difference of the steric requirements of the two carbenes is too large to be neglected and accounts for the failure to obtain a linear relationship of the logarithms of the relative rates in olefin additions. The same observation was made by Doering on comparing dibromo- with dichlorocarbene.[4]

Experimental

Materials.—The chlorocyclopropanes used for standardization of the vapor phase chromatograph were synthesized following the procedures described in the preceding paper.[1] Cyclohexene (Eastman Kodak Co., white label), 2,3-dimethylbutene-2, 2-methylbutene-2 (Matheson, Coleman and Bell, 99%) and pentene-1 (Matheson, Coleman and Bell, 99%) were purified before use by fractional distillation. Isobutylene (Matheson, "pure grade"), *cis*-butene-2 (Philips Hydrocarbons, "pure grade") and *trans*-butene-2 (Philips Hydrocarbons, "research grade") were used without further purification. *n*-Butyllithium was prepared by standard procedure from butyl bromide and lithium in diethyl ether. Methylene chloride ("reagent grade") was used unpurified.

Vapor Phase Chromatograms.—Vapor phase chromatograms were carried out with a Fisher–Gulf Partitioner equipped with integrator. The separations were effected by the use of a 12-ft. column charged with TCP on firebrick. Suitable temperatures were determined for each separation (50 to 140°), and helium flow rates of 60 to 80 ml./min. gave satisfactory resolution. The sensitivity of the detector cell for each product was determined by chromatographing known mixtures of the chlorocyclopropanes and determination of the peak area. Two such runs with different ratios of chlorocyclopropanes have been carried out for each pair of products.

Test for Product Stability.—A mixture of chlorocyclopropanes of the following composition was prepared: 1-chloro-2,2,3,3-tetramethylcyclopropane (I), 5.02 mmoles; 1-chloro-2,2,3-trimethylcyclopropane (II) (both isomers), 4.85 mmoles; 1-chloro-2,2-dimethylcyclopropane (III), 4.81 mmoles; 1-chloro-2,3-*trans*-dimethylcyclopropane (IV), 5.29 mmoles. The mixture was dissolved in pentane (30 ml.) and methylene chloride (8.4 g.). To this solution was added over a period of 30 minutes *n*-butyllithium (50 mmoles) at −35°. The reaction mixture was washed with water and analyzed by v.p.c. The ratios of chlorocyclopropanes were found to be 1.06 (I):1.05 (II):1.00 (III):1.05 (IV) (*vs.* 1.04:1.01:1.00:1.10 for the composition of the starting mixture).

Competition Runs.—The competition runs were carried out in a three-neck flask equipped with stirrer, addition funnel and nitrogen inlet tube. Both olefins (0.25 mole of each) and methylene chloride (0.1 mole) were added and cooled to −35°. To this solution was added *n*-butyllithium (0.05 mole) over a period of 30 minutes. The temperature was kept between −35 and −40°. After addition was complete the reaction mixture was washed with water, dried and analyzed by v.p.c.; *trans/cis* isomer ratios were found to be: 1-chloro-2,2,3-trimethylcyclopropane, 1.6; 1-chloro-2,3-*cis*-dimethylcyclopropane, 5.5; 7-chlorobicyclo[4.1.0]heptane, 3.2; 1-chloro-2-*n*-propylcyclopropane, 3.4.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.]

The Alleged Role of Nitroxyl in Certain Reactions of Aldehydes and Alkyl Halides[1]

BY PETER A. S. SMITH AND GEORGE E. HEIN[2]

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The reaction of primary alkyl halides with Piloty's acid ($C_6H_5SO_2NHOH$) or Angeli's salt ($Na_2N_2O_3$), reported by Angeli to give aldoximes, has been shown to proceed by alkylation of the benzenesulfonhydroxamate or nitrohydroxamate ion, respectively, rather than by alkylation of nitroxyl, HNO, which these compounds generate. Sodium nitrosyl does not convert alkyl halides to oximes, nor does it convert aldehydes to hydroxamic acids (Angeli–Rimini aldehyde test). The rate of breakdown of Angeli's salt to nitrite and nitroxyl has been found to follow first-order kinetics, and to be unaffected by a change in solvent from water to ethanol, but it is markedly retarded by sodium hydroxide. Alkaline nitration of cyclohexylhydroxylamine gives cyclohexanone oxime through the unstable N-cyclohexylnitrohydroxamate anion. The O-acetyl and O-tetrahydropyranyl derivatives of Piloty's acid can be alkylated efficiently on the nitrogen to give isolable products, which can be converted to aldoximes by hydrolytic cleavage of the blocking group and treatment with base. By the various methods mentioned benzyl and 2,4,6-trimethylbenzyl chlorides and ethyl and hydrocinnamyl iodides have been converted to the corresponding oximes.

Introduction

The substance nitroxyl, HNO (or its hydrate, $HN(OH)_2$) has had a long history as a hypothetical intermediate in various reactions, but has nevertheless been consigned to obscurity by being completely ignored by numbers of otherwise comprehensive treatises on inorganic chemistry. Latimer and Hildebrand[3] provide a notable exception to this. Although nitroxyl itself has not been isolated (it has, however, been trapped in a frozen argon matrix[4]), its sodium salt, NaNO, has been known for many years from its direct formation from sodium and nitric oxide.[5] The principal interest in nitroxyl, however, has been in its role as an intermediate in various reactions in which hyponitrite or nitrous oxide is formed from substances containing only a single nitrogen atom. These reactions have been correlated by the assumption that a characteristic reaction of nitroxyl is dimerization to hyponitrous acid, which in turn readily decomposes to nitrous oxide (eq. 1).

$$2HNO \longrightarrow HON{=}NOH \longrightarrow N_2O + H_2O \quad (1)$$

Recently, renewed attention has been given to nitroxyl as a species that can be eliminated from organic molecules. Examples are the nitrosative degradation of tertiary amines[6] (eq. 2) and the Nef reaction[7,8] (eq. 3). The latter reaction when ap-

(1) Presented at the 135th National Meeting of the American Chemical Society, Boston, Mass., April, 1959. From the doctoral thesis of G. E. Hein, 1959.

(2) National Science Foundation Predoctoral Fellow.

(3) W. M. Latimer and J. H. Hildebrand, "Reference Book of Inorganic Chemistry," The Macmillan Co., New York, N. Y. 1941.

(4) H. W. Brown and G. C. Pimentel, *J. Chem., Phys.*, **29**, 883 (1958).

(5) A. Joannis, *Compt. rend.*, **118**, 713 (1894); E. Zintl and A. Harder, *Ber.*, **66**, 760 (1933).

(6) P. A. S. Smith and H. G. Pars, *J. Org. Chem.*, **24**, 1325 (1959).

(7) E. E. van Tamelen and R. J. Thiede, THIS JOURNAL, **74**, 2615 (1952).

(8) M. F. Hawthorne, *ibid.*, **79**, 3471 (1957).

plied to the *aci* forms of primary nitro alkanes is

$$(RCH_2)_3N \xrightarrow{HNO_2} (RCH_2)_3\overset{+}{N}NO \longrightarrow (RCH_2)_2\overset{+}{N}{=}CHR + HNO \quad (2)$$

$$R_2C{=}NOOH \longrightarrow R_2C\begin{matrix}OH\\NO\end{matrix} \longrightarrow R_2C{=}O + HNO \quad (3)$$

the reverse of a reaction (eq. 4) postulated by Angeli[9] to account for the familiar

$$R{-}CH{=}O + HNO \longrightarrow R{-}CH\begin{matrix}OH\\NO\end{matrix} \longrightarrow R{-}C\begin{matrix}O\\NHOH\end{matrix} \quad (4)$$

Angeli–Rimini test for aldehydes,[10] in which a hydroxamic acid is formed from the reaction of an aldehyde with benzenesulfonhydroxamic acid ("Piloty's acid") and certain other hydroxylamine derivatives. Another reaction with organic compounds attributed to nitroxyl by Angeli is alkylation,[9] a process by which a reactive alkyl halide is converted to an oxime (eq. 5). In this paper we

$$R{-}CH_2{-}X + HNO \longrightarrow R{-}CH_2{-}NO \longrightarrow R{-}CH{=}NOH \quad (5)$$

report an investigation of these last two reactions, which we conclude do not after all involve nitroxyl, but are instead reactions competing with nitroxyl-generating reactions.

Results and Discussion

Alkylation of Piloty's Acid and Angeli's Salt.—The principal sources of nitroxyl for laboratory use are Piloty's acid,[11] $C_6H_5SO_2NHOH$, and "Angeli's salt",[9] $Na_2[O_2NNO]$ (sodium nitrohydroxamate). In basic aqueous solution each generates hyponitrite, together with benzenesulfinate or nitrite, respectively. We first investigated the reaction of Piloty's acid with benzyl chloride in alkaline medium under varied conditions. Both aqueous and alcoholic solutions were used, the alkalinity of the solutions was varied, and the mole-ratio of benzyl chloride to Piloty's acid was varied from 1 to 2. The principal product was in all cases benzyl phenyl sulfone, accompanied by the solvolysis products, benzyl alcohol and benzyl ethyl ether. Ethyl and hydrocinnamyl iodide gave entirely analogous results.

Angeli's alkylation experiments were carried out using sodium nitrohydroxamate rather than Piloty's acid, insofar as one can tell from the meager published reports.[9] In our hands this salt reacted with benzyl chloride in 95% ethanol solution to give benzyl alcohol, benzaldehyde, benzoic acid, 3,4,5-triphenylisoxazole, benzyl ethyl ether, phenylnitromethane and 3,5-diphenyl-1,2,4-oxadiazole (an air-oxidation product of benzaldoxime[12]), but no benzaldoxime. In an experiment in dimethylformamide solution, the same substances were formed (with the exception of the ether), but the proportion of isoxazole was larger, and a small amount (*ca.* 1%) of benzaldoxime was isolated. The use of cadmium nitrohydroxamate in place of the sodium salt did not significantly change these results, nor did the use of other solvents (acetone, benzene, ethyl ether) when they did not prevent reaction entirely.

In confirmation of Angeli's report, ethyl iodide was found to give some acetaldoxime, but the yield was very poor. Owing to the greater difficulty of isolation and characterization of this compound, further work with ethylation was not attempted. Butyl bromide gave no oxime.

Benzhydryl bromide was treated with Angeli's salt in acetonitrile solution, and the products were separated by chromatography on alumina. They were benzhydrol, benzophenone, dibenzhydryl ether, O-benzhydrylbenzophenoxime and N-benzhydrylacetamide. The yield of the oxime derivative, which presumably arose from alkylation of benzophenone oxime formed first, was poor (1.5%).

β-Phenylethyl chloride and hydrocinnamyl iodide reacted with Angeli's salt in aqueous ethanol in a much cleaner fashion, and gave oximes in yields of 20 to 30% in different experiments. Since the latter example provided the best instance of the reaction under investigation, it was studied more intensively; the yield of hydrocinnamaldoxime and the amount of unconsumed hydrocinnamyl iodide were determined as functions of time, amount of excess alkali and water content of the solvent. The results are shown in Tables I and II. The experiments were carried out at the reflux temperature of the solutions, but one experiment carried out at room temperature for 12 hours gave sensibly the same yield of oxime and recovery of alkyl iodide as did the reflux temperature experiment that was stopped at one and a half hours, showing that the rates of the alkylation reaction and of the competing reactions are affected to nearly the same degree by changes in temperature.

TABLE I

REACTION OF HYDROCINNAMYL IODIDE WITH ANGELI'S SALT AS AFFECTED BY SOLVENT COMPOSITION

	3.5-hour reaction time		
Water content of ethanol, %	Conversion to oxime, %	Recovered R–I, %	Corrected yield, %
0	12	71	42
5	23.5	44	42
10	19.5	10	21.5
15	18	1.7	18.5
20	13	0	13
70	<7.5	0	<7.5

TABLE II

REACTION OF HYDROCINNAMYL IODIDE WITH ANGELI'S SALT AS AFFECTED BY ADDED BASE

in 95% alcohol, 3.5-hour reaction time			
Mole ratio NaOH/R–I	Conversion to oxime, %	Recovered R–I, %	Corrected yield, %
0	26	21	33
0.042	19	49	37
.083	14	39	23
.17	11	33	16
1.0	0	14	0
2.0	0	0	0

Owing to the variable quality of different batches of Angeli's salt, which cannot be satisfactorily

(9) A. Angeli, *Ahrens Samm. Chem. Tech. Vorträge*, **13**, 2 (1908).

(10) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Thomas Y. Crowell Co., New York, N. Y., 1947, p. 123.

(11) O. Piloty, *Ber.*, **29**, 1559 (1896).

(12) E. Beckmann, *ibid.*, **22**, 1588 (1889).

purified, the set of experiments recorded in each table utilized the same batch of salt. The three sets of experiments represented by Tables I, II and III made use of separate batches of Angeli's salt, however, and experiments from one set cannot properly be compared with those of another. The differences among batches appear to lie largely in the degree of decomposition, and thus in the nitrite content. Batches prepared and handled under the most nearly anhydrous conditions gave the highest conversions and corrected yields. A control experiment in which no Angeli's salt was used gave a 97% recovery of hydrocinnamyl iodide after 3.5 hours, but one in which an equivalent of sodium nitrite was substituted for Angeli's salt showed no more than a trace of alkyl iodide left after 3.5 hours. It appears that nitrite ion is the best of those nucleophiles available, and its presence, arising from the decomposition of Angeli's salt (eq. 6), is responsible for the generally low level of the yields and for the erratic recovery percentages.

$$2Na_2N_2O_3 \longrightarrow 2NaNO_2 + Na_2N_2O_2 \qquad (6)$$

Rate of Decomposition of Nitrohydroxamate.—For comparison with these results, the decomposition of Angeli's salt was studied in solution spectrophotometrically. Addison[13] has shown that it has an absorption maximum at 250 mμ, and nitrite absorbs at 365 mμ. As Addison reports, the extinction coefficient of different batches of Angeli's salt varies considerably, and an accurate rate constant could not be determined. The logarithm of the optical density varies linearly with time, however, suggesting a pseudo-first-order rate for the disappearance of the salt. The slope of the plot does not change significantly with solvent compositions from 100% water to 100% ethanol, implying that the solvent is not involved in the rate-determining step. The rate was markedly slower in solutions containing added base, however (*vide* Fig. 1), an observation that had been made qualitatively by earlier investigators.[14,15] These results can be best correlated by the interpretation that it is the monobasic anion, O_2N–NHO^- (presumably in equilibrium with tautomers), that decomposes in the rate-determining step as in eq. 7. This is parallel to the decomposition of Piloty's acid in alkaline solution (eq. 8). Since ethanol is a much weaker

$$O_2N—NHO^- \longrightarrow NO_2^- + HNO \qquad (7)$$

$$C_6H_5SO_2NHO^- \longrightarrow C_6H_5SO_2^- + HNO \qquad (8)$$

acid than water, but the rate of decomposition of Angeli's salt is the same in either solvent, we conclude that the monobasic nitrohydroxamate ion is a weaker acid than either, and that Angeli's salt is therefore largely solvolyzed to the monobasic anion in both solvents. (The precipitation of the neutral salt from ethanol solution when Angeli's salt is prepared presumably reflects a much lower solubility of the neutral relative to the monobasic salt.)

Reactions of Sodium Nitrosyl.—For comparison with the foregoing experiments using the classical sources of nitroxyl, sodium nitrosyl, NaNO, was

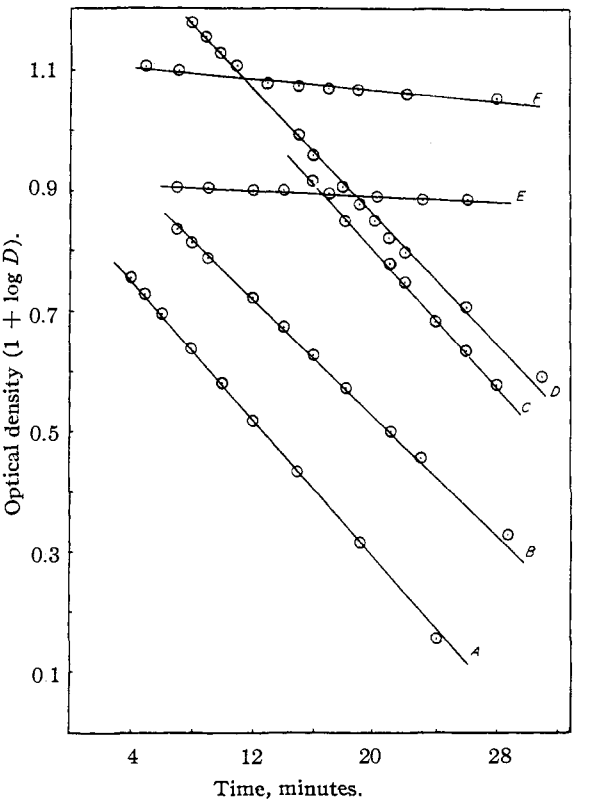


Fig. 1.—Decomposition of sodium nitrohydroxamate in solution as followed by ultraviolet absorption at 250 mμ: A, in 95% ethanol; B, in water; C, in 50% ethanol; D, in 80% ethanol; E, in 0.04 *N* NaOH; F, in 0.1 *N* NaOH ($Na_2N_2O_3$ concentrations differ among runs, but are about 10^{-4} *M*).

investigated in similar reactions. Its decomposition in solution is known to follow the same path in the latter stages, giving hyponitrite (by dimerization of HNO) and from it nitrous oxide.[5] When sodium nitrosyl was treated with alkyl halides in aqueous alcoholic solutions, the only organic products we could detect were those which would have been formed had the equivalent amount of sodium hydroxide been used instead; that is, alcohol and ether. In no instance were we able to find a nitrogenous organic product or other evidence that alkylation of sodium nitrosyl had occurred to a significant extent. This contrast with the behavior of Piloty's acid and Angeli's salt led us to try sodium nitrosyl as a reagent for the Angeli–Rimini test for aldehydes. No trace of hydroxamic acid could be detected by the customary ferric chloride color reaction, whether reaction with aldehyde was carried out on the dry salt or in solution. For control purposes, small amounts of Piloty's acid or Angeli's salt were added to selected reaction mixtures of sodium nitrosyl and aldehyde; in such experiments the formation of hydroxamic acid was invariably detected, confirming that the reaction environment was compatible for the Angeli–Rimini reaction if the right reagent was used.

Interpretations.—The evidence thus implies that nitroxyl is not responsible for either the Angeli–Rimini reaction or the conversion of alkyl halides to oximes. These reactions must therefore arise

(13) C. C. Addison, G. A. Gamlen and R. Thompson, *J. Chem. Soc.*, 338 (1952).

(14) G. Kortum and G. Finckh, *Z. physik. Chem.*, **1348**, 32 (1940).

(15) K. S. Naik, C. C. Shah and S. Z. Patel, *J. Indian Chem. Soc.*, **23**, 284 (1946).

from the precursors of nitroxyl, namely, Piloty's acid and nitrohydroxamate. If either of these should become alkylated at the hydroxylamine nitrogen, the products in basic solution would be homologs of the anions of equations 7 and 8 presumed to be the intermediates that break down to form nitroxyl. In this case, however, nitroxyl would not be formed, but the homologous nitroso compounds, which would readily tautomerize to oximes (eq. 9).

$$RCH_2X + {}^{-}O_2NNO^{-} \longrightarrow O_2NNO^{-} \longrightarrow \underset{\displaystyle CH_2R}{\overset{|}{}} \quad NO_2^{-} + RCH_2NO \qquad (9)$$

The formation of oximes is thus seen to be directly competitive with nitroxyl formation, which can arise only from the unalkylated anions. Furthermore, displacement on the alkyl halide by hydroxamate is competed with by all other nucleophiles that may be present, the most significant being nitrite, alkoxide, hydroxide, oximate and hyponitrite. Thus it is that small amounts of base, although reducing protonation to the monobasic anion, increase the corrected yield of oxime because of retarded breakdown of the monobasic nitrohydroxamate ion, but larger amounts exert a progressively opposing influence by competing for the alkyl halide.

Nitrite, an inevitable product, is particularly effective in competing for alkyl halide, as has been shown, and nitro alkanes and alkyl nitrites or their transformation products are to be expected as by-products. The 3,4,5-triphenylisoxazole isolated from the reaction of benzyl chloride with Angeli's salt is a known condensation product of phenylnitromethane in basic medium,[16] and some phenylnitromethane itself could be detected (*vide posteriori*). The bulk of the benzaldehyde formed must have arisen from benzyl nitrite, which would certainly be formed. Alkyl nitrites are known to decompose to carbonyl compounds readily on heating.[17] Benzaldoxime, of course, could not be the source of benzaldehyde, since oximes are not hydrolyzed in basic solution.

When Piloty's acid is used instead, benzenesulfinate ion, a good nucleophile, is an inevitable accompanying product. Displacement by it leads to sulfones, and indeed, phenyl benzyl sulfone is the principal product arising from benzyl chloride and Piloty's acid. The predominance of this product simply indicates that benzylation of benzenesulfonhydroxamate is slower than its breakdown to nitroxyl and benzenesulfinate. It is significant that benzaldehyde is not formed, the path by which it can arise from Angeli's salt through alkyl nitrite not being possible with Piloty's acid.

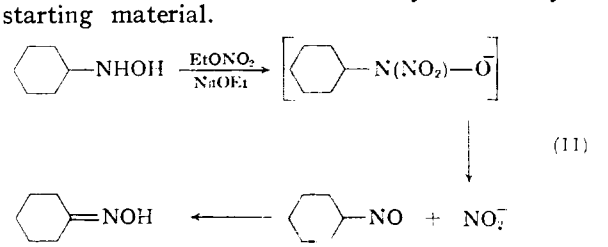
The effect of the water content of the solvent (Table I) cannot be due to an increase of the rate of decomposition of Angeli's salt to nitroxyl, for we have shown that this rate is essentially unaffected by changes in solvent composition. On the other hand, the rapid decrease of the amount of recovered alkyl halide with increasing water content shows that it is other competing reactions that are promoted; presumably they are displacement reactions of some kind. The change from 100% ethanol to aqueous solutions involves both an increase in the polarity of the medium, and an increase in the solubility of Angeli's salt. Since Angeli's salt is only slightly soluble in absolute alcohol, the reaction mixtures were initially heterogeneous in the mixtures with low water content. Both of these effects of increasing water content are ones that increase O-alkylation over N-alkylation of ambident anions,[18,19] to which class nitrohydroxamate belongs. We do not know the structure or the subsequent fate of O-alkylated nitrohydroxamate, but it cannot reasonably lead to oxime. (Elimination of hyponitrite or nitramide, as the structure may require, would lead to aldehyde; such a reaction may have contributed to the formation of the considerable quantities of benzaldehyde obtained from benzyl chloride, and benzophenone from benzhydryl bromide.) Furthermore, the increased concentration of nitrohydroxamate (and thus of nitrite) also in solution in the more aqueous systems would accelerate total alkylation, leading to more rapid destruction of alkyl halide, as observed.

Since the Angeli–Rimini reaction cannot be brought about with sodium nitrosyl, it, too, must be a reaction of the precursors of nitroxyl. It presumably occurs through addition of the carbonyl carbon to the hydroxylamine nitrogen, followed by separation of nitrite or benzenesulfinate to give the α-nitroso alcohol structure presumed to be an intermediate in the Nef reaction; the usual tautomerization of the CH–NO structure leads to the observed hydroxamic acids (eq. 10).

$$R{-}CHO + A{-}NHO^{-} \longrightarrow R{-}CHOH{-}NA{-}O^{-} \longrightarrow A^{-} + RCHOH{-}NO \longrightarrow R{-}CONHOH \qquad (10)$$

A = NO_2 or $C_6H_5SO_2$

Nitration of Organic Hydroxylamines.—The intermediate formed by alkylation of nitrohydroxamate (eq. 9) is the anion of an N-nitro hydroxylamine. It should therefore be attainable by alkaline nitration of a hydroxylamine already bearing an N-alkyl group. To confirm this analysis, cyclohexylhydroxylamine was treated with ethyl nitrate in the presence of sodium ethoxide. Cyclohexanone oxime, the expected decomposition product of the N-nitrohydroxylamine, was obtained in 32% yield (eq. 11). An attempt to obtain nitrosobenzene by nitration of phenylhydroxylamine under similar conditions failed, however. An unsuccessful attempt was also made to prepare a structure which might result from O-alkylation of nitrohydroxamate; treatment of hydrocinnamyloxyamine with ethyl nitrate and sodium ethoxide led only to recovery of starting material.



(11)

(16) E. P. Kohler and G. R. Barrett, THIS JOURNAL, **46**, 2110 (1924).

(17) H. Brunner, *Ber.*, **9**, 1744 (1876); N. Kornblum and E. P. Oliveto, THIS JOURNAL, **71**, 226 (1949).

(18) N. Kornblum, R. A. Smiley, R. K. Blackwood and D. C. Iffland, *ibid.*, **77**, 6269 (1955).

(19) N. Kornblum and A. P. Lurie, *ibid.*, **81**, 2705 (1959).

Derivatives of Piloty's Acid.—The intermediate formed by alkylation of benzenesulfonhydroxamate, analogous to that formed by alkylation of nitrohydroxamate, is an N-benzenesulfonyl-N-alkylhydroxylamine (or its anion), a known class of compound. By acid hydrolysis they regenerate benzenesulfonic acid and alkylhydroxylamine, but when exposed to base they break up into benzenesulfinate and a C-nitroso compound or the tautomeric oxime (eq. 12).[20] This is an example of the Raschig rule for the direction of hydrolytic cleavage of S–N bonds; it is also a confirmation of the reaction path postulated in the foregoing discussion.

$$C_6H_5SO_2{-}NCHR_2{-}OH \xrightarrow{OH^-} [C_6H_5SO_2NCHR_2{-}O^-] \longrightarrow C_6H_5SO_2^- + ON{-}CHR_2 \longrightarrow R_2C{=}NOH \quad (12)$$

The success of this reaction raises the question of why alkylation of Piloty's acid is such a poor route to oximes. We concluded that it may be that benzenesulfonhydroxamate is a relatively poor displacing agent, so that its fragmentation, which is known to be very fast, effectively forstalls N-alkylation. We proposed to circumvent these obstacles by substituting the hydroxyl group of Piloty's acid with an easily removable group. Such substitution would serve to prevent both O-alkylation and breakdown into benzenesulfinate and nitroxyl, and thus give maximum opportunity for N-alkylation. This result was accomplished by both acetylation and tetrahydropyranylation.

Treatment of potassium benzenesulfonhydroxamate with acetic anhydride in benzene gave O-acetylbenzenesulfonhydroxamic acid in good yield, along with some of the previously known O,N-diacetyl compound. Successful preparation of the monoacetyl compound is quite sensitive to conditions; benzene was found to be the best solvent, probably because the monoacetyl product is relatively insoluble in it. Ether was not a satisfactory solvent. Toluene-sulfonhydroxamic acid gave a lower ratio of mono- to di-acetyl product when acetylated as the potassium salt in benzene. Benzoylation of potassium benzenesulfonhydroxamate gave mostly dibenzoyl derivative and at best only 9% of the O-benzoyl derivative.

O-Acetylbenzenesulfonhydroxamic acid is alkylated in 65% yield by benzyl chloride in ethanol containing approximately an equivalent of sodium hydroxide. Hydrocinnamyl iodide did not work under these conditions, however; decomposition of the acid was faster, and phenyl hydrocinnamyl sulfone was produced. The silver salt, which was prepared by precipitation with silver nitrate from neutralized solutions of O-acetylbenzenesulfonhydroxamic acid, was alkylated successfully by a variety of alkyl halides, and in this manner ethyl and hydrocinnamyl iodides and 2,4,6-trimethylbenzyl chloride were successfully employed. Isopropyl iodide, however, yielded no N-alkyl product, and appeared to suffer elimination instead.

The N-alkyl-O-acetylbenzenesulfonhydroxamates were hydrolyzed rapidly by hot, dilute sodium bicarbonate to give oximes of the aldehydes corresponding to the alkyl groups, in yields up to 90%. It was found to be unnecessary to isolate the alkylated intermediates, and alkyl halides could thus be converted to aldoximes in one combined operational step involving only quite mild conditions. Presumably the product of the hydrolysis step is the N-alkylbenzenesulfonhydroxamate anion, which rapidly breaks up to give oxime. Hydrolysis in acidic solution would be expected to give the N-alkylbenzenesulfonhydroxamic acid, a stable species in the absence of base, which undergoes slow hydrolysis in acidic solution to give N-alkylhydroxylamine. However, when we treated N-hydrocinnamyl-O-acetylbenzenesulfonhydroxamic acid with refluxing 10% ethanolic hydrogen chloride, hydrocinnamaldoxime was isolated in 76% yield. Apparently elimination of benzenesulfinate occurs before separation of the acetyl group, but we have not investigated this reaction further.

A significant side-product in many of our experiments in which O-acetylbenzenesulfonhydroxamic acid was treated with base was benzenesulfonamide. We have not determined which of several reasonable paths may be responsible for its formation.

Reaction with dihydropyran converted Piloty's acid into O-tetrahydropyran-2-ylbenzenesulfonhydroxamic acid in 23.5% yield, accompanied by 2% of O,N-bis-tetrahydropyran-2-ylbenzenesulfonhydroxamic acid and 35% of benzenesulfinic acid. Treatment of the O-tetrahydropyranyl compound with benzyl chloride and alcoholic sodium hydroxide gave 60% of a benzyl derivative, which could be hydrolyzed by dilute hydrochloric acid to the known N-benzylbenzenesulfonhydroxamic acid, which gives benzaldoxime on treatment with alkali. Tetrahydropyranyl N-hydrocinnamylbenzenesulfonhydroxamate was prepared analogously in 70% yield. Hydrolysis to the free acid (not isolated) and treatment with alkali gave 35% of hydrocinnamaldoxime.

Angeli's alkylation reaction can thus be accomplished through isolated intermediates if the hydroxyl group of Piloty's acid is blocked, although it cannot be accomplished when breakdown to nitroxyl occurs first. Furthermore, the general method is potentially useful in synthesis, inasmuch as it provides a non-oxidative conversion of alkyl halides to aldoximes (and thus to aldehydes or nitriles), and it succeeds with non-benzylic primary alkyl halides and with hindered benzylic ones, both of which usually give unsatisfactory results in the Sommelet reaction.[21]

Experimental[22]

Sodium Nitrohydroxamate (I).—Sodium nitrohydroxamate was prepared by a simplified version of Angeli's[9] procedure. To a solution of 120 g. (3.0 moles) of sodium hydroxide in 800 ml. of methanol was added a solution of 69.5 g. (1.0 mole) of hydroxylamine hydrochloride in 45 ml. of hot water. The suspension was cooled in an ice-bath and filtered to remove salt. To the filtrate was added 119 g. (1.0 mole) of butyl nitrate (Bios Chemical Co.) over 15 min. with stirring and cooling. The solid was washed with

(20) F. Raschig, "Schwefel und Stickstoff-Studien," Verlag Chemie, Leipzig, 1924.

(21) S. J. Angyal, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, Chapt. 4.

(22) Melting and boiling points are uncorrected. Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Infrared spectra were recorded from Nujol mulls or as liquid films on a Perkin-Elmer model 21 infrared spectrophotometer.

methanol and dried in a vacuum desiccator to yield 71 g. (58%) of white, microcrystalline powder.

The same reaction was also run with equal success using commercial ethyl nitrate and freshly prepared methyl nitrate as nitrating agents.

Reaction of Sodium Nitrohydroxamate and Benzyl Chloride in Aqueous Ethanol.—A mixture of 19.0 g. (0.15 mole) of benzyl chloride, 25.0 g. (0.20 mole) of sodium nitrohydroxamate and 50 ml. of 95% ethanol was stirred for 4 hours at reflux on a steam-bath, cooled and filtered, the filtrate distilled under water vacuum to remove solvent, and the remaining mass distilled through a six-inch Vigreux column at 50 mm. to give the fractions: I, b.p. 37–40°, 5.85 g., $n^{24}D$ 1.3667; II, b.p. 127–144°, wt. 4.35 g., $n^{24}D$ 1.5332; III, b.p. 145–151°, wt. 2.90 g., $n^{24}D$ 1.5465. Fraction III was identified as benzaldehyde by its odor, infrared spectrum, refractive index (reported[23] n_D 1.5468) and conversion to its 2,4-dinitrophenylhydrazone, m.p. 235–236° (reported[24] m.p. 235°), and its semicarbazone, m.p. 207–209°, undepressed upon admixture with an authentic sample. Fraction II appeared to be a mixture containing benzyl ethyl ether and benzaldehyde, detectable by its odor, and isolated as its methone derivative; 0.5 g. of fraction II yielded 0.30 g. of the methone, m.p. 190.5–193.5° (reported[25] m.p. 192°). Fraction I appeared to be essentially aqueous alcohol. Assuming fraction III to be pure benzaldehyde, the total yield was 25%. The solid residue from the distillation was washed with 5% sodium hydroxide, dissolved in hot acetone, filtered and recrystallized in fractions by addition of increasing amounts of water to the mother liquor, to give two products in three crops: 0.15 g., m.p. 202–208.5°; 0.30 g., m.p. 104–106°; and 0.2 g., m.p. 103.5–106°. After three recrystallizations from acetone the higher melting material was identified as 3,4,5-triphenylisoxazole, m.p. 205–207° (reported[16] m.p. 210°).

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.82; H, 5.09; N, 4.71; mol. wt., 297. Found: C, 84.66; H, 5.17; N, 4.57; mol. wt. (Rast, camphor), 278.

The low melting compound on recrystallization from aqueous ethanol had m.p. 106–106.5°, and was identified as 3,5-diphenyl-1,2,4-oxadiazole (reported[12] m.p. 108°), undepressed when mixed with a sample prepared by the potassium ferricyanide oxidation of benzaldoxime.

Acidification of the basic extract from the distillation residue gave 0.55 g. (3%) of benzoic acid, m.p. 120.5–121.5° (identified by mixed melting point).

In a similar experiment where the acidified reaction mixture was treated with dinitrophenylhydrazine reagent without prior attempts at separation, a 36% yield of purified benzaldehyde dinitrophenylhydrazone was obtained. In another experiment, 16% of crude benzoic acid, m.p. 116–121°, was obtained by acidifying the total base-soluble fraction of the reaction mixture.

Reaction of Sodium Nitrohydroxamate and Benzyl Chloride in Dimethylformamide.—A mixture of 25.3 g. (0.20 mole) of benzyl chloride, 30.5 g. (0.25 mole) of sodium nitrohydroxamate and 100 ml. of dimethylformamide was stirred and warmed gradually for 0.5 hour, whereupon an exothermic reaction set in which raised the temperature to 80°. The mixture was stirred until it returned to room temperature, then filtered, and the liquid portion distilled. The solid residue was washed with water to leave 1.05 g. (3%) of triphenylisoxazole, m.p. 203–206°. Acidification of the water wash yielded 2.05 g. (8.5%) of benzoic acid, m.p. 121–122.5°, after sublimation. The original liquid portion was distilled on a steam-bath under aspirator vacuum to remove solvent. The distillate yielded 2.5% of benzaldehyde, isolated as its dinitrophenylhydrazone (1.4 g.), m.p. 221–226°. The residue was distilled through a 9-inch Vigreux column and collected in six fractions: I, 1.5 g., b.p. 85–90° (17 mm.); II, 1.4 g., b.p. 93–97° (16 mm.); III, 4.7 g., b.p. 98–101° (16 mm.); IV, 2.5 g., b.p. 99–103° (17 mm.); V, 0.7 g., b.p. 104–107° (17 mm.); VI, 0.3 g., b.p. 112–120° (16 mm.), and a residue, wt. approximately 5 g.

The first two fractions appeared to consist largely of dimethylformamide.

Infrared spectra showed that V contained over 95% of benzyl alcohol and that III and IV contained the same alcohol as major constituents. The other discernible component in the spectrum of V was benzaldoxime. After several weeks, VI solidified and was shown to be benzaldoxime by comparison with a known sample. The distillation residue was washed with water, leaving 2.6 g. of a high-melting solid material which could not be identified. It exploded on heating, and attempts to recrystallize it from a variety of organic solvents yielded only triphenylisoxazole.

Reaction of Hydrocinnamyl Iodide with Sodium Nitrohydroxamate in Aqueous Alcohol.—In a typical experiment 2.46 g. (0.01 mole) of hydrocinnamyl iodide and 2.40 g. of sodium nitrohydroxamate (0.0195 mole) were refluxed in 25 ml. of solvent for the desired length of time; a solid phase was present at all times. The mixture was rapidly brought to room temperature and 25 ml. of water and 25 ml. of ether were added. The basic aqueous layer was separated and the ether washed with 15 ml. of 10% sodium hydroxide in two portions. The basic extracts were combined, diluted with 15 ml. of water and neutralized with carbon dioxide. The oxime which precipitated out was filtered, dried and weighed. It was found that, on the average, the filtrate contained 0.107 g. of oxime, so this amount is included in the yields reported in Tables I, II and III. Variation of the ratio of Angeli's salt to alkyl halide showed that yields leveled off at between one and two molar equivalents of Angeli's salt, of which some then remained unreacted.

Variation of Yield with Reaction Time.—In these experiments the solvent was 95% ethanol. After extraction with base, alcoholic silver nitrate was added to the acidified ether layer to assay unconsumed alkyl halide; from the weight of silver iodide recovered, yield and conversion were calculated (see Table III).

TABLE III

EFFECT OF REACTION TIME ON THE REACTION OF HYDROCINNAMYL IODIDE WITH ANGELI'S SALT

Reaction time, hr.	Oxime, g.	Conversion, %	AgI, g.	Recovered R–X, %	Corrected yield, %
1:00	0.163	11	1.406	60	27
1:30	.212	14	1.149	45	26
2:30	.237	16	0.826	35	25
3:00	.391	26	.150	6.4	28
3:30	.407	27	.096	4.1	29
5:00	.319	21	.053	1.6	22
6:00	.265	18	.032	1.3	18
7:00	.270	18	.031	1.3	18
10:00	.248	17	...	..	17

In an experiment similar to the 3.5-hour one reported in Table III, the product mixture was filtered, evaporated, taken up in 60–70° petroleum ether and chromatographed on alumina. From 7.5 g. (0.0305 mole) of hydrocinnamyl iodide and 6.0 g. (0.049 mole) of Angeli's salt there was obtained 1.455 g. (32%) of oxime, m.p. 88–95°, and 0.615 g. (8.2%) of recovered hydrocinnamyl iodide, corresponding to a corrected yield of 34%. The other chromatographic fractions, all oils, accounted for roughly 30% of the material. All the fractions seemed impure, but they contained much hydrocinnamyl alcohol and some hydrocinnamaldehyde as shown by comparison of the spectra with those of known samples.

Variation of Yield with Solvent.—In this set of experiments the reaction time was kept constant at 3.5 hours and the amounts of reactants used were the same as in the previous set of experiments. The results are recorded in Table I. The volume of the solution was sufficient so that the alkyl halide was completely dissolved in the hot solution down through 85% aqueous ethanol. The solubility of the salt increased considerably with increasing water content; in 80% ethanol complete solution occurred much earlier.

Effect of Added Base.—Solutions of sodium hydroxide in 95% ethanol were prepared and mixed with 2.46 g. of hydrocinnamyl iodide and 2.40 g. of sodium nitrohydroxamate such that when the volume was adjusted to 25 ml., the ratios of NaOH to hydrocinnamyl iodide were those given in Table II. The reaction time was 3.5 hours.

(23) O. Schmidt, *Ber.*, **36**, 2479 (1903).

(24) T. Curtius and D. M. Dedichen, *J. prakt. Chem.*, [2] **50**, 265 1894).

(25) D. Vorländer and O. Strauss, *Ann.*, **309**, 379 (1899).

Other Factors.—For control purposes the effects of other factors on the reaction were also studied. In all experiments the solvent was 95% ethanol. Refluxing 1.05 g. of hydrocinnamyl iodide alone in the solvent for 3.5 hours resulted in 97% recovery, by silver iodide assay. Refluxing 2.46 g. of hydrocinnamyl iodide with 0.65 g. of sodium nitrite in 25 ml. of solvent resulted in complete destruction of the alkyl iodide.

Rate of Decomposition of Sodium Nitrohydroxamate.—The decomposition of sodium nitrohydroxamate was followed on a Beckman DU spectrophotometer by observing the decrease in the absorption peak at 250 mμ. Samples of the salt (usually 0.1 g.) were dissolved rapidly in a measured quantity (usually 100 ml.) of solvent, and aliquots withdrawn at measured intervals, diluted where necessary, and placed in the absorption cell. The results are summarized in Fig. 1, which shows that the plots of log D against time are linear, consistent with first-order kinetics. The half-life in the absence of added alkali is about 10 minutes.

On extrapolation of the curves so obtained to zero time it was possible to calculate a maximum extinction coefficient. As previously observed by Addison,[13] the spectra of different samples of sodium nitrohydroxamate are not entirely reproducible, but the values obtained here are in good agreement with his. In 0.1 N and 0.2 N sodium hydroxide solutions, log E at 250 mμ was estimated to be 3.82 and 3.95, respectively. Addison calculated 3.92 for pure sodium nitrohydroxamate in 0.1 N sodium hydroxide solution. The presence of nitrite was observed by its absorption at 365 mμ.

Benzhydryl Bromide and Sodium Nitrohydroxamate in Acetonitrile.—A mixture of 3.7 g. (0.015 mole) of benzhydryl bromide, 3.60 g. (0.295 mole) of sodium nitrohydroxamate and 40 ml. of freshly distilled acetonitrile was refluxed for 4 hours, cooled, filtered, and the solvent evaporated on a steam-bath. The residue was taken up in a 2:3 mixture of petroleum ether (b.p. 60–70°) and carbon tetrachloride and chromatographed on an alumina column. The first substance eluted was dibenzhydryl ether, wt. 538 mg. (21%), m.p. 104–107.5°; recrystallization from ethanol raised the m.p. to 107–108° (reported[26] m.p. 109°). The second compound to be eluted was O-benzhydrylbenzophenoxime, wt. 37 mg. (1.5%), m.p. 98–100.5°; recrystallization from ethanol raised the m.p. to 101.5–102°, undepressed by mixture with an authentic sample.[27] The third substance eluted was benzophenone, wt. 583 mg. (21%), obtained as an oil whose infrared spectrum and that of the 2,4-dinitrophenylhydrazone prepared from it were superimposable on that of authentic samples.

The fourth substance eluted was identified as N-benzhydrylacetamide, m.p. 142–146° (reported[28] m.p. 146–147°), wt. 142 mg. (4%). Recrystallization from petroleum ether–ethyl acetate mixture gave a pure sample, m.p. 146–146.5°.

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.94; H, 6.67; N, 6.27.

The fifth substance eluted was benzhydrol, wt. 362 mg. (13%), m.p. 60–65°. Recrystallization from aqueous ethanol raised the m.p. to 64–66°, undepressed by mixture with an authentic sample. Intermediate fractions consisting of obvious mixtures amounted to 354 mg.

Other Attempted Alkylations of Sodium Nitrohydroxamate.—Benzyl chloride was refluxed with suspensions of sodium nitrohydroxamate in ethyl ether, benzene or acetone. No ionic chloride could be detected even when refluxing was continued for over 2 days, nor could the formation of aldehyde or oxime be detected. Butyl bromide formed no detectable aldehyde or oxime when refluxed for up to 12 hours with sodium nitrohydroxamate in 95% or dilute ethanol or in ethyl ether.

β-Phenylethyl Iodide and Sodium Nitrohydroxamate.—Phenylacetaldoxime was prepared from β-phenylethyl iodide and sodium nitrohydroxamate in 95% ethanol in 20–25% yield by a procedure analogous to the one used with hydrocinnamyl iodide. The reaction was not studied extensively because, in addition to the solvolysis reactions observed in other systems, this reaction was further complicated by the production of tars, presumably arising from a competing elimination reaction.

(26) A. Zagoumeny, *Ann.*, **184**, 176 (1877).

(27) A. C. Cope and A. C. Haven, Jr., THIS JOURNAL, **72**, 4901 (1950).

(28) H. L. Wheeler, *Am. Chem. J.*, **26**, 354 (1901).

Attempted Alkylation of Sodium Nitrosyl.—Sodium nitrosyl[5] (6.2 g., 0.12 mole) was added slowly at room temperature to a stirred solution of 10.0 g. (0.08 mole) of benzyl chloride in absolute ethanol. After stirring for 1 hour the mixture was distilled and yielded 8.1 g. (74%) of benzyl ethyl ether, b.p. 85–88° (26 mm.), $n^{25}D$ 1.4921 (reported[29] b.p. 78° (18 mm.), $n^{20}D$ 1.4957). No evidence for the formation of benzaldehyde or benzaldoxime could be obtained.

Acetonitrile and dimethylformamide (DMF) were also employed as solvents; with them strictly anhydrous conditions were required to avoid hydrolysis of the solvents. No evidence of the formation of benzaldehyde or benzaldoxime could be obtained by heating benzyl chloride and sodium nitrosyl in dimethylformamide from which water had been removed by azeotropic distillation with benzene.[30] Treatment of the acidified reaction mixture with 2,4-dinitrophenylhydrazine resulted in no detectable hydrazone formation, and an infrared spectrum of the residue after removal of solvent by distillation suggested the presence of no compounds other than benzyl chloride and benzyl alcohol. The reaction in acetonitrile gave similar results.

Attempted Angeli Reaction with Sodium Nitrosyl.—Several experiments were attempted using acetaldehyde, benzaldehyde or hydrocinnamaldehyde. Since sodium nitrosyl reacts rapidly with hydroxylic solvents, the freshly prepared solid was added to a rapidly stirred solution of the aldehyde in aqueous alcohol. The addition was performed both at room temperature and at reflux and the solution was periodically tested for the presence of hydroxamic acid by the ferric chloride color reaction; in no case did color develop. In several experiments Piloty's acid or sodium nitrohydroxamate was added to portions of the reaction mixtures at various times. In each case these reagents immediately reacted leading to positive ferric chloride tests.

The reaction was also attempted without solvents by mixing aldehyde directly with solid sodium nitrosyl. If the system was exposed to the atmosphere, an exothermic reaction occurred resulting in polymerization of the aldehyde, but no traces of hydroxamic acid could be detected by the ferric chloride test.

Attempted Nitration of N-Phenylhydroxylamine.—N-Phenylhydroxylamine[31] was treated with ethyl nitrate in ethereal ammonia solution, according to the procedure described by Marvel[32] for the nitrosation of phenylhydroxylamine. No evidence of reaction could be detected, even when the solution was warmed; neither heat nor precipitate was formed. The only material recovered was phenylhydroxylamine (20%).

Attempted Nitration of N-Cyclohexylhydroxylamine.—To a solution of 0.25 g. (0.010 mole) of sodium in 25 ml. of absolute ethanol was added 0.58 g. (0.005 mole) of N-cyclohexylhydroxylamine[33]; most of it dissolved. A solution of 0.50 g. (0.0055 mole) of ethyl nitrate in 5 ml. of absolute ethanol was added slowly at room temperature to the resulting suspension. A mild exothermic reaction set in and the temperature rose to 30°, remaining there for about 1 hour. After 3 hours the resulting clear solution was evaporated on a steam-bath to leave a slurry, which was taken up in the minimum amount of water, and carefully neutralized with dilute hydrochloric acid. Recrystallization from petroleum ether (b.p. 30–40°) of the semi-solid so obtained gave 0.18 g. (32%) of cyclohexanone oxime, m.p. 87.5–88.5° (reported[34] m.p. 90°), undepressed by an authentic sample.

Benzenesulfonhydroxamic (Piloty's) Acid and its Salts.—Piloty's acid, m.p. 122–125°, was prepared by a simplified version of the procedure used by Piloty.[11]

The sodium and potassium salts of Piloty's acid were prepared in greater than 90% yield by precipitation from alcoholic solutions of the acid with stoichiometric amounts of concentrated, alcoholic solutions of the appropriate base. Because of their evident instability, these salts were not purified for analysis, but were used forthwith.

(29) J. von Braun, *Ber.*, **43**, 1351 (1910).

(30) L. Maier and E. Rochow, THIS JOURNAL, **79**, 5884 (1957).

(31) O. Kamm, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 445.

(32) C. S. Marvel, *ibid.*, p. 177.

(33) G. Vavon and A. L. Berton, *Bull. soc. chim. France*, [4] **37**, 301 (1925).

(34) M. Konovalov, *J. Russ. Phys.-Chem. Soc.*, **30**, 960 (1898).

Reaction of Piloty's Acid with Benzyl Chloride. (a) With One Equivalent.—Although reaction was carried out under a variety of conditions, the only product isolated was phenyl benzyl sulfone in 70 to 95% yield. The reaction was run in ethanol at room temperature and at reflux, with simultaneous addition of all reactants or with slow addition of Piloty's acid or of base. The amount of sodium hydroxide added varied from one to five equivalents. In every case fine white needles began to appear after some time and cooling of the reaction mixture caused most of the sulfone to precipitate. Addition of water to the ethanol or evaporation precipitated the remaining sulfone. In a typical run 8.3 g. (0.05 mole) of benzyl chloride, 4.0 g. (0.10 mole) of sodium hydroxide and 10.0 g. (0.058 mole) of Piloty's acid were dissolved in 85 ml. of 95% ethanol and refluxed for 3 hours, cooled, and the precipitate collected. Concentration of the filtrate gave a second crop; total 10.5 g. (91%), m.p. 143–146°. The filtrate did not give a significant precipitate with 2,4-dinitrophenylhydrazine reagent. Recrystallization from 95% ethanol raised the melting point to 145.5–147° (reported[35] 147°), undepressed when mixed with an authentic sample of phenyl benzyl sulfone.

(b) **With Two Equivalents.**—A solution of 5.2 g. (0.03 mole) of Piloty's acid in 10 ml. of 95% ethanol was dropped rapidly into a solution of 2.4 g. (0.06 mole) of sodium hydroxide and 7.5 g. (0.06 mole) of benzyl chloride in 40 ml. of 95% ethanol. The salt of Piloty's acid precipitated during the addition but dissolved as the reaction proceeded. The mixture was refluxed with stirring for 2.5 hours; the solid which separated on cooling was collected and recrystallized from ethanol, giving 3.3 g. (47.5%) of benzyl phenyl sulfone, m.p. 143–147°. The liquid portion of the reaction was distilled on a steam-bath, and the residual paste was washed with water and recrystallized from ethanol, leaving 0.8 g. (11.5%) of sulfone, m.p. 143.5–146.5°. Carbon dioxide was bubbled into the aqueous filtrate to precipitate any weak acids, but nothing separated. On acidification with concentrated hydrochloric acid, however, 1.2 g. (28%) of crude benzenesulfinic acid, m.p. 79–80.5° (reported[36] m.p. 83–84°), was obtained, identified by conversion to benzyl phenyl sulfone by treatment with benzyl chloride and base, and to phenylmercuric chloride by reaction with mercuric chloride. Ether was added to the distillate from the reaction and it was extracted with 20% aqueous sodium hydroxide. Neutralization with carbon dioxide gave no precipitate, but acidification with hydrochloric acid gave a small additional amount of benzenesulfinic acid. Concentration of the dried ($CaSO_4$) neutral layer precipitated more benzyl phenyl sulfone (0.7 g., 10%). The filtrate from this had a distinct odor of benzyl chloride, and addition of ethanolic silver chloride and dilute nitric acid to an aliquot precipitated silver chloride corresponding to 15% of the benzyl chloride originally added. Treatment of another aliquot with 2,4-dinitrophenylhydrazine precipitated a small amount of benzaldehyde dinitrophenylhydrazone, corresponding to less than 2% of the original benzyl chloride. The infrared spectrum of the solution suggested that most of the remaining material consisted of benzyl chloride, benzyl alcohol and benzyl ethyl ether. The sum (0.029 mole) of the sulfone and sulfinic acid isolated accounts for 97% of the Piloty's acid, while the sum (0.03 mole) of sulfone and silver chloride accounts for 50% of the benzyl chloride.

Other attempts to alkylate Piloty's acid in base gave sulfone as the only identified product besides solvolysis products of the alkyl halides employed. Several reactions were attempted with hydrocinnamyl iodide in ethanol and aqueous ethanol systems both at reflux and at room temperature. Base concentration was also varied from one equivalent to ten. In no case could any weak acid, *i.e.*, oxime, be detected by neutralizing suitable fractions with carbon dioxide, nor did the reaction mixtures give significant precipitation with 2,4-dinitrophenylhydrazine reagent.

O-Acetylbenzenesulfonhydroxamic Acid.—To 25 g. (0.118 mole) of potassium benzenesulfonhydroxamate suspended in 100 ml. of sodium-dried benzene was added dropwise 10.2 g. (0.10 mole) of freshly distilled acetic anhydride while the temperature was kept at 10 ± 2.5° with external cooling. The mixture was stirred for 0.5 hour after the addition was completed, while it was allowed to come to room temperature. The resulting paste was filtered and the residue was washed thoroughly with water to leave 14.8 g. (58.5% based on potassium benzenesulfonhydroxamate, 69% based on acetic anhydride) of O-acetylbenzenesulfonhydroxamic acid, m.p. 89.5–92.5°. Recrystallization from benzene (once) and water (three times) gave an analytical sample, m.p. 92.5–94°.

Anal. Calcd. for $C_8H_9NO_4S$: C, 44.66; H, 4.22; N, 6.51; S, 14.54. Found: C, 44.58; H, 4.31; N, 6.50; S, 14.96.

The compound was soluble in 5% sodium bicarbonate; its infrared spectrum showed one ester carbonyl stretching band at 1770 cm.$^{-1}$ and only one band above 3200 cm.$^{-1}$, corresponding to the lower frequency band of the two found in this region for Piloty's acid.

Evaporation of the original benzene filtrate gave a solid, which on washing with 5% sodium bicarbonate and water yielded 2.15 g. (7.7% based on potassium benzenesulfonhydroxamate, 17% based on acetic anhydride) of O,N-diacetyl benzenesulfonhydroxamate, m.p. 83–85° (reported[11] m.p. 85°). This material was insoluble in base and showed infrared absorption at 1795 cm.$^{-1}$, corresponding to ester carbonyl, and at 1725 cm.$^{-1}$, corresponding to amide carbonyl; there was no absorption above 3200 cm.$^{-1}$. Evaporation of the aqueous washings from the monoacyl fraction gave a solid, which was recrystallized from water with considerable loss to yield approximately 0.5 g. (2.8%) of benzenesulfonamide, m.p. 147–149° (reported[37] m.p. 152–153°), undepressed by mixture with an authentic sample.

N-Benzyl O-Acetylbenzenesulfonhydroxamate.—A solution of 1.1 g. (5.1 mmoles) of O-acetylbenzenesulfonhydroxamic acid and 0.38 g. (3.0 mmoles) of benzyl chloride in 20 ml. of 95% ethanol and enough 5% aqueous sodium hydroxide to give an initial *p*H of about 8 was refluxed for one hour. The mixture was then cooled and concentrated, and successive crops of solid precipitates filtered off. The first and second crops yielded 0.545 g., m.p. 97.5–100°, and 0.045 g., m.p. 92–100°, respectively (total yield 65%). They showed identical infrared spectra and three recrystallizations from aqueous ethanol gave an analytical sample, m.p. 99.5–101.5°.

Anal. Calcd. for $C_{15}H_{15}NO_4S$: C, 59.01; H, 4.95; N, 4.59. Found: C, 59.15; H, 5.05; N, 4.44.

The third crop gave 55 mg. (7%) of benzenesulfonamide, m.p. (crude) 137–149°, identified by comparison of its infrared spectrum with that of an authentic specimen.

Hydrolysis of N-Benzyl O-Acetylbenzenesulfonhydroxamate.—A suspension of 1.0 g. (3.3 mmoles) of N-benzyl O-acetylbenzenesulfonhydroxamate in 25 ml. of 5% sodium hydroxide was refluxed for 25 minutes, cooled and filtered. The residual solid proved to be unreacted starting material, 235 mg. (24%), m.p. 95–100°. To the filtrate was added 20 ml. of ether, and the organic material, which had a strong odor of benzaldehyde, was extracted with two 10-ml. portions of 10% sodium hydroxide. The basic, aqueous layer was neutralized with carbon dioxide, extracted with ether, and the extracts were dried over calcium chloride and saturated with dry hydrogen chloride to precipitate 175 mg. (44%) of hydrochloride, which was converted to benzaldoxime, m.p. 129–131° (reported[38] m.p. 130°), undepressed when mixed with an authentic sample.

Silver O-Acetylbenzenesulfonhydroxamate.—A solution of 2.46 g. of silver nitrate in 10 ml. of water was added rapidly to a freshly prepared solution of 3.10 g. of O-acetylbenzenesulfonhydroxamic acid in 14.5 ml. of 1 *N* sodium hydroxide. The precipitated gray silver salt was filtered at once, washed with water and ether, and dried *in vacuo* in the dark; wt. 3.91 g. (84%). Because of its evident stability, purification for analysis was not attempted. Alternatively, 1.00 g. of the acid was dissolved in 20 ml. of dry ether and the ammonium salt was precipitated by bubbling in dry ammonia while cooling in ice. The salt, which weighed 0.96 g., was dissolved in 10 ml. of ice-water and a solution of 0.705 g. of silver nitrate in 5 ml. of water was added rapidly. The precipitate of white silver salt was washed with water and dried *in vacuo* in the dark; wt. 1.05 g. (70%). While this method results in a some-

(35) R. Otto and W. Otto, *Ber.*, **21**, 1695 (1888).
(36) W. Peters, *ibid.*, **38**, 2570 (1905).
(37) T. Curtius and F. Lorenzen, *J. prakt. Chem.*, [2] **58**, 176 (1898).
(38) E. Beckmann, *Ber.*, **20**, 2766 (1887).

what lower yield, the product is of better quality for use in alkylations.

N-Hydrocinnamyl O-Acetylbenzenesulfonhydroxamate.—In an opaque flask 0.73 g. (2.98 mmoles) of hydrocinnamyl iodide and 1.00 g. (2.98 mmoles) of the foregoing white silver salt were refluxed for 5 hours in 20 ml. of dry, redistilled acetonitrile. The precipitated silver salts were filtered off, the solvent evaporated, and the resulting oil triturated with petroleum ether (b.p. 30–40°). The solid which slowly formed was recrystallized from aqueous ethanol, and gave 0.65 g. (66%) of product, m.p. 97–99°. Four recrystallizations from ethanol gave an analytical sample, m.p. 99–99.5°, without excessive loss or other evidence of decomposition.

Anal. Calcd. for $C_{17}H_{19}NO_4S$: C, 61.25; H, 5.75; N, 4.20. Found: C, 61.02; H, 5.67; N, 4.07.

The foregoing procedure was one of several attempted. Reaction in many solvents was possible: stirring for several days in dry ether gave a 43% yield; in ethanol a lower yield was obtained.

Hydrolysis of N-Hydrocinnamyl O-Acetylbenzenesulfonhydroxamate. (a) With Base.—Refluxing for 3 hours 250 mg. (0.75 mmole) of N-hydrocinnamyl O-acetylbenzenesulfonhydroxamate suspended in 15 ml. of 5% sodium bicarbonate and 3 ml. of 95% ethanol, cooling the mixture and collecting the precipitate gave 85 mg. (71%) of hydrocinnamaldoxime, m.p. 72–85°. Concentration of the filtrate on a steam-bath, cooling and filtering gave 5 mg. more. Acidification of the filtrate with dilute hydrochloric acid gave another 10 mg. of the same product, for a total crude yield of 90%. Comparison of infrared spectra and a mixture melting point confirmed the identity.

(b) With Acid.—Refluxing for 2 hours 200 mg. (0.60 mmole) of N-hydrocinnamyl O-acetylbenzenesulfonhydroxamate in 14 ml. of 10% ethanolic hydrogen chloride, cooling and partial neutralization with 5% sodium hydroxide caused an oil to separate, which solidified on cooling and standing. It was dissolved in excess 5% sodium hydroxide and reprecipitated with concentrated hydrochloric acid to yield 68 mg. (76%) of hydrocinnamaldoxime, m.p. 85.5–88°, undepressed by mixture with an authentic sample.

N-2,4,6-Trimethylbenzyl O-Acetylbenzenesulfonhydroxamate.—An ethereal suspension of 1.26 g. (7.5 mmoles) of 2,4,6-trimethylbenzyl chloride[39] and 3.22 g. (0.010 mole) of silver O-acetylbenzenesulfonhydroxamate was refluxed in the dark for 24 hours, then cooled, filtered to remove silver salts and evaporated to a paste. Recrystallization from ethanol gave 2.22 g. (85%) of product, m.p. 119–121°. Four recrystallizations from aqueous ethanol and two from carbon tetrachloride–ligroin mixture gave an analytical sample, m.p. 121.5–123°.

Anal. Calcd. for $C_{18}H_{21}NO_4S$: C, 62.24; H, 6.10. Found: C, 62.29; H, 6.29.

2,4,6-Trimethylbenzaldoxime.—Refluxing 1.4 g. (8.6 mmoles) of N-2,4,6-trimethylbenzyl O-acetylbenzenesulfonhydroxamate, 35 ml. of 5% sodium bicarbonate and 15 ml. of ethanol for 4 hours, filtering hot from a small amount of insoluble material, and cooling precipitated 0.56 g. (85%) of oxime, m.p. 176–180° (reported[40] m.p. 180–181°).

Attempted Alkylations Using Isopropyl Iodide.—Isopropyl iodide and silver O-acetylbenzenesulfonhydroxamate were brought together in acetonitrile, ether or benzene as solvent. In each case silver iodide was formed in nearly stoichiometric amount, and some O-acetylbenzenesulfonhydroxamic acid was recovered (up to 28%), but nothing recognizable as N-isopropyl O-acetylbenzenesulfonhydroxamate could be found. No more than traces of acetone could be detected with 2,4-dinitrophenylhydrazine reagent.

Acetaldehyde Dinitrophenylhydrazone.—A mixture of 1.50 g. (4.7 mmoles) of silver O-acetylbenzenesulfonhydroxamate, 365 mg. (2.35 mmoles) of ethyl iodide and 20 ml. of dry ether was refluxed in the dark for 10 hours. Evaporation of the filtered solution left an oil, which was treated with 5% ethanolic sodium hydroxide for one hour, then acidified and distilled into 2,4-dinitrophenylhydrazine solution, where it precipitated 380 mg. (73%) of crude acetaldehyde dinitrophenylhydrazone. Recrystallization from ethanol gave 300 mg. (57%) of pure product, m.p. 143.5–145.5° (reported[41] m.p. 147°), undepressed by mixture with an authentic sample.

O-Benzylbenzenesulfonhydroxamic Acid and O,N-Dibenzoyl Benzenesulfonhydroxamate.—To a stirred suspension of 5.7 g. (0.027 mole) of potassium benzenesulfonhydroxamate in 20 ml. of sodium-dried benzene was added 6.1 g. (0.027 mole) of freshly distilled benzoic anhydride, while the temperature was kept below 15°. The solution was stirred for a few minutes after addition was complete and then allowed to come to room temperature while stirring was continued. The resulting slurry was filtered and the solid taken up in water and ether. Acidification of the water layer yielded 2.0 g. of benzoic acid. The original filtrate and the ether extract were combined and evaporated leaving a paste, which was extracted with 2% sodium hydroxide. The neutral residue weighed 5.2 g. (51%), m.p. 111–116°. Three recrystallizations from aqueous ethanol gave an analytical sample, m.p. 114.5–116°. Its infrared spectrum and analysis were consistent with O,N-dibenzoyl benzenesulfonhydroxamate.

Anal. Calcd. for $C_{18}H_{20}NO_5S$: C, 62.99; H, 3.97; N, 3.67. Found: C, 62.77; H, 3.97; N, 3.49.

Acidification of the basic extract precipitated 0.7 g. (9%) of benzoyl benzenesulfonhydroxamate, m.p. 78–83°. Recrystallization from aqueous ethanol (five times) gave an analytical sample, m.p. 89.5–91.5°.

Anal. Calcd. for $C_{13}H_{11}NO_4S$: C, 56.32; H, 4.00. Found: C, 56.35; H, 4.13.

Phenyl Hydrocinnamyl Sulfone.—On refluxing 1.1 g. (5.0 mmoles) of O-acetylbenzenesulfonhydroxamic acid and 615 mg. (2.5 mmoles) of hydrocinnamyl iodide in 25 ml. of absolute ethanol with 5 ml. of 5% aqueous sodium hydroxide for 2 hours, cooling, filtering from a small amount of solid and evaporating much of the ethanol, 300 mg. (46%) of a solid, m.p. 81–83.5°, was obtained. This product was identical with phenyl hydrocinnamyl sulfone obtained from the reaction of Piloty's acid with hydrocinnamyl iodide in basic solution, under conditions the same as those which converted benzyl chloride to benzyl phenyl sulfone. Recrystallization from ethanol (twice) gave an analytical sample, m.p. 83–83.5°.

Anal. Calcd. for $C_{15}H_{16}SO_2$: C, 69.21; H, 6.20. Found: C, 69.28; H, 6.12.

O-Tetrahydropyran-2-ylbenzenesulfonhydroxamic Acid.—Slow addition of 4.9 g. (0.058 mole) of redistilled, sodium-dried dihydropyran to 10.0 g. (0.058 mole) of Piloty's acid in 100 ml. of dry ether with or without addition of 2 drops of concentrated sulfuric acid resulted in an exothermic reaction. Extraction with base after two hours of stirring gave a transient blue-green color; neutralization with carbon dioxide precipitated 3.5 g. (23.5%) of O-tetrahydropyran-2-ylbenzenesulfonhydroxamic acid, m.p. 115–121°. Recrystallization from benzene-petroleum ether mixture (twice), methanol (three times) and acetone (once) gave an analytical sample, m.p. 117.5–123°.

Anal. Calcd. for $C_{11}H_{15}NSO_4$: C, 51.36; H, 5.88; N, 5.45. Found: C, 51.35%; H, 5.98; N, 5.38.

Further acidification of the aqueous solution with hydrochloric acid gave 2.8 g. (35%) of benzenesulfinic acid, m.p. 78–81°. The original ethereal solution yielded 0.50 g. (2%) of **O,N-bis-tetrahydropyran-2-ylbenzenesulfonhydroxamate**, m.p. 109–114° after recrystallization from petroleum ether–carbon tetrachloride mixture (three times) and methanol (twice).

Anal. Calcd. for $C_{16}H_{23}NSO_5$: C, 56.29; H, 6.79; N, 4.10. Found: C, 56.32; H, 6.71; N, 4.13.

N-Benzyl O-Tetrahydropyran-2-ylbenzenesulfonhydroxamate.—A mixture of 1.23 g. (4.9 mmoles) of O-tetrahydropyran-2-ylbenzenesulfonhydroxamic acid, 0.63 g. (5.0 mmoles) of benzyl chloride and 1 ml. of 20% sodium hydroxide solution in 10 ml. of ethanol was refluxed 2 hours, then cooled and filtered from some salt. Careful addition of water to the warmed filtrate and subsequent refrigeration precipitated 1.0 g. (60%) of the desired product, m.p. 83–86°. Recrystallization from aqueous methanol (six times) gave an analytical sample, m.p. 86–87°.

Anal. Calcd. for $C_{18}H_{21}NSO_4$: C, 62.24; H, 6.10; N, 4.03. Found: C, 62.15; H, 6.23; N, 3.95.

(39) W. T. Nauta and J. W. Dienske, *Rec. trav. chim.*, **55**, 1000 (1936).

(40) R. Scholl and F. Kacek, *Ber.*, **36**, 331 (1903).

(41) C. F. H. Allen, THIS JOURNAL, **52**, 2957 (1930).

N-Benzylbenzenesulfonhydroxamic Acid.—Hydrolysis of 0.60 g. (2.3 mmoles) of N-benzyl O-tetrahydropyran-2-ylbenzenesulfonhydroxamate by refluxing with 10 ml. of 2% hydrogen chloride in 50% aqueous ethanol for 2 hours, cooling the mixture and diluting the water gave 0.39 g. (85.5%) of N-benzylbenzenesulfonhydroxamic acid, m.p. 87–91° after recrystallization from benzene, undepressed by mixture with an authentic sample. The analysis corresponded to the presence of a half-mole of benzene of crystallization, in agreement with Piloty's original report[11] of this compound obtained from benzenesulfonyl chloride and N-benzylhydroxylamine.

Anal. Calcd. for $C_{13}H_{13}O_3NS \cdot {}^1/_2C_6H_6$: C, 63.55; H, 5.33; N, 4.63. Found: C, 63.89; H, 5.42; N, 4.29, 4.40.

N-Hydrocinnamyl O-Tetrahydropyran-2-ylbenzenesulfonhydroxamate.—Refluxing 1.60 g. (6.2 mmoles) of O-tetrahydropyran-2-ylbenzenesulfonhydroxamic acid with 1.23 g. (5.0 mmoles) of hydrocinnamyl iodide and 1.5 ml. of 20% sodium hydroxide solution in 10 ml. of 95% ethanol gave 1.24 g. (70%) of product, m.p. 80.5–82°. Five recrystallizations from ethanol gave an analytical sample, m.p. 81.5–83°.

Anal. Calcd. for $C_{20}H_{25}NO_4S$: C, 63.98; H, 6.71; N, 3.73. Found: C, 63.95; H, 6.84; N, 3.66.

Hydrolysis of 0.85 g. (2.3 mmoles) of the foregoing compound by refluxing in 50% aqueous ethanol for 2 hours followed by dilution with water gave an oil which could not be crystallized. The oil was refluxed for 0.5 hour in dilute ethanolic sodium hydroxide, and the cooled solution was then diluted with water and extracted with ether. Neutralization of the aqueous layer with carbon dioxide gave 120 mg. (35%) of hydrocinnamaldoxime, m.p. 83–87°.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, CASE INSTITUTE OF TECHNOLOGY, CLEVELAND 6, OHIO]

Chlorination of Aromatic Compounds by Antimony Pentachloride[1,2]

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Investigation of the reaction of antimony pentachloride with halobenzenes and toluene indicates that chlorination proceeds by electrophilic substitution involving an attacking species of low activity, as evidenced by the almost exclusive *ortho–para* orientation. Preliminary dissociation of the metal chloride is deemed unlikely, since the *ortho/para* ratio produced by chlorination of chlorobenzene or toluene by antimony pentachloride is substantially lower than that obtained from catalytic chlorination with chlorine gas. The reactions with mesitylene and pentamethylbenzene were also studied. Theoretical aspects of the chlorination reaction are discussed.

Introduction

Since the appearance, in 1862, of the first report[4] on the chlorination of aromatic compounds by antimony pentachloride, the reaction has received relatively little attention, except as a route to polychlorinated compounds. Thus, Steiner[5] isolated decachlorobenzophenone, hexachlorobenzene and pentachlorobenzoic acid from the reaction of benzophenone with an excess of the pentachloride at elevated temperatures. It was not until recently, however, that a study, preliminary in nature, of the mechanism of aromatic chlorination by antimony pentachloride was reported.[6]

The purpose of the present work was to elucidate the mechanism of aromatic chlorination by antimony pentachloride. Included in this study were the halobenzenes, toluene, mesitylene and pentamethylbenzene.

Results and Discussion

Early work[7] established the general equation for chlorination by antimony pentachloride. On the basis of our investigations, the reaction is considered to proceed by electrophilic substitution, as evidenced by the predominant *ortho–para* orientation in the halobenzene series and with toluene.

$$ArH + SbCl_5 \rightarrow ArCl + SbCl_3 + HCl$$

TABLE I

ANTIMONY PENTACHLORIDE AND AROMATIC COMPOUNDS

C_6H_5X,[a] X =	Temp., °C.	Time, hr.	ClC_6H_4X B.p., °C.	ClC_6H_4X Yield, %	o, %	m, %	p, %
F[b]	43–49	2	127–128	83[c]	4	<1[d]	96[e]
Cl	41–59	2	170–172	82	15	1	84
Br	31–56	1	192–194	83	25	1	74
I	4–17	1	129–135[f]	36[g]	50[e]	<1[d]	50
CH_3	18–31	2.5	156	87[h]	47	2	51

[a] C_6H_5X (2 moles) and $SbCl_5$ (0.5 mole). [b] Run at half scale; reaction mixture was distilled directly. [c] Calcd. for C_6H_4ClF: C, 55.20; H, 3.09. Found: C, 55.41; H, 3.45. [d] No detectable *m*-isomer. [e] By difference. [f] At 55 mm. [g] See Experimental section for other products. [h] Plus 1.1 g. of distillation residue consisting of chlorotoluene and dichlorotoluene by infrared analysis.

In addition, this interpretation is consistent with the order of reactivity of the aromatic component (toluene > benzene > chlorobenzene), based on a comparison of "initiation temperatures," as well as on kinetic evidence.[8] The increasing amount of *ortho* substitution as the atomic number of the halogen increases has been encountered with other electrophilic reagents,[6,9] and is explained on the basis of the inductive effect of the substituent.

It has been assumed that antimony pentachloride acts by preliminary dissociation to free chlorine which then functions as the actual chlorinating agent.[4,10]

$$SbCl_5 \rightleftharpoons SbCl_3 + Cl_2$$

$$ArH + Cl_2 \xrightarrow{SbCl_3} ArCl + HCl$$

(1) Part IV of a series on "Reactions of Metal Halides with Organic Compounds"; presented in part at the 136th Meeting of the American Chemical Society in Atlantic City, N. J., September, 1959, Abstracts of Papers, p. 23P.

(2) From the Ph.D. thesis of Allen K. Sparks, Case Institute of Technology, 1960.

(3) Allied Chemical Corp. Fellow, 1958–1960.

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(5) K. Steiner, *Monatsh.*, **36**, 825 (1915); *C. A.*, **10**, 181 (1916).

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(7) A. Rosenheim and W. Stellman, *Ber.*, **34**, 3377 (1901).

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