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Gas Chromatographic Identification of Aldehydes and Ketones in Toxicological Analyses

A number of methods [*1–5*] are available for the identification of aldehydes and ketones by gas chromatography (GC). Baker et al [*1*] used a column packed with Porapak Q for the direct determination of the lower alcohols, acetone and acetaldehyde, in blood; a similar method was used to identify these same components in milk [*2*]. The analysis of compounds containing an isolated carbonyl group, as their 2,4 dinitrophenylhydrazones, has been reported [*3,4*] and in a recent paper the GC analysis of aldehydes and ketones as their acetals and ketals was described [*5*].

This report describes a convenient method for the gas chromatographic identification of some aldehydes and ketones routinely encountered in toxicological analyses.

Experimental

Instrumentation

Two Gas Chromatographs were used for Analysis—1. A Varian model 1200 gas chromatograph (Varian Associates, Walnut Creek, Calif.) equipped with a flame ionization detector and a 0–5 mV Speedomax type G recorder (Leeds & Northrup Co., Philadelphia, Pa.) and containing a 6 ft coiled aluminum (¼-in. outside diameter) column packed with 15 percent Hallcomid M-18 on 80–100 mesh as Chrom Q acid washed (AW) hexamethyldisilanized (HMDS) (Chromatographic Specialties Ltd., Brockville, Ontario, Canada) was used. The operating conditions for the results shown in Fig. 1 and Fig. 2 were as follows:

Injection port temperature 240°C;
Column temperature 85°C;
Detector temperature 260°C;
Carrier gas (nitrogen) flow rate approximately 50 ml/min.

2. A Varian model 2100 gas chromatograph equipped with a flame ionization detector and a Varian 0–1 mV recorder Model 30 and containing a 4 ft glass U-shaped column (¼-in. outside diameter) packed with 3 percent OV-1 on 80–100 mesh Gas Chrom Q, AW HMDS was used under the following conditions (see Fig. 3 for results):

Injection port temperature 240°C;
Column temperature 200°C;

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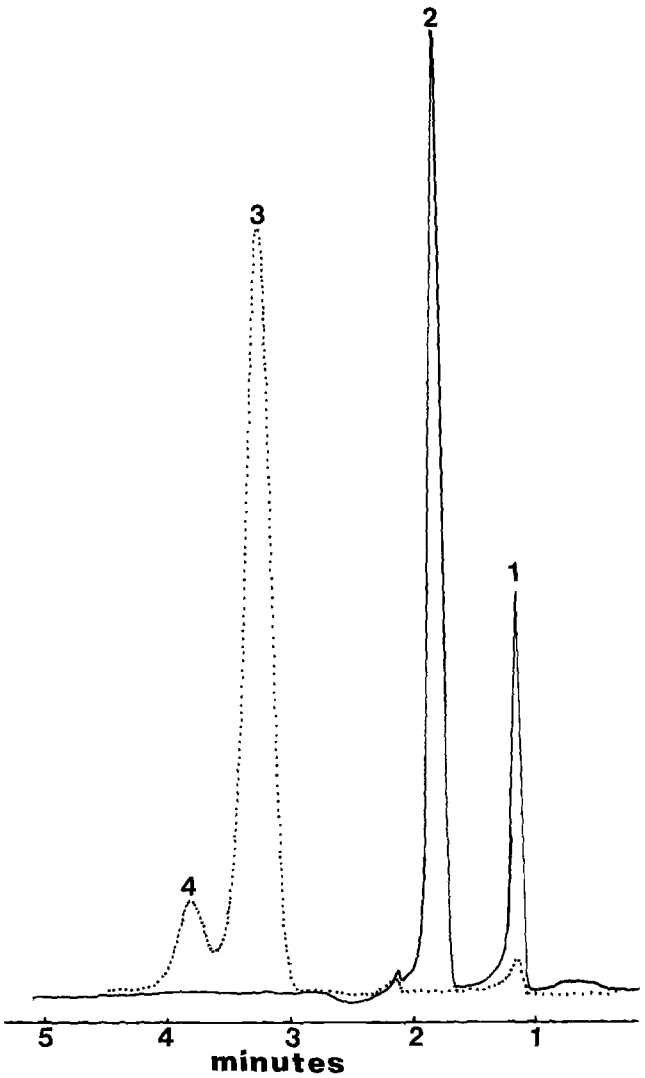

FIG. 1—*The solid line indicates the gas chromatographic response to blood containing acetaldehyde [1] (0.13 percent volume/volume) and acetone [2] (0.13 percent volume/volume). The dotted line indicates the response to the same blood after treatment with $NaBH_4$ producing ethanol [3], isopropanol [4]. The column temperature was 85°C.*

Detector temperature 320°C;
Carrier gas (nitrogen) flow rate approximately 50 ml/min.

A column temperature of 260°C and an injection port temperature of 280°C was used for the analysis of Haloperidol.

A 6 ft U-shaped glass column (¼-in. outside diameter) packed with 3 percent OV 17 on 80–100 mesh Gas Chrom Q AW HMDS (Chromatographic Specialties Ltd.) was used for the analysis of Diethylpropion under the following conditions:

Injection port temperature 240°C;
Column temperature 130°C;

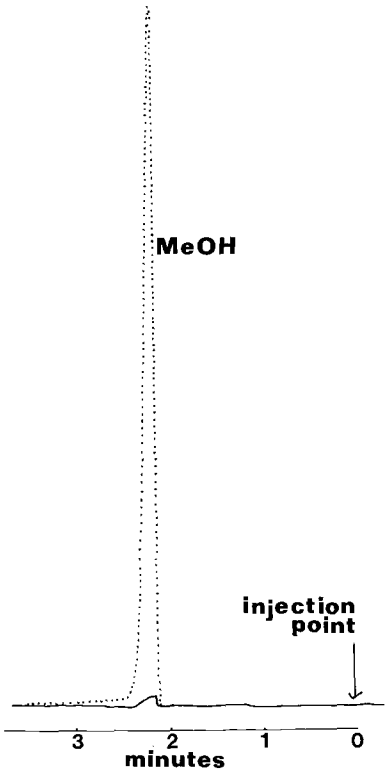

FIG. 2—*The solid line indicates the gas chromatographic response to an aqueous solution of ethylene glycol (200 mg percent) to which solid potassium meta-periodate was added. The dotted line indicates the response to the same solution after treatment with $NaBH_4$. (2.5 μl injected in both cases). The column temperature was 85°C.*

Detector temperature 320°C;
Carrier gas (nitrogen) flow rate approximately 50 ml/min.

Materials

Sodium borohydride powder 98 percent (Fisher Scientific Co., Fairlawn, N.J.)
Acetaldehyde, practical grade (Matheson, Coleman & Bell, Norwood, Cincinnati, Ohio)
Acetone, laboratory grade (Double distilled)
Ethylene glycol, laboratory grade (Fisher Scientific)
Potassium meta-periodate, analytical grade (J. T. Baker Chemical Co., Phillipsburg, N.J.)
Methadone (Dow Chemical of Canada, Sarnia, Ontario)
Ethanol, laboratory grade (Redistilled)
Diethylpropion (tenuate) (Merrell Co., Cincinnati, Ohio)
Haloperidol (haldol) (McNeil Labs., Ft. Washington, Pa.)

Procedures

To a sample of blood or urine (0.5 ml) in a centrifuge tube was added 1 ml of distilled water followed by a small amount (1–2 mg) of solid sodium borohydride; if excess frothing occurred, the sample was centrifuged. After approximately 10 min at room temperature a

few microlitres of the resulting solution were injected directly into the gas chromatograph. This procedure was used for those compounds containing an isolated carbonyl group which on reduction gave alcohols which can be analyzed on the GC columns that are normally used in routine alcohol analysis, for example, Hallcomid, Porapak R, etc.

Tissue extracts of drugs [6] were taken up in a small volume of ethanol (approximately 0.5 ml) and sodium borohydride (1–2 mg) added; after approximately 10 min a few microlitres of the ethanol solution were injected directly into the gas chromatograph.

Results and Discussion

The identification of any substance by gas chromatography alone has its limitations; the degree of certainty is increased, however, if the substance is analyzed on two or more stationary phases of different type, or if a derivative of the substance can be formed and shown by analysis to be identical to a standard previously prepared.

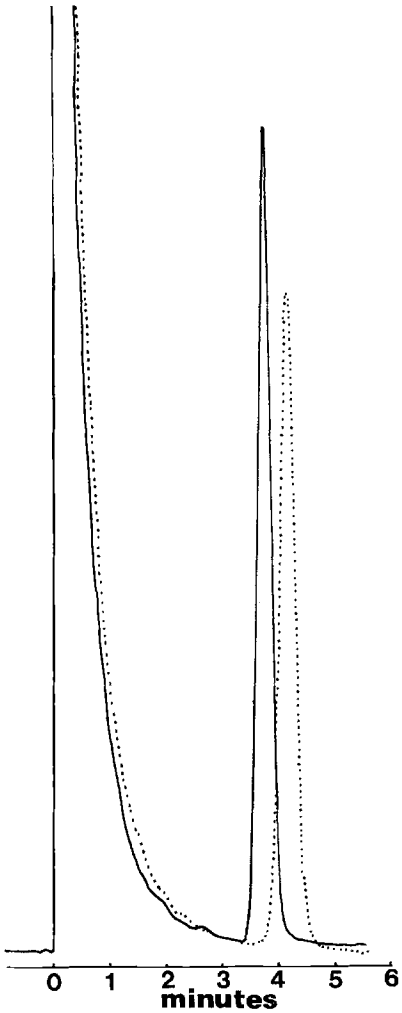

FIG. 3—*The solid line indicates the gas chromatographic response to an ethanolic solution of methadone (50 mg percent). The dotted line dicates the response after treatment of the same methadone solution with* $NaBH_4$. *The column temperature was 200°C.*

Figure 1 illustrates the change in GC response when a mixture of acetaldehyde and acetone in blood is reduced to ethanol and isopropanol respectively. The stationary phase used was 15 percent Hallcomid M-18 although similar results were obtained with Porapak R.

The response of a flame ionization detector to formaldehyde is poor and the stationary phases normally used in alcohol analysis do not separate formaldehyde from methanol [7]. Figure 2 illustrates the increase in detector response when an aqueous solution of ethylene glycol and potassium meta-periodate (this reaction produces formaldehyde [8]) was treated with sodium borohydride; the increase in response provides a convenient confirmatory test for formaldehyde, ethylene glycol, and any other glycol which produces formaldehyde on periodate oxidation.

There are a number of drugs and drug metabolites that contain an isolated carbonyl group that can be reduced with sodium borohydride. Figure 3 illustrates the "peak shift" that occurs in the GC response to an ethanolic solution of methadone treated with sodium borohydride. Diethylpropion (Tenuate) and Haloperidol (Haldol) were both readily reduced with sodium borohydride; although in the former case, it was necessary to raise the column temperature (130°– 150°C on 3 percent OV 17) in order to elute the reduction product in a reasonable time.

Summary

A convenient method for the identification of some common aldehydes and ketones is described. Treatment of aqueous or alcoholic solutions of aldehydes and ketones with solid sodium borohydride results in the formation of the corresponding alcohols which are analyzed on the same GC column as the original carbonyl compounds.

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