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Note

Development of a successful gas chromatographic method of analyzing *o*-aminobenzenesulfonic acids via their sulfonyl chlorides

ADEL AMER, EARL G. ALLEY and CHARLES U. PITTMAN, Jr.*
University/Industry Chemical Research Center, Department of Chemistry, Mississippi State University, Mississippi State, MS 39762 (U.S.A.)
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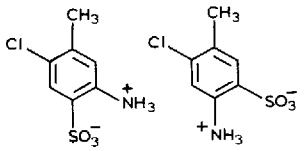
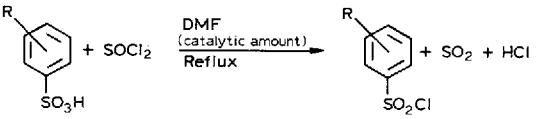
o-Aminobenzenesulfonic acids are very important pigment and dye intermediates[1]. Two commercially important examples include "C-amine" (I) and B-acid (II) used in the formulation of a variety of azo pigments. The commercial interest in such compounds is reflected in many investigations of their chromatographic behavior including separations by paper[2], thin-layer[3], gas–liquid (GLC)[4] and liquid[5–9] chromatography. Because of the exceptional selectivity, sensitivity and convenience of GLC its successful application to the analysis of derivatives such as I and II would constitute a valuable methodology. In particular, we have had a need for a second method [to complement high-performance liquid chromatographic (HPLC) methods] which could search for difficult to separate isomers and impurities that have common retention times in our HPLC separation studies.



I II

Early investigations by Kirkland[10] resulted in methods by which a variety of arylsulfonic acids and their salts could be analyzed by GLC via their sulfonyl chloride derivatives. In that work, arylsulfonic acids were reacted with thionyl chloride in the presence of catalytic amounts of N,N-dimethylformamide (DMF) to give smooth conversion to the corresponding sulfonyl chloride:



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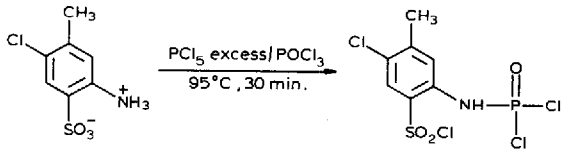
The sulfonyl chlorides were readily chromatographed using various silicone oil liquid phases on Chromosorb, Celite and firebrick supports. However, Kirkland[10] notes that unfortunately this method failed when the amino group was present as a substituent.

In 1973 Parsons[4] attempted to extend the thionyl chloride method to aminobenzenesulfonic acids without success. Only non-volatile products of unknown identity were obtained. However, he found that treating moist aminobenzenesulfonic acids with excess PCl_5–$POCl_3$ resulted in a dual derivatization reaction, giving compounds which were assigned structure III:



III

While direct mass spectrometric (MS) and nuclear magnetic resonance (NMR) spectral proof for structure III was not achieved, this structure was consistent with further derivatization chemistry employed. Furthermore, derivatives such as III were volatile enough to be amenable to GLC analyses. Thus, a complex mixture consisting of sulfanilic acid, 3-amino-*p*-toluenesulfonic acid and several aminochlorotoluenesulfonic acids and aminodichlorotoluenesulfonic acids was derivatized with PCl_5–$POCl_3$ at 95°C for 30 min and separated using packed column, GLC (OV-17 on diatomaceous earth, 170°C isothermal then increased at 10°C min^{-1} to 245°C). The use of reaction temperatures of 110°C or above led to complex product mixtures.

The purpose of this paper is to clarify the chemistry involved when aminobenzenesulfonic acids are reacted with $SOCl_2$–DMF. Further, we present a suitable means of converting aminobenzenesulfonic acids to the corresponding sulfonyl chlorides using PCl_5. This resulted in a suitable GLC method for analyzing aminobenzenesulfonic acids as their more volatile sulfonyl chlorides, thereby achieving what Kirkland[10] and Parsons[4] originally set out to do.

EXPERIMENTAL

Synthetic part

Pyridinium o-aminobenzenesulfonates. Aminobenzenesulfonic acid derivatives, such as I (9 mmole), were suspended in pyridine (5 ml). Each mixture was warmed to 60°C for 10 min with stirring and then left at room temperature for 1 h. The white precipitate was filtered, washed with diethyl ether and dried to yield the corresponding pyridinium salt in quantitative yield: pyridinium salt of I, m.p. > 300°C: ^1H NMR {[$^2H_6$]dimethylsulfoxide (DMSO-d_6)} δ 2.17 (s, 3H, CH_3), 6.53 (s, 2H, NH_2), 6.7, 7.5 (2s, 2H, ArH), 7.9–9.10 (m, 5H, pyrH); pyridinium salt of II, m.p. > 300°C: ^1H NMR (DMSO-d_6) δ 2.20 (s, 3H, CH_3), 7.02, 7.62 (2s, 2H, ArH), 7.77–9.23 (m, 7H, NH_2 and pyrH); pyridinium salt of V, m.p. >300°C; ^1H NMR (DMSO-d_6) δ 2.48 (s, 3H, CH_3), 6.33 (s, 2H, NH_2), 6.68,7.68 (2s, 2H, ArH), 7.78–9.12 (m, 5H, pyrH).

o-Aminobenzenesulfonyl chlorides VI–VIII

The pyridinium salts of the mixed *o*-aminobenzenesulfonic acids I, II and V (prepared as described above) (0.33 mmole of each) and phosphorus pentachloride (1.0 mmole) were mixed and heated, (external oil bath) at 95°C for 40 min, to give the corresponding sulfonyl chlorides VI, VII and VIII (eq. 4). The product mixture was analyzed by dilution with toluene and GLC analysis (see *Instrumentation*).

N,N-Dimethyl-N'-(3-methyl-4-chlorobenzene-6-sulfonic acid)formamidine (IV). A suspension of I (0.0135 mole) in $SOCl_2$ (3 ml, 0.041 mole) and DMF (1.5 ml, 0.019 mole) was stirred at room temperature for 1 h and then heated at 50°C for 1 h. The mixture was then cooled and diluted with cold water (20 ml). A precipitate was filtered, washed with water and dried. HPLC analysis (see *Instrumentation*) showed that only the title compound was formed. It was recrystallized from distilled water to give colorless needles of IV; yield = 70% (0.0095 moles); m.p. = 302–305° (decomp.); ^{1}H NMR (DMSO-d_6) δ 2.38 (s, 3H, CH_3-Ar), 3.20, 3.43 (2s, 6H, $N(CH_3)_2$), 7.67, 7.73 (2s, 2H, ArH), 9.00 (bs, 2H, N = CH and the acidic proton). $C_{10}H_{13}ClN_2O_3S$ requires: C = 43.40, H = 4.73, N = 10.13, S = 11.59, Cl = 12.81. Found: C = 43.42, H = 4.68, N = 10.11, S = 11.73, Cl = 12.82.

Instrumentation

o-Aminosulfonyl chlorides were detected on a Perkin-Elmer Sigma 2 gas chromatograph equipped with flame ionization detector, using a 30 m × 0.25 mm I.D. fused-quartz capillary column with a bonded DB-5 stationary phase. The temperature was held at 100°C for 1 min and then programmed at 10°C min^{-1} to 275°C. The injector temperature was 275°C. Helium was used as carrier gas. Formamidine IV was detected on a Series 3 Perkin-Elmer HPLC instrument with a Perkin-Elmer LC-75 spectrophotometric detector using an analyzing wavelength of 245 nm. The chromatogram was obtained using a Supelcosil LC-18 reversed-phase column, 250 mm × 4.6 mm I.D. and a phosphate buffered methanol–tetrabutylammonium hydroxide mobile phase (pH 7.3) pumped at a flow-rate of 1.5 ml min^{-1} and pressure of 2050 p.s.i. The mobile phase was prepared by mixing equivalent volumes of the phases A and B described in ref. 5. ^{1}H NMR spectra (in DMSO-d_6) were recorded on a Varian EM-360A spectrometer with tetramethylsilane as the standard. Chemical shifts are given on the δ scale. Mass spectra were recorded at 70 ev with a Finnagin 4500 GC–MS instrument. Melting points were determined with Melt-Temp melting point apparatus and are uncorrected.

RESULTS AND DISCUSSION

It has long been known that DMF catalyzes the reaction of sulfonic acids with thionyl chloride and prevents the formation of sulfonic anhydrides[11–13]. Upon treating 2-amino-4-methyl-5-chlorobenzenesulfonic acid (I) with excess thionyl chloride in the presence of excess DMF at 50°C we, like Parsons[4] and Kirkland[10], were unable to synthesize the desired 2-amino-4-methyl-5-chlorobenzenesulfonyl chloride. Instead, a more polar compound (Fig. 1) with a m.p. of 302–305°C was isolated by recrystallization from distilled water. A combination of IR and ^{1}HNMR spectroscopy and MS and elemental analyses confirmed the structure was that of N,N-dimethyl-N'-(3-methyl-4-chlorobenzene-6-sulfonic acid)formamidine, IV:

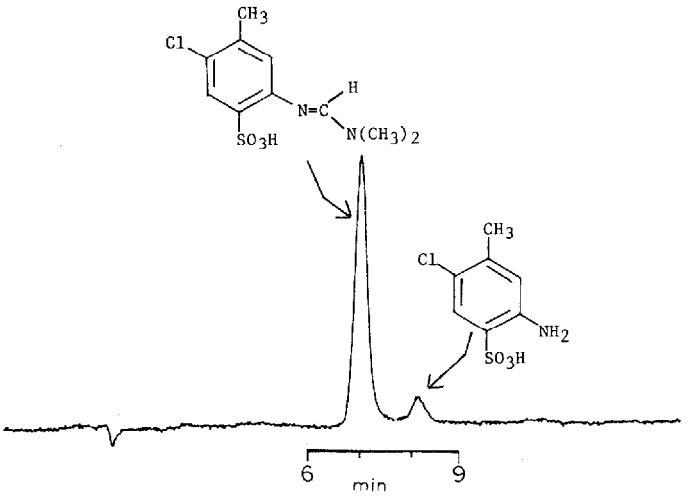
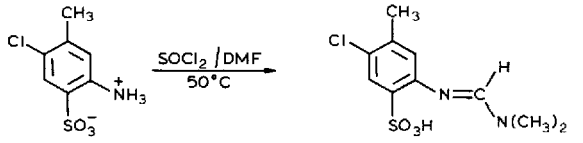


Fig. 1. HPLC chromatogram of the reaction mixture of I with DMF–SO_2Cl.

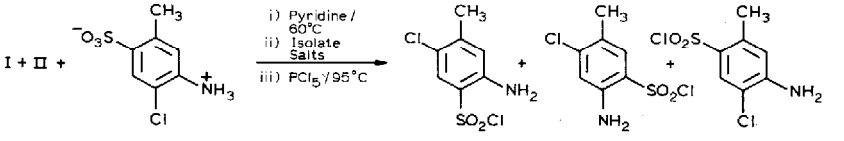


IV

Thus, DMF participates in this deep-seated reaction to give a formamidine group at the original amino group.

The IR spectrum (KBr) of IV exhibits an intense band at 1710 cm^{-1} (–CH=N stretching). The two magnetically non-equivalent formamidine methyl groups resonate at δ 3.17 and 3.40 ppm in the ^{1}HNMR spectrum and the 3-methyl group occurs as a singlet at δ 2.37. The –CH=N and –SO_3H protons appear as a broad signal (area = 2H) at δ 9.0 ppm and one of these exchanges with deuterium oxide, as is expected. The mass spectrum (70 eV) gives a large peak at m/z 276 attributed to $M^{+\cdot}$. The formation of IV explains the inability of Parsons[4] and Kirkland[10] to develop suitable GLC methods using thionyl chloride derivatizations of aminobenzenesulfonic acids.

The successful conversion of aminobenzenesulfonic acids to their corresponding sulfonyl chlorides was then carried out by first preparing the corresponding pyridinium salts and then reacting these salts with PCl_5:



V VI VII VIII

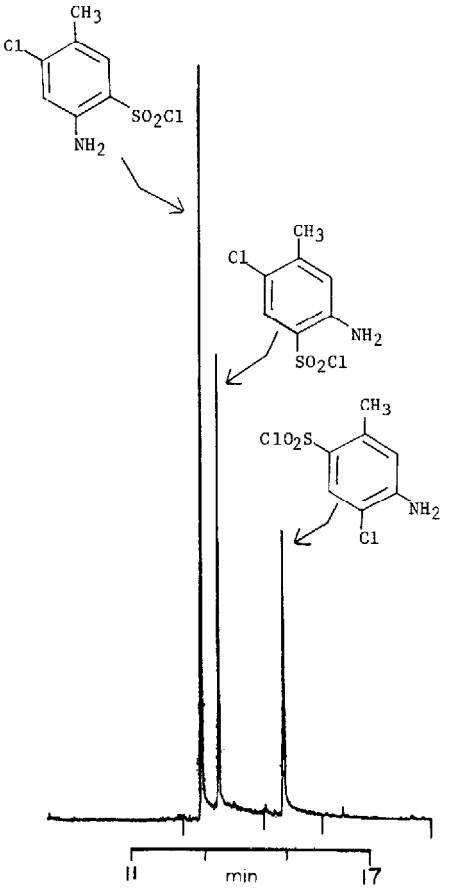


Fig. 2. Typical capillary gas chromatograms obtained according to the described method.

This method led to a successful capillary column method to analyze mixtures of aminobenzenesulfonic acids because the sulfonyl chlorides were suitably volitile and did not hydrolyze during GLC analyses. For example, a mixture of I, II and V could be converted quantitatively to their pyridinium salts by heating in excess pyridine at 60°C. The pyridinium salt mixture from sulfonic acids I, II and V was then reacted with PCl_5 at 95°C to give complete conversion to corresponding sulfonyl

TABLE I

MASS SPECTRAL DATA OF COMPOUNDS VI, VII AND VIII

Compound	*Relative intensity*						
	m/z 239	*m/z 156*	*m/z 140*	*m/z 114*	*m/z 104*	*m/z 99*	*m/z 77*
VI	65.49	38.23	100.00	30.27	18.23	5.66	58.76
VII	35.96	41.26	100.00	3.80	31.13	2.10	73.84
VIII	28.52	63.97	100.00	–	44.32	–	97.88

chlorides VI–VIII. The sulfonyl chlorides were readily chromatographed using a 30-m capillary column with a DB-5 stationary phase programmed from 100 to 275°C (Fig. 2).

The sulfonyl chlorides VI, VII and VIII were also individually prepared from their parent aminobenzenesulfonic acids I, II and V, respectively, using this method. Furthermore, their structures were confirmed by MS. Each isomer showed molecular ion peaks at m/z 239 and base peaks at m/z 140 due to the loss of SO_2Cl fragments. The isomers VI, VII and VIII are easily distinguished by comparing the relative intensities of the peaks at m/z 239, 156, 140, 114, 104, 99 and 77 (Table I). Thus, the pyridinium salt/phosphorus pentachloride method is useful for GC–MS analysis of aminobenzenesulfonic acid derivative mixtures.

The success in using the pyridinium salts as precursors to the aminobenzenesulfonyl chlorides is due to two factors. First, pyridine is released during the reaction with PCl_5. It probably complexes with PCl_5 (or $POCl_3$), thereby lowering the tendency of these derivatives to react with the arylamine group to give derivaties similar to III. Neither III nor its isomers were detected by GLC or GC–MS analyses in this work. Secondly, by avoiding the use of DMF, the problem of formamidine formation is eliminated. Finally, it should be noted that the sulfonyl chloride, VI, was not obtained when the pyridinium salt of I was simply heated with thionyl chloride, in the absence of DMF.

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