

Colorimetric Recognition of Aldehydes and Ketones

Zheng Li, Ming Fang, Maria K. LaGasse, Jon R. Askim, and Kenneth S. Suslick*

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-dinitrohydrazine, 4,4'-azodianiline, and pararosani-line (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 H₂SO₃ from the dehydrolysis and loss of SO₂ 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).

[*] Dr. Z. Li, M. Fang, Dr. M. K. LaGasse, Prof. Dr. K. S. Suslick
Department of Chemistry
University of Illinois at Urbana-Champaign
600 S Matthews Ave, Urbana, IL 61801 (USA)
E-mail: ksuslick@illinois.edu

Dr. J. R. Askim
National Institute of Standards and Technology
Gaithersburg, MD (USA)

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:
<https://doi.org/10.1002/anie.201705264>.

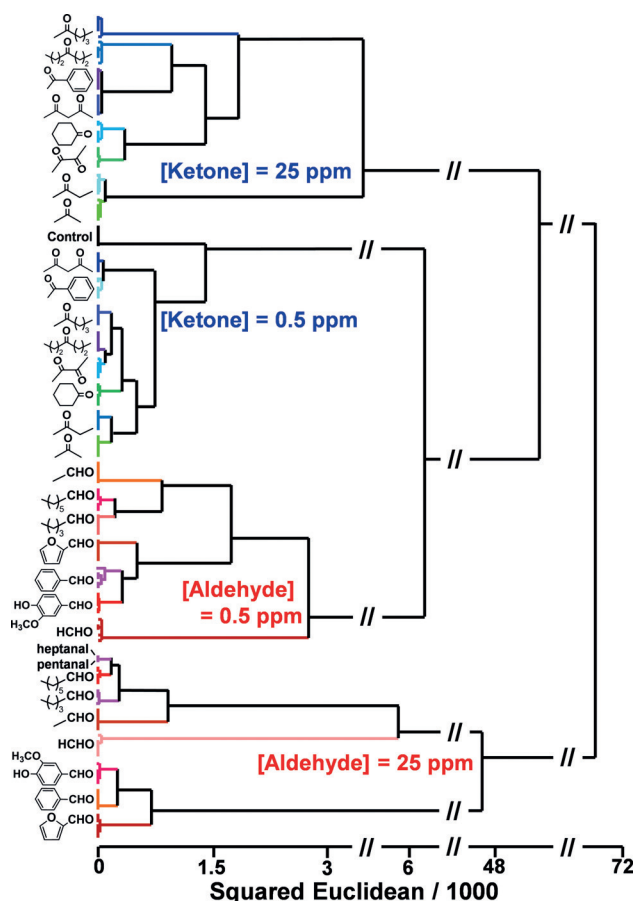


Figure 3. Hierarchical cluster analysis (HCA) for sensor array response of 7 aldehydes and 8 ketones at 25 and 0.5 ppm and a N_2 control. All analytes were run in quintuplicate trials. Only one error in clustering was observed: one trial of pentanal at 25 ppm mistaken as heptanal.

“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-oxidation of liquor vapors converts ethanol into acetaldehyde or acetic acid

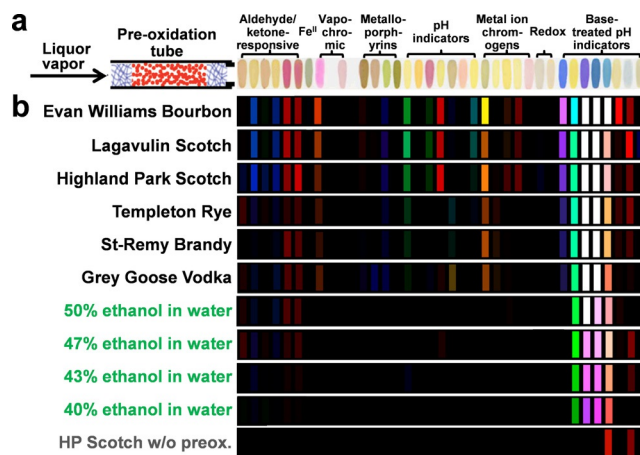


Figure 4. a) Scheme showing the pre-oxidation of liquor vapors before exposing to the sensor array. b) 2-min sensor array response with pre-oxidation to six liquor samples and four ethanol controls, as well as the Highland Park (HP) Scotch without pre-oxidation; each pattern is the average of three independent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

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 vapo-chromic 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.

Acknowledgement

We acknowledge funding in part through a Senior Scientist Mentor Award of the Camille and Henry Dreyfus Foundation. K.S.S. wishes to recognize the happy occasion of the 85th, 85th, 80th, and 75th birthdays of his mentors, Professors James P. Collman, Fred C. Anson, John I. Brauman, and Robert G. Bergman, respectively.

Conflict of interest

The authors declare no conflict of interest.

Keywords: aldehydes · colorimetric sensor arrays · ketones · liquors

How to cite: *Angew. Chem. Int. Ed.* **2017**, *56*, 9860–9863
Angew. Chem. **2017**, *129*, 9992–9995

-
- [1] H. Maarse, *Volatile Compounds in Foods and Beverages*, Marcel Dekker, New York, **1991**.
- [2] a) J. R. Askim, M. Mahmoudi, K. S. Suslick, *Chem. Soc. Rev.* **2013**, *42*, 8649–8682; b) L. You, D. Zha, E. V. Anslyn, *Chem. Rev.* **2015**, *115*, 7840–7892; c) N. A. Rakow, K. S. Suslick, *Nature* **2000**, *406*, 710–713.
- [3] a) S. E. Stitzel, M. J. Aernecke, D. R. Walt, *Annu. Rev. Biomed. Eng.* **2011**, *13*, 1–25; b) R. A. Potyrailo, C. Surman, N. Nagraj, A. Burns, *Chem. Rev.* **2011**, *111*, 7315–7354; c) F. Röck, N. Barsan, U. Weimar, *Chem. Rev.* **2008**, *108*, 705–725; d) A. Hierlemann, R. Gutierrez-Osuna, *Chem. Rev.* **2008**, *108*, 563–613.
- [4] a) D. J. Wales, J. Grand, V. P. Ting, R. D. Burke, K. J. Edler, C. R. Bowen, S. Mintova, A. D. Burrows, *Chem. Soc. Rev.* **2015**, *44*, 4290–4321; b) E. Comini, *Mater. Today* **2016**, *19*, 559–567.
- [5] a) A. Roth, H. Li, C. Anorma, J. Chan, *J. Am. Chem. Soc.* **2015**, *137*, 10890–10893; b) L. Feng, C. J. Musto, K. S. Suslick, *J. Am. Chem. Soc.* **2010**, *132*, 4046–4047.
- [6] H. Jin, T.-P. Huynh, H. Haick, *Nano Lett.* **2016**, *16*, 4194–4202.
- [7] K. M. Frazier, T. M. Swager, *Anal. Chem.* **2013**, *85*, 7154–7158.
- [8] S. H. Lim, L. Feng, J. W. Kemling, C. J. Musto, K. S. Suslick, *Nat. Chem.* **2009**, *1*, 562–567.
- [9] Z. Li, H. Li, M. K. LaGasse, K. S. Suslick, *Anal. Chem.* **2016**, *88*, 5615–5620.
- [10] a) J. R. Askim, Z. Li, M. K. LaGasse, J. M. Rankin, K. S. Suslick, *Chem. Sci.* **2016**, *7*, 199–206; b) Z. Li, W. P. Bassett, J. R. Askim, K. S. Suslick, *Chem. Commun.* **2015**, *51*, 15312–15315.
- [11] a) Z. Li, K. S. Suslick, *ACS Sens.* **2016**, *1*, 1330–1335; b) M. Śliwińska, P. Wiśniewska, T. Dymerski, J. Namieśnik, W. Wardencki, *J. Agric. Food Chem.* **2014**, *62*, 1423–1448; c) U. Khulal, J. Zhao, W. Hu, Q. Chen, *RSC Adv.* **2016**, *6*, 4663–4672; d) S. Qian, H. Lin, *Anal. Chem.* **2015**, *87*, 5395–5400.
- [12] F. Feigl, V. Anger, *Spot Tests in Organic Analysis*, 7th ed., Elsevier, Amsterdam, **1966**.
- [13] J. R. Askim, K. S. Suslick, *Anal. Chem.* **2015**, *87*, 7810–7816.
- [14] a) J. Li, C. Hou, D. Huo, M. Yang, H.-b. Fa, P. Yang, *Sens. Actuators B* **2014**, *196*, 10–17; b) S. Srinives, T. Sarkar, A. Mulchandani, *Sens. Actuators B* **2014**, *194*, 255–259.
- [15] a) J. Janata, *Principles of Chemical Sensors*, 2nd ed., Springer, New York, **2009**; b) R. A. Johnson, D. W. Wichern, *Applied Multivariate Statistical Analysis*, 6th ed., Prentice Hall, Upper Saddle River, NJ, **2007**.
- [16] P. Flach, *Machine Learning: The Art and Science of Algorithms that Make Sense of Data*, Cambridge University Press, Cambridge, **2012**.
- [17] a) J. Han, C. Ma, B. Wang, M. Bender, M. Bojanowski, M. Hergert, K. Seehafer, A. Herrmann, U. H. F. Bunz, *Chem.* **2017**, *2*, 817–824; b) E. Bihar, Y. Deng, T. Miyake, M. Saadaoui, G. G. Malliaras, M. Rolandi, *Sci. Rep.* **2016**, *6*, 27582; c) A. Rico-Yuste, V. González-Vallejo, E. Benito-Peña, T. de las Casas Engel, G. Orellana, M. C. Moreno-Bondi, *Anal. Chem.* **2016**, *88*, 3959–3966; d) E. Ghanem, H. Hopfer, A. Navarro, M. Ritzer, L. Mahmood, M. Fredell, A. Cubley, J. Bolen, R. Fattah, K. Teasdale, L. Lieu, T. Chua, F. Marini, H. Heymann, E. Anslyn, *Molecules* **2015**, *20*, 9170; e) S. C. McCleskey, P. N. Floriano, S. L. Wiskur, E. V. Anslyn, J. T. McDevitt, *Tetrahedron* **2003**, *59*, 10089–10092.
- [18] H. Lin, M. Jang, K. S. Suslick, *J. Am. Chem. Soc.* **2011**, *133*, 16786–16789.

Manuscript received: May 22, 2017

Accepted manuscript online: June 28, 2017

Version of record online: July 17, 2017