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## DERIVATIZATION PROCEDURE FOR THE DETERMINATION OF CHLOROACETYL CHLORIDE IN AIR BY ELECTRON CAPTURE GAS CHROMATOGRAPHY

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### SUMMARY

A gas chromatographic method is described for the determination of chloroacetyl chloride (CAC) in air in the presence of monochloroacetic acid (MCA). Air containing CAC was bubbled through a reactant solution of 2,4,6-trichlorophenol (TCP) and pyridine in toluene to produce the derivative 2,4,6-trichlorophenyl chloroacetate (TCPC). Excess TCP was removed by extractions with 1 *N* sodium hydroxide, and TCPC was determined via electron capture gas chromatography. An average recovery of  $76 \pm 4\%$  (mean  $\pm$ S.D.) was obtained when CAC was added directly to the reactant solution. When air samples containing CAC were scrubbed and analyzed, recoveries averaged  $70 \pm 5\%$  (mean  $\pm$ S.D.). The quantitative detection limit ( $2.5 \times$  noise) was 1 ng CAC/ml in the extracted organic layer [1 ppb\*\* in air for a 5-l sample]. The general applicability of this method for volatile acid halides was also explored.

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### INTRODUCTION

Chloroacetyl chloride (CAC) is a member of a very reactive class of compounds used in industry as chemical intermediates. Because of their highly reactive nature, acid halides may present a significant personnel hazard<sup>1</sup>, although no threshold limit value (TLV) for CAC has been proposed by the American Conference of Governmental Industrial Hygienists. In order to determine CAC in industrial environments and to monitor test chamber concentrations during inhalation toxicology studies, it was necessary to develop an analytical method more sensitive and specific than any of those presently available.

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\*\* Throughout this article the American billion ( $10^9$ ) is meant.

Indirect methods involving reactions and subsequent colorimetric determination<sup>2</sup> or dechlorination of acid chlorides and determination as chloride ion in solution<sup>3,4</sup> have been described. Typically these methods lack specificity and the desired sensitivity. However, Rusch *et al.*<sup>5</sup> claim a detection limit for dimethylcarbamoyl chloride in air in the low ppb range by reaction with 4-(*p*-nitrobenzyl)pyridine to form the highly colored dihydropyridine derivative and Crummett and McLean<sup>6</sup> obtained similar sensitivity for phosgene by ultraviolet spectrometry after derivatization with aniline.

Methods for measuring acid halides directly by gas chromatography have been described<sup>7,8</sup>; however, these typically involve difficult and/or exotic chromatographic techniques. Espisito *et al.*<sup>9</sup> have recently circumvented most of these problems in determining phosgene to sub-ppb levels in air.

Greatly enhanced chromatographic properties and increased response can be imparted to acid halides by derivatization prior to analysis. Acid chlorides have been analyzed as their methyl esters<sup>10</sup> and their N,N-diethyl amides<sup>11</sup>. Dahlberg and Kihlman<sup>12</sup> converted acid chlorides to their isopropyl esters before analysis via electron capture gas chromatography. They claim detection limits of  $10^{-11}$  mole/ $\mu$ l (1  $\mu$ g/ml) for CAC and  $10^{-12}$  mole/ $\mu$ l for dichloroacetyl chloride and trichloroacetyl chloride.

Although the highly specific and sensitive method described herein has been tailored specifically for the determination of CAC, several other acid chlorides were derivatized under identical reaction conditions and the derivatives identified to emphasize the general utility of this procedure.

## EXPERIMENTAL

### Materials

Calcium hydride and sodium hydroxide and the organic solvents acetone, hexane, methanol, pyridine and toluene were all of analytical reagent grade. The toluene was stored over calcium hydride and pyridine over sodium hydroxide pellets to reduce and maintain the water content at a consistent and acceptable level. Dimethyldichlorosilane (DMCS), used for deactivating glassware, was obtained from Pierce (Rockford, Ill., U.S.A.).

Chloroacetyl chloride (97% pure) and 2,2,3-trichloropropionyl chloride were supplied by Dow Chem. (Midland, Mich., U.S.A.). Acetyl chloride, dichloroacetyl chloride and 2,4,6-trichlorophenol (TCP) (98% pure) were obtained from Aldrich (Milwaukee, Wisc., U.S.A.). Pentafluorophenol was obtained from Peninsular Chem. Research (Gainesville, Fl., U.S.A.). 1,4-Dibromonaphthalene (DBN), the internal standard, was obtained from Eastman-Kodak (Rochester, N.Y., U.S.A.) and was used without further purification.

The 2,4,6-trichlorophenyl chloroacetate (TCPC) was prepared by scaling up the derivatization procedure described below. The TCPC was purified by recrystallization twice from hexane. The other reaction products, 2,4,6-trichlorophenyl 2,2,3-trichloropropionate (TCPT), 2,4,6-trichlorophenyl acetate (TCPA), 2,4,6-trichlorophenyl dichloroacetate (TCPD) and pentafluorophenyl chloroacetate (PFPC), were prepared as was TCPC above, but were not recrystallized.

### Apparatus

A Varian Series 2400 gas chromatograph equipped with a  $^{63}\text{Ni}$  electron capture detector was used. A 1.7 m  $\times$  2 mm I.D. glass column was packed with a bonded polyester liquid phase on Chromosorb W-AW (100–120 mesh) and conditioned prior to use for 24 h at 200° with an argon–methane (95:5) gas flow-rate of 30 ml/min. A Hewlett-Packard 5750 gas chromatograph equipped with a flame ionization detector (FID) was used for purity confirmation of synthesized compounds. A 1 m  $\times$  2 mm I.D. glass column was packed with 3% SP-2100 on Supelcoport (80–100 mesh) and conditioned prior to use for 24 h at 230° with a helium gas flow-rate of 30 ml/min.

A Finnigan Model 3200 mass spectrometer equipped with a chemical ionization source and a Model 6110 data package was used for structure confirmation. A Perkin-Elmer R-32 nuclear magnetic resonance (NMR) spectrometer was also employed for structure elucidations and purity estimations.

A Model G portable pump (Mine Safety Appliance Co.) was used in the air sampling system. The air flow-rates were determined with a Brooks rotameter, Model 1355-00CIFA.

### Air sampling

Air was passed through two 30-ml impingers in series at a rate of 0.5 l/min for 10.0 min. Each impinger contained 20.0 ml of a dry toluene reactant solution (0.14 g TCP, 0.1 ml pyridine and 4.0  $\mu\text{g}$  DBN per 20 ml solution). No volume corrections were necessary after sampling. All glassware used in the air sampling apparatus was deactivated with 30% DMCS in toluene followed by washes with methanol and acetone.

### Gas chromatography (GC)

Samples were extracted with 2  $\times$  20 ml of aqueous 1 *N* sodium hydroxide solution. Aqueous extracts were discarded. 2  $\mu\text{l}$  of the extracted toluene solution were injected onto the analytical chromatographic column under the following conditions: argon–methane (95:5) carrier gas at 30 ml/min; column temperature, 150°; injection port temperature, 175°;  $^{63}\text{Ni}$  electron capture detector at 220°; electrometer at  $8 \times 10^{-10}$ . The retention times for TCP, DBN, TCPC and TCPD were 1.3 min, 2.1 min, 2.6 min and 2.8 min, respectively (Fig. 1).

The purity of the synthesized ester was estimated by area percent calculations of the flame ionization responses for solutions of *ca.* 10 mg/ml ester in acetone under the following conditions: 1  $\mu\text{l}$  injection onto the SP-2100 column; helium carrier gas at 30 ml/min; column temperature, 200°; injection port temperature, 200°; flame ionization detector at 250°; electrometer,  $8 \cdot 10^3$ .

### Recoveries

Recoveries were determined in two different experiments. First, synthetic samples were prepared by spiking 20.0 ml of reactant solution with 0.2–2.0  $\mu\text{l}$  of solutions containing 5.64 mg or 11.28 mg (4.0 or 8.0  $\mu\text{l}$ ) CAC per 20.0 ml dry toluene (Table I). After 10 min the samples were extracted as described above. Secondly, the air sampling apparatus was used to simulate actual sampling conditions by injecting 0.2–2.0  $\mu\text{l}$  of the above dilute CAC solutions into the inlet arm of the leading impinger.

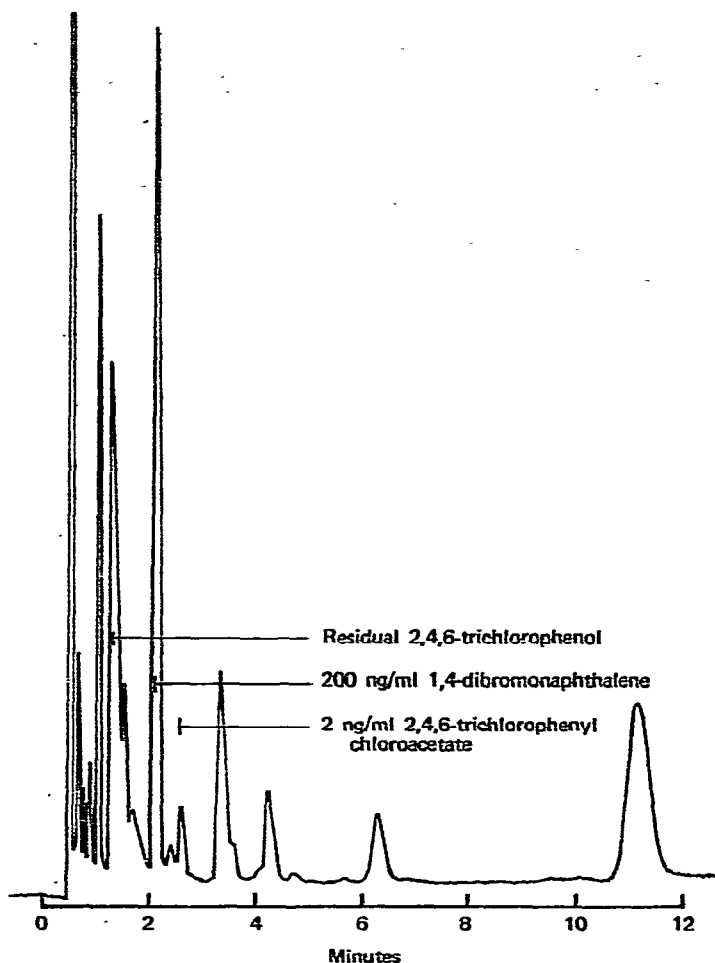


Fig. 1. Typical chromatogram. Instrument: Varian 2400 ECD ( $^{63}\text{Ni}$ ); column: 1.7 m  $\times$  2 mm I.D. glass packed with a bonded polyester packing on Chromosorb W-AW; carrier gas: argon-methane (95:5) at 30 ml/min; temperatures: column 150°, injector 175°, detector 220°; range:  $10^{-10}$ ; attenuation: 8; injection volume: 2.0  $\mu\text{l}$ .

Air was passed through the system at 0.5 l/min for 10 min after the injection. The samples were then extracted as described above (Table II).

### Spectrometry

Identification of the reaction products was performed via the direct probe on the Finnigan Model 3200 chemical ionization mass spectrometer (CI-MS). The probe temperature was increased gradually from 70° to 400°. The methane reactant gas was adjusted to yield an ion source pressure of 450  $\mu\text{m}$ .

Structures and approximate purities of the reaction products were determined by nuclear magnetic resonance (NMR) using the following conditions: 90 MHz proton NMR; reference standard, tetramethylsilane; temperature, 37°; sweep time,

TABLE I

RECOVERY DATA OBTAINED BY SPIKING CAC DIRECTLY INTO REACTANT SOLUTION

Sample no.	Equivalent concentration of TCPC added as CAC (ng/ml)	TCPC found (ng/ml)	Recovery (%) <sup>*</sup>
1	68.5	51.1	75
2	68.5	52.9	77
3	34.3	26.6	78
4	102.8	73.4	71
5	68.5	52.4	76
6	48.0	33.2	69
7	89.1	61.8	69
8	68.5	55.0	80
9	68.5	50.9	74
10	68.5	52.4	76
11	68.5	51.4	75
12	20.6	17.3	84
13	116.5	80.6	69
14	27.4	22.3	81
15	54.8	43.8	80
16	68.5	56.0	82
17	68.5	53.6	78
18	82.2	62.9	76

\* Average recovery = 76;  $\delta = 4$ ;  $2\delta = 9$ .

TABLE II

RECOVERY DATA OBTAINED BY SPIKING CAC INTO AIR SAMPLING STREAM

Sample no.	TCPC added as CAC ( $\mu\text{g}$ )	TCPC found in impinger 1 ( $\mu\text{g}$ )	TCPC found in impinger 2 ( $\mu\text{g}$ )	Carry-over (%) <sup>**</sup>	Total TCPC found ( $\mu\text{g}$ )	Recovery (%) <sup>***</sup>
1	2.06	1.40	0.05	3	1.45	70
2	1.37	0.90	0.08	8	0.98	72
3	1.37	0.79	0.08	10	0.87	64
4	0.96	0.70	0.04	5	0.74	77
5	0.41	0.34	ND <sup>*</sup>	0	0.34	82
6	1.10	0.65	0.06	9	0.71	65
7	0.55	0.35	0.04	10	0.39	70
8	1.37	0.88	0.07	7	0.95	69
9	1.78	1.15	0.02	2	1.17	66
10	1.78	1.17	0.10	8	1.27	71
11	2.06	1.39	0.04	3	1.43	70
12	1.37	0.85	0.04	5	0.89	65

\* ND = Not detected with a detection limit of 0.02  $\mu\text{g}$  TCPC in 20 ml solution.

\*\* Average carry-over = 6%.

\*\*\* Average recovery = 70;  $\delta = 5$ ;  $2\delta = 10$ .

300 sec; filter 2;  $H_1$  level 9; sensitivity 4; solvents, deuterated acetone for TCPC and deuterated chloroform for the others; concentration, 10–50% by weight; 4-mm sample tubes.

## RESULTS

The response for TCPC was shown to be linear from 2 ng/ml to at least 200 ng/ml in toluene. The response for the internal standard, DBN, was shown to be linear from 20 ng/ml to at least 460 ng/ml. The recovery results obtained by spiking CAC directly into the reactant solution (Table I) averaged  $76 \pm 4\%$  (mean  $\pm$ S.D.). When the CAC was added directly to the air stream ahead of the first impinger (Table II) the average recovery dropped to  $70 \pm 5\%$  (mean  $\pm$ S.D.). This decrease in recovery may be due to the reaction of CAC with atmospheric moisture.

To test the effect of moisture build-up in the reactant solution during sampling, six recoveries were obtained using toluene saturated with water as the solvent for the reactant solution. The average yield for these six samples dropped by 5% relative to yields obtained under the same conditions but with dry toluene.

The average carry-over of reaction product into the second impinger was 6% (Table II). This carry-over could possibly be diminished by replacing the impingers with the generally more efficient fritted-glass sparger-tubes.

The TCPC prepared in bulk and used as the authentic standard for this work was characterized by NMR, CI-MS and FID-GC. It is a white solid melting at 69.0–69.5° and yields a single peak by FID-GC. The proton NMR spectrum was consistent with the proposed structure showing a two-proton singlet at 4.85  $\delta$  corresponding to the chloroacetyl protons and another two-proton singlet at 7.78  $\delta$  corresponding to the aromatic protons. No evidence of the aromatic protons of TCP was observed at 7.38  $\delta$ . The  $M + 1$  ion ( $m/e$  273) was the base peak in the chemical ionization mass spectrum of TCPC. The isotope ratios for the  $M + 1$  ion were indicative of four chlorine atoms. No  $M + 29$  or  $M + 41$  reactant ions were observed. The major fragmentation ions were  $m/e$  196 and  $m/e$  197, each with three chlorine atoms.

The structures of TCPT, TCPA, TCPD and PFPC were likewise confirmed by NMR and CI-MS, but no recovery data were generated for these compounds.

## DISCUSSION

Acid halides react with halogenated phenols in the presence of pyridine to give stable ester derivatives which exhibit excellent gas chromatographic properties. A halogenated phenol was chosen as the derivatization reagent because: (1) the resulting ester yields a very strong response for electron capture detection, and (2) the excess reagent can be quantitatively removed by extraction. The retention times for the species of interest may be varied by choosing a different halogenated phenol (*e.g.*, using a fluorinated phenol for the less volatile aromatic acid halides, etc.).

The TCPC recovery was not increased by allowing the reaction to continue after the 10-min sampling period; however, the recovery was proportional to the excess of TCP in the reactant solution with 53% recovery for a 0.10 g/20 ml concentration and 76% recovery for a concentration of 0.14 g/20 ml. The limiting factor for increasing the recovery this way is the amount of TCP which may be removed by extraction prior to analysis by electron capture GC.

Changing the concentration of pyridine in the reactant solution had no effect on recoveries. However, if a catalytic amount of pyridine was not added, recoveries decreased drastically and were inconsistent. Pyridine is thought to catalyze this re-

action by forming an acylpyridinium chloride salt with CAC which then reacts with the phenol. Pyridine also acts as an acid scavenger in the system. TCPC was shown to be stable for at least 2 days when the reactant solution was left in contact with the 1 *N* sodium hydroxide solution; however, the presence of an excess of HCl will cause rapid hydrolysis of the ester.

It is suspected that monochloroacetic acid (MCA) will be present in finite amounts in air samples containing CAC due to water hydrolysis of the acid chloride. MCA was added to the reactant solution at concentrations as high as 50  $\mu\text{g/ml}$  with no TCPC being detected. The detection limit for TCPC was 2 ng/ml or 0.001 mole % of the MCA added. However, the corresponding chloroacetic anhydride did react with a high yield apparently forming one mole of ester per mole of anhydride added. In fact, anhydrides have been applied previously as derivatizing agents for the determination of phenols<sup>13</sup>.

The detection limit ( $2.5 \times$  noise) for CAC is 1 ng/ml reaction solution (2.4 ng TCPC/ml). This corresponds to 1 ppb CAC in air when using 20 ml of reactant solution and 5 l of air. The absolute detection limit can conceivably be lowered to the sub-ppb range, if needed, by increasing the air volume collected.

The bonded polyester gas chromatographic column packing used in this procedure was prepared at The Dow Chemical Co. Publication of the preparation and applications of this and other bonded chromatographic packings is planned for the near future<sup>14</sup>. This packing permits significantly more efficient separations as compared to conventional coated packings and exhibits shorter retention times for most compounds which allows the use of much lower column temperatures. Conventional packed columns can be substituted in this procedure but will result in longer analysis times and less sensitivity.

## CONCLUSIONS

The proposed method is a sensitive and specific procedure for the determination of chloroacetyl chloride in air. Recoveries in two different experiments were  $76 \pm 4\%$  (mean  $\pm$  S.D.) and  $70 \pm 5\%$  (mean  $\pm$  S.D.). A quantitative detection limit ( $2.5 \times$  noise) of 1 ppb can be achieved with a 5-l air sample. This technology may be feasible for the determination of other acid halides in air.

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