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Propofol analysis using a TiO_2 nanotube-based gas sensor and a solid electrolyte CO_2 sensor

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Abstract

For the development of gas sensors applied to organic gas detection, the preparation of sample gases containing organic vapors with controlled concentrations is sometime necessary in accurately evaluating the gas sensor properties. In this study, using a diffusion method where liquid samples were heated and vaporized under a carrier gas flow, we prepared standard sample gases containing 2,6-diisopropylphenol (propofol), which are breath markers for diabetes and anesthesia depth, respectively. We used a NASICON ($Na_3Zr_2Si_2PO_{12}$; Na^+ conductor)-based CO_2 sensor combined with a Pt/Al_2O_3 combustion catalyst to prepare propofol gases with known concentrations. We demonstrated that the prepared propofol gases with constant concentrations were effectively detected by Au loaded-TiO_2 nanotube sensors.

Key words: TiO_2, $Na_3Zr_2Si_2PO_{12}$, semiconductor, solid electrolyte, propofol

Introduction

Human breath analysis is a promising technique as a real-time medical diagnostics that allows noninvasive monitoring and detection of illnesses. Human breath contains a wide variety of compounds, including inorganic gases such as NO and volatile organic compounds (VOCs) such as ethanol and acetone. Their concentrations are closely associated with those in blood, and as such changes in the concentration are indicative of person's medical conditions. Recently, the analysis of 2,6-diisopropylphenol (propofol) in blood and breath has attracted considerable attention. Its chemical structure is shown in Fig. 1. Propofol is intravenously administered hypnotic agent used for induction and maintenance of anesthesia and for sedation of patients in intensive care units. The determination of propofol concentrations in expiratory air likely allows the real-time monitoring of changes in its concentration in blood during anesthesia. High-performance gas sensors with a compact size and low cost, if available, would provide an inexpensive and efficient way to rapidly screen for certain diseases.

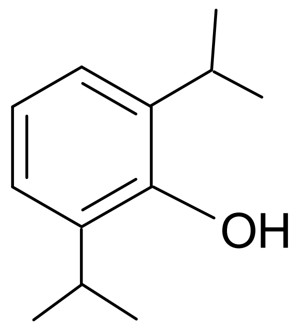

Fig. 1. Chemical structure of 2,6-diisopropylphenol (propofol).

However, existing sensors for VOC detection still have problems, i.e., low sensitivity, low selectivity, and interference from high humidity contained in breath. Thus, further sensor development is highly desirable. We have recently developed TiO_2 nanotube-based gas sensors [1,2]. Nanostructured films made from TiO_2 nanotubes provided effective pores in the films for gas diffusion and gave high sensitivity to VOCs like toluene and alchol. In this study, we applied this sensor for the detection of propofol.

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However, continuous preparation of standard propofol gases is necessary for the investigation of the properties of the sensors. Standard propofol gases are not commercially availavel. To prepare standard propofol gases, we used a simple system of determining organic gas concentrations in sample gases prepared by a diffusion method where a liquid sample was heated and vaporized [3,4]. In this system, organic compounds in sample gases are decomposed to CO_2 via catalytic combustion and the resulting CO_2 is detected using a solid-state CO_2 sensor. Organic vapor concentrations are determined from the CO_2 concentration determined with the CO_2 sensor according to their stoichiometric complete combustion reactions. We demonstrated that the system could continuously monitor and determine the ethanol vapor concentration in a sample gas stream prepared by heating liquid ethanol, and that the sample gas thus prepared could be used for the accurate evaluation of gas sensor properties for VOC detection.

In this study, we further examined the feasibility of our developed system for the determination of concentrations of propofol. The propofol gases thus prepared and concentration analyzed were used to study the properties of TIO_2 nanotube-based gas sensors for the detection of propofol.

Experimental

TiO_2 nanotube-based sensors were fabricated by a hydrothermal process and a screen printing method [1]. A TiO_2 commercial powder (P-25, Degussa) was hydrothermally treated with a NaOH solution (10 mol/L) at 230°C for 24 h in a Teflon-lined autoclave. After the treatment, the TiO_2 powder was washed with an HCl solution (0.2 mol/L) under ultrasonic irradiation for 1 h. Then, the obtained products were carefully washed with D.I. water to remove Cl- ions, filtered, and dried to recover TiO_2 nanotubes. The resulting nanotubes were calcined at 600°C for 1 h, and then subjected to a ball-milling treatment using a planet-type ball-mill for 3 h. Gold nanopaticles were deposited on TiO_2 nanotubes by a photochemical method in a manner reported elsewhere [5]. The prepared nanotubes (1.0 g) were dispersed in D.I. water (100 mL) containing ethanol (10 mL), and then a designated amount of $HAuCl_4$ (0.5-2.0 wt%) was added in the suspension. Ethanol was used as an electron donor. UV light (250 W) was irradiated to the suspension for 3 h under stirring. The obtained Au-loaded TiO_2 nanotubes were washed with D.I. water, filtered, and dried to recover Au-loaded TiO_2 nanotubes, which were then calcined at 600°C for 1 h. Transmission electron microscopy (TEM) was used to observe the morphology of deposited Au particles. The loading amount of Au was tuned by changing the concentration of $[AuCl_4]^-$ in a precursor solution and determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES).

The obtained TiO_2 nanotubes coated with Au nanoparticles were deposited on an Al_2O_3 substrate with gold electrodes. The film was calcined at 600°C in air. The structure of the fabricated sensor was shown in Fig. 2 (a). The sensor response of the TiO_2 sensor was defined as Rair/Rgas, where Rair and Rgas are the electric resistances in air and in a test gas, respectively. The TiO_2 sensor was operated at 450-550°C.

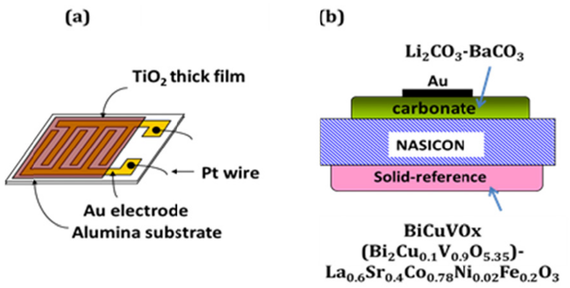


Fig. 2. The structures of (a) TiO_2-based sensor and (b) the CO_2 sensor.

The solid-state CO_2 sensor was fabricated by depositing a carbonate layer on a NASICON (Na+ conductor; $Na_3Zr_2SiPO_{12}$) sintered disk. The NASICON disk was prepared by a sol-gel method. As an auxiliary layer, Li_2CO_3-$BaCO_3$ was deposited on the NASICON disk. BiCuVOx-based solid reference electrode was attached to the NASICON disk. The detailed fabrication process was reported elsewhere [6, 7]. The electromotive force (EMF) of the device was measured with an electrometer. The sensor was operated at 500°C.

The propofol sensing properties of the TiO_2 films were measured in a gas-flow apparatus shown in Fig. 3. Sample gases containing propofol in air were prepared by a diffusion method using a standard gas generator (Permeater PD-1B, GASTEC) [3, 4]. Liquid propofol was placed in a capillary container and heated at 50°C to vaporize propofol. The generated vapor was delivered to a chamber where the TiO_2 sensor was placed. Synthetic air was used as a carrier gas.

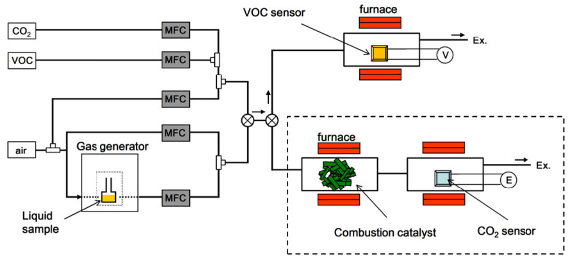


Fig. 3. Experimental setup for measuring the sensing properties of TiO_2-based sensors and preparing standard propofol gases.

The concentration of propofol in the sample gas was determined by decomposing propofol at the catalyst chamber shown in Fig.3. A Pt/Al_2O_3 catalyst was used to completely decompose propofol into CO_2. The catalyst was heated at 500°C with an electric furnace. The resulting CO_2 contained in the sample gas was delivered to the chamber where the CO_2 sensor was placed.

Fig. 4 shows a typical calibration curve of the CO_2 sensor. The EMF of the device was linear to the logarithm of CO_2 concentration, following the Nernst behavior. From this curve, the concentration of CO_2 in sample gases can be determined.

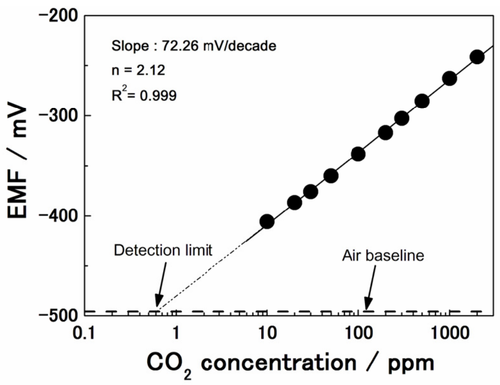


Fig. 4. Calibration curve of the CO_2 sensor.

Results and Discussion

We first analyzed the propofol concentration in sample gases with the CO_2 sensor. Fig. 5 shows the response of the CO_2 sensor to CO_2 formed after the combustion of propofol gases prepared by the diffusion method. The propofol concentration was determined according to the simple complete combustion reaction of propofol.

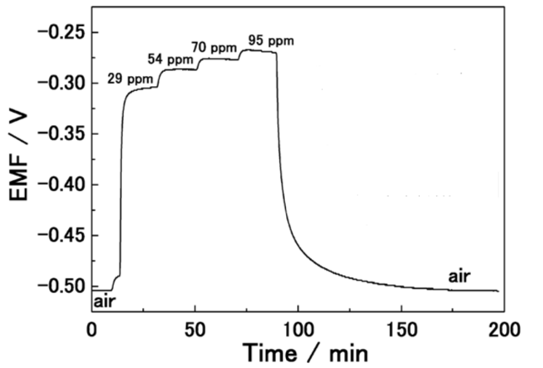
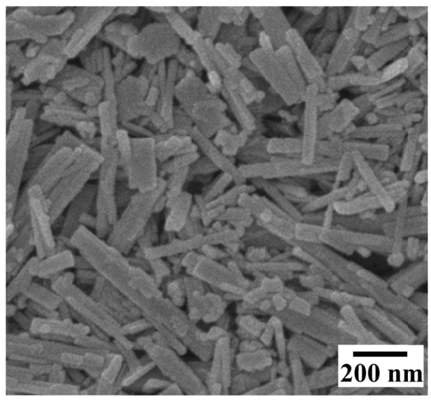


Fig. 5. Dynamic transient of the EMF of the CO_2 sensor in response to propofol gases with different concentrations. The concentrations of propofol was determined from the calibration curve of the CO_2 sensor.

The concentration of propofol was successfully controlled by changing the mixing rate of the parent propofol gas and a synthetic air. Accordingly, the response of the CO_2 sensor changed as shown in Fig.5. It is noteworthy that the present method allowed for the continuous generation of propofol gas and in-situ determination of its concentration in sample gases.

Fig. 6 shows the SEM and TEM images of TiO_2 nanotubes decorated with Au nanoparticles. The SEM image shows the porous structure of the sensing film. This structure allows for the diffusion of large sized gas such as propofol deep inside the sensing film. The highly anisotropic shape of the nanotubes successfully formed the observed porous structure. The TEM image clearly showed that Au nanoparticles were loaded on the nanotubes. An average particle size was ca. 20-50 nm at 0.92 wt %. Increasing the Au loading amount led to an increase in the particle size of Au.



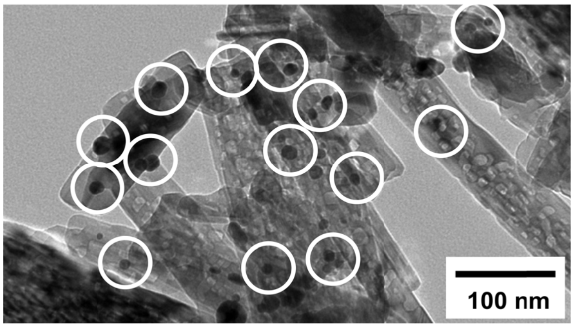


Fig. 6. SEM and TEM images of TiO_2 nanotubes loaded with Au.

Fig. 7 shows the dependence of sensor response of the TiO_2-based gas sensor. The device responded well to changes in propofol concentration, demonstrating its high sensitivity to propofol. The sensor response was improved by depositing Au nanoparticles on nanotubes. An improvement of catalytic activity of TIO_2 nanotubes is possibly due to the observed increase in the sensor response. The highly dispersed state of Au nanoparticles on nanotubes may also contribute to the high sensitivity.

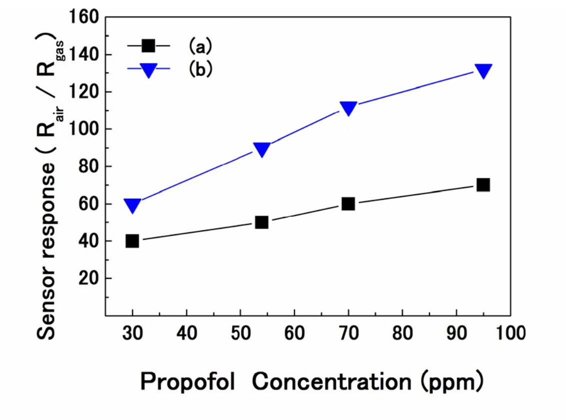


Fig. 7. Dependence of sensor responses of TiO_2 nanotube devices on propofol concentration at 500°C (a) TiO_2 nanotubes, (b) loaded with Au at 0.92 wt.%.

Conclusion

Inorder to detect 2,6-diisopropylphenol (propofol) for breath analysis, we have fabricated TIO_2 nanotube-based gas sensor by a hydrothermal method. The sensor showed high sensitivity to propofol, which was prepared by a diffusion method using a liquid sample. The concentration of propofol in the prepared sample gas was detemined by a solid electrolyte CO_2 sensor combined with a combustion catalyst. The present study demonstrated that the developed system is useful for the analysis and contineous generation of volatile organic gases.

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