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Note

Influence of ethylene glycol on diminishing decomposition of carbamazepine following methylation with trimethylanilinium hydroxide

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Carbamazepine (Tegretol, Geigy, Ardsley, N.Y., U.S.A.) has been shown to be extremely effective in the treatment of convulsive disorders and trigeminal neuralgia. Carbamazepine is most often determined by gas–liquid chromatographic (GLC) methods[1–5]. The determination of carbamazepine by GLC is complicated by thermal decomposition giving multiple peaks during chromatography. Various derivatization techniques have been reported but none of these has been generally accepted. Permethylation by trimethylanilinium hydroxide (TMAH) is a well established method for the derivatization of anticonvulsants prior to GLC. When phenobarbital and carbamazepine are derivatized by this reagent both undergo decomposition giving rise to major breakdown products. Very recently Kelly[6] reported that the addition of certain polyhydric alcohols (ethylene glycol, 1,2-propanediol and glycerol) to TMAH suppressed to a significant degree the decomposition of phenobarbital giving a single peak. No mention was made of the effect of these solvents in suppressing the decomposition of carbamazepine. Prior to the publication of the paper by Kelly we had found that the addition of 1% ethylene glycol to TMAH was instrumental in suppressing the decomposition of phenobarbital and also carbamazepine.

EXPERIMENTAL

GLC was carried out on a Perkin-Elmer 3920 instrument equipped with a flame ionization detector and employing a glass column, 6 ft. × 2 mm I.D. packed with 3% OV-17 on Chromosorb W HP (Perkin-Elmer, Norwalk, Conn., U.S.A.). Operating temperatures were: oven, 240°; injection port, 280°; detector, 280°. Nitrogen was employed as the carrier gas at a flow-rate of 30 ml/min.

RESULTS AND DISCUSSIONS

Fig. 1 shows the chromatograms obtained before and after the addition of the ethylene glycol. We add the ethylene glycol directly to the TMAH when received and have not noticed any loss in the efficiency of this combination. This reagent combination now serves as a basis for a gas chromatography–mass spectrometry

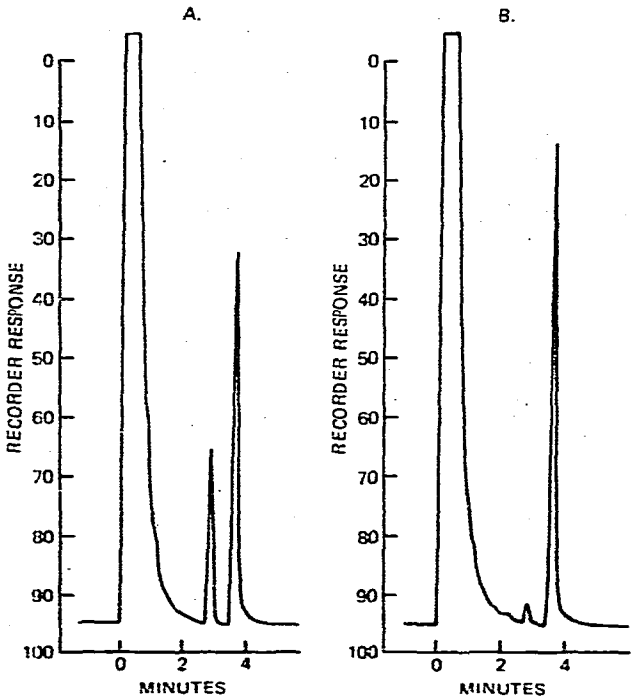

Fig. 1. Gas chromatograms obtained before (A) and after (B) the addition of ethylene glycol to TMAH.

method for the simultaneous determination of phenobarbital, carbamazepine, primidone and dilantin with 5-(*p*-methylphenyl)-5-phenylhydantoin (MPPH) used as the internal standard. Details of this method can be obtained upon request. The role of these alcohols in suppressing the decomposition of phenobarbital and carbamazepine is not clear; nevertheless, we consider that this observation will be of considerable value to those laboratories interested in determining anticonvulsants by gas chromatography.

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