k_S/k_O expected if the enzyme used the metaphosphate mechanism.[9]

(9) Support of this work by the National Institutes of Health is gratefully acknowledged.

Ronald Breslow, Ira Katz
Department of Chemistry, Columbia University
New York, New York 10027

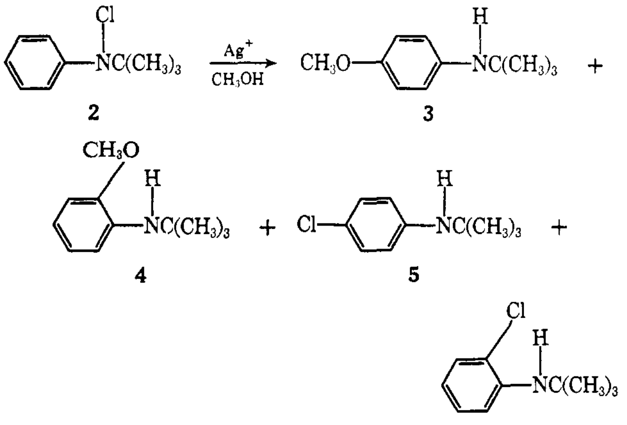
Received October 16, 1968

Anilenium Ions. Intermediates in the Nucleophilic Substitution of Anilines[1]

Sir:

In general, nucleophilic aromatic substitution is found to occur on aromatic systems abundantly substituted with electron-withdrawing groups and in the special case of diazonium salts.[2] We wish to report at this time a simple method which makes possible the nucleophilic substitution of anilines under extremely mild conditions.

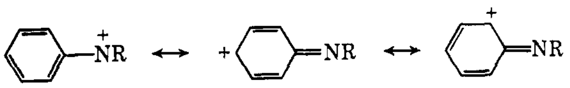
Recently, it was proposed that the chlorination of the aromatic ring of anilines[3] and the rearrangement of N-chloroanilides[2b,4] to *o*- and *p*-chloroaniline derivatives occur *via* N-chlorination,[5] followed by heterolysis of the N–Cl bond to yield an amide anion and positive chlorine, which electrophilically attacks the aromatic ring. Our studies on the reactions of nitrenium ions[1] suggested to us that in the presence of silver ion the N–Cl bond might be heterolytically cleaved to yield divalent electron-deficient nitrogen and chloride anion.[6] In order to test this hypothesis we prepared N-chloro-N-methylaniline (**1**)[5,7] and N-chloro-N-*t*-butylaniline (**2**).[7,8] When **2** was treated with methanolic silver perchlorate or methanolic silver trifluoroacetate at −8°, we obtained a mixture of **3**, **4**, **5**, and **6** in yields of 39, 6, 6, and 28%,[9] respectively, for a total yield of 79% based on unrecovered N-*t*-butylaniline (which generally accounted for *ca.* 5–10% of **2**). The formation of **3** as the major product clearly demonstrated the nucleophilic character of this reaction.



Undoubtedly the formation of both **3** and **4** required nucleophilic attack by methanol (a relatively poor nucleophile) on the aromatic ring.[10] When the reaction was carried out at −8° in the absence of silver ion no trace of either **3** or **4** was found. This non silver ion catalyzed reaction, which gave 8% N-*t*-butylaniline, 52% **6**, and 14% **5**, was considerably slower than the corresponding silver ion catalyzed reaction. In addition the *o*- to *p*-chloro-N-*t*-butylaniline ratio was 4.6 in the silver ion catalyzed reaction and 3.7 in the non silver ion catalyzed reaction.[11]

N-Chloro-N-methylaniline (**1**) gave results very similar to those obtained with **2**. Under silver ion catalyzed conditions at −20° we obtained N-methyl-*p*-anisidine (30%), N-methyl-*o*-anisidine (1%), *p*-chloro-N-methylaniline (6%), *o*-chloro-N-methylaniline (9%), and N-methylaniline (5%). The over-all yield (51%) from **1** was considerably lower than that from **2** due to the slow oxidation of the reaction products by silver ion.

Several mechanistic questions remain to be answered in relation to these substitution reactions. It is not clear whether the reaction is S$_N$2′ or S$_N$1′; that is, whether the reaction is a silver ion assisted displacement or whether a discrete "anilenium" ion such as **7** is formed. Since carbon should be able to bear a positive charge more readily than nitrogen, it would be anticipated that the charge on **7** would be predominantly delocalized into the ring with **8** and **9** being the principal resonance contributors. This would explain the formation of the observed anisole derivatives.



7 **8** **9**

One question which cannot be answered on the basis of the data presently available is whether the formation of the rearranged chloroanilines occurs in a separate reaction involving reverse heterolytic cleavage of the N–Cl bond to yield positive chlorine which then electrophilically attacks the ring or whether the *o*- and *p*-chloroanilines are arising *via* a tight ion pair involving **7**. The second possibility has the advantage that a

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(1) Paper V in a series on the chemistry of nitrenium ions. For previous papers in this series see (a) P. G. Gassman and B. L. Fox, *Chem. Commun.*, 153 (1966); (b) P. G. Gassman and B. L. Fox, *J. Am. Chem. Soc.*, **89**, 338 (1967); (c) P. G. Gassman and R. L. Cryberg, *ibid.*, **90**, 1355 (1968); (d) P. G. Gassman, F. Hoyda, and J. Dygos, *ibid.*, **90**, 2716 (1968).

(2) For reviews of nucleophilic aromatic substitution see: (a) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951); (b) E. D. Hughes and C. K. Ingold, *Quart. Rev.* (London), **6**, 34 (1952); (c) J. F. Bunnett, *ibid.*, **12**, 1 (1958); (d) R. Sauer and R. Huisgen, *Angew. Chem.*, **72**, 294 (1960); (e) S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963).

(3) R. S. Neale, R. G. Schepers, and M. R. Walsh, *J. Org. Chem.*, **29**, 3390 (1964).

(4) K. M. Johnston, G. H. Williams, and H. J. Williams, *Chem. Ind.* (London), 991 (1966).

(5) P. Haberfield and D. Paul, *J. Am. Chem. Soc.*, **87**, 5502 (1965).

(6) This appeared even more likely in view of the acid-catalyzed rearrangement of arylhydroxylamines: H. E. Heller, E. D. Hughes, and C. K. Ingold, *Nature*, **168**, 909 (1951). See also R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 176 (1964).

(7) N-Chloro-N-methylaniline (**1**) and N-chloro-N-*t*-butylaniline (**2**) were prepared *via* reaction of N-methylaniline and N-*t*-butylaniline with sodium hypochlorite at −8°. Compounds **1** and **2** routinely titrated for greater than 95% active chlorine. Reductive removal of the active chlorine showed that only traces of material with a chlorinated aromatic ring were formed under the conditions used to prepare **1** and **2**.

(8) N-*t*-Butylaniline was prepared according to the procedure of A. Bell and M. B. Knowles, U. S. Patent 2,692,287 (1956); *Chem. Abstr.*, **50**, 2666*e* (1956).

(9) In refluxing methanol in the presence of excess silver trifluoroacetate the yields of **3**, **4**, **5**, and **6** were 35, 5, 6, and 22%, respectively. This experiment was carried out by dripping a solution of **2** into a refluxing solution of silver trifluoroacetate in methanol.

(10) Under the reaction conditions **5** and **6** were not converted to either **3** or **4**.

(11) An *o*- to *p*-chloro-N-*t*-butylaniline ratio of 1.85 has been reported[3] for the reaction of N-*t*-butylaniline with N-chlorosuccinimide in refluxing benzene.

single type of heterolytic cleavage can account for all of the products.[12] Experimentation is in progress which should allow us to distinguish between these two possible routes to the *o*- and *p*-chloroanilines.

Since N-chloroaniline derivatives can be prepared rapidly in high yield and in a high state of purity *via* reaction of the corresponding aniline with sodium hypochlorite, the use of these intermediates in the synthesis of a wide variety of substituted aromatic amines should be possible. We are presently investigating a variety of applications of this potentially important nucleophilic aromatic substitution reaction.

Acknowledgment. We wish to thank the National Cancer Institute of the Public Health Service for Grant CA-07110 which supported this research.

[12] We have previously shown that chlorine can migrate from nitrogen to carbon with dramatic silver ion catalysis in high yield[1c] *via* the intermediacy of a tight ion pair.

[13] Alfred P. Sloan Research Fellow, 1967–1969.

[14] National Defense Education Act Predoctoral Fellow, 1967–1969.

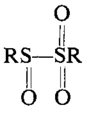
Paul G. Gassman,[13] Gerald Campbell,[14] Ronald Frederick
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210

Received October 4, 1968

Synthesis and Properties of a Sulfinic Anhydride[1]

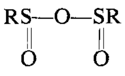
Sir:

Previously all attempts[2,3] to prepare the anhydride **2** of any sulfinic acid have led to the preparation of the isomeric sulfinyl sulfone **1**. We wish to report the first



$$\mathrm{R}\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}-\overset{\substack{\mathrm{O}\\ \|}}{\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}}\mathrm{R}$$

1

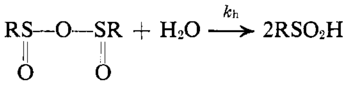


$$\mathrm{R}\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}-\mathrm{O}-\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}\mathrm{R}$$

2

preparation of such an anhydride (**2a**, R = *t*-Bu) and to indicate some significant differences between its properties and those of **1**.

Careful acidification of a cold solution of magnesium 2-methyl-2-propanesulfinate[4] gives 2-methyl-2-propanesulfinic acid (**3a**), which can be converted to the corresponding sulfinyl chloride by treatment with an equimolar quantity of thionyl chloride in ether. The sulfinyl chloride was added to a stirred suspension of silver 2-methyl-2-propanesulfinate[4] in ether at −5 to −10°. After 3 hr the mixture was filtered, and the ether was removed at 0°. The residue was purified by several low-temperature recrystallizations from ether, giving 2-methyl-2-propanesulfinic anhydride (**2a**, R = *t*-Bu) in 50% yield, mp 45–46°.[5] Proof that the compound was a sulfinic anhydride was provided (1) by its facile hydrolysis (eq 1) to **3a**, isolated in 73% yield by

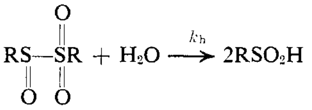


$$\mathrm{R}\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}-\mathrm{O}-\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}\mathrm{R} + \mathrm{H_2O} \xrightarrow{k_h} 2\mathrm{RSO_2H} \qquad (1)$$

2a **3a**

precipitation as its benzenediazo sulfone derivative, $\mathrm{C_6H_5N{=}NSO_2Bu}$-*t* (**4**), mp 65–66°,[6] and (2) by its infrared spectrum (in $\mathrm{CHCl_3}$), which was entirely different in the 7.5–9.3-μ region from those of three known sulfinyl sulfones (**1b**,[7] R = $\mathrm{CH_3}$; **1c**,[7] R = *n*-Bu; and **1d**,[2] R = *p*-$\mathrm{CH_3C_6H_4}$). All three of the latter possess a strong band at 7.6 μ due to the sulfone group, another absorption due to this group in the region 8.5–9.0 μ, and a strong band due to the sulfinyl group at 9.2 μ. In contrast, **2a** shows *only* a *single* strong band at 8.8 μ, an appropriate wavelength for a sulfinyl group which is bonded to carbon and an electron-withdrawing oxygen function.[9]

Sulfinic anhydride **2a** differs markedly from sulfinyl sulfones **1b–d** in the susceptibility of its hydrolysis to acid catalysis. In aqueous dioxane the hydrolysis of sulfinyl sulfones (eq 2) is not subject to acid catalysis



$$\mathrm{R}\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}-\overset{\substack{\mathrm{O}\\ \|}}{\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}}\mathrm{R} + \mathrm{H_2O} \xrightarrow{k_h} 2\mathrm{RSO_2H} \qquad (2)$$

(Table I and ref 3a). In sharp contrast the hydrolysis of sulfinic anhydride **2a** (eq 1) in the same medium shows definite acid catalysis (Table I), k_h being given by an expression of the form

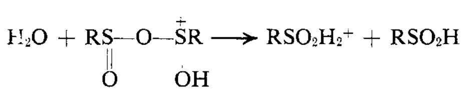
Table I. Rates of Hydrolysis in Acidic 60% Dioxane at 21.4° [a]

	$k_h \times 10^3$, sec^{-1}				
	$C_{\mathrm{HClO_4}}$, *M*				
Compound	0.01	0.10	0.30	0.50	0.60
1b, R = $\mathrm{CH_3}$	12	12			
1c, R = *n*-Bu	2.7	2.6		2.6	
2a, R = *t*-Bu	0.15	0.20	0.35	0.51	0.61

[a] Followed spectrophotometrically by measuring the decrease in optical density at 250 mμ for **1b** and **1c** and at 238 mμ for **2a**.

$$k_h = k_0 + k_H(\mathrm{H^+}) \qquad (3)$$

Since $(k_H{}^{\mathrm{D_2O}}/k_H{}^{\mathrm{H_2O}}) = 1.35$, the $k_H(\mathrm{H^+})$ term in eq 3 is presumably associated with a mechanism (eq 4) involving attack of water on protonated **2a** (**5**).[10]



$$\mathrm{H_2O} + \mathrm{R}\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{S}}-\mathrm{O}-\underset{\mathrm{OH}}{\overset{+}{\mathrm{S}}}\mathrm{R} \longrightarrow \mathrm{RSO_2H_2^+} + \mathrm{RSO_2H} \qquad (4)$$

5

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[1] This research was supported by the National Science Foundation, Grant GP-6952.

[2] (a) H. Bredereck, A. Wagner, H. Beck, and R. J. Klein, *Ber.*, **93**, 2736 (1960); (b) H. Bredereck, A. Wagner, E. H. Beck, H. Berlinger, and K.-G. Kottenhahn, *Angew. Chem.*, **70**, 268 (1958).

[3] (a) J. L. Kice and G. Guaraldi, *J. Am. Chem. Soc.*, **89**, 4113 (1967); (b) J. L. Kice and N. E. Pawlowski, *ibid.*, **86**, 4898 (1964).

[4] H. Rheinbolt, F. Mott, and E. Motzkus, *J. Prakt. Chem.*, [2] **134**, 257 (1932).

[5] *Anal.* Calcd for $\mathrm{C_8H_{18}O_3S_2}$: C, 42.45; H, 7.96. Found: C, 42.60; H, 7.64. The nmr spectrum ($\mathrm{CCl_4}$) showed a sharp singlet at τ 8.78; the ultraviolet spectrum (dioxane) showed $\lambda_{\max}$ 238 mμ (ϵ 2300); upon addition of water to the solution this $\lambda_{\max}$ gradually disappears due to hydrolysis of **2a** to **3a**.

[6] *Anal.* Calcd for $\mathrm{C_{10}H_{14}N_2O_2S}$: C, 53.07; H, 6.23. Found: C, 53.36; H, 5.97.

[7] The two sulfinyl sulfones **1b** and **1c**, previously unreported, were synthesized from the appropriate sulfinyl chloride and the sodium salt of the corresponding sulfinic acid by procedures analogous to those used for the synthesis of **1d**.[2,3,8]

[8] Satisfactory analyses were obtained for **1b** and **1c**. Their ultraviolet spectra (dioxane) have no clearly defined maximum above 220 mμ, only a broad shoulder extending from about 240–260 mμ (ϵ ~3000); on addition of water to the solution this absorption at 240–260 mμ disappears more or less rapidly due to hydrolysis of **1**. The nmr spectrum of **1b** consists of two sharp singlets, one at τ 7.15 and the other at τ 6.83.

[9] L. J. Bellamy in "Organic Sulfur Compounds," Vol. 1, N. Kharasch, Ed., Pergamon Press, Oxford, 1961, p 48. See also the spectrum of ethyl *p*-toluenesulfinate shown in ref 2a.

[10] If the $k_H(\mathrm{H^+})$ term were due to unimolecular dissociation of **5** (an A1 mechanism), $k_H{}^{\mathrm{D_2O}}/k_H{}^{\mathrm{H_2O}}$ would be much larger (1.9–2.6).[11]