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Note

Identification of bromotetrachlorophenol in commercial pentachlorophenol samples

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Over 50 million pounds of pentachlorophenol (PCP) are produced each year in the U.S.A.[1] for use as a wood preservative, fungicide and bacteriacide. The National Toxicology Program (NTP) initiated toxicity studies on this compound because of the high potential for human exposure resulting from the widespread use of PCP. Three commercial samples of PCP, a purified, an intermediate, and a technical grade preparation, were selected for study. Prior to toxicity testing, these three samples were investigated to determine the identities and concentrations of any manufacturing by-products which could compromise the toxicity study. The presence of toxic manufacturing by-products of PCP such as chlorinated dibenzodioxins, dibenzofurans, diphenyl ethers, biphenyls, toluenes, benzenes, and related phenolic compounds, has been well documented[2]. However, brominated compounds have not been reported previously as by-products of PCP synthesis. This study summarizes the identification and quantitation of 2-bromo-3,4,5,6-tetrachlorophenol (BTCP) as a major contaminant in all three commercial preparations.

EXPERIMENTAL

Reagents

N-Methyl-N-nitro-N-nitrosoguanidine (97%), 2,3,5,6-tetrachlorophenol (98%) and 3,4,5,6-tetrachlorophenol (97% purity) were purchased from Aldrich. All organic solvents and additional reagent chemicals were ACS reagent grade.

Sample preparations

Preparation of methylated derivatives. Diazomethane derivatizing agent was freshly prepared from N-methyl-N-nitro-N-nitrosoguanidine, MNNG, according to the procedure described by McKay and co-workers[3,4].

PCP (0.1 g) was placed in a 60-ml septum vial and dissolved in diethyl ether (2–5 ml). Diazomethane reagent (10 ml) was added and the vial sealed. One hour later an additional 5 ml of diazomethane was added, the vial again sealed and allowed to sit for 24 h. The next day, 1.0% acetic acid was added dropwise until the excess

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diazomethane was consumed. The methylated sample was then dried under a gentle stream of dry nitrogen. The residue was dissolved in 5 ml of benzene, quantitatively transferred to a 10-ml volumetric flask and diluted to volume with benzene.

Preparation of non-methylated PCP samples. PCP (0.1 g) was weighed into a 10-ml volumetric flask and diluted to volume with benzene.

Synthesis of bromotetrachlorophenol standards

2-Bromotetrachlorophenol was synthesized from 3,4,5,6-tetrachlorophenol by a procedure similar to that described by Scott[5]. The following modifications were made. The excess brominating reagent was reduced by titration with thiosulfate. The aqueous reaction mixture was then extracted twice with toluene. The toluene solutions were combined to yield a final solution theoretically containing 30 mg/ml of 2-bromo-3,4,5,6-tetrachlorophenol. 4-Bromotetrachlorophenol was also synthesized from 2,3,5,6-tetrachlorophenol following this same method. The identities of the two bromotetrachlorophenol isomers were confirmed by gas chromatography–mass spectrometry (GC–MS). Additionally, each compound yielded a single peak by GC.

Instrumental

BTCP was identified and quantitated in the three PCP samples by capillary GC–MS. Full mass scan and high resolution GC–MS techniques were used.

GC–MS analyses were performed on a Finnigan MAT 311-A spectrometer interfaced via a DB-5, 15 m × 0.25 mm I.D. J&W fused-silica capillary column to a Varian 2700 gas chromatograph equipped with a J&W on-column injection system. A temperature program of 80 to 325°C at 8°C/min with a 2-min initial hold was used. Helium carrier gas at a linear velocity of 15 cm/sec was used. The source temperature was maintained at 270°C. The transfer and helium separator temperatures were held at 300°C. Electron energy was 70 eV with a 2.0 mA emission current. The accelerator and electron multiplier voltages were 3000 V and −1600 V, respectively. Resolution was 750 for full mass scan and 5000 (10% valley) and 10,000 (50% valley) for high-resolution GC–MS. The data type was exponential centroid (1.18 sec/scan) in the 50–500 mass range. An Incos 2400 data system was used for data collection.

RESULTS

The reconstructed ion-current chromatograms (RICs) of the non-methylated and derivatized samples of technical grade PCP are shown in Figs. 1 and 2, respectively. The RICs of the purified and intermediate grades of PCP are not included but resembled the RICs presented for the technical grade sample. The impurity of interest eluted on the trailing edge of the major peak. The peaks representing the major component and a known impurity, tetrachlorophenol, are labeled on the RICs for elution order comparison.

Mass spectra of the impurity in the methylated and non-methylated technical grade PCP samples are presented in Figs. 3 and 4, respectively. A mass spectrum of the synthesized 2-bromo-3,4,5,6-tetrachlorophenol is shown in Fig. 5.

The molecular ion for the non-methylated impurity was observed at m/z 308. Specific ion plots showed high intensity ions at m/z 308, 228, 165, 130, 95 and 60. The fairly intense ion at m/z 228, $[M-80]^{+\cdot}$, suggested that bromine was present and

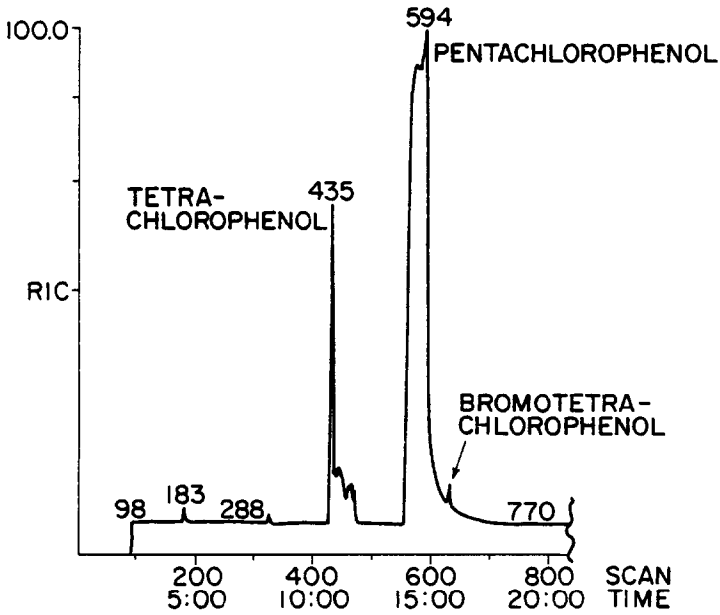

Fig. 1. Reconstructed ion-current chromatogram for non-methylated pentachlorophenol sample. Time in min.

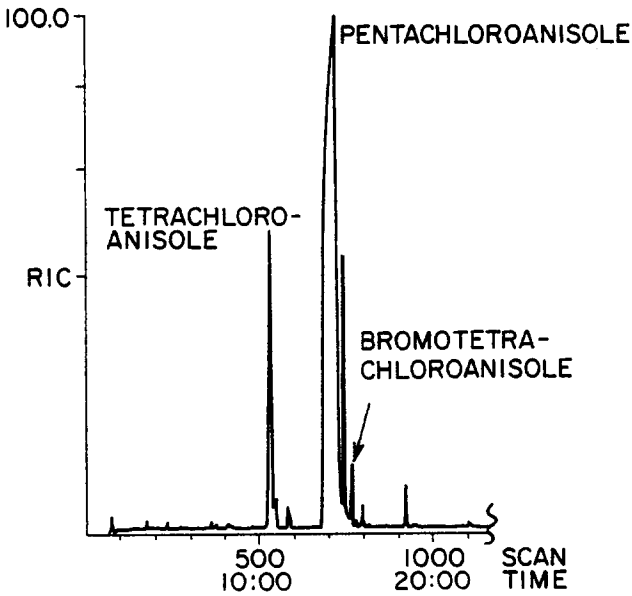

Fig. 2. Reconstructed ion-current chromatogram for derivatized pentachlorophenol sample.

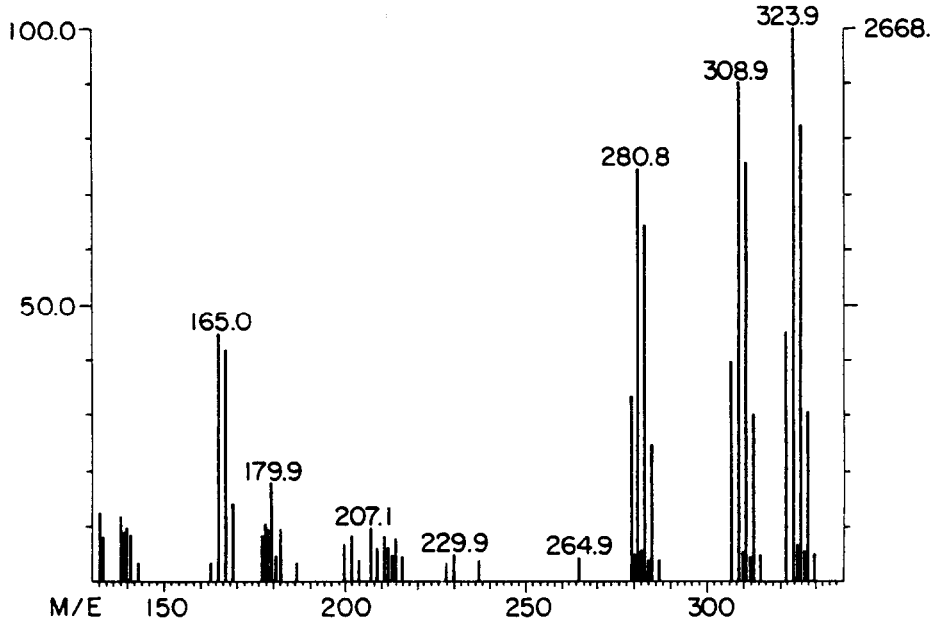

Fig. 3. Mass spectrum for derivatized impurity.

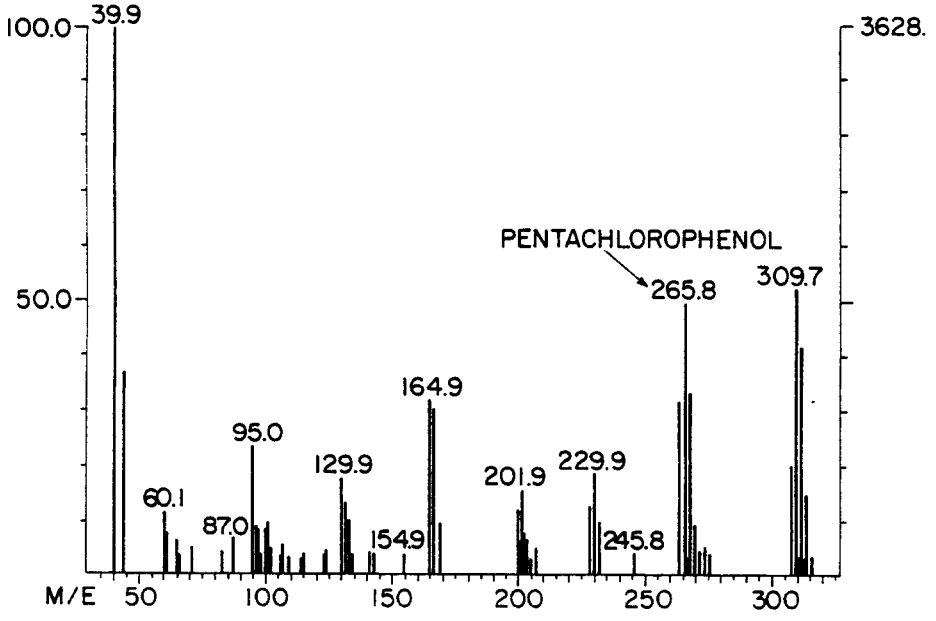

Fig. 4. Mass spectrum for untreated impurity.

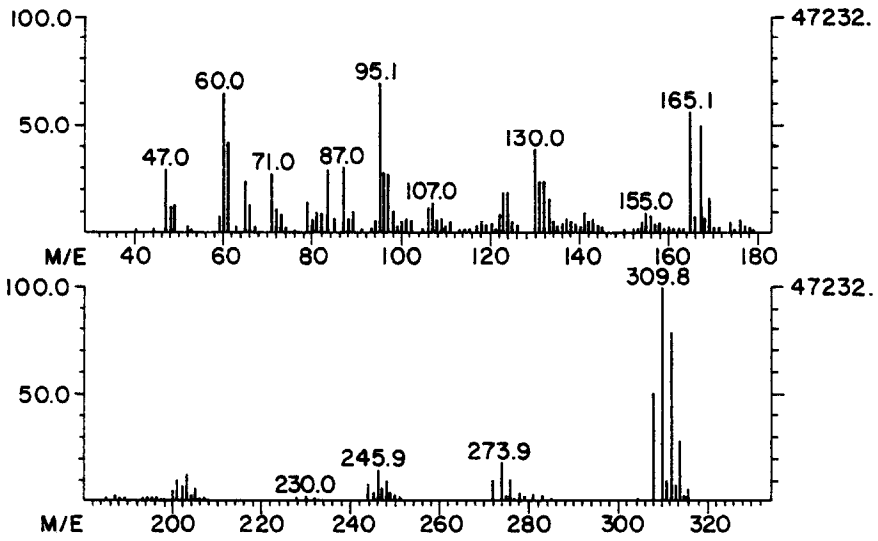

Fig. 5. Mass spectrum for 2-bromo-3,4,5,6-tetrachlorophenol standard.

fragmented as hydrogen bromide. This initial loss of 80 atomic mass units (a.m.u.) from the molecular ion also indicated that the bromine was *ortho* to the hydroxyl group. The loss of 80 a.m.u. from the $[M]^+$ was also observed for the synthesized 2-bromo-3,4,5,6-tetrachlorophenol but not the 4-bromo-2,3,5,6-tetrachlorophenol. Four chlorines could be accounted for in the fragmentation scheme. The loss of 63 a.m.u. from *m/z* 228 was probably due to loss of a CClO unit, or loss of CO [*m/z* 228 → *m/z* 200) followed by loss of a chlorine (*m/z* 200 → *m/z* 165). Three consecutive losses of 35 a.m.u. (*m/z* 165 → *m/z* 130 → *m/z* 95 → *m/z* 60) accounted for the three additional chlorines.

Specific ion plots revealed relatively weak ions at *m/z* 272, 244 and 209. A loss of 79 a.m.u. from the ion observed at *m/z* 209 to yield an ion at *m/z* 130 again indicated bromine was present. The ion observed at *m/z* 272 indicated a loss of hydrogen chloride from the molecular ion (*m/z* 308 → *m/z* 272). The remaining three chlorines were observed at *m/z* 244 → *m/z* 209 and *m/z* 130 → *m/z* 95 → *m/z* 60.

These same ions were also observed in the mass spectrum of the 2-bromo-3,4,5,6-tetrachlorophenol standard.

The theoretical ratio of $[M]^+$-$[M+2]^+$-$[M+4]^+$-$[M+6]^+$ for four chlorines and one bromine is 44:100:84:33, which compares well to the isotope ratio observed for the molecular ion cluster of the impurity, 43:100:84:32. The isotope clusters and intensities for the 2-bromo-3,4,5,6-tetrachlorophenol standard were similar as well, 44:100:84:32.

The exact mass of the impurity was determined by high resolution GC–MS. The required mass for the molecular ion of bromotetrachlorophenol is 307.796. The observed mass for the impurity molecular ion, determined by peak matching, was 307.795 (n = 3). The difference between the required and observed mass was only 1.0 ma.m.u.

A spiking experiment was performed to confirm retention time data. The im-

purity peak representing BTCP was enhanced when the technical grade PCP sample was spiked with the 2-bromo-3,4,5,6-tetrachlorophenol standard.

The concentration of BTCP in the three PCP samples was *ca.* 0.1% when quantitated by GC–MS peak area comparison against the synthesized standard (assuming quantitative yield). Based on this quantitation data, the calculated bromine content would be *ca.* 0.03% in each of the three samples. Elemental analysis for bromine in the technical grade PCP performed by Galbraith Labs., was 0.03%, in agreement with the calculated value.

DISCUSSION

The results obtained from this analysis suggest that bromotetrachlorophenol may be a common contaminant in PCP preparations. BTCP has probably not been detected in the numerous analyses concerned with the identification of PCP manufacturing by-products because it is not resolved from the PCP peak by traditional chromatographic methods. Recent developments in capillary GC and GC–MS provided the additional resolution needed to separate the two components.

The bromine found in BTCP is probably introduced as an impurity in the chlorine sources used for the synthesis of PCP. The two most widely used methods for production of PCP are the electrophilic chlorination of phenol in the presence of a catalyst at elevated temperatures, and the alkaline hydrolysis of pentachlorobenzene.

The identification of BTCP in these samples is significant because of its potential toxicity and the high probability of human exposure to this compound due to the widespread use of PCP. The quantitation of BTCP at *ca.* 0.1% in all three grades of PCP is also significant because it indicates that present purification methods are inadequate at removing this compound from the bulk samples.

REFERENCES

1 *Synthetic Organic Chemicals, United States Production and Sales*, U.S. International Trade Commission, USITC Publication No. 776, 1974, p. 185.
2 B. A. Schmetz, P. A. Keeler and P. J. Gehring, *Toxicol. Appl. Pharmacol.*, 28 (1974) 151.
3 A. F. McKay, *J. Amer. Chem. Soc.*, 70 (1948) 11974.
4 A. F. McKay *et al.*, *Can. J. Res.*, 28 (1950) 683.
5 W. Scott, in Furnman and Howell (Editors), *Standard Methods of Chemical Analysis*, Vol. II, Part D, 1939, p. 2253.