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Colorimetric Recognition of Aldehydes and Ketones

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Abstract: *A colorimetric sensor array has been designed for the identification of and discrimination among aldehydes and ketones in vapor phase. Due to rapid chemical reactions between the solid-state sensor elements and gaseous analytes, distinct color difference patterns were produced and digitally imaged for chemometric analysis. The sensor array was developed from classical spot tests using aniline and phenylhydrazine dyes that enable molecular recognition of a wide variety of aliphatic or aromatic aldehydes and ketones, as demonstrated by hierarchical cluster, principal component, and support vector machine analyses. The aldehyde/ketone-specific sensors were further employed for differentiation among and identification of ten liquor samples (whiskies, brandy, vodka) and ethanol controls, showing its potential applications in the beverage industry.*

Development of a sensitive, rapid, and inexpensive method for in situ determination of aldehydes and ketones has many important applications, including chemical toxin detection, security screening, food inspection, and disease monitoring. As examples: formaldehyde is a significant indoor pollutant and known human carcinogen; acetone and acetoacetate are indicators of ketosis in diabetics; a variety of aliphatic or aromatic aldehydes and ketones (e.g., vanillin, diacetyl, and furfural are produced during fermentation and aging of beers and liquors) contribute heavily to the aroma of many beverages.[1]

The optoelectronic nose, a highly portable chemical analyzer that tracks the pattern-based response of colorimetric sensor arrays, has recently emerged as a versatile approach for the identification and differentiation of chemically diverse liquid or gaseous analytes.[2] The pattern of color changes in an array of cross-reactive, chemically responsive dyes are chemical "fingerprints" unique to each odorant or odorant mixture, in a fashion reminiscent of the pattern of olfactory receptors response in animals. Prior electronic nose technologies[3] for aldehyde/ketone detection have used metal oxides,[4] organic fluorescent or colorimetric probes,[5] metallic nanoparticles[6] and carbon-based resistors.[7] The sensors used by traditional electronic noses are inherently built into the electronics and, to be reversible and reusable, must utilize only weak interactions (primarily physisorption) between the sensors and the analytes. The necessity of weak interactions, however, limits sensitivity, diminishes selectivity, and makes them susceptible to environmental interference (e.g., changes in humidity). Such systems generate low dimensional data (typically with $>90\%$ of the total variance in a single dimension), which substantially limits differentiation among similar analytes.[2a,3c]

In the past decade, our group has developed inexpensive, disposable colorimetric sensor arrays, which in essence are digitalized multidimensional extensions of litmus paper.[2a] These sensor arrays use diverse chemoresponsive dyes in which color changes originate from a wide range of dye–analyte interactions, including Lewis and Brønsted acid-base interactions, redox reactions, vapochromic polarity interactions, as well as physisorption. Quantitative measurement of color changes upon exposure to volatiles by digitally imaging provides a highly multidimensional response unique to the volatiles' interactions with the sensor elements. Colorimetric sensor arrays have proven applications to environmental monitoring,[8] medical diagnosis,[9] security screening,[10] and food safety.[11]

In order to improve our discriminatory power among volatile carbonyls (e.g., aldehydes, ketones, and esters), we have now explored specific amine-containing indicators for the selective vapor discrimination of aliphatic or aromatic aldehydes and ketones at ppm and sub-ppm levels. Our newly designed colorimetric formaldehyde or ketone detection methods are based on nucleophilic addition to a carbonyl group by an amine in the formation of an imine, which gives a difference UV-vis absorption band.[5b] Inspired by qualitative spot tests, such as Brady's or Schiff test,[12] we chose three aniline or phenylhydrazine compounds as the sensor components: 2,4-dinitrobydrazine, 4,4′-azodianiline, and pararosaniline (Figure 1 a).

To optimize the sensor response, printable chemically responsive inks were formulated from one of three amine-based dyes with added acids (see Figure 1 b and the Materials and Experimental Section in the Supporting Information). The arrays were then exposed to pre-mixed vapors of aldehydes or ketones at desired concentrations and scanned using our recently developed handheld device[13] (Figures S1 and S2). It is interesting to find that sulfurous acid, the standard reagent used in Schiff tests,[12] is unable to induce the characteristic color change in the sensor array, presumably due to the decomposition of H_2SO_3 from the dehydrolysis and loss of SO_2 during the sensor array drying and storage (see Scheme S1 for the proposed mechanism). The use of sulfuric acid or *p*-toluenesulfonic acid, however, enhances the sensor response substantially (Figure S3).

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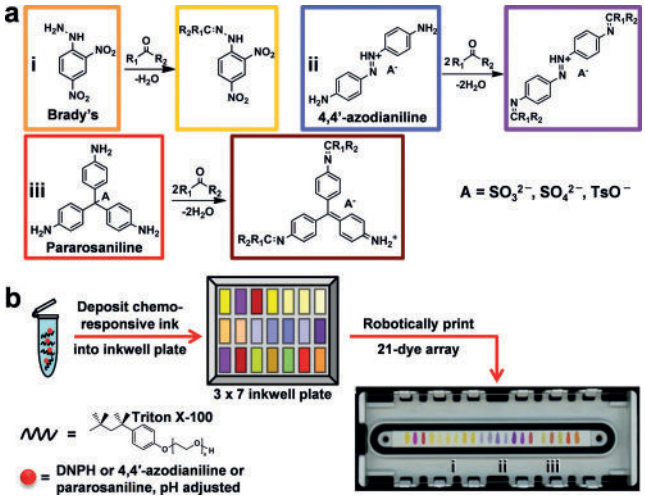

Figure 1. Designed aldehyde/ketone-responsive colorimetric sensor array. a) Three aldehyde/ketone-responsive dyes 2,4-dinitrobydrazine (i), 4,4′-azodianiline (ii) and pararosaniline (iii) with their color change reactions with carbonyl compounds. b) Preparation of a linearized 21-element sensor array.

The final sensor array for detection of aldehydes and ketones uses these carbonyl-sensitive dyes in optimized formulations and contains 21 bar spots (see Figure 1b and Table S1). The sensor response of 7 aldehydes and 8 ketones at 25 and 0.5 ppm, respectively were tested in quintuplicate; the responses are shown in Figure 2. The sensor array responses provide easily distinguishable patterns for each carbonyl. The intensity of color change is largely dependent on the reactivity of the different aldehydes and ketones during the nucleophilic addition: i) aldehydes are generally more responsive than ketones; ii) aliphatic aldehydes more than aromatic ones; iii) reactivity diminishes as the length of the carbon chain grows. These trends in reactivity originate from the electrophilicity of carbonyl groups in the various analytes.

As a method for quantitative determination of aldehydes or ketones, sensor responses of six representative analytes were evaluated at their PEL concentrations for 2 min exposures. Based on the array response curves near the PEL, limits of detection (LODs) were extrapolated to an analyte concentration where S/N = 3. Table 1 lists our estimated LODs (ranging from 40 to 840 ppb), which are all below 10% of their respective PELs and substantially better than other colorimetric or chemiresistor methods, which are reported at ppm levels.[7,14] We observe very little response in our arrays to changes in humidity (Figure S4), in large part due to our use of hydrophobic formulations on hydrophobic membranes.

Table 1: The extrapolated limits of detection (LODs) of six analytes based on results of 2 min exposure and their ratios to permissible exposure levels (PELs).

	PEL [ppm][a]	LOD [ppm]	LOD/PEL [%]
Formaldehyde	0.75	0.04	5.3
Acetaldehyde	200	0.22	0.11
Furfural	5	0.43	8.6
Methyl ethyl ketone	200	0.32	0.16
Phenylacetone	200	0.60	0.30
Cyclohexanone	50	0.84	1.7

[a] PEL = permissible exposure level, 8 h day^{-1}.

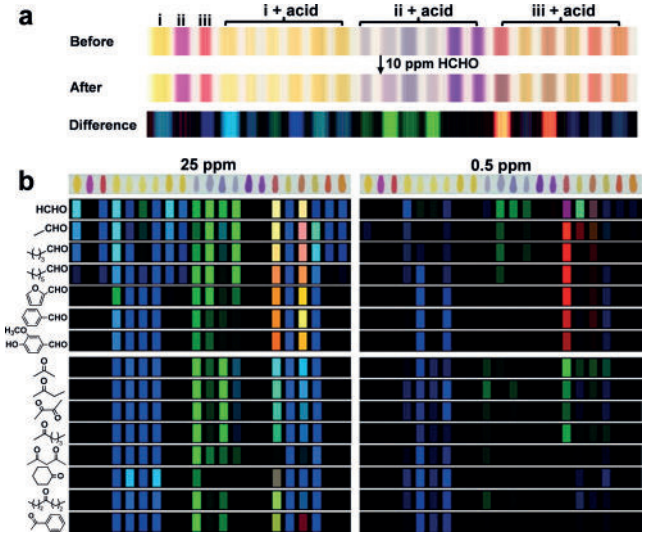

Figure 2. Sensor response to aldehydes and ketones. a) Before-exposure, 2 min after-exposure and color difference profile of the array for a typical measurement on 10 ppm formaldehyde. The array components were described in Table S1. b) Color difference profiles of 7 aldehydes and 8 ketones at 25 and 0.5 ppm after 2 min exposure; average of 5 replicates with RGB color range expanded for visualization from 3 to 8 bits per color (i.e., range of 3–10 expanded to 0–255).

To evaluate the differentiating capability of the sensor array, a standard statistical method, hierarchical cluster analysis (HCA),[15] was employed. As shown in Figure 3, successful discrimination was achieved among 15 aldehydes and ketones at two vapor concentrations (plus a N_2 control). In clustering 155 total trials, only one error occurred (specifically, one pentanal trial mistaken for heptanal): i.e., the overall accuracy of the HCA of these data is >99.4%. Remarkably, the categories shown in the dendrogram are consistent with the structural and electronic properties of the analytes: the aliphatic aldehydes produce one cluster, aromatic ones another, and all the ketones are tightly associated, at both 25 ppm and 0.5 ppm levels.

In order to measure the dimensionality of our data, principal cluster analysis (PCA, an unsupervised, model-free method[15]) was used. The colorimetric sensor array probes a wide range of intermolecular interactions, and so a high level of dispersion was anticipated. The PCA scree plot (Figure S5) shows that 19 principal components (PCs) are needed to account for 95% of the total variance of the data.

Unlike unsupervised clusterification methods (e.g., HCA and PCA), support vector machine analysis (SVM) is a predictive method that is designed to classify incoming data that is not part of a training database. SVM classification is based on pairwise class prediction and focuses on the data most likely to be misclassified (i.e., data vectors near the decision boundary for any given class pair, the so-called

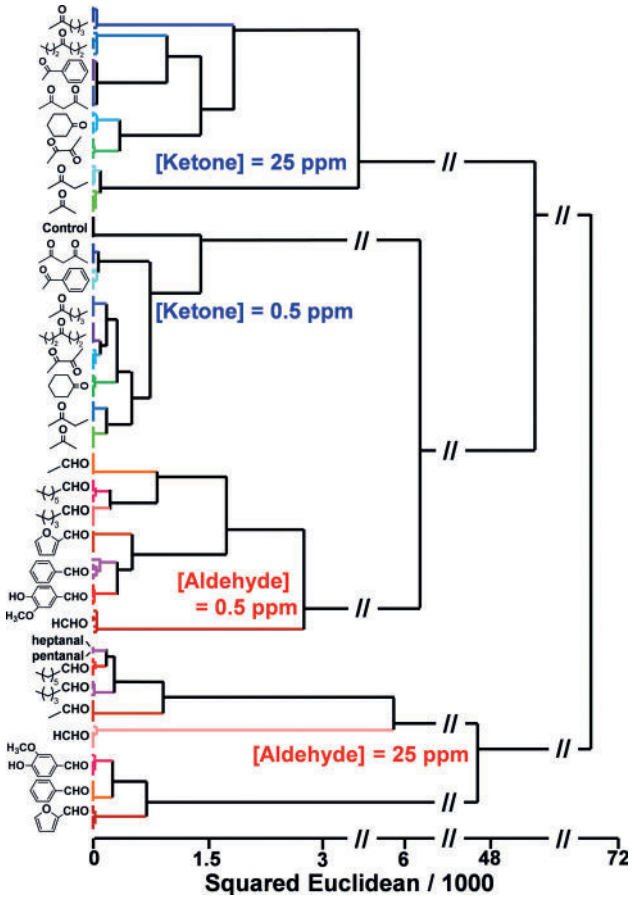

Figure 3. Hierarchical cluster analysis (HCA) for sensor array response of 7 aldehydes and 8 ketones at 25 and 0.5 ppm and a N_2 control. All analytes were run in quintuplicate trials. Only one error in clustering was observed: one trial of pentanal at 25 ppm mistaken as heptanal.

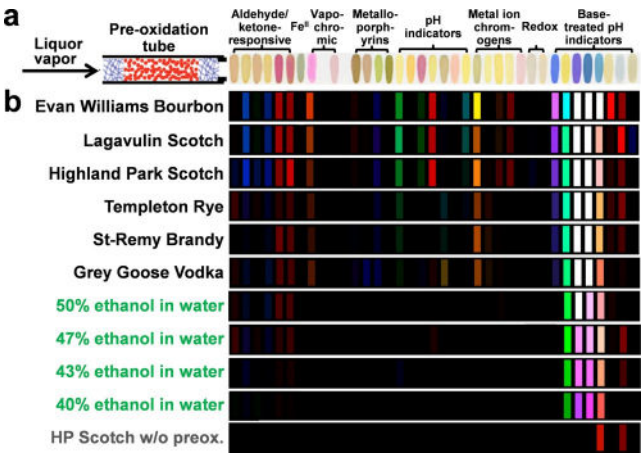

Figure 4. a) Scheme showing the pre-oxidation of liquor vapors before exposing to the sensor array. b) 2-min sensor array response with pre-oxidation to six liquor samples and four ethanol controls, as well as the Highland Park (HP) Scotch without pre-oxidation; each pattern is the average of three independent trials; color range expanded from 3 to 8 bits per color.

"support vectors") to create optimized decision boundaries that best separate the data for each given pair of classes in high dimensional space. The result of each pairwise comparison gives a vote that is used to determine the final classification.[10a,16] The results of SVM analysis are shown in Table S2: SVM analysis shows no errors observed in 155 trials using a standard leave-one-out permutation model, i.e., the error rate is $< 0.65\,\%$.

Various other classes of VOCs were tested to assess the selectivity of our aldehyde and ketone specific sensor array. As hoped, very little response is observed to alcohols, amines, carboxylic acids, esters, ethers, halocarbons, nitriles, and sulfides, even at higher concentrations (Figure S6). The sensor array is probing primarily the electrophilicity of carbonyl groups, and so these results are inherent in the lower electrophilicity of these other classes of compounds.

There remains substantial interest in the analytical community for quality control and assurance of alcoholic beverages.[17] For the identification of liquors, we therefore incorporated our newly developed aldehyde/ketone-sensitive dyes in a broader, 36-element colorimetric sensor arrays (Table S3, Figure 4), integrated with pre-oxidation reagent (i.e., H_2CrO_4/Al_2O_3, Figure 4a). The pre-oxidization of liquor vapors converts ethanol into acetaldehyde or acetic acid which are more responsive to the sensor array.[18] This more generalized sensor array is responsive not only to aldehydes/ketones, but also to a wider range of VOCs, and contains chemoresponsive sensors including pH indicators for carboxylic acids, Lewis acid/base indicators (for sulfides, amines, etc.), redox indicators for polyphenols, and vapochromic dyes for ethanol.

This generalized sensor array was tested against the complicated volatile mixtures present in the headspace gas of each liquor. Collected in triplicate trials, the scaled color difference maps shows distinctive sensor response patterns unique to each liquor or ethanol control (Figure 4b). Each liquor has its own distinct aroma produced during production and aging in wood barrels that arise from a highly diverse set of compounds including esters, disulfides, fatty acids, aldehydes, ketones, monoterpenes and phenols.[1] Aqueous ethanol controls over a range of relevant ethanol concentrations were also tested; these show relatively simple response patterns (Figure 4b) uncomplicated by the presence of any congeners. The color difference profiles of the liquors and ethanol controls are all easily differentiated. HCA (Figure S7) and 3D PCA (Figure S8) show excellent differentiation among all samples and permit clear separation of ethanol controls from the liquors.

In conclusion, a colorimetric sensor array has been developed for the identification of volatile aldehydes and ketones at ppb levels. The sensor components were derived from classical spot tests and optimized to induce strong changes in color rapidly upon exposure to aldehydes or ketones. A handheld reader of the sensor arrays allows for the discrimination of aliphatic or aromatic aldehydes and ketones within 2 minutes, with high accuracy of classification $> 99\,\%$. A generalized sensor array was tested against not only individual compounds but also against the complex odors of liquor samples, revealing its promising applications in the food and beverage industry for quality control and assurance.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: aldehydes · colorimetric sensor arrays · ketones · liquors

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