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PRODUCTION OF CITRAL FROM GERANIOL

II*. CAPILLARY GAS CHROMATOGRAPHIC–MASS SPECTROMETRIC INVESTIGATION OF TWO DIFFERENT OXIDATION REACTIONS USING A GRAPHITE POROUS-LAYER OPEN-TUBULAR COLUMN WITH A LARGE COATING RATIO OF POLAR LIQUID PHASE

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SUMMARY

The preparation of porous-layer open-tubular columns for gas–liquid chromatography with graphitized thermal carbon black as a solid support and a polar stationary phase is described. The application of these columns is demonstrated by an example.

The reaction products from two oxidation reactions for the production of synthetic citral have been analysed by combined gas chromatography–mass spectrometry. About 30 trace substances resulting from redox reaction and cyclization of the starting materials were found.

INTRODUCTION

The production of citral of good quality in high yields is of economic interest as citral (a mixture of geranial and neral) is a key intermediate in the synthesis of important polyisoprenoid substances such as vitamin A; it is also a starting material in the perfume industry.

In a previous paper[1], it was demonstrated that conventional gas chromatography (GC) could be used effectively for monitoring the major products during the production of citral by chemical oxidation of geraniol and nerol:

* Part I, ref. 1.

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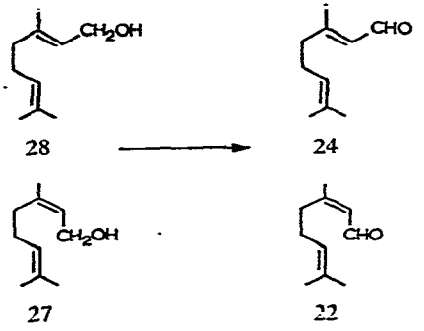


The choice of the best oxidizing agent (in terms of cost, ease of use and yields) and batch control during the reaction were easily carried out following a 30-min analysis using a conventional column packed with a polar stationary phase (polyethylene glycol PEG 1500). Chromic acid in glacial acetic acid ($K_2Cr_2O_7$–AcOH) is the reagent of choice and the compounds accounting for 99% (w/w) of the resulting product can be identified by conventional GC. In an alternative process, chromic anhydride in pyridine (CrO_3–Py) was used, although this costly reagent is flammable, which may limit its use in industrial processes.

The presence of impurities which either are formed during the oxidation or which pre-exist in the starting material may dramatically affect the quality of the resulting citral oil, although these products usually amount to 3% or less of the total oxidation products. As conventional GC cannot monitor these trace substances effectively, a more detailed study of the side-products of the two selected oxidative reactions ($K_2Cr_2O_7$–AcOH and CrO_3–Py) has been carried out by means of capillary-column GC and combined gas chromatography–mass spectrometry (GC–MS). This work was made possible by adopting a new type of porous-layer open-tubular (PLOT)[2] column in which graphitized thermal carbon black (GTCB) is used as a solid support and a strongly polar stationary phase is employed.

EXPERIMENTAL

The starting geraniol (Firmenich, Basle, Switzerland) is a mixture of geraniol (96%), nerol (2%), citronellol (1.5%) and trace amounts of citrals. It is free of more or less volatile substances (see Fig. 2).

Oxidation of geraniol

The two methods investigated are standard procedures for the oxidation of allyl alcohols and the detailed operating conditions are described in the literature[3], so that only a brief description is given here.

Reaction A. Geraniol was oxidized with $K_2Cr_2O_7$ in glacial acetic acid–benzene (1:1) for 45 min at 64°. After extraction and washing, the resulting oil (95% recovery) was distilled under vacuum (0.1 torr) and the 35–76° cut collected. The overall conversion and recovery was 90%.

Reaction B. A CrO_3–pyridine complex was cautiously prepared by slowly adding CrO_3 to pyridine as described elsewhere[3,4]. Geraniol was added, and the resulting solution was left overnight at room temperature. The reaction was stopped by addition of water, and the oxidized oil (90% yield) was recovered as above.

Gas chromatography

A wall-coated open-tubular (WCOT) column was prepared by etching an open-tubular column with dry HCl and coating with polyethylene glycol (PEG 20M) according to a procedure described by Alexander *et al.*[5].

A graphite PLOT column was prepared according to the method described by Vidal-Madjar *et al.*[6]: glass tubes were cleaned by percolation of a chromic acid solution and 15–25-m capillary columns (0.4–0.6 mm I.D.) were prepared using a home-made glass drawing machine. The capillary tube was filled by pushing in a suspension of 5% GTCB (Cabott Corp., Billerica, Mass., U.S.A.) in dichloromethane containing 0.25% of squalane. One end was sealed, and the solvent was evaporated at 140° in a home-made, modified version of the apparatus described by Ilkova *et al.*[7]. The squalane used here as a suspension stabilizer was then removed by heating the column overnight at 180° under a stream of dry argon.

The stationary phase was coated on the carbon layer by percolation of a 20% solution of free fatty acid phase (FFAP) in methylene chloride through the column. The columns were connected to the gas chromatograph (Varian 2700) using short (5-cm) glass-to-metal connections[8], two conventional SS-102-1 Swagelok nuts, and two no-hole 1/16-in. Vespel ferrules (Alltech SF-100/0-V) drilled to 0.5 mm. This arrangement is both vacuum- and pressure-tight (up to 6 bar), it withstands temperatures up to 320° and the ferrules are re-usable after dismantling. The standard 1/4-in. injector of the chromatograph was converted into a Grob-type capillary injector[9] by inserting a simple device made easily from available spare parts as shown in Fig. 1. An aliquot of the pure citral oil (0.3–1 μl) was injected through this device while maintaining a stream-splitting ratio of 1:20–1:50 depending on the analysis.

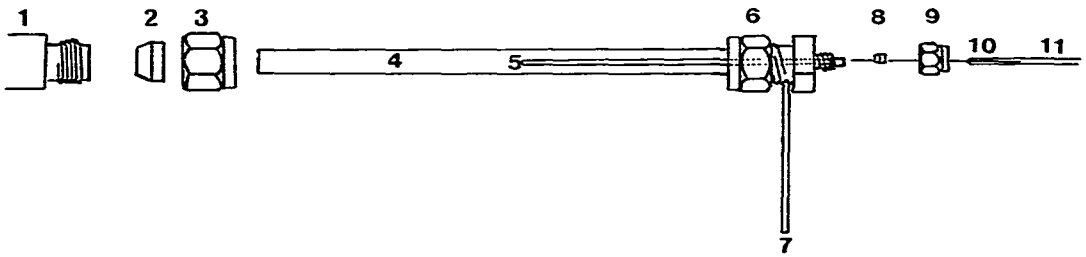


Fig. 1. Schematic diagram showing a glass adaptor for standard 1/4-in. injector and a coupling method for connecting GTCB PLOT columns to the injector: 1 = 1/4-in. injector end fitting; 2 = 1/4-in. Vespel ferrule; 3 = 1/4-in. Swagelok nut; 4 = glass tube (6 mm O.D.) filled with silanized glass beads; 5 = glass-lined metal tube (1.5 × 0.7 mm) with bottom fitted in component 6; 6 = modified 1/4-in. to 1/16-in. Swagelok reducing union; 7 = connection to a fine metering needle valve; 8 = 1/16-in. no-hole Vespel ferrule drilled to 0.5 mm; 9 = 1/16-in. Swagelok nut; 10 = Dilver P metal tubing fusable to glass; 11 = glass capillary column.

Gas chromatography–mass spectrometry

A DuPont Model 21-492-B GC–MS apparatus equipped with a DuPont Model 094-B2 disc-based data system was used for spectra acquisition and processing. Scanning of masses 200–27 was performed repetitively at 1 sec/decade with a flyback time of 3 sec. The GTCB PLOT column was either directly coupled to the MS source or directed to a single-stage glass-jet separator after addition of 5 ml/min of make-up helium.

RESULTS AND DISCUSSION

Capillary gas chromatography

It has been shown that the chromatography of closely related polar substances such as the isomeric terpene alcohols (geraniol, nerol and linalool) and aldehydes is best obtained on polar stationary phases[10]. The practical realization of stable glass capillary columns coated with polar stationary phases is a long-standing problem which has recently been solved by modifying the glass surface. Dehydration[11] and chemical treatment with HF[12] or HCl[5,13] followed by silanization or other deactivation methods[14] are accepted procedures, and the resulting surface can be coated with most polar and apolar phases by using the static or the dynamic coating procedures.

In this study, a glass capillary column (20 m × 0.2 mm I.D.) coated with PEG 20M was prepared. A GC trace of the geraniol raw material and of the resulting oxidation products from reaction with $K_2Cr_2O_7$–CH_3COOH are shown in Fig. 2. Good separation and resolution and absence of tailing on the peaks of the polar substances can be observed. However, because of a low loadability, the use of this column in GC–MS failed to produce clear spectra for most of the trace constituents of the mixture. To alleviate similar problems which frequently occur in GC–MS, columns with a lower phase ratio and a higher loading capacity are used, as discussed by McFadden[15]. There are reports of similarly trace analyses of essential oils by using very long (200–300-m) large-bore (0.75 mm I.D.) metal capillary columns[16]. The use of short PLOT columns is an alternative solution.

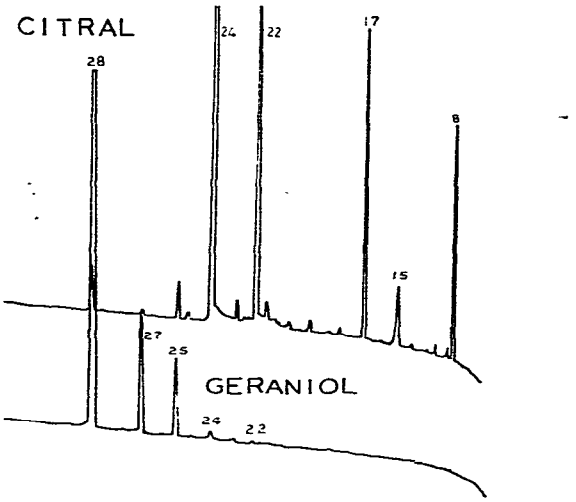


Fig. 2. Gas chromatographic analysis of geraniol raw material (bottom trace) and of oxidation products of geraniol from reaction A (top trace). PEG 20M WCOT column, 20 m × 0.2 mm I.D.; inlet pressure, 1 bar; temperature 115–200° at 2°/min. Peaks are identified in Table I.

Glass PLOT columns prepared with a finely divided support such as silanized pure silica powder (Silanox) can be easily prepared[17,18]. However, our results and those of other workers[19] have shown that the resulting column is better coated with

non-polar or moderately polar stationary phases when using the dynamic coating procedure. Poor results are obtained with polar phases.

Until recently, GTCB was used mainly to prepare packed columns for gas–solid chromatography (GSC). Because of the high surface energy of GTCB and the poor mechanical stability of the particles, classical columns are difficult to pack with GTCB, their efficiency is only average and their permeability is low. On the other hand, PLOT columns made with a porous layer of pure GTCB have great potential interest for GSC[6,20,21] as they are easy to prepare and have a high permeability.

Some interesting results have been obtained by adding small amounts (0.5–2%, w/w) of stationary phase to the GTCB in packed[22–24] and PLOT columns[6]. A further step was to try to add larger amounts of stationary phase (up to 20%, w/w, relative to GTCB). Under such conditions, it was demonstrated that pure gas–liquid partition controls the separation and adsorption plays no significant part; GTCB then behaves as an inert solid support. The use of GTCB in PLOT columns offers several practical advantages over other inert solid materials: its surface is free from any specific adsorption sites so no tailing of polar material will occur, it can be coated with many different stationary phases, including polar stationary phases such as PEG 20M, or FFAP using the dynamic coating procedure. These attractive features were explored during the following practical analysis.

In this study of oxidized citral oil, one of the GTCB PLOT columns, a 20-m column heavily loaded (10% w/w) with FFAP, was used. In a separate test, as many as 15,000 plates for linalool at 110° (capacity factor, $k' = 3.8$) were measured. This moderate plate efficiency results from the large bore of the PLOT column used (0.6 mm I.D.).

An on-column load of about 50 μg of oxidized mixture was generally suitable for obtaining mass spectra from amounts of substances less than 0.5%. No significant loss of separating power was observed when such a high load of substances was injected on to the column. Higher loads were prevented mainly because of problems with the mass spectrometer, as contamination of the source block with excess of sample was a risk and the mass spectra were distorted due to saturation of the ion-counting recorder system when microgram amounts of a pure substance entered the source.

Chromatograms of the oxidized products of geraniol oil from reactions A and B are shown in Fig. 3, and compounds identified being listed in Table I. The elution order for terpenes was found to be the same on a heavily loaded GTCB PLOT column and on a WCOT column coated with the same stationary phase[25]. This suggests a low degree of adsorption on the carbon layer.

GC–MS identification of citral by-products

Geraniol oil yields, in both oxidations, the expected citrals [geranial (24) and neral (22)], citronellal (15) and a wide variety of trace products. To our knowledge, many of these oxidation products have not previously been reported to occur from reactions A and B.

Both fractions were obtained by distillation of the raw reaction mixture, but trace amounts of solvents from the reaction and the washing interfere with some of the early eluting peaks. This effect occurs for benzene, toluene, xylene and pyridine in B; chloroform in A results from the cleaning of the injection syringe.

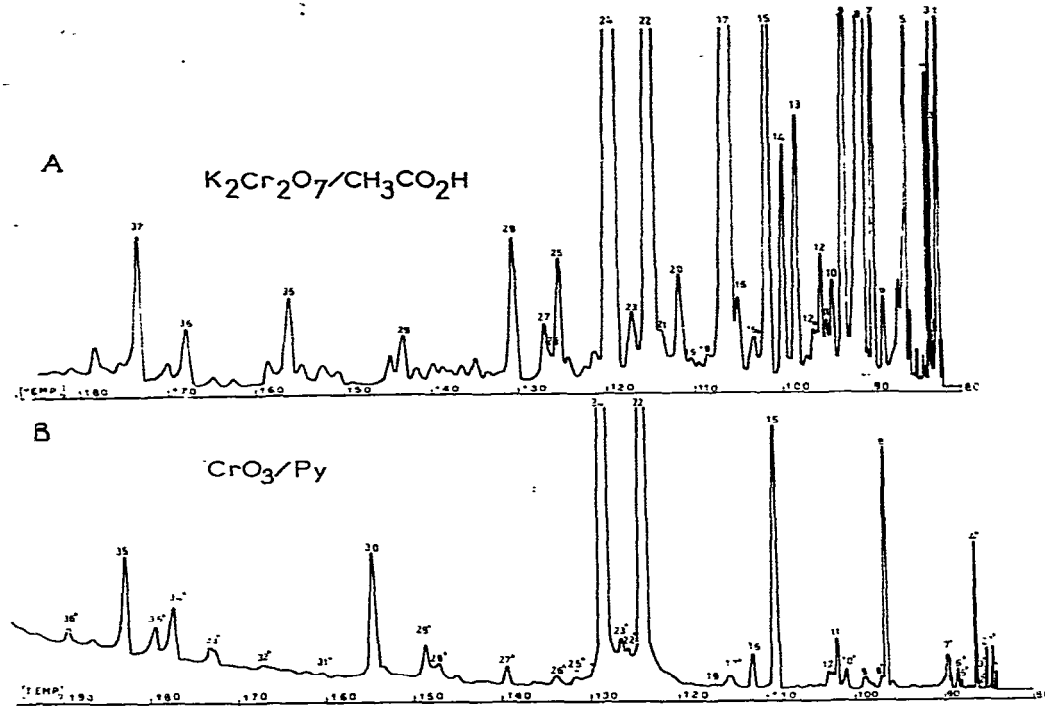


Fig. 3. GC plot of the analysis of the oxidation products of geraniol when reacted with (A) $K_2Cr_2O_7$–CH_3COOH and (B) CrO_3–Py. GTCB PLOT column coated with FFAP. Inlet pressure, (A) 2 bar and (B) 1 bar; temperature, 80–200° at 2°/min. Peaks are identified in Table I.

TABLE I

IDENTIFICATION OF PEAKS IN FIGS. 2 AND 3

Peak No.		*Mol.wt.**	*Formula*	*Substance***
A	*B*			
1	1	84	C_6H_{12}	Cyclohexane
—	1′	98	C_7H_{14}	Methylcyclohexane
2	2	58	C_3H_6O	Acetone
—	2′	78	C_6H_6	Benzene
3	—	118	$CHCl_3$	Chloroform
—	3′	128	C_9H_{20}	2,6-Dimethylheptane
4	—	126	C_9H_{18}	Isopropylcyclohexane
—	4′	92	C_7H_8	Toluene
5	—	142	$C_8H_{14}O_2$	5,6-Epoxy-2-heptanone (tent.)
—	5′	126	C_9H_{18}	2,6-Dimethyl-2-heptene
6	—	128	$C_8H_{16}O$	6-Methyl-2-heptanone
—	6′	106	C_8H_{16}	Xylene
7	—	128	$C_8H_{16}O$	2,5-Dimethylcyclohexanol (tent.)
—	7′	79	C_5H_5N	Pyridine
8	8	126	$C_8H_{14}O$	6-Methylhept-5-en-2-one
—	8′	(158) 143	$C_{10}H_{22}O$	2,6-Dimethylheptan-2-ol (tent.)

TABLE I *(continued)*

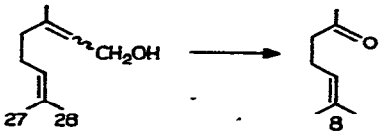
Peak No.		*Mol.wt.**	*Formula*	*Substance***
A	*B*			
9	9	140	$C_9H_{16}O$	2,6-Dimethyl-5-heptenal
10	—	150	$C_{10}H_{14}O$	Thymol
—	10′	150	$C_{10}H_{14}O$	Isopiperitenone, carvone, (tent.)
11	11	150	$C_{10}H_{14}O$	Perillen
12	12	152	$C_{10}H_{16}O$	Unknown (acyclic terpene alcohol?)
12_o	—	152	$C_{10}H_{16}O$	Cyclocitral (2-isopropenyl-5-methylcyclopentane-1-carboxaldehyde ?)
13	—	(170) 155	$C_{10}H_{18}O_2$	Linalool oxide
14	—	(170) 155	$C_{10}H_{18}O_2$	Linalool oxide
15	15	154	$C_{10}H_{18}O$	Citronellal
—	15_o	(156) 138	$C_{10}H_{20}O$	Menthol, carvomenthol (tent.)
16_o	—	110	$C_7H_{10}O$	3 Methyl-2-cyclohexenone (tent.)
16	16	112	$C_7H_{12}O$	3-Methyl-3-cyclohexenol (tent.)
17	—	154	$C_{10}H_{18}O$	Linalool
—	17′	152	$C_{10}H_{16}O$	Unknown (acyclic terpene alcohol?)
18	—	154	$C_{10}H_{18}O$	Terpinen-4-ol
19	19	166	$C_{10}H_{14}O_2$	6,7-Dihydroperillaketone (tent.)
20	—	152	$C_{10}H_{16}O$	Carvotanacetone (tent.)
21	—	152	$C_{10}H_{16}O$	Isogeranial
22	22	152	$C_{10}H_{16}O$	Neral
—	22′	162		Unknown
23	—	152	$C_{10}H_{16}O$	Isogeranial
—	23′	152	$C_{10}H_{16}O$	Piperitone
24	24	152	$C_{10}H_{16}O$	Geranial
25	—	156	$C_{10}H_{20}O$	Citronellol
—	25′	152	$C_{10}H_{16}O$	Isogeranial
26	—	154	$C_{10}H_{18}O$	Isogeraniol
27	—	154	$C_{10}H_{18}O$	Nerol
28	—	154	$C_{10}H_{18}O$	Geraniol
—	26′	156	$C_{10}H_{20}O$	Citronellol (+ contaminating substance showing M^+ 176 and 161)
—	27′	168	$C_{10}H_{16}O_2$	Monoepoxygeranial
—	28′	152	$C_{10}H_{16}O$	1-*p*-Menthene-9-al (tent.)
—	29′			Low mass end similar to that of isopulegol or piperitol
—	32′	166	$C_{10}H_{14}O_2$	Oxopiperitone (tent.)
—	33′	164	$C_{10}H_{12}O_2$	Best match found: isopropyltropolone
—	34′	168	$C_{10}H_{16}O_2$	Unknown
—	35′	184	$C_{10}H_{16}O_3$	Diepoxygeranial
35	35	184	$C_{10}H_{16}O_3$	Diepoxygeranial
36	—	156		Unknown
37	—	184	$C_{10}H_{16}O_3$	Diepoxygeranial

* A clear molecular ion was found for all peaks, except for peaks 8′, 13, 14 and 29′. A $M^+ - 15$ peak was found for peaks 8′, 13 and 14.

** (tent.) = tentative identification based on correlation with reference spectra[35] and manual interpretation. Published mass spectral data were not found for peaks 12, 12_o, 19, 27′, 29′–32′, 35–37 and 35′.

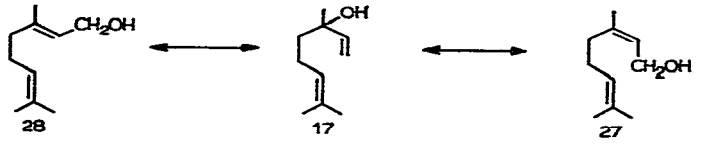
Trace amounts of the three constituents of the starting material are still present in A (peaks 25, 27 and 28). Geraniol and nerol were not detected in B, whereas citronellol was tentatively identified under peak 26'.

The major side-product from reactions A and B is the unsaturated ketone 8, resulting from oxidative double-bond cleavage:



A similar reaction can account for the presence of acetone (2).

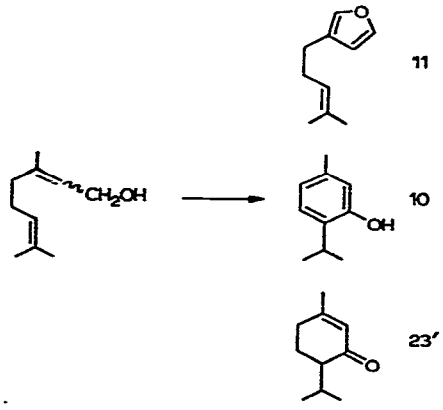
Reaction A yields many acid-catalysed isomerization products which do not occur under the conditions of reaction B. Linalool is present exclusively and in a high amount in A, resulting from the following isomerization scheme[26]:



During the reaction, linalool gave in turn different by-products such as linalool oxide (13 and 14) resulting from cyclization of 6,7-epoxylinalool[27]. Linalool oxide occurs naturally in orange peel and grapefruit essence[28,29].

Synthetically produced citrals often yield many double-bond positional isomers of geranial and citronellal, such as in both mixtures where isogeranial (21, 23 and 25') and isogeraniol (26) were encountered. Precise location of the double bonds is difficult to derive from the mass spectra, although some positional isomers are known to be more probable[30].

Another set of by-products result from cyclization and redox reactions. Perillen (11), piperitone (23') and thymol (10) are examples of such by-products, and have been also found in plants containing natural citral[31–33]:



The oxidation of an alcohol to an aldehyde sets free a hydrogen molecule, which in turn may saturate a double bond, and thus it may explain the occurrence of partially or completely reduced terpene fragments.

Peaks eluting later than the starting material correspond to various citral oxides showing a molecular weight higher than that of geraniol and citronellol. Tentative identification, based solely on their mass spectra, was assumed for geranial (or isomer) monoepoxides (27′, 29′ and 30′) and diepoxides (35, 35′ and 37). Epoxidation of citral by peracids was reported to occur at both the 2,3- and 6,7-positions[27,34]; a similar reaction may have caused the formation of the different monoepoxides encountered here. Monocyclic terpene oxides could explain the mass spectra at peaks (32′ and 33′), but further work is necessary to provide firmer evidence.

Some acidic by-products are usually formed during the oxidation of citral, but they were eliminated here during the reaction work-up which, includes washing with water and $NaHCO_3$ solution.

The sum of all the by-products, not including citral, the remainder of the geraniol oil and the main by-products (8 and 15 in A and 8 in B) amount to about 1 % of the total material.

Fig. 3 and Table I show that the relative abundance and the nature of many by-products differ significantly. To be of industrial use, both mixtures need to be further purified by means of $NaHSO_3$, as previously described[1].

CONCLUSION

The separation of two synthetically prepared citrals has been a test for demonstrating some practical performances of a GTCB PLOT column. Good selectivity for terpenes with a similar skeleton but different functional groups and a high sample load have been shown to be important parameters for this analysis. Work is now in progress to reduce the inner diameter of the columns and to improve the coating procedure so that a wide variety of different stationary phases can be used.

ACKNOWLEDGEMENTS

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