INTRODUCTION:
The profiling of synthesis impurities is of utmost importance in forensic chemistry. This poster presents an overview of impurities formed during the peracid oxidation of anethole (the major component of anise oil) in the synthesis of PMA.

SYNTHESIS:
- **Performic acid**: Created by adding 6.8 g 30% H2O2 to 24.0 g HCOOH.
- **Peracid oxidation**: The performic acid was added to a solution of 6.0 g anethole in 30 mL acetone at such a rate that the temperature did not exceed 38°C. After addition, reaction was allowed to continue for 12 hours.

  - Extracting the reaction mixture with 2 x 50 mL dichloromethane and washing the organic phase with 50 mL water yielded 8.2 g of a yellow oil.
  - The glycol (esters) are refluxed in a mixture of methanol and dilute sulfuric acid to obtain the ketone 4-methoxyphenyl-2-propanone, a precursor of 4-methoxyamphetamine (PMA) in the Laboratory reaction.

**FIGURE 2**: A typical chromatogram of a peracid oxidation reaction mixture (split 1:50). Substances A-D are formed due to oxidative cleavage of anethole and are discussed in Fig. 3; E is 4-methoxyphenyl-2-propanone. Substance X is a tetrasubstituted tetrahydrofuran (THF), of which the formation is detailed in Fig. 4.

**FIGURE 3**: The reaction scheme shows the oxidative cleavage of anethole, yielding anisaldehyde (A), the latter is converted to O-formyl-4-methoxyphenol (B). The glycol (esters) are refluxed in a mixture of methanol and dilute sulfuric acid to obtain the ketone 4-methoxyphenyl-2-propanone, a precursor of 4-methoxyamphetamine (PMA) in the Laboratory reaction.

**Mass spectra**: methyl chavicol (A), 4-methoxyphenol (B), O-formyl-4-methoxyphenol (C) and anisaldehyde (D)

**FIGURE 4**: The intermediary epoxide (cf Fig. 1) is hydrolyzed to a stable carbocation, which is able to react with anethole itself to form an instable intermediate. The latter is converted to a tetrasubstituted THF (X) via an intramolecular reaction.

**INSTRUMENTATION:**
- GC/MS analysis by Agilent 6890 Plus GC coupled to Agilent 5973N MSD.
- **Column**: VF-5MS factorFour (30 m x 0.250 mm x 0.25 µm); **carrier gas**: He, flow rate of 1 mL/min.
- **oven programming**: 50°C (1 min), 35°C/min to 100°C, 10°C/min to 270°C (20 min).
- **MSD**: EI mode (70 eV), 36-500 amu, 4.00 min solvent delay.

**DISCUSSION:**

**IMPURITY FORMATION**

1. **Oxidative cleavage of anethole**
The oxidative cleavage of anethole will yield anisaldehyde, which in turn is converted to O-formyl-4-methoxyphenol according to the Baeyer-Villiger reaction. The latter substance is hydrolyzed to 4-methoxyphenol. Screening of the reaction mixture also demonstrates the presence of methyl chavicol (also present in anise oil and MS similar to anethole).

2. **2,4-Dimethyl-3,5-bis(4'-methoxyphenyl) tetrahydrofuran**
This substituted tetrahydrofuran (THF) is formed during the peracid oxidation of anethole. The anethole epoxide (cf Fig. 1) can convert spontaneously to a carbocation intermediate, which in turn can react with anethole to form the tetrasubstituted THF (cf Fig. 4).

Theoretically, this THF can have 4 different diastereomers (cf MS Fig. 4, denominated as X). The chromatogram and extracted ion chromatogram for m/z 312 in Fig. 2 illustrates that the applied capillary column separates the THF in 3 diastereomers (cf Fig. 2).

**CONCLUSION:**

Peracid oxidation impurities are formed via different routes. Both 4-methoxyphenol (Fig. 3B) and the tetrasubstituted THF (Fig. 4X) are specific for the peracid oxidation of anethole and are utile markers for forensic chemists.