow solid, mp 305–308° (97% yield). soluble in NaOH but insoluble in $NaHCO_3$ solution. Two crystallizations from acetone raised the melting point to 329–331°; $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1670.

Anal. Calcd for $C_{16}H_{13}N_3O_5$: C, 58.71; H, 4.00; N, 12.84; O, 24.44. Found: C, 58.65; H, 3.91; N, 12.99; O, 24.37.

b. From Methyl 4-Nitro-2,5-dimethoxybenzoylformate. The keto ester V (R = CH_3, 250 mg, 9.3×10^{-4} mole) and *o*-phenylenediamine (300 mg, 0.0028 mole) were refluxed in 10 ml of benzene and worked up as above to yield 160 mg (52%), mp 332–333°, identical in infrared spectrum with the product of I.

Ethyl 4-Nitro-2,5-dimethoxyphenylacetate. 4-Nitro-2,5-dimethoxyphenylacetic acid (3.5 g, 0.0145 mole) in 200 ml of ethanol and two drops of concentrated H_2SO_4 was refluxed overnight and the solution neutralized with 5% sodium bicarbonate solution to yield 4.1 g of crude ethyl ester, mp 70–83°. Recrystallization from acetone–hexane yielded pale yellow needles, 3.6 g (0.0134 mole), mp 72, 82–83° (85%). The analytical sample was obtained by recrystallizing three times from ethanol to yield yellow prisms, mp 87–88°; $\nu_{\max}^{\text{KBr}}$ in cm^{-1}: 1740.

Anal. Calcd for $C_{12}H_{15}NO_6$: C, 53.53; H, 5.62; N, 5.20; O, 35.65. Found: C, 53.75; H, 5.71; N, 5.26; O, 35.41.

α-Chloro-α-chlorosulfenylphenylacetyl Chloride (XI). Dry pyridine (2 ml) was added dropwise to a solution of 8 g (0.059 mole) of phenylacetic acid in 50 ml of thionyl chloride (freshly opened) with cooling and stirring. A yellow color developed. The mixture was refluxed overnight under anhydrous conditions. After the thionyl chloride was removed by vacuum distillation, the residual oil was treated with two 100-ml portions of dry ether. The ether solution was decanted from an insoluble residue (discarded) and evaporated to dryness. A 93% yield (14 g) of crude product was obtained. This was dissolved in 100 ml of dry hexane and passed through a Florisil–hexane column. The product was eluted with hexane as the first fraction: 9 g (61% yield), a slightly yellowish oil; $\nu_{\max}^{\text{Liq}}$ in cm^{-1}: 1780 (s), 1811 (s).

Anal. Calcd for $C_8H_5OSCl_3$: C, 37.6; H, 1.9; S, 12.5; Cl, 41.5. Found: C, 37.6; H, 1.9; S, 12.2; Cl, 41.5.