Journal of Chromatography, 473 (1989) 276–280
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 21 487

Note

Gas chromatographic analysis of sulphonic acids as their sulphonamide derivatives

HIROYUKI KATAOKA, TSUNEKI OKAZAKI and MASAMI MAKITA*
Faculty of Pharmaceutical Sciences, Okayama University, Tsushima, Okayama 700 (Japan)
(First received October 7th, 1988; revised manuscript received March 6th, 1989)

The analysis of aliphatic and aromatic sulphonic acids by gas chromatography (GC) has been carried out after their conversion into the volatile derivatives by desulphonation with acids[1–3], alkali fusion[4–6], sulphonyl chlorination[7–9] or fluorination[10], sulphonyl esterification[7,11–15], trimethylsilylation[16], and reduction to the thiol[17,18]. However, the usefulness of these methods may be limited by the time-consuming derivatization process. Further, the sulphonyl halides and the esters of sulphonic acids are generally unstable and are apt to undergo thermal decomposition during the GC analysis.

It appeared to us that dibutylamide derivatives of sulphonic acids would be potentially useful for GC, especially as we had already succeeded in the GC analysis of taurine (2-aminoethanesulphonic acid) as its N-acyldibutylamide derivatives[19,20]. The sulphonic acid function of N-acyltaurine was converted into the corresponding dibutylamide derivative in nearly quantitative yield by a convenient procedure involving ion-pair extraction, followed by chlorination and amidation. We have therefore studied the GC analysis of a variety of sulphonic acid compounds as their dibutylamide derivatives and report the results in this paper.

EXPERIMENTAL

Reagents

Methane-(C_1) and 2,4,6-trimethylbenzenesulphonic acids as the free acids and 1-propane-(C_3), 1-pentane-(C_5), 1-heptane-(C_7), 1-nonane-(C_9), 1-tridecane-(C_{13}), 1-octadecane-(C_{18}), benzene-, *p*-toluene-, 2,4-dimethylbenzene- and α-naphthalenesulphonic acids as the sodium salts were purchased from Tokyo Kasei Kogyo (Tokyo, Japan). C_1–C_9 and aromatic sulphonic acids were dissolved in water and C_{13} and C_{18} sulphonic acids were dissolved in 30% ethanol. These standard solutions were prepared so as to contain 0.1 mg/ml of each acid. Anthracene (Nakarai Chemicals, Kyoto, Japan) was dissolved in methylene chloride at a concentration of 0.05 mg/ml and used as an internal standard (I.S.). Tetraalkylammonium salts were purchased from Nakarai Chemicals and used as 10% methanolic solutions. Tetraalkylammonium hydroxide solutions were prepared from their salts with silver oxide as described earlier[19]. Thionyl chloride (Nakarai Chemicals) was used after distillation. Dibutylamine (DBA) (Nakarai Chemicals) was used as a 2 *M* solution in acetonitrile. All other chemicals were of analytical-reagent grade.

0021-9673/89/$03.50

Gas chromatography

GC analysis was performed using a Shimadzu Type 4CM-PF gas chromatograph equipped with a 1.5 m × 3 mm I.D. glass column packed with 1.0% silicon SE-54 on Uniport HP (100–120 mesh) and with flame ionization detection (FID). The packed column was conditioned at 290°C for 24 h with nitrogen at a flow-rate of 30 ml/min. The operating conditions are given in the caption of Fig. 3. Peak heights for sulphonic acids and the I.S. were measured and the peak-height ratios were calculated for the construction of a calibration graph.

Gas chromatography–mass spectrometry

A Shimadzu-LKB 9000 gas chromatograph–mass spectrometer with the same type of column as used for GC–FID was employed under the following conditions: trap current, 60 μA; ionizing voltage, 70 eV; accelerating voltage, 3.5 kV; ion-source temperature, 250°C; separation temperature, 240°C; and helium flow-rate, 40 ml/min.

Analytical derivatization procedure

An aliquot of the sample solution (containing 2–50 μg of each sulphonic acid) was pipetted into a 10-ml Pyrex glass tube with a PTFE-lined screw-cap. After the total reaction volume had been made up to 1 ml with distilled water, 0.05 ml of 10% tetrahexylammonium chloride[a] or tetrabutylammonium bromide[a] and 2 ml of methylene chloride were added and the tube was shaken with a shaker set at 300 rpm (up and down) for 3 min at room temperature. After centrifugation for 1 min, the organic layer was transferred to another tube and the solvent was evaporated to dryness under a stream of nitrogen. To the residue was added 0.2 ml of thionylchloride, and the tube was tightly capped and heated at 80°C for 10 min. The excess of thionyl chloride was removed at 50°C under a stream of nitrogen. To the residue was added 0.2 ml of 2 *M* DBA solution, and the mixture was incubated at 80°C for 5 min after tightly capping. The reaction mixture was acidified with 1 ml of 20% orthophosphoric acid and then extracted twice with 3 ml of diethyl ether. To the ether extracts was added 0.4 ml of anthracene (I.S.) solution and the solvent was evaporated to dryness at 50°C. After the residue had been dissolved in 0.2 ml of ethyl acetate, the solvent was

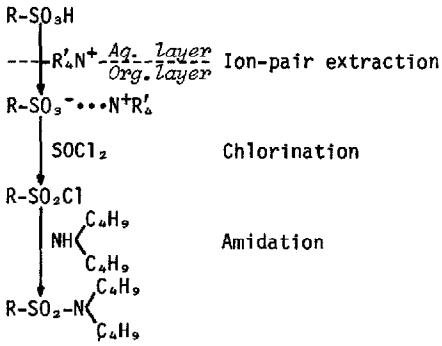

Fig. 1. Derivatization of sulphonic acids. R, R′ = alkyl or aryl.

[a] Tetrahexylammonium chloride and tetrabutylammonium bromide were used for the hydrophilic sulphonic acids (C_1–C_9) and the lipophilic sulphonic acids (C_{13}, C_{18} and aromatic), respectively.

dried over anhydrous sodium sulphate and 2 μl of this solution were injected into the GC–FID system. The derivatization process is summarized in Fig. 1.

RESULTS AND DISCUSSION

In the first step of the derivatization, sulphonic acids are extracted from the aqueous phase into methylene chloride by an ion-pair extraction technique[21] using tetraalkylammonium as counter ion. The influence of the nature of the counter ion on this extraction was investigated. Table I shows that tetrahexylammonium and tetrabutylammonium are the most satisfactory counter ions for the hydrophilic sulphonic acids (C_1–C_9 aliphatic) and the lipophilic sulphonic acids (higher aliphatic and aromatic), respectively, although the optimum counter ion varies with the class and type of sulphonic acid. On the other hand, it was found that the Cl^- and Br^- forms of the tetraalkylammonium salts were as effective here as the OH^- form, whereas the I^- and ClO_4^- forms were not useful. Chlorination of the sulphonic acid function with thionyl chloride was accomplished within 10 min at 80°C. The reaction of sulphonyl chlorides with DBA proceeded rapidly at 80°C and gave the corresponding sulphonamide derivatives. The total derivatization process could be performed within 30 min.

The structures of the derivatives were confirmed by GC–MS. The mass spectrum of the dibutylamide derivative of *p*-toluenesulphonic acid is shown in Fig. 2. The molecular ion peak (M^+) with the postulated *m/z* 283 and the prominent fragment ion peaks, *m/z* 240 ($M^+ - C_3H_7$), 155 [$M^+ - N(C_4H_9)_2$] and 91 [$M^+ - SO_2N(C_4H_9)_2$] were observed and were useful for structure elucidation.

The derivatives were found to be very stable under normal laboratory conditions and no thermal decomposition was observed during the GC analysis. Typical chromatograms are shown in Fig. 3.

In order to test the linearity of the calibration graph, various amounts of sulphonic acids ranging from 2 to 50 μg were derivatized in a mixture and aliquots representing 40–1000 ng of the acids were injected into the GC system. In each in-

TABLE I

INFLUENCE OF THE NATURE OF THE ALKYLAMMONIUM AS COUNTER ION ON THE ION-PAIR EXTRACTION OF ALIPHATIC AND AROMATIC SULPHONIC ACIDS

Alkylammonium hydroxide	*Peak-height ratio[a] for sulphonic acids[b]*											
	C_1	C_3	C_5	C_7	C_9	C_{13}	C_{18}	*B*	*T*	*X*	*M*	*N*
Tetraethylammonium	0	0	0	0.030	0.217	0.990	0.720	0.020	0.019	0.019	0.022	0.039
Tetrapropylammonium	0	0	0.014	0.275	0.841	0.985	0.720	0.057	0.150	0.253	0.388	0.441
Tetrabutylammonium	0.017	0.083	0.587	0.828	0.957	0.954	0.682	0.909	1.068	0.991	0.882	0.700
Tetrapentylammonium	0.387	0.618	0.904	0.946	1.030	0.953	0.682	1.048	1.123	1.021	0.921	0.663
Tetrahexylammonium	0.850	0.935	1.056	0.963	0.981	0.832	0.595	0.530	0.679	0.586	0.697	0.366
Tetraheptylammonium	0.932	0.978	0.973	0.663	0.490	0.624	0.446	0.332	0.314	0.218	0.331	0.129
Tetraoctylammonium	0.780	0.650	0.656	0.417	0.281	0.352	0.321	0.308	0.304	0.221	0.328	0.113

[a] Peak-height ratios are given relative to the internal standard (anthracene).

[b] C_1–C_{18} = aliphatic; B = benzene-; T = toluene-; X = 2,4-dimethylbenzene-; M = 2,4,6-trimethylbenzene-; N = α-naphthalenesulphonic acids.

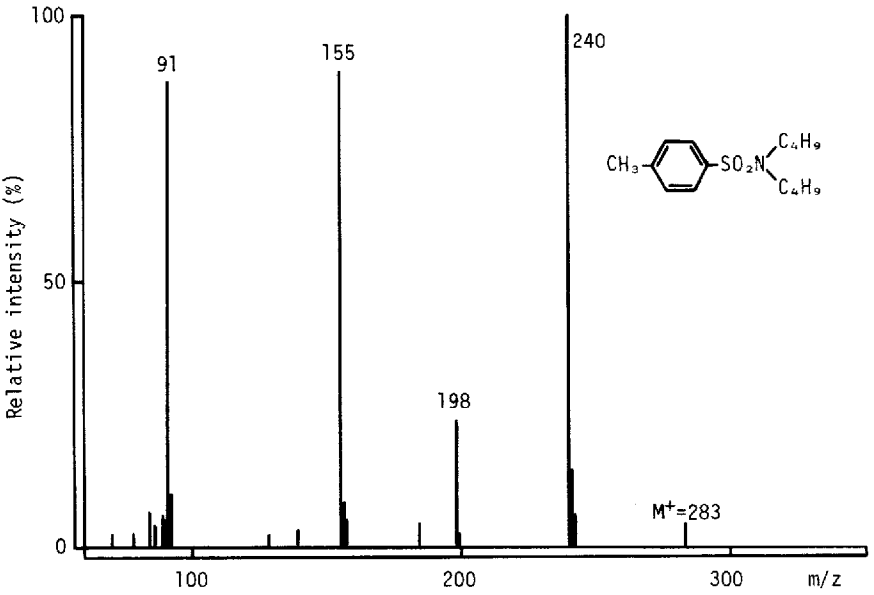

Fig. 2. Mass spectrum of dibutylamide derivative of *p*-toluenesulphonic acid.

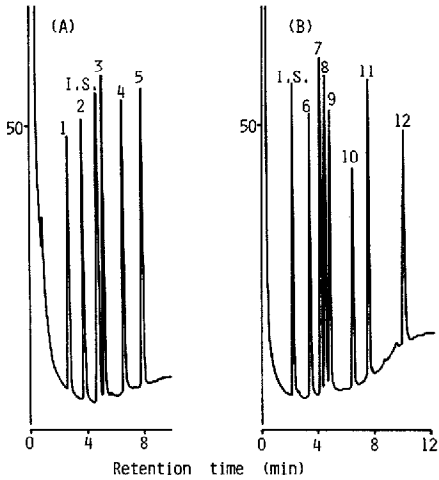

Fig. 3. Gas chromatography of mixtures of sulphonic acids as the corresponding dibutylamide derivatives. GC conditions: column, 1.0% silicone SE-54 on Uniport HP (100–120 mesh), 1.5 m × 3 mm I.D., glass; column temperature, (A) programmed at 15°C/min from 100 to 250°C and (B) programmed at 15°C/min from 140 to 285°C; injection and detector temperatures, 290°C; nitrogen flow-rate, 45 ml/min. Peaks: 1 = methane-; 2 = 1-propane-; 3 = 1-pentane-; 4 = 1-heptane-; 5 = 1-nonane-; 6 = benzene-; 7 = *p*-toluene-; 8 = 2,4-dimethylbenzene-; 9 = 2,4,6-trimethylbenzene-; 10 = α-naphthalene-; 11 = 1-tridecane; 12 = 1-octadecanesulphonic acid; I.S. = anthracene. Each peak represents 400 ng of the acid.

TABLE II

LINEAR REGRESSION DATA FOR SOME SULPHONIC ACIDS

Sulphonic acid	*No. of data*	*Regression line*[a]	*Correlation coefficient (r)*
C_1	15	$y = 43.09x - 6.95$	0.9963
C_7	15	$y = 48.30x - 3.90$	0.9977
C_{13}	15	$y = 46.93x + 5.47$	0.9995
p-Toluene-	15	$y = 53.80x - 5.85$	0.9996
α-Naphthalene-	15	$y = 34.63x - 6.17$	0.9973

[a] y = Peak-height ratio; x = amount of each sulphonic acid.

stance, a linear relationship was obtained and the reproducibility was found to be satisfactory (Table II).

These experiments have conclusively demonstrated that aliphatic and aromatic sulphonic acids can be succesfully analysed at the microgram level by GC of their sulphonamide derivatives.

REFERENCES

1 J. D. Knight and R. House, *J. Am. Oil Chem. Soc.*, 36 (1959) 195.
2 E. A. Setzkorm and A. B. Carel, *J. Am. Oil Chem. Soc.*, 40 (1963) 57.
3 S. Nishi, *Bunseki Kagaku*, 14 (1965) 912.
4 S. Nishi, *Bunseki Kagaku*, 14 (1965) 917.
5 T. Nakagawa, K. Miyajima and T. Uno, *J. Gas Chromatogr.*, 6 (1968) 292.
6 S. Siggia, L. R. Whitlock and J. C. Tao, *Anal. Chem.*, 41 (1969) 1387.
7 J. J. Kirkland, *Anal. Chem.*, 32 (1960) 1388.
8 J. B. Himes and I. J. Dowbak, *J. Gas Chromatogr.*, 3 (1965) 194.
9 J. S. Parson, *J. Chromatogr. Sci.*, 11 (1973) 659.
10 J. S. Parson, *J. Gas Chromatogr.*, 5 (1967) 254.
11 W. Funasaka, T. Kojima and T. Toyota, *Bunseki Kagaku*, 14 (1965) 815.
12 A. Heywood, A. Mathias and E. Williams, *Anal. Chem.*, 42 (1970) 1272.
13 K. M. Baker and G. E. Boyce, *J. Chromatogr.*, 117 (1976) 471.
14 A. El Homsi, B. Gilot and J. P. Canselier, *J. Chromatogr.*, 151 (1978) 413.
15 A. M. Nardillo, R. C. Castells, E. L. Arancibia and M. L. Caslla, *Chromatographia*, 25 (1988) 618.
16 J. Eagles, *Anal. Chem.*, 43 (1971) 1697.
17 T. Ishii, K. Yamane, H. Kato and K. Kunishiro, *Yukagaku*, 24 (1975) 23.
18 H. Oka and T. Kojima, *Bunseki Kagaku*, 28 (1979) 410.
19 H. Kataoka, S. Yamamoto and M. Makita, *J. Chromatogr.*, 306 (1984) 61.
20 H. Kataoka, N. Ohnishi and M. Makita, *J. Chromatogr.*, 339 (1985) 370.
21 E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis*, Verlag Chemie, Weinheim, 1982.