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Note

Gas chromatographic method for the determination of 2-amino-1,3-propanediol (Serinol)

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2-Amino-1,3-propanediol (Serinol) is an intermediate employed in the synthesis of Iopamidol, a non-ionic, water-soluble iodinated contrast medium[1]. As in radiology it might be employed as an angiographic contrast medium in highly concentrated aqueous solution (*ca.* 80%), the purity of the raw material used becomes an extremely important factor for the maintenance of possible impurities at low levels. As the presence of impurities in the final product depends mostly on the purity of the intermediates, for Serinol we required a suitable analytical system that would operate selectively and with sufficient precision with either aqueous solutions or the substance as such.

There is little published information on Serinol, and only two paper chromatographic methods[2,3] and one direct chromatographic method[4], mainly qualitative, have appeared. We therefore developed a method for the determination of Serinol through its N,O-acylation with trifluoroacetic anhydride (TFAA) and subsequent gas chromatography (GC). The derivatization reaction with TFAA was adopted as the first choice for an amino alcohol[5,6].

EXPERIMENTAL

Materials

Unless otherwise stated, all reagents were analytical-reagent grade products from E. Merck (Darmstadt, G.F.R.).

The sample of Serinol was prepared as described in the literature[7]. The product obtained was then purified several times as its oxalate: acidimetric assay, 99.5%; thin-layer chromatography, single spot at $R_F = 0.55$ in the solvent system water–dioxane–25% ammonia (6:3:0.5) and detection with chlorine vapour + 1% *o*-toluidine (Fertigplatten DC-Si 60 F_{254}).

A 20% (w/v) solution of triacetin in chloroform was used as an internal standard.

Instruments and operating conditions

Gas chromatography. GC analyses were carried out on a Carlo Erba Model FV 2350 gas chromatograph equipped with a flame-ionization detector. The glass column (2 m × 3 mm I.D.) was packed with 5% OV-225 on Chromosorb W HP

(80–100 mesh) (Carlo Erba). The packed column was conditioned for 24 h at 200° (nitrogen flow-rate 20 ml/min). The injector and detector temperatures were 250°, the column temperature 150° and the carrier gas (nitrogen) flow-rate 30 ml/min.

Gas chromatography–mass spectrometry (GC–MS). A Perkin-Elmer Model 270 mass spectrometer operating at 70 eV (emission 80 μA) was used. The glass chromatographic column (2 m × 3 mm I.D.) was packed with 5% OV-225 on Chromosorb W HP (80–100 mesh) and operated at 150° with a helium flow-rate of 30 ml/min.

Infrared (IR) spectroscopy. A Perkin-Elmer Model 257 spectrophotometer was used. The IR spectrum of the trifluoroacetyl derivative of Serinol was taken from a thin film between two sodium chloride plates.

Nuclear magnetic resonance (NMR) spectroscopy. A Varian EM 390 spectrometer operating for protons at 90 MHz was used. The spectrum of the trifluoroacetyl derivative was taken in an approximately 30% solution of $CDCl_3$.

Derivatization procedure

(a) Aqueous solutions of Serinol. Six aqueous solutions of Serinol were prepared at concentrations from 1.5 to 15%. Aliquots of 100 μl of these solutions (16.5–165 μmoles) were placed in 10-ml glass-stoppered conical centrifuge tubes and treated carefully with 2 ml of TFAA (14.3 mmoles), cooling the tubes in an ice–water bath. The reaction mixture was allowed to stand for 20 min at room temperature and 100 μl of a chloroform solution of the internal standard were added to each tube.

(b) Pure Serinol. Serinol (15–20 mg; 165–220 μmoles) was weighed into a glass-stoppered conical centrifuge tube and dissolved at 40° in 200 μl of TFAA (1400 μmoles). The reaction mixture was allowed to stand for 20 min at room temperature and then 100 μl of the chloroform solution of the internal standard were added.

Gas chromatographic analysis

An amount of 1 μl of the solutions from the derivatization reaction was injected into the gas chromatograph. For Serinol samples from aqueous solutions (procedure a) the sensitivity used was $1.28 \cdot 10^{-9}$ A, while for Serinol as such (procedure b) it was $1.28 \cdot 10^{-8}$. In both instances, the internal standard and the derivative were eluted with retention times of 14.8 and 18.6 min, respectively (Fig. 1).

Preparation and characterization of the derivative

A 1-g amount of Serinol (0.011 moles) was treated with 10 ml of TFAA (0.071 mole) and heated at 40° for 2 h. After evaporation of the excess of TFAA in a rotating flask under vacuum, the oily residue was distilled (b.p. 125°/3 mm); $n_D^{20} = 1.3693$; $d_{20} = 1.6175$. The product obtained was characterized by IR and NMR spectroscopy, and GC–MS, with the following results.

In IR spectroscopy (liquid film), the main bands were at 3320 and 3100 (νNH. amide) 2975, 2905, 1795 (νC=O, ester), 1712 (νC=O, amide I), 1550 (δNH + νCN amide II), 1466, 1400, 1350 (νCN + δNH amide III), 1125 and 1160 (νC–O–ester). 772, 730 and 720 cm^{-1}.

In NMR spectroscopy there was a multiplet at δ4.60 (5H, $2CH_2$ + 1CH) and broad doublet at δ6.93 (NH) ppm.

GC revealed only one peak with a retention time of 18.6 min, as cited in the

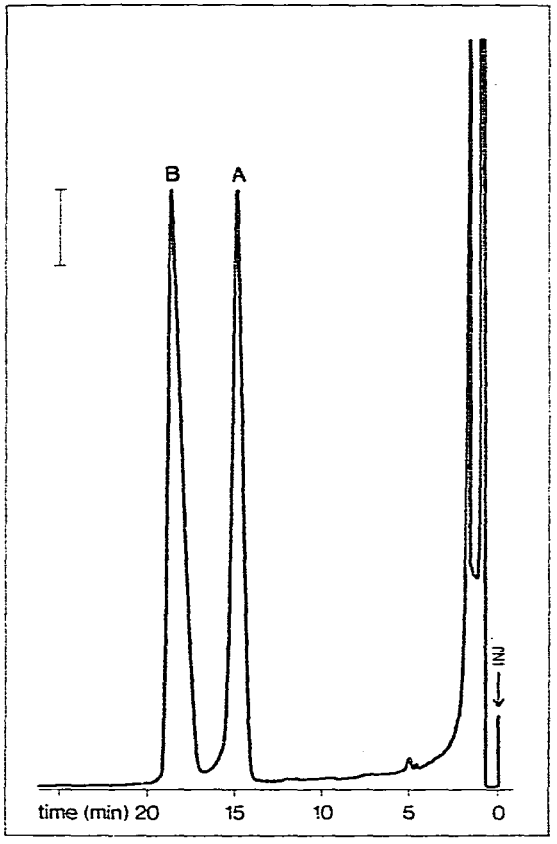

Fig. 1. Gas chromatogram of a sample containing 19.950 mg of Serinol after derivatization with TFAA and procedure b. (A) internal standard; (B) Serinol derivative.

previous section. This peak, analyzed in conjunction with a mass spectrometer, showed, in addition to a molecular ion at $m/e = 379$, a fragmentation typical of a N,O-trifluoroacetyl derivative (Fig. 2).

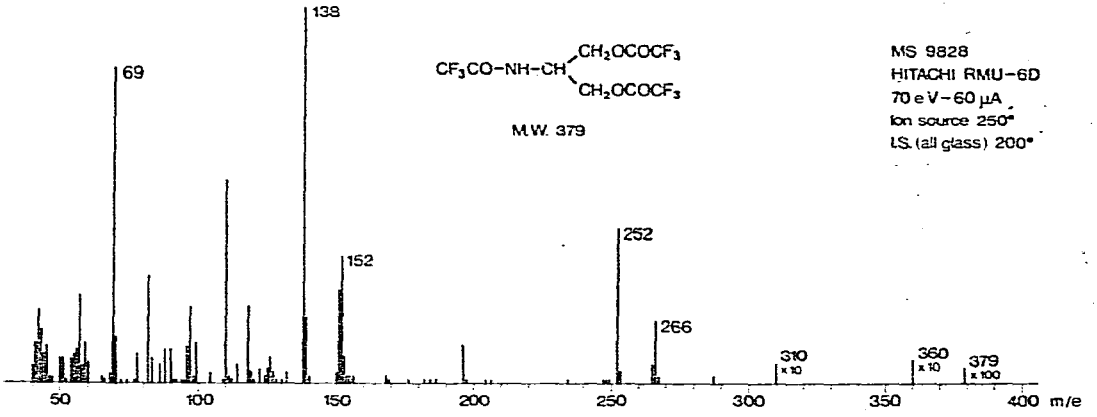

Fig. 2. Mass spectrum of the N,O-trifluoroacetyl derivative of Serinol.

TABLE I

RESULTS FOR DETERMINATION OF SERINOL IN AQUEOUS SOLUTION

Serinol taken (g per 100 ml)	*Serinol peak height (scale divisions)*	*Internal standard peak height (scale divisions)*	*Peak-height ratio*	*Serinol found*	
				g per 100 ml	*%*
1.52	7.3	75.0	0.097	1.54	+1.3
3.11	15.3	74.5	0.205	3.09	−0.6
6.06	30.1	74.0	0.407	5.98	−1.3
8.98	46.1	74.0	0.623	9.08	+1.1
12.04	62.6	75.5	0.829	12.03	−0.1
15.15	76.8	73.5	1.045	15.13	−0.1

RESULTS

The analytical results obtained after derivatization of the aqueous solutions of Serinol are reported in Table I.

The efficiency of the method was shown by the regression line analysis[8], $y = a + bx$, where y represents Serinol concentration (g per 100 ml) and x the peak-height ratio of Serinol to internal standard. The following values were found:

$$y = 14.328x + 0.154 \text{ and } s_{xy} = 0.054,\ s_b = \pm 0.0663$$
$$s_a = \pm 0.0418,\ r = 0.99994.$$

One of the samples analysed (15.15% solution) by CG–MS gave only one peak with an MS profile like that reported in Fig. 2. To evaluate the precision of analytical procedure b, ten replicate analyses were carried out and the results are reported in Table II. The results show that the precision of the method was within ±0.6%.

TABLE II

PRECISION OF ANALYTICAL PROCEDURE b

Serinol taken (mg)	*Serinol peak height (scale division)*	*Internal standard peak height (scale divisions)*	*Peak height ratio*	*Serinol found (mg)*	*Δ (%)*
19.340	78.7	80.4	0.9789	19.361	0.11
19.373	79.2	81.3	0.9742	19.268	−0.54
20.243	83.4	82.0	1.0171	20.116	−0.63
17.788	77.8	85.5	0.9099	17.996	1.17
15.264	63.4	82.2	0.7713	15.255	0.06
20.520	88.8	86.4	1.0278	20.328	−0.93
17.924	70.0	76.8	0.9115	18.028	0.58
15.689	64.0	80.4	0.7960	15.743	0.34
19.963	81.7	81.9	0.9976	19.731	−1.16
19.550	79.0	79.0	1.0000	19.778	0.93

CONCLUSIONS

By the derivatization reaction with TFAA, a method has been developed for the determination of Serinol both in aqueous solution and as the pure substance. The method is easy to carry out and sufficiently precise and selective. Structural analysis of the derivative formed from Serinol showed that it is the N,O-trifluoroacetyl derivative.

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