# Detecting Disease through Breath: The Power of Chemoselective Reagents

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## Introduction

One of the greatest problems facing modern cancer treatments is developing efficient non-invasive cancer detection methods. Regarding these methods, chemical analysis of volatile organic compounds (VOCs) in exhaled breath has shown potential.[1] Many of these VOCs are carbonyl compounds, mainly ketones and aldehydes; for example, formaldehyde, acetaldehyde, and acrolein. These carbonyls are included in products of gas emissions from industry, traffic, and other pollution. They are both an environmental cause of human disease and can result from internal diseases. Many of them are detrimental to human health and have been shown to contribute to cardiovascular disease after continuous exposure.[2] The VOCs of interest for my project are derivatives of aldehydes, which are products of lipid peroxidation in the body. High concentrations of these aldehydes in exhaled breath can be linked to cancer.

Therefore, the synthesis and production of chemical reagents that selectively react with these aldehydes would have great potential to be detected as a biomarker of disease in the body. This approach has led to several viable products. A process was developed to use a promising and specifically reactive compound with carbonyl, 2-(aminooxy) ethyl-*N*,*N*,*N*-trimethylammonium iodide (ATM).[3] ATM was synthesized in the oxidation of air samples to allow for the detection of ATM-carbonyl. The use of the ATM reagent to detect lipid peroxidation derived aldehydes through this process holds great promise for the detection of disease.

## Methodology & Results

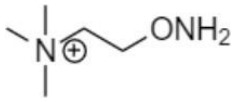


**Figure 1** – *ATM.*

ATM was used to test for these aldehydes in air samples through usage of a silica microreactor. The microreactor chip consisted of an interior of micropillars which were coated in a set amount of ATM- based salt in a methanol bath. Ambient air was then passed through the pillars. The ATM was shown to react readily with both ketones and aldehydes via oximation reactions, where a positive charge (from ATM's ammonium) is added onto the ATM-carbonyl adducts. This ionization allowed the aldehydes in the air samples to combine with ATM in an adduct structure, and therefore, the detection of the adduct via Mass Spectroscopy (MS).

[1] Hanna, G. B.; Boshier, P. R.; Markar, S. R.; Romano, A. Accuracy and Methodologic Challenges of Volatile Organic Compound-Based Exhaled Breath Tests for Cancer Diagnosis: A Systematic Review and Meta-Analysis: A Systematic Review and Meta-Analysis. *JAMA Oncol.* 2019, *5* (1), e182815.
[2] Secondhand Smoke Exposure and Cardiovascular Effects; The National Academies: Washington, DC, 2010; p 228
[3] Li, M.; Li, Q.; Nantz, M. H.; Fu, X.-A. Analysis of Carbonyl Compounds in Ambient Air by a Microreactor Approach. *ACS Omega* 2018, *3* (6), 6764–6769.

## Conclusions & Discussion

Measurement of these specific aldehydes through this process of oximation and subsequent ionization of carbonyl adducts has proven fruitful, allowing the levels of many dangerous compounds to be determined in a relatively quick and simple method. As mentioned in the results, the ATM reagent binds to both aldehydes and ketones, although the aldehydes are the compounds that want to be measured. Therefore, a reagent that would more selectively react with aldehydes would be a worthy endeavor.

The development of ATM-carbonyl through this process is a powerful idea from the field of chemistry and is promising for the quick and non-invasive detection of cancer. Current methods of cancer detection are physically taxing for many individuals, and the inconvenience alone dissuades many people from getting more regular testing. If more methods existed that would allow a patient to quickly, and through little trouble, learn of any signs of cancer, imagine how many more cases would be caught early on. These chemical tests could be the future for how we monitor cancer, and hopefully result in early treatment and longer life expectancies.