Highly Enantioselective Graphene-Based Chemical Sensors Prepared by Chiral Noncovalent Functionalization

Xiaobo Shang,*‡ Cheol Hee Park,*‡ Gwan Yeong Jung,§ Sang Kyu Kwak,*§ and Joon Hak Oh,*‡§

1Department of Chemical Engineering, Pohang University of Science and Technology (POSTECH), 77 Cheongam-ro, Pohang 37673, Korea
2School of Chemical and Biological Engineering, Institute of Chemical Processes, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, Korea
§Department of Energy Engineering, School of Energy and Chemical Engineering, Ulsan National Institute of Science and Technology (UNIST), 50 UNIST-gil, Ulsan 44919, Korea

Supporting Information

ABSTRACT: As a basic characteristic of the natural environment and living matter, chirality has been used in various scientific and technological fields. Chiral discrimination is of particular interest owing to its importance in catalysis, organic synthesis, biomedicine, and pharmaceutics. However, it is still very challenging to effectively and selectively sense and separate different enantiomers. Here, enantio-differentiating chemosensor systems have been developed through spontaneous chiral functionalization of the surface of graphene field-effect transistors (GFETs). GFET sensors functionalized using noncovalent interactions between graphene and a newly synthesized chiral-functionalized pyrene material, Boc-L-Phe-Pyrene, exhibit highly enantioselective detection of natural acrylic monoterpenoid enantiomers, that is, (R)-(+)− and (S)-(−)−-β-citronellol. On the basis of a computational study, the origin of enantio-differentiation is assigned to the discriminable charge transfer from (R)-(+)− or (S)-(−)−-β-citronellol into graphene with a significant difference in binding strength depending on surface morphology. The chemosensor system developed herein has great potential to be applied in miniaturized and rapid enantioselective sensing with high sensitivity and selectivity.

KEYWORDS: graphene transistors, chiral sensors, chemical sensors, noncovalent interactions, enantioselectivity

1. INTRODUCTION

Chirality plays a very important role in various fields of scientific and technological research and has great potential to be applied in key areas such as chemical synthesis, pharmaceutics, catalysis, fundamental physics, and biomedicine.1 As most biological compounds and many pharmaceuticals are chiral, sensing and separating chiral compounds is of great importance.2 In many cases, one enantiomer of chiral drugs such as 3,4-dihydroxyphenylalanine has the desired effect (e.g., healing properties), while the other has an undesirable effect (e.g., toxicity).3 Therefore, there is a need for selective discrimination and separation of enantiomers. While chiral discrimination has great potential to be applied in many areas, it remains challenging because of the difficulty of discriminating between enantiomers that have nearly identical properties and the same chemical composition, different only in steric conformation.4 However, when chiral chemicals interact with another chiral entity (typically a molecular receptor) to produce enantio-specific interactions, their biological and physiological properties can differ dramatically. By making use of this principle, separation and detection of optical isomers can be carried out using offline analytical techniques such as chromatography. Other chiral discrimination methods include microwaves,5,6 photoelectron circular dichroism,7 chiral light,8−10 cavity-enhanced polarimeters,11 and magnetic substrates.12

Compared to other methods, amperometric chemo sensors based on field-effect transistors (FETs) are attractive owing to advantages such as their rapid sensing ability, high sensitivity, ease of handling, small size, and need for only a small volume of samples.13−15 To date, FET-based sensors have been widely used in artificial skin technology, environmental monitoring, light sensing, drug delivery, and food safety detection.15 However, among the various applications of FET-based sensing, chiral sensing is still one of the most challenging applications of FET-based sensors. Torsi et al. successively reported a bilayer-structured organic field-effect transistor (OFET)-based sensing technology for enantioselective detec-
tion of terpene flavor molecules of biological origin at an unprecedentedly low concentration and a sensitive and quantitative capacitance-modulated transistor based on functionalization of gate electrodes using odorant binding proteins for the differential detection of chiral odorant molecules.\textsuperscript{4,10} Recently, molecularly imprinted polymer-based extended-gate OFET chemosensors have also been reported to enantioselectively sense chiral phenylalanine.\textsuperscript{3} Further in-depth research on topics such as the synthesis of novel chiral materials, as well as chiral sensing methods and mechanisms, will expedite the development of the chiral sensing platforms.

In particular, graphene-based field-effect transistors (GFETs) are promising for sensing applications owing to the intrinsic chemical inertness of graphene and the high sensitivity of the FET platform.\textsuperscript{17–19} However, sensitizer molecules and structures need to be introduced for high selectivity and broad sensing applications. Noncovalent functionalization of graphene by π-interactions is an attractive synthetic method because it offers the possibility of attaching functional groups to graphene, while preserving the graphene lattice and electrical performance.\textsuperscript{22,23} π−π interactions, which can be affected by several factors related to aromatic molecules, such as electron-donating or withdrawing ability, planarity, and the substituents, are one of the most intriguing noncovalent interactions. For example, pyrene-substituted materials have larger planar aromatic structures that strongly anchor them to the hydrophobic surface of graphene sheets via π−π interactions without disrupting graphene’s conjugation.\textsuperscript{22–25}

In the present study, we synthesized a pyrene-functionalized material (Boc-L-Phe-Pyrene) and utilized it as UV−vis and fluorescent probes for enantioselective sensing of the biomolecule β-citronellol, which is prevalent in essential oils of various aromatic plant species and has various pharmacological and anti-anxiety effects, such as antibacterial, antifungal, antispasmodic, hypotensive, vasorelaxant, anticonvulsant, antiinociceptive, and anti-inflammatory activities.\textsuperscript{26–29} More interestingly, Boc-L-Phe-Pyrene was used as the chiral functional layer on the graphene surface of GFET-based sensors using π−π noncovalent interactions for the enantioselective sensing of β-citronellol. On the basis of computational studies, including density functional theory (DFT) and molecular dynamics (MD) simulations, we suggest an enantioselective sensing mechanism: Boc-L-Phe-Pyrene with oblique morphology exhibits different binding strengths with enantiomeric β-citronellol, leading to differences in the charge transfer (CT) amount into graphene. For future applications, we also demonstrate the fabrication of a flexible enantioselective sensor device. The highly selective and sensitive detection of β-citronellol enantiomers with a low concentration using the Boc-L-Phe-Pyrene/graphene bilayer-structured system will enable new strategies for FET-based chiral sensing.

2. EXPERIMENTAL SECTION

2.1. Materials and Instrumentation. All starting materials were purchased from Aldrich and used without further purification. All solvents were ACS grade unless otherwise noted. The absorption spectra were measured using a Cary 5000 UV−vis−NIR spectrophotometer for solutions. Photoluminescence (PL) spectra were recorded on an FP-6500 spectrophotometer (JASCO). An Agilent 5500 scanning probe microscope running with a NanoScope V controller was used to obtain atomic force microscopy (AFM) images. AFM images were recorded in a high-resolution tapping mode under ambient conditions. Raman spectroscopic analysis was conducted at a wavelength of 532 nm (WITec, Micro Raman). The electrical performances of fabricated GFETs and GFET-based enantioselective sensors were measured using a Keithley 4200-SCS semiconductor parameter analyzer.

2.2. Synthesis and Characterization of Boc-L-Phe-Pyrene. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (6.2 mmol), 4-dimethylaminopyridine (2.8 mmol), triethylamine (4.1 mmol), and 1-pyrenemethanol (2.1 mmol) were successively added to a solution of N-(tert-butyloxy carbonyl)-1-phenylalanine (1.89 mmol) in 25 mL of dichloromethane (DCM) at room temperature, and the mixture was stirred overnight. Then, the reaction mixture was concentrated in vacuo. The residue was diluted with DCM and sequentially extracted with saturated NaHCO\textsubscript{3} aqueous solution, water, and brine. The final product was purified by column chromatography (yield: 57\%). (S)-Pyrenyl 1-ylmethyl 2-((tert-butyloxy carbonyl)amino)-3-phenylpropanoate: 1\textsuperscript{H} NMR (400 MHz, CDCl\textsubscript{3}): 8 8.00–8.26 (m, 9H), 6.86–7.12 (m, 5H), 5.80–5.95 (m, 2H), 4.92–5.03 (m, 1H), 4.61–4.71 (m, 1H), 2.95–3.10 (m, 2H), 1.40 (s, 9H) ppm. \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): 171.9, 131.2, 130.7, 129.7, 129.2, 128.4, 128.0, 127.3, 126.5, 125.6, 124.9, 124.6, 124.6, 122.8, 65.5, 54.5, 38.3, 28.3 ppm (Figure S1). Elemental analysis (% calc) for C\textsubscript{36}H\textsubscript{38}N\textsubscript{2}O\textsubscript{4}: C, 77.19; H, 6.21; N, 3.75. Found (%): C, 77.15; H, 6.20; N, 3.68. HRMS (MALDI-TOF, m/z): M\textsuperscript{+} calculated for 479.2097; found, 479.2095.

2.3. Sensor Device Fabrication on SiO\textsubscript{2}/n+Si Wafer. A graphene film was grown on the copper foil by the conventional chemical vapor deposition method using H\textsubscript{2} and CH\textsubscript{4} gas. After the growth of graphene, poly(methyl methacrylate) (PMMA) was coated on the graphene surface. Copper foil under the graphene film was etched using ammonium persulfate (\((\text{NH}_4)_2\text{S}_2\text{O}_8\)) aqueous solution (0.1 M). Then, the PMMA/graphene was wet-transferred on the SiO\textsubscript{2} (300 nm)/n+Si wafer and annealed at 130 °C for 30 min. The PMMA-supporting film was removed using acetone. For deposition of the Boc-L-Phe-Pyrene layer, the devices were immersed in a N,N-dimethylformamide (DMF) solution of Boc-L-Phe-Pyrene for 12 h. Next, the devices were rinsed in an excess amount of DMF and annealed to remove residual solvent. Source and drain electrodes were deposited in a thickness of 40 nm by thermal evaporation of Au using a patterned shadow mask.

2.4. Fabrication of Flexible Sensor Devices. A flexible sensor was fabricated on an indium tin oxide (ITO)-deposited polyethylene naphthalate (PEN) substrate, in which ITO and PEN serve as the gate electrode and the substrate, respectively. As a flexible dielectric layer, SU-8 10 diluted with γ-butyrolactone (γ-butyrolactone/SU-8 10 = 7:3 by volume ratio) was spin-coated at 7000 rpm for 120 s, and films were annealed at 95 °C for 1 min.\textsuperscript{30} The SU-8 10 film was exposed to UV light to induce cross-linking and annealed at 110 °C for 1 h. The preparation processes for the graphene film, Boc-L-Phe-Pyrene layer, and electrodes were the same as described above.

2.5. MD Simulation. The induced dipole moments of Boc-L-Phe-Pyrene on the graphene for each chiral enantiomer of β-citronellol were investigated using MD simulations. First, three types of morphologies were chosen as model systems by varying the angle between the aromatic plane and functional group in the Boc-L-Phe-Pyrene molecules (i.e., “vertical”, “oblique”, and “horizontal” shapes). After full optimization by DFT calculation, a 3 × 3 × 1 supercell structure was created, and the vacuum was fully introduced in the z-direction (i.e., 44.5 Å × 51.3 Å × 100.0 Å). Subsequently, the equilibrium binding configurations for each (R)−(+)- or (S)−(−)-β-citronellol at a fixed pressure condition of 1 atm were identified by grand canonical Monte Carlo (GCMC) simulation\textsuperscript{31} (i.e., ~70 chiral citronellol molecules adsorbed on each Boc-L-Phe-Pyrene/graphene system). Using these configurations as the initial structure, NVT (isothermal) MD simulations were performed for 10 ns at room temperature with a time-step of 1 fs. All MD simulations were carried out using COMPASSII forcefield.

2.6. DFT Calculation. DFT calculations were used to investigate the binding energy (BE) and CT of Boc-L-Phe-Pyrene/graphene in
the presence of (R)-(+) or (S)-(−)-β-citronellol. First, three morphological systems consisting of Boc-1-Phe-Pyrene and graphene were constructed by applying a vacuum in the z-direction (i.e., 14.8 × 17.1 × 35.0 Å³). With these models, the initial binding configurations of a single (R)-(+) or (S)-(−)-β-citronellol were identified by GCMC simulations. Subsequently, after full optimization of the systems, the BEs of (R)-(+) or (S)-(−)-β-citronellol on the Boc-1-Phe-Pyrene/graphene systems were calculated as follows

\[
BE = E_{\text{pyrene/G+ch.}} - E_{\text{pyrene/G}} - E_{\text{ch.}}
\]

where \( E_{\text{pyrene/G+ch.}} \), \( E_{\text{pyrene/G}} \), and \( E_{\text{ch.}} \) represent the total energies of Boc-1-Phe-Pyrene/graphene systems adsorbed by (R)-(+) or (S)-(−)-β-citronellol, bare Boc-1-Phe-Pyrene/graphene systems, and an isolated single (R)-(+) or (S)-(−)-β-citronellol molecule, respectively. All DFT calculations were performed using the DMol³ program.41 The equilibrium binding configuration of (R)-(+) or (S)-(−)-β-citronellol on the Boc-1-Phe-Pyrene/graphene systems were calculated by group-based summation and an atom-based force field (ff)(a radius of 15.5 Å) scheme.

2.7. GCMC Simulation. GCMC simulations of the (R)- and (S)-enantiomers of β-citronellol were performed using the Sorption program.41 The equilibrium binding configurations of (R)-(+) or (S)-(−)-β-citronellol were investigated at a fixed pressure of 1 atm and at room temperature. The systems were equilibrated for 1.0 × 10⁶ MC steps and analyzed for the next 1.0 × 10⁶ MC steps. The nonbond interactions, including electrostatic and van der Waals forces, were estimated by group-based summation and an atom-based cutoff (a radius of 15.5 Å) scheme.

3. RESULTS AND DISCUSSION

Pyrene-based materials are widely used in photochemical research because of their unique properties.42 Our pyrene-based chiral material, Boc-1-Phe-Pyrene, was synthesized by esterification between 1-pyrenemethanol and N-(tert-butoxycarbonyl)-L-phenylalanine. The UV-vis and PL spectra of pyrene-functionalized material in tetrahydrofuran (THF) solutions (5 × 10⁻⁷ M) are illustrated in Figure 1. For the Boc-1-Phe-Pyrene, the absorption spectra in THF exhibited three main peaks at 344, 327, and 315 nm, corresponding to the 0→0, 0→1, and 0→2 transitions of well-resolved vibronic structures of the chiral molecule, respectively. Fluorescence studies of Boc-1-Phe-Pyrene in THF (5 × 10⁻⁷ M) showed the mirror image of the UV–vis spectra with three main peaks at the wavelengths of 415, 396, and 376 nm.

UV–vis spectroscopy is widely used in molecular sensing and has various advantages for determining enantiomeric excess (ee), such as rapid measurement and simple instrumentation. When the absorbance lies in the visible range, it is possible to quickly detect the ee value by the naked eye.43 Fluorescence is another optical technique that has been used to determine ee. The fluorescence instrument is highly sensitive, rapid, relatively inexpensive, and can be used for real-time analyses. Therefore, the development of enantioselective UV–vis and fluorescence sensors for the recognition of chiral organic molecules has attracted great interest.43–45 To assess the enantioselective response of Boc-1-Phe-Pyrene toward β-citronellol, we measured the absorption and emission spectra of Boc-1-Phe-Pyrene (Figure 1c,d) with each enantiomer of β-citronellol. In the presence of either (R)-(+) or (S)-(−)-β-citronellol at a concentration of 5 × 10⁻⁴ M, the maximum wavelength of fluorescence and absorbance kept constant, while the intensities of both fluorescence and absorbance of the Boc-1-Phe-Pyrene (5 × 10⁻⁷ M) were quenched.

Interestingly, the intensities were always reduced more for (R)-(+) β-citronellol than (S)-(−)-β-citronellol in both UV–vis and PL spectra. We surmise that the enantiomeric sensing mechanism of Boc-1-Phe-Pyrene can be related to the different association constants of Boc-1-Phe-Pyrene with the enantiomeric analyte of β-citronellol.46–48

For the use of Boc-1-Phe-Pyrene in enantioselective sensing, we fabricated a GFET sensor device using functionalized graphene with a Boc-1-Phe-Pyrene layer via noncovalent π–π interactions.45 A schematic illustration of the chiral-functionalized GFET sensor fabrication process is shown in Figure 2a (see details in the Experimental Section). The film characteristics of pristine graphene and Boc-1-Phe-Pyrene/graphene were analyzed using AFM and Raman spectroscopy. The AFM height image of pristine graphene shows a clean and flat surface with a root-mean-square roughness (Rq) of 0.253 nm (Figure 2b), while the Boc-1-Phe-Pyrene/graphene film exhibits a clearly different surface morphology with a higher Rq of 0.447 nm, which explains the successful attachment of Boc-1-Phe-Pyrene onto the surface (Figure 2c). The thickness of Boc-1-Phe-Pyrene layers deposited on graphene is about 2 nm, when estimated from the AFM height profile (Figure S2). Raman spectra of the pristine graphene film showed a 2D band (2675 cm⁻¹), G band (1582 cm⁻¹), and high intensity ratio of 2D/G (I₂D/I_G) over 4, which indicates typical characteristics of monolayer graphene (Figure 2d). In addition, the high quality of graphene is confirmed by the low intensity of the D band (1343 cm⁻¹), which is an indicator of graphene defects. However, Boc-1-Phe-Pyrene/graphene films show apparent differences from the pristine graphene film in Raman spectra. For example, the Raman spectra of the Boc-1-Phe-Pyrene/graphene film exhibit an increase in the intensity of the G band and position shifts of the 2D and G bands from 2675 and 1582 to 2680 and 1588 cm⁻¹, respectively, which might be related to the stacking of Boc-1-Phe-Pyrene on the top of the graphene film and the p-type doping effect of...
Electrical properties of pristine graphene- and Boc-L-Phe-Pyrene/graphene-based transistor devices are shown in Figure S3 (Supporting Information). The source−drain current ($I_D$) as a function of gate voltage ($V_G$) for the pristine graphene transistor shows typical properties of p-channel-operated graphene transistor devices, with a Dirac point of 10 V. However, the Boc-L-Phe-Pyrene/graphene transistor device clearly shows a current−voltage characteristic of p-type doped devices, with a Dirac point shifted to a positive $V_G$ region above 50 V. This reflects the p-type doping effect of Boc-L-Phe-Pyrene, which is consistent with the upshift of 2D band and G band positions in Raman spectra of the Boc-L-Phe-Pyrene/graphene film (Figure 2d). The hole carrier mobility ($\mu_h$) of the devices was calculated based on current−voltage characteristics using the following equation:

$$\mu_h = \frac{g_m L}{V_D W C_g}$$

Figure 3. Concentration-dependent chiral β-citronellol vapor sensing signals from (a) pristine graphene sensors and (b) Boc-L-Phe-Pyrene/graphene sensors fabricated on SiO$_2$/Si wafer. $I_0$ is the baseline current. Solid lines are the interpolating calibration curves. Ten sensor devices were tested for statistical analysis. (c) Continuous enantioselective sensing responses of a Boc-L-Phe-Pyrene/graphene sensor device for chiral β-citronellol vapor with a concentration of 100 ppm ($V_D = -0.1 $ V; $V_G = -20 $ V) and (d) magnified plot of the dotted area in (c).

To demonstrate the enantioselective chemical sensing properties of the Boc-L-Phe-Pyrene/graphene system, we used the vapor of (R)-(+)−β-citronellol and (S)-(−)−β-citronellol enantiomers as the sensing analytes in the fabricated graphene originated from the pyrene derivative functional layer.50,51
Table 1. Average Drain Current Changes for Boc-L-Phe-Pyrene/Graphene-Based Sensors and Pristine Graphene Sensors upon Exposure to Various Concentrations of \( \beta \)-Citronellol Vapors

<table>
<thead>
<tr>
<th>analyte</th>
<th>100 ppm</th>
<th>80 ppm</th>
<th>60 ppm</th>
<th>40 ppm</th>
<th>20 ppm</th>
<th>10 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R)-(+)(-)-citronellol</td>
<td>-1.27 ( \pm ) 0.07</td>
<td>-1.10 ( \pm ) 0.10</td>
<td>-1.04 ( \pm ) 0.08</td>
<td>-1.04 ( \pm ) 0.08</td>
<td>-1.01 ( \pm ) 0.07</td>
<td></td>
</tr>
<tr>
<td>(S)-(+)(-)-citronellol</td>
<td>-9.49 ( \pm ) 0.52</td>
<td>-6.40 ( \pm ) 0.26</td>
<td>-5.57 ( \pm ) 0.12</td>
<td>-4.95 ( \pm ) 0.12</td>
<td>-4.49 ( \pm ) 0.12</td>
<td></td>
</tr>
</tbody>
</table>

*Ten sensor devices for each active layer were tested for statistical analysis.

Ten sensor devices for each active layer were tested for statistical analysis. Standard deviation.

For vapor phase sensing, the devices were operated in the p-channel mode \( (V_D = -0.1 \, V, \, V_G = -20 \, V) \), and the analyte liquids were vaporized using customized sequential vaporization tools as reported by Torsi et al.\(^{1}\) For the analyte vapor concentration estimation, the theoretical saturation concentration of \( \beta \)-citronellol vapor was simply calculated using the Clausius–Clapeyron equation. The analyte vapor concentration was controlled by mixing analyte vapor with nitrogen gas using a customized gas flow control system. The schematic diagram of the customized vapor phase sensing system is shown in Figure S4 (Supporting Information).

Figure 3a shows the change in drain current in the pristine graphene-based sensor devices as a function of the analyte vapor concentration. The change in channel current \( (I_D - I_{D_0}) \) of the pristine graphene sensor showed a decrease in p-channel current when both \((R)-(+)\) and \((S)-(+)\)\(-\)-\( \beta \)-citronellol vapors were exposed to the sensor devices, and the increase in current reduction was consistent with the enhancement of the analyte vapor concentration. As expected, the pristine graphene sensor shows almost the same level of current reduction for \((R)-(+)\) and \((S)-(+)\)-\( \beta \)-citronellol vapors, which means that the pristine graphene itself is not able to enantioselectively sense enantiomeric citronellol. However, the Boc-l-Phe-Pyrene/graphene-based sensor device exhibits obvious differences under exposure to \( \beta \)-citronellol enantiomer vapors compared to pristine sensors (Figure 3b). The Boc-l-Phe-Pyrene/graphene-based sensor device always reduced the channel current more for \((S)-(+)\)-\( \beta \)-citronellol vapor than for the other enantiomer \((R)-(+)\)-\( \beta \)-citronellol. We tested vapor concentration ranges from 100 to 2 ppm; however, we could not test vapor concentrations lower than 2 ppm owing to the limited vapor dilution properties of our customized vapor sensing system. The sensitivity for enantiomeric analytes, which was defined as the ratio of the channel current change with regard to the analyte concentration change, was measured from the slope of calibration curves in Figure 3b. Measured sensitivities were \(-6.7 \pm 0.57 \, nA \, per \, ppm \) for \((R)-(+)\)-\( \beta \)-citronellol and \(-9.1 \pm 0.87 \, nA \, per \, ppm \) for \((S)-(+)\)-\( \beta \)-citronellol, respectively. These sensitivities obtained from our sensor system showed remarkable enhancement when compared with the previously reported sensitivity of \( \beta \)-citronellol enantiomers obtained from the organic thin-film transistor-based sensor system \([0.04 \pm 0.01 \, nA \, per \, ppm \) for \((R)-(+)\)-\( \beta \)-citronellol and \(-0.08 \pm 0.01 \, nA \, per \, ppm \) for \((S)-(+)\)-\( \beta \)-citronellol, respectively].\(^{5} \) The theoretical limit of detection for both enantiomers, estimated from the calibration curves, was 1.45 ppm for \((R)-(+)\)-\( \beta \)-citronellol and 1.06 ppm for \((S)-(+)\)-\( \beta \)-citronellol, respectively.\(^{5} \) The response time, defined as the time required to reach 36.8% \( (=e^{-1}) \) of the maximum current change\(^{5} \) for \((R)-(+)\) and \((S)-(+)\)-\( \beta \)-citronellol sensing, was 2.25 and 1.53 s, respectively.

Interestingly, the level of current reduction for the Boc-l-Phe-Pyrene/graphene sensor for analyte vapor exposure was lower than that of the pristine graphene sensor. The lower level of current reduction with the Boc-l-Phe-Pyrene/graphene sensor can be attributed to the existence of the Boc-l-Phe-Pyrene interlayer, which limits the direct approach of the analyte molecule to the graphene layer and interactions between analyte vapor and graphene channels. In addition, we investigated multiple sensing responses at 100 ppm of \((R)-(+)\) and \((S)-(+)\)-\( \beta \)-citronellol vapor using the Boc-l-Phe-Pyrene/graphene-based sensor and found stable and repeatable multiple sensing signals with obvious differences in intensity.
for (R)-(−)- and (S)-(−)-β-citronellol vapors (Figure 3c,d). A comparison of sensing signals between the Boc-1-Phe-Pyrene/graphene-based sensor and pristine graphene-based sensor is presented in Table 1. These results clearly demonstrate the enantioselective chemical sensing properties of the sensor device and also show that the adsorption of a chiral functionalized Boc-1-Phe-Pyrene layer on the graphene device can provide enantioselective sensing properties to graphene-based sensor devices.

The results plotted in Figure 3 clearly show that the interaction between Boc-1-Phe-Pyrene and β-citronellol vapor on the graphene-based sensor reduces the amount of channel current. We speculated that the difference in the level of channel current reduction occurred because the electron-donating effects of the chiral analyte differed for the (R)- and (S)-enantiomers of β-citronellol when the analytes were adsorbed on the Boc-1-Phe-Pyrene layer (Figure 4a). Thus, to verify a signature of enantioselective sensing, we investigated the induced dipole moment on the Boc-1-Phe-Pyrene layer by performing MD simulations. We considered highly plausible morphological systems (i.e., “vertical”, “oblique”, and “horizontal” shapes) by varying the angle between the aromatic plane and the functional group of Boc-1-Phe-Pyrene molecules (see Figure S5 and “MD Simulation” in the Experimental Section). Interestingly, the induced dipole moments exhibited different trends depending on the surface morphology (Figures 4b and S6). In the vertical morphology, the dipole moment differences induced by (R)-(−)- or (S)-(−)-β-citronellol were small, whereas in other morphologies, the induced polarity of Boc-1-Phe-Pyrene was predominant to one side [i.e., (R) > (S) for horizontal morphology and (R) < (S) for oblique morphology]. Thus, on the basis of our results, we suggest that the oblique morphology may have been dominantly present on the surface which is consistent with experimental results in Figure 3. To investigate this further, we compared the binding strengths of (R)-(−)- or (S)-(−)-β-citronellol adsorbed on the Boc-1-Phe-Pyrene/graphene system using DFT calculations (see Figure S7 and “DFT Calculation” in the Experimental Section). The oblique morphology exhibited a significant difference in BE according to the chirality of β-citronellol (i.e., −37.4 kcal mol⁻¹ for (R)-(−)-β-citronellol and −45.3 kcal mol⁻¹ for (S)-(−)-β-citronellol), resulting in the substantial differences in CT to graphene. Notably, Mulliken charge analyses showed that electron donation to graphene, which was induced by the interaction between Boc-1-Phe-Pyrene and β-citronellol, was observed for all model systems regardless of surface morphology. On the basis of these results, the differences in BE due to the different chirality of β-citronellol induced differences in the level of CT and subsequently the dipole moment, which was the cause of the different levels of channel current reduction in the device.

To enable further applications of the enantioselective chemical sensor, we fabricated a flexible version using a plastic substrate and a polymer dielectric layer (Figure S8) that could easily be bent, as shown in Figure 5a. To demonstrate the enantioselective chemical sensing capability of the flexible sensor, we exposed it to (R)-(−)- and (S)-(−)-β-citronellol vapors and measured current changes. Similar to the results...
obtained from wafer-based sensors, we found clear differences in the level of drain current reduction depending on the chirality of the β-citronellol enantiomer vapor. The average change in drain current for (R)-(−)-β-citronellol vapor sensing was −1.33 μA, while for (S)-(−)-β-citronellol vapor sensing, it was −1.62 μA (Figure 5b,c). This shows that flexible sensors can easily be fabricated with reproducible enantioselective sensing responses that are consistent with those obtained using wafer-based sensor devices.

4. CONCLUSIONS

In summary, we synthesized the chiral-functionalized pyrene molecule Boc-l-Phe-Pyrene and utilized it for enantioselective discrimination of β-citronellol enantiomers. The Boc-l-Phe-Pyrene molecule itself showed chiral discrimination properties with different UV−vis and PL responses in solution-phase sensing of (R)-(+) and (S)-(−)-β-citronellol. Device-based chiral discrimination of the given β-citronellol enantiomers was accomplished by GFETs via noncovalent interactions between Boc-l-Phe-Pyrene and graphene. Both pristine graphene films and graphene/Boc-l-Phe-Pyrene films were characterized by AFM and Raman spectroscopy to establish the successful deposition of Boc-l-Phe-Pyrene on the graphene surface. The resulting chemosensors could successfully identify β-citronellol enantiomers with high sensitivity. On the basis of computational studies, the binding interactions between (R)-(−)- or (S)-(−)-β-citronellol and the Boc-l-Phe-Pyrene/graphene system significantly differ according to the chirality of β-citronellol, leading to substantial differences in the CT from enantiomer citronellol to graphene and in the induced dipole moments. Furthermore, we successfully fabricated a flexible GFET-based enantioselective sensor. Given the fact that FET-based chiral sensing is still rare and challenging, this study paves the way for the development of highly sensitive and enantioselective chemosensors.

■ ASSOCIATED CONTENT

# Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsami.8b13517.

NMR spectra; GFET performances; experimental process; and simulation results (PDF)

■ AUTHOR INFORMATION

Corresponding Authors
*E-mail: skkwak@unist.ac.kr (S.K.K.).
*E-mail: joonhoh@snu.ac.kr (J.H.O.).

ORCID

Sang Kyu Kwak: 0000-0002-0332-1534
Joon Hak Oh: 0000-0003-0481-6069

Author Contributions

X.S. and C.H.P. contributed equally to this work. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Samsung Research Funding Center of Samsung Electronics under project number SRFC-MA1602-03. S.K.K. acknowledges financial support from the NRF of Korea (NRF-2014R1A1A1009799) and computational resources from UNIST-HPC.

■ REFERENCES

Monoterpene Alcohol, Reduces Nociceptive and Inflammatory
Barreto, E. O.; Oliveira, A. P.; Quintans, L. J. Citronellol, a
V.; De Sousa, D. P.; Badaue-Passos, D.; de Lucca, W.; Brito, F. A.;
Approximation Made Simple.
ACS Applied Materials & Interfaces
Composites of Graphene with Large Aromatic Molecules.
Dispersions of Noncovalently Functionalyzed Graphene from Graphite
and Their Multifunctional High-Performance Applications. Nano
Lee, D. J.; Kong, B.-S.; Paik, K.-W.; Jeon, S. Enhanced Thermal
Conductivity of Epoxide-Graphene Composites by Using Non-Oxidized
Hybrid Photodetectors with Ultrahigh Photoresponsivity. Small
2014, 10, 3700–3706.
(27) de Sousa, D. P.; Gonçalves, J. C. R.; Quintans-Júnior, L.; Cruz,
J. S.; Araújo, D. A. M.; de Almeida, R. N. Study of Anticoagulant
Effect of Citronellol, a Monoterpenoid Alcohol, in Rodents. Neurosci.
(28) Bastos, J. F. A.; Moreira, I. J. A.; Ribeiro, T. P.; Medeiros, I. A.;
(41) DS BIOVIA. Materials Studio 2018; Dassault Systèmes: San Diego, 2018.