Tetrahedron Letters 54 (2013) 2890–2893

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Two-dimensional sensor array for discrimination of amines

Jung-Deog Lee, Jong-In Hong *

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, Republic of Korea

ARTICLE INFO

Article history:
Received 28 February 2013
Accepted 27 March 2013
Available online 6 April 2013

Keywords:
Sensor array
Discrimination of amines
Molecularly imprinted polymers
Metalloporphyrin
Linear discriminant analysis

ABSTRACT

A two-dimensional sensor array was prepared for the discrimination of various amines. A simple combination of four molecularly imprinted polymers and three dyes was used to produce a 12-channel sensor array capable of discriminating between structurally similar amines.

Chemical sensing using sensor arrays is based on the utilization of arrays of differential receptors. Since all sensors or receptors in an array might not be selective to a specific analyte, data analysis of the responses of various analytes by pattern recognition is performed to facilitate discrimination between structurally similar analyte molecules.[1] Sensor arrays are promising tools because they enable accurate analysis, owing to their responsiveness to a broad range of analytes, and because the synthesis of these sensors requires minimal effort. Previously, classical electronic noses have been developed, which utilize metal oxide sensors, surface acoustic wave sensors, metal oxide field effect transistors, or conducting polymers.[2] More recent studies have demonstrated the use of colorimetric sensor arrays that utilize metalloporphyrins, calix[4]pyrroles, and Zn(salicylaldimine).[3]

Several groups have reported on the discrimination of amines by pattern recognition using molecularly imprinted polymers (MIPs), dyes, or kinetic spectral data.[4] Herein, we present a two-dimensional (2D) sensor array that can be used for the discrimination of various structurally similar amines. This sensor array has 12 channels and is composed of sensor elements that can be easily obtained through a simple combination of MIPs and metalloporphyrin dyes. A simple combination of two orthogonal arrays yields an array with diverse components; furthermore, this combination amplifies the discriminating power of the resulting sensor array.

Two arrays were selected in this study: an array of molecularly imprinted polymers and an array of metalloporphyrin dyes. Figure 1 shows the amines selected as target analytes. The analytes include primary amines (**A1**, **A2**, and **A5**), secondary amines (**A3** and **A4**), amines having other functional groups (**A2**, **A3**, and **A4**), and pharmaceutical (**A3**). It would not be an easy task to discriminate between the various sets of different amines by employing conventional methods.

Although, in general, analytes can be efficiently discriminated by using an MIP array, the introduction of a signaling unit into the polymer matrix is rather difficult. Therefore, in most studies on MIPs, spectroscopically active analytes were used or the binding of analytes to the MIPs was examined using an indicator displacement assay (IDA).[5] A metalloporphyrin array can be used to identify analytes; further, metalloporphyrins also provide useful information such as distinct absorbance and fluorescence patterns upon binding to analytes.[6] However, elaborate design and synthesis of porphyrin derivatives are required for the analysis of structurally similar compounds. In order to enhance the discriminating power of the sensor array, we utilized the positive aspects of both MIPs and metalloporphyrins. For constructing the MIP array, four polymers were prepared by thermal polymerization using methacrylic acid (MAA) and ethylene glycol dimethacrylate (EDMA) in acetonitrile. **P0** is a non-imprinted polymer, while **P1**–**P3** are imprinted polymers prepared using **A1**–**A3**, respectively, as templates (Table S1). The dye array comprises three metalloporphyrins that are prepared using 5,10,15,20-tetrakis-(3,5-di-*tert*-butylphenyl)-21*H*, 23*H*-porphine.[7] A sensor array with twelve channels could be easily prepared by the combination of four MIPs (**P0**–**P3**) and three metalloporphyrin dyes (Zn(II)-por, Co(II)-por, and Co(III)-por).

For example, **P0**·Zn(II)-por indicates that polymer **P0** and dye Zn(II)-por were employed for sensing an analyte (Table S2).

The general process adopted for sensing an analyte is shown in Scheme 1. First, a mixture of analytes and MIPs is equilibrated. Then, the MIPs are removed by syringe filters, and the remaining

* Corresponding author. Tel.: +82 2 880 6682; fax: +82 2 889 1568.
E-mail address: jihong@snu.ac.kr (J.-I. Hong).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.03.118

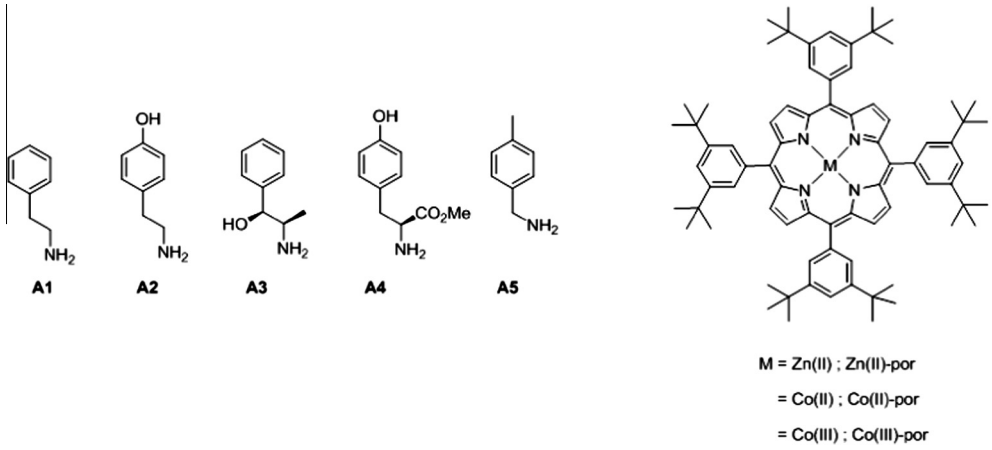
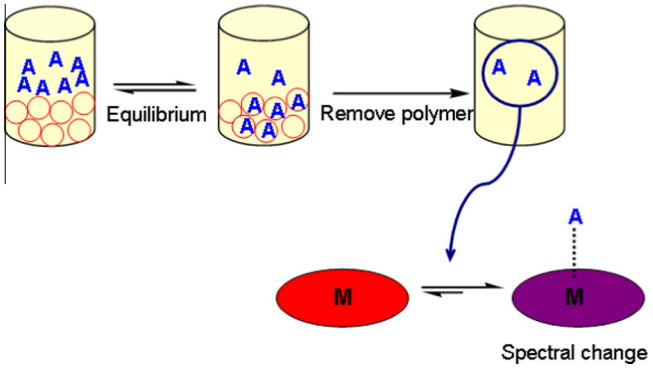


Figure 1. Analytes and metalloporphyrin dyes. **A1**: Phenethylamine, **A2**: tyramine, **A3**: (+)-norephedrine, **A4**: L-tyrosine methyl ester, **A5**: 4-methylbenzyl amine.



Scheme 1.

unbound analytes (supernatant) are treated with a solution of each metalloporphyrin, which results in a spectral change in each dye. It is noteworthy that this method can be used for easily detecting analytes using spectroscopy, and is useful for sensing spectroscopically inactive analytes. Next, we attempted to determine the relationship between the spectral change and the binding of the analytes to the MIPs. For this purpose, we measured the absorbance of the supernatant using the batch rebinding test and determined the spectral change induced by the supernatant observed for the dye solution. For the rebinding study (Fig. 2), different amounts of polymer **P3** were added to 4 mL of a 6 mM solution of an analyte (**A3**) in chloroform, and the resulting solution was shaken for 30 min. Subsequently, the UV spectrum of the supernatant was obtained. Further, 1.5 mL of the same supernatant solution was mixed with 1.5 mL of 5 μM Zn(II)-por in chloroform, and the absorbance of the resulting solution was measured. The graph shown in Figure 2a reveals that the absorbance of the supernatant decreased with increasing amounts of **P3**; this indicates that a greater amount of **A3** was bound to **P3**. A similar relationship was observed between **P3** and the absorbance of Zn(II)-por, as shown in Figure 2b; as the amount of **P3** increased, the absorbance of Zn(II)-por decreased at 430 nm and simultaneously increased at 421 nm. Thus, it was confirmed that the binding of an analyte is indicated by a spectral change, which can, therefore, be considered to be a response of the polymer toward the analytes.

The sensor array **P0**·Zn(II)-por–**P3**·Zn(II)-por, which had four channels and contained only one dye Zn(II)-por, was initially tested to discriminate between the analytes **A1**–**A5**. For evaluating the responses of the sensor elements, 4 mL of a 3 mM solution of an analyte in chloroform was shaken for 30 min in the presence of 20 mg

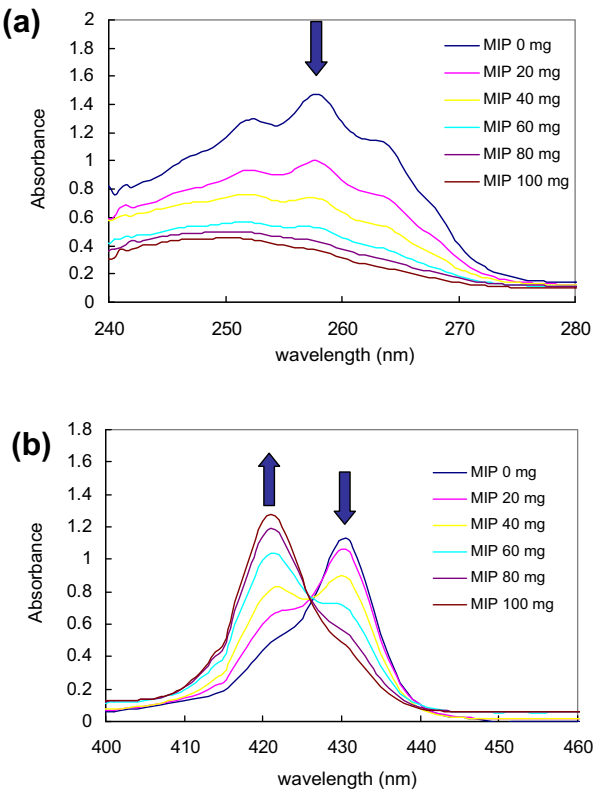


Figure 2. Absorbance change in (a) supernatant and (b) Zn(II)-por observed for binding of **A3** with **P3**.

of polymer. Next, 0.75 mL of the supernatant solution was mixed with 0.75 mL of a solution of 5 μM Zn(II)-por in chloroform; the absorbance of the resulting solution was measured. The response was recorded as the ratio of the observed absorbance (A, 421 nm) to the initial absorbance (Ai, 421 nm), that is, A/Ai, where Ai was measured from 1.5 mL of a 2.5 μM dye solution. Six replicates were conducted, and the entire data were consolidated in a 4 × 30 matrix data sheet (4 sensors × 5 analytes × 6 replicates). The analytes were discriminated by means of statistical analysis. The numerical responses obtained using the **P0**·Zn(II)-por–**P3**·Zn(II)-por array were consolidated in a 4 × 30 matrix, after which, a linear discriminant analysis (LDA) was performed to reduce the dimensionality of the data. Two different LDA plots are shown in Figure 3. Figure 3a represents the case in which all the analytes were successfully dis-

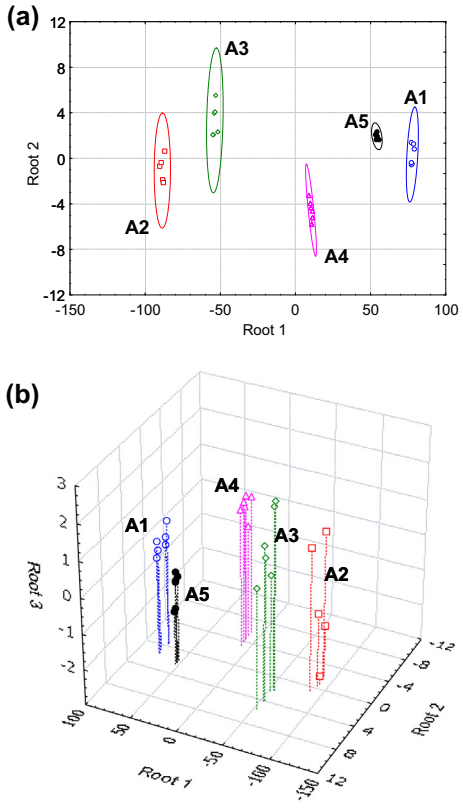


Figure 3. LDA plots from the four-channel sensor array **P0**·Zn(II)-por–**P3**·Zn(II)-por for identification of analytes **A1**–**A5**: (a) 2D LDA plot, (b) 3D LDA plot

criminated at a 95% confidence level. It is noteworthy that along with **A1**–**A3**, **A4**–**A5** could also be classified even though they were not employed in the imprinting procedures. The three-dimensional LDA plot shown in Figure 3b also shows a clear distinction between the analytes. At this stage, it could be inferred that the four-channel sensor array is capable of independently identifying all the analytes **A1**–**A5**.

Next, the response patterns of the entire sensor array **P0**·Zn(II)-por–**P3**·Co(III)-por, in which all three dyes were used, were obtained. The experimental conditions were the same, the only exception being that 150 μL of the supernatant solution was mixed with 1.5 mL of a 2.5 μM dye solution when Co(II)-por and Co(III)-por were included. Further, when Co(II)-por and Co(III)-por were included, the response was recorded as the ratio of the observed absorbance to the initial absorbance of the dye, that is, A (413 nm)/Ai (413 nm), where Ai was the absorbance measured for a mixture of 150 μL chloroform and 1.5 mL 2.5 μM dye solution. Six replicates were conducted and the entire data were consolidated in a 12 × 30 matrix data sheet (12 sensors × 5 analytes × 6 replicates). LDA for the entire sensor array was performed to reduce the dimensionality of the data. Two LDA plots are shown in Figure 4. As expected, the entire sensor array was found to be capable of successfully discriminating all the analytes, with a higher degree of visual differentiation. It can be inferred that the entire 12-channel sensor array enhances the discriminating power of the MIP array (Fig. 4a). This inference is similar to that drawn on the basis of the LDA results mentioned previously. Further, by taking the third vector from the LDA analysis into consideration, we obtain three-dimensional (3D) patterns for the complete array; a clear distinction between all the analytes is observed in these patterns (Fig. 4b).

In summary, we have demonstrated the use of a new type of sensor array for the discrimination of various amines. A 12-channel array was constructed using four polymers and three dyes. The

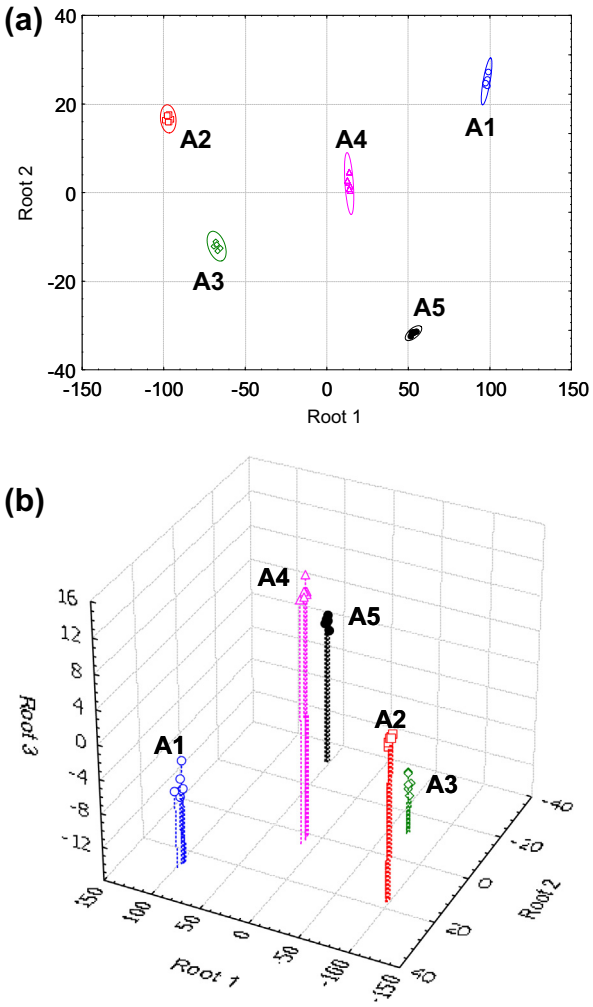


Figure 4. LDA plots obtained when the entire 12-channel sensor array **P0**·Zn(II)-por–**P3**·Co(III)-por is used for identification of analytes **A1**–**A5**: (a) 2D LDA plot, (b) 3D LDA plot.

effectiveness of the proposed sensing mechanism was verified by obtaining the response patterns of the sensors and analyzing them by LDA; various structurally similar amines were successfully discriminated. Moreover, the array was capable of classifying **A4**–**A5** even though no receptors were specifically designed for these analytes. While previous works using an MIP array or a metalloporphyrin array are successful for the discrimination of amines, it is notable that the orthogonal combination of MIPs and metalloporphyrins increases the discrimination ability, as shown in the current two-dimensional sensor array. The inclusion of a higher number of dyes provided enhanced discriminating power without any synthetic modifications. Thus, the array has potential for application as a sensing system with a specificity as high as those of natural systems.

Acknowledgements

This work was supported by an NRF Grant funded by the MEST (Grant No. 2012-0000159).

Supplementary data

Supplementary data (experimental procedures and data analysis) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.03.118.

References and notes

1. (a) Albert, K. J.; Lewis, N. S.; Schauer, C. L.; Sotzing, G. A.; Stitzel, S. E.; Vaid, T. P.; Walt, D. R. *Chem. Rev.* **2000**, *100*, 2595–2626; (b) Jurs, P. C.; Bakken, G. A.; McClelland, H. E. *Chem. Rev.* **2000**, *100*, 2649–2678.
2. (a) Heilig, A.; Bârsan, N.; Weimar, U.; Schweizer-Berberich, M.; Gardner, J. W.; Göpel, W. *Sens. Actuators, B* **1997**, *43*, 45–51; (b) Getino, J.; Horrillo, M. C.; Gutierrez, J.; Ares, L.; Robla, J. I.; Garcia, C.; Sayago, I. *Sens. Actuators, B* **1997**, *43*, 200–205; (c) Reichert, J.; Coerdt, W.; Ache, H. J. *Sens. Actuators, B* **1993**, *13*, 293–296; (d) Hoyt, A. E.; Ricco, A. J.; Bartholomew, J. W.; Osbourn, G. C. *Anal. Chem.* **1998**, *70*, 2137–2145; (e) Sommer, V.; Tobias, P.; Kohl, D.; Sundgren, H.; Lundström, I. *Sens. Actuators, B* **1995**, *28*, 217–222; (f) Gardner, J. W.; Pearce, T. C.; Friel, S.; Bartlett, P. N.; Blair, N. *Sens. Actuators, B* **1994**, *18*, 240–243; (g) Freund, M. S.; Lewis, N. S. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 2652–2656; (h) Doleman, B. J.; Lonergan, M. C.; Severin, E. J.; Vaid, T. P.; Lewis, N. S. *Anal. Chem.* **1998**, *70*, 4177–4190.
3. (a) Rakow, N. A.; Suslick, K. S. *Nature* **2000**, *406*, 710–713; (b) Baldini, L.; Wilson, A. J.; Hong, J.; Hamilton, A. D. *J. Am. Chem. Soc.* **2004**, *126*, 5656–5657; (c) Palacios, M. A.; Nishiyabu, R.; Marquez, M.; Anzenbacher, P., Jr. *J. Am. Chem. Soc.* **2007**, *129*, 7538–7544; (d) Germain, M. E.; Knapp, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 5422–5423.
4. (a) Greene, N. T.; Morgan, S. L.; Shimizu, K. D. *Chem. Commun.* **2004**, 1172–1173; (b) Greene, N. T.; Shimizu, K. D. *J. Am. Chem. Soc.* **2005**, *127*, 5695–5700; (c) Shimizu, K. D.; Stephenson, C. J. *Curr. Opin. Chem. Biol.* **2010**, *14*, 743–750; (d) Rakow, N. A.; Sen, A.; Janzen, M. C.; Ponder, J. B.; Suslick, K. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4528–4532; (e) Bang, J. H.; Lim, S. H.; Park, E.; Suslick, K. S. *Langmuir* **2008**, *24*, 13168–13172; (f) Hasani, M.; Emami, F. *Anal. Methods* **2012**, *4*, 1339–1349.
5. (a) Matsui, J.; Higashi, M.; Takeuchi, T. *J. Am. Chem. Soc.* **2000**, *122*, 5218–5219; (b) Lee, J.-D.; Greene, N. T.; Rushton, G. T.; Shimizu, K. D.; Hong, J.-I. *Org. Lett.* **2005**, *7*, 963–966; (c) Manesiotis, P.; Hall, A. J.; Sellergren, B. *J. Org. Chem.* **2005**, *70*, 2729–2738; (d) Urraca, J. L.; Moreno-Bondi, M. C.; Orellana, G.; Sellergren, B.; Hall, A. *J. Anal. Chem.* **2007**, *79*, 4915–4923.
6. (a) Sen, A.; Suslick, K. S. *J. Am. Chem. Soc.* **2000**, *122*, 11565–11566; (b) Zhang, C.; Suslick, K. S. *J. Am. Chem. Soc.* **2005**, *127*, 11548–11549.
7. Metalloporphyrins were prepared according to literature procedures (a) Crossley, M. J.; Thordarson, P.; Bannerman, J. P.; Maynard, P. J. *J. Porphyrins Phthalocyanines* **1998**, *2*, 511–516; (b) Miyamoto, T. K.; Sugita, N.; Matsumoto, Y.; Sasaki,, Y.; Konno, M. *Chem. Lett.* **1983**, *12*, 1695–1698; (c) Urbani, M.; Iehl, J.; Osinska, I.; Louis, R.; Holler, M.; Nierengarten, J.-F. *Eur. J. Org. Chem.* **2009**, 3715–3725; (d) Zhu, W.; Sintic, M.; Ou, Z.; Sintic, P. J.; McDonald, J. A.; Brotherhood, P. R.; Crossley, M. J.; Kadish, K. M. *Inorg. Chem.* **2010**, *49*, 1027–1038.