Applications of Chromic Acid–Celite Columns to Micro- and Semimicro Preparations of Fatty Aldehydes

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In a convenient two-phase procedure, columns of Celite 545 charged with aqueous chromic acid are used to oxidize microgram and milligram amounts of fatty alcohols to the corresponding aldehydes with approximately a 70% yield. The original configuration and position of the double bond is fully maintained during the oxidation of unsaturated alcohols.

This laboratory has reported the use of microcolumns of Analytical Grade Celite (AGC) charged with aqueous chromic acid to cleave and locate double bonds in methyl esters and in olefins (1). Earlier, a similar system, differing only in the ratio of chromic acid, water, and AGC, was shown to be highly efficient in oxidizing micromole amounts of saturated secondary alcohols to the corresponding ketones (2). Observing that the substitution of another type of Celite, i.e., Celite 545,[2] for AGC results in a lowering of the oxidizing potency of aqueous chromic acid to a point where double bonds are not attacked and primary alcohol groups are oxidized to the corresponding aldehyde in a respectable yield, we developed a simple micro- and semimicro method for preparing fatty aldehydes from the more readily accessible alcohols. Although a number of procedures utilizing chromium trioxide–pyridine-based systems for preparing aldehydes from alcohols in potentially higher yield were available (3,4), none of them seemed as convenient or as adaptable to microscale synthesis as the proposed method.

METHODS

Preparation of chromic acid on Celite 545. Chromium trioxide (1 g) was dissolved in 2 ml of distilled water in a mortar, and the solution was ground with 5 g of Celite 545 until the mixture was homogeneously yellow-orange. The impregnated Celite was kept at room temperature in a tightly stoppered bottle, and it maintained its reaction characteristics for at least 6 months.

[1]Agricultural Research Service, U.S. Department of Agriculture.

[2]Reference to brand or firm name does not constitute endorsement by the U.S. Department of Agriculture over others of a similar nature not mentioned.

Preparation of aldehydes at the microgram level. For preparing microgram amounts of aldehydes, approximately 1-cm-long columns of the impregnated Celite were made in melting-point capillaries, using the technique described previously (1). From 0.4 to approximately 200 μg of the alcohol dissolved in up to 6 μl of methylene chloride was applied to the column, by placing the tip of a 10-μl syringe on the surface of the column bed and expelling the solution slowly onto the column. Ater 10 min, the column was eluted with CS_2 using the pressure device described earlier (1).[3] The effluent was removed as thoroughly as possible with a hypodermic syringe and was examined by gas–liquid and thin-layer chromatography (tlc).

Preparation of aldehydes at the milligram level. For preparing milligram amounts of aldehydes, the procedure was as follows. The chromic acid–Celite 545 powder (1 g) was packed tightly in a column[4] with a tamping rod and 0.5 ml of a dichloromethane solution containing from 2 to about 200 μmol of the alcohol was pipetted onto the column. This volume wetted about 80–90% of the powder. After 10 min, the column was eluted with 5–6 ml of dichloromethane using slight air pressure. Some of the alcohols, especially the unsaturated ones, were contaminated with some color from the column packing. This color was easily removed by permitting the effluent to flow through a 0.5-g bed of dry Celite 545 contained in a column.[4]

The carbonyl compounds in an aliquot of the effluent were converted to 2,4-dinitrophenylhydrazones which were purified by tlc, if necessary, and were assayed spectrophotometrically (5).

Thin-layer chromatography. For preparative work, precoated 8 × 8-in. silica gel G plates, 500 μm thick (Analtech, Newark, Del.), were used. The plates were prewashed in benzene and then were spotted with up to approximately 30 mg of the alcohol oxidation products. After development, the major band was removed by scraping, and the aldehyde was eluted with 3% methanol in dichloromethane.

For argentation tlc, 250-μm-thick silica gel G plates were placed, adsorbent side down, in a tray containing 10% $AgNO_3$ in acetonitrile. The plates were removed, blotted, and air dried 1 hr in semidarkness.

Analytical tlc was conducted on 250-μm-thick precoated silica gel G plates without preliminary treatment. All tlc separations were made using benzene as solvent. Spots were detected by spraying with 3% copper acetate in 8.5% H_3PO_4 and heating at 170–200°C.

Gas–liquid chromatography. Gas–liquid chromatography (glc) was conducted on (a) an 8 ft × ⅛ in. column containing 7.5% ethylene glycol adipate and 2% H_3PO_4 on 90–100 mesh Anakrom ABS, programmed from 65 to 195°C at 6°C/min; and on (b) a 4 ft × ⅛ in. column containing 3% JXR

[3]Hexane, benzene, CCl_4, or CH_2Cl_2 can also be used.

[4] Disposable Pasteur "Super" pipets, 10 mm o.d. × 5.75 in., sold by Matheson Scientific Company, Moorestown, N.J., were used.

TABLE 1

YIELD OF ALDEHYDES FROM OXIDATION OF FATTY ALCOHOLS ON A CHROMIC ACID–CELITE 545 COLUMN

Fatty alcohol	Amount on column (μmol)	Yield[a] (%)
1-Decanol	47	75
10-Undecen-1-ol	199	69
Lauric	10	72
Myristic	101	72
Palmitic	51	75
Stearic	62	71
Oleic	90	72
Elaidic	61	70
cis-Vaccenic	69	74
trans-Vaccenic	44	60
Petroselenic	56	66
Petroselaidic	43	69
Linoleic	52	75
Linoelaidic	51	69
Linolenic	50	75
1-Octacosanol	2	72

[a] Determined colorimetrically on tlc-purified 2,4-dinitrophenylhydrazones.

on 80–100 mesh Gas-Chrom Q, programmed from 65 to 270°C at 10°C/min. Columns were stainless steel and silanized; helium was the carrier gas, supplied at a pressure of 30 ml/min.

Mass spectrometry. To confirm the identity of the oxidation products, we used mass spectrometry. The LKB GC-MS system was utilized, and conditions were similar to those published earlier (6).

Nuclear Magnetic Resonance (NMR). Proton spectra were obtained on a Bruker Model WH-90. Samples were analyzed in $CDCl_3$ with tetramethylsilane as an internal standard.

RESULTS AND DISCUSSION

The fatty alcohols examined and the yields of aldehyde produced in the milligram-scale oxidation procedure are listed in Table 1. By preparative tlc, the yields of pure aldehyde determined gravimetrically were approximately 5% lower than those listed.

Other components identified in the oxidation mixture were the ester (12–20%)[5] formed by condensation of alcohol and aldehyde followed by oxidation of the hemiacetal (7); the fatty acid (5–10%); small amounts (1–

[5]glc Column (b) was used to examine esters with 24 or more carbons. All other components were examined on glc column (a).

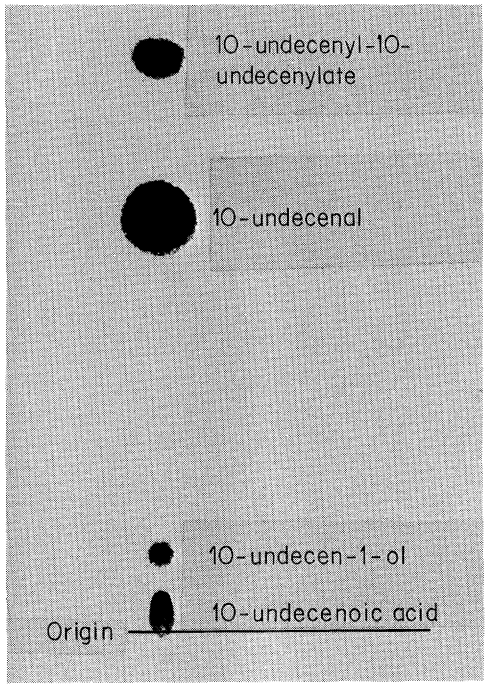

FIG. 1. Typical thin-layer chromatographic separation of the products of oxidation of fatty alcohols by chromic acid on Celite 545. Oxidation products from 10-undecen-1-ol. Adsorbent: silica gel G; solvent: benzene.

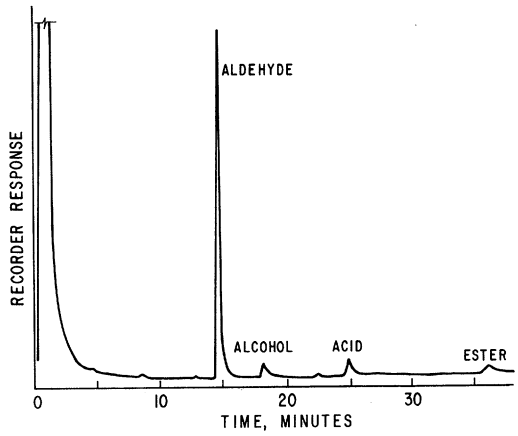

FIG. 2. Gas–liquid chromatographic separation of products of oxidation of 10-undecen-1-ol by chromic acid on Celite 545. Peaks are, respectively, 10-undecenal, 10-undecen-1-ol, 10-undecenoic acid, and 10-undecenyl-10-undecenylate. Column: 8 ft × ⅛ in. EGA–H_3PO_4. For conditions, see text.

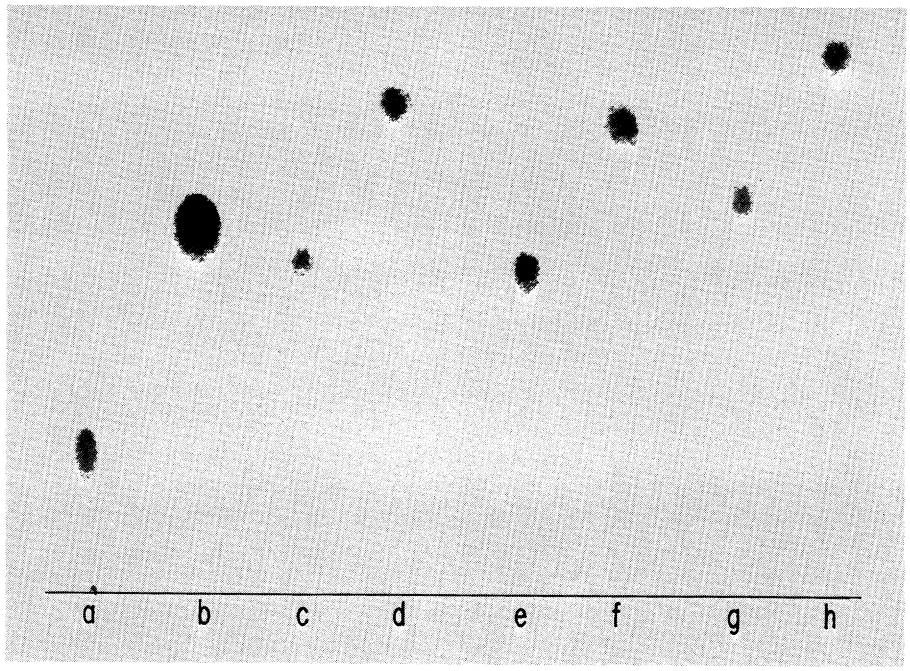

FIG. 3. Argentation thin-layer chromatographic separation of unsaturated aldehydes obtained by preparative tlc of oxidation products of fatty alcohols by chromic acid on Celite 545. Spots are from left to right: linoleyl, linoelaidyl, *cis*-vaccenyl, *trans*-vaccenyl, petroselenyl, petroselaidyl, oleyl, and elaidyl aldehydes. Adsorbent: Silica gel G–$AgNO_3$; solvent: benzene.

5%) of unreacted alcohol; and traces of unidentified products. Typical tlc and glc analyses are shown in Figs. 1 and 2, respectively. The same products were identified in the microgram-scale oxidations, and yields were approximately the same as judged by comparison of gas chromatograms.

The integrity of double bonds was fully maintainted during oxidation of unsaturated alcohols. Argentation tlc (Fig. 3) and NMR analysis[6] showed that no *cis–trans* isomerization had occurred. There also was no indication (by glc) that double bonds had oxidized. Analysis for double-bond position (6)[7] showed that no migration had taken place.

Dichloromethane was the preferred solvent for the oxidation. Benzene was also satisfactory. It was noted, however, that when solvents less polar

[6]The NMR analysis was applicable to monoethenoid aldehydes only and could detect a minimum of 10–15% contamination of one isomer in another.

[7]The method for locating double bonds was modified in that the scission products obtained from the hydrocarbon side of the double bond in monoethenoid aldehydes were gas chromatographed as free acids instead of as methyl esters.

than benzene (e.g., CCl_4, CS_2, and *n*-hexane) were tried, slight scission of double bonds occurred, and, also, somewhat higher amounts of fatty acids were formed. This suggests that some type of adsorption of the unsaturated fatty alcohol onto the surface of the support might be a prerequisite for double-bond oxidation and for further oxidation of the aldehyde function. It may also suggest an explanation for the marked difference in the reactivities of chromic acid supported on AGC as opposed to Celite 545. In this connection it should be mentioned that acid-washing of Celite 545 did not alter its properties relative to unwashed Celite 545. AGC is an acid-washed Celite. Thus, the difference in reactivities of chromic acid supported on Celite 545 and on AGC is due to some other factor. Three different lots of Celite 545 all behaved similarly.

Primary alcohols shorter than decanol give much poorer yields of aldehydes, the oxidation proceeding to the carboxylic acid. This was more marked with 1-hexanol than with 1-octanol and may indicate that increased water solubility of an alcohol will give a lower yield of aldehyde.

Fatty aldehydes are potential constituents of lipids, capable of being generated from plasmalogens and glyceryl-alk-1-enyl ethers, both classes being widely distributed in animal lipids. The proposed method offers a rapid and simple way to prepare these aldehydes, as needed, from the more conveniently stored alcohols.

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