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Note

Liquid chromatographic separation of four stereoisomers of cyclothiazide

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It has previously been reported that cyclothiazide, a diuretic drug, can be separated by thin-layer chromatography into two or three spots[1]. The separation of three components by high-performance liquid chromatography has also been reported[2,3]. However, none of these methods completely resolved the components. UV analysis of the peaks using a laser diode array detector showed the same maxima and

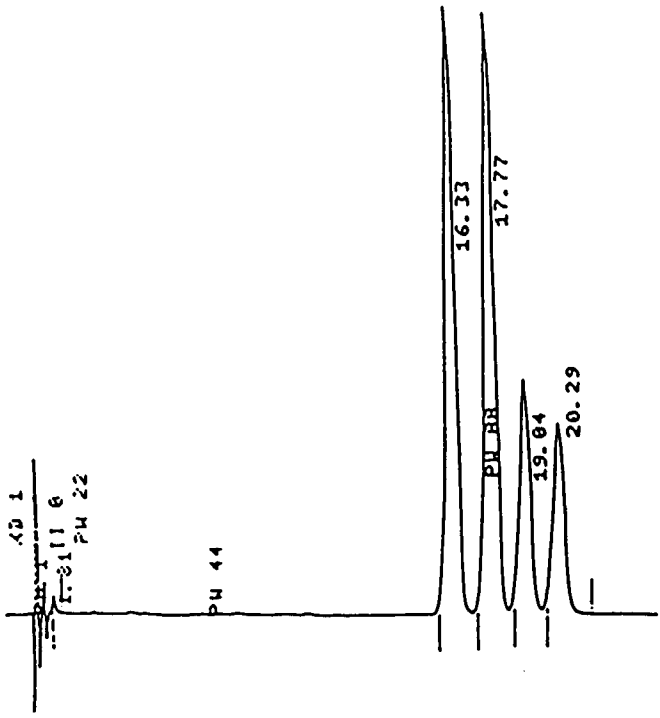

Fig. 1. Chromatogram of cyclothiazide. A 25-μl injection of a 0.5 mg/ml solution on a Waters 150 × 4.6 mm Nova-Pak column eluted at 1.0 ml/min with acetonitrile–tetrahydrofuràn–water–acetic acid (18:10:71.7:0.3) and with UV detection at 271 nm.

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zene-1,3-disulfonamide with 5-norbornene-2-carboxaldehyde[4]. This latter compound may exist as two geometric isomers. A sample obtained from Aldrich was found to contain two components, 3:1 by area, using gas chromatography on a 6 ft. × 1/4 in. glass column packed with 10% Carbowax 20M on 80–100 mesh Supelcoport and operated at 140°C (see Fig. 2). A sample obtained by acid hydrolysis of cyclothiazide USP gave similar results.

Therefore if the synthesis produces the endo and exo products in a 1:1 ratio, the theoretical distribution of the four isomers of cyclothiazide would be expected to be 37.5:37.5:12.5:12.5, in reasonable agreement with that found experimentally.

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