ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2019, **55**, 10768

Received 9th July 2019,
Accepted 12th August 2019

DOI: 10.1039/c9cc05245c

rsc.li/chemcomm

Reaction-based chiroptical sensing of ClO^- using circularly polarized luminescence *via* self-assembly organogel†

Jun Gong,‡[a] Maoxing Yu,‡[b] Chunfei Wang,[a] Jingyun Tan,[a] Shichao Wang,[a] Shiyin Zhao,[a] Zujin Zhao,[b] Anjun Qin,[b] Benzhong Tang[b] and Xuanjun Zhang*[a]

By covalent combination of a chiral amino acid, lipid, and achiral phenothiazine derivative, a reaction-based chiroptical probe, PTZ-D, was obtained. PTZ-D could self-assemble into a chiral organogel realizing the chirality transformation from a chiral amino acid to a self-assembled system and displaying unprecedented chiroptical monitoring of ClO^- with switchable CPL signals.

Fluorescent probes have developed rapidly in the past decades, while the investigation only focuses on achiral chromophore scaffolds emitting unpolarized light,[1] which inevitably suffer from the interference of background because of the common existence of autofluorescence. In recent years, chiroptical technologies have attracted great attention in recognizing polarized light owing to the high specificity. In the field of optoelectronic technologies, organic semiconductors have been used in field-effect transistors to detect circularly polarized luminescence (CPL), which has great significance in the development of CPL detecting devices.[2] Additionally, a kind of chiral oligothiophene material has been developed to discriminate the direction of illumination.[3] In the field of chiroptical sensing, circular dichroism (CD) spectroscopy, the most widely used chiroptical tool, has been extensively used to investigate the absolute configurations of chiral compounds.[4] However, reaction-based CD sensing of achiral species has been limited due to the shortage of suitable probes. Recently, we synthesized an effective CD probe to detect ClO^- with switching CD signals.[5a] Despite the advantages of CD spectroscopy, as absorption spectroscopy, CD only reflects the structural properties in the ground state of a molecule. In contrast, circularly polarized luminescence (CPL) is correlated with the excited states, displaying the difference in the emission intensity between left- and right-circularly polarized light.[6] Additionally, emission spectroscopy is normally much more sensitive than absorption spectroscopy and has a larger application range. Thereby, we aim to design a kind of probe emitting CPL signals; only the polarized light from the target-triggered CPL probe can be collected, and other unpolarized light will be automatically filtered out, which will dramatically increase spatial resolution and selectivity.

Until now, some CPL biosensors have been reported, which are activated or enhanced by the generation of metal ion coordination bonds,[7] photoisomerization[8] or concentration variation.[9] Although these probes could show CPL-changing, even CPL-switching properties, they were not reaction-based. Their further application was limited by single triggered fashion of the scaffolds involved in the probes. In order to further expand the application range of CPL, the design of reaction-based CPL sensors has become necessary because of adjustable reaction sites and tuneable emission wavelength.

The extent of CPL can be conveniently indicated through the luminescence dissymmetry factor (g_{lum}), whose values range between −2 and +2.[10] Kawai and co-workers found that the self-assembly could amplify the g_{lum} value, because the excitonic couplings between individual chromophores were gathered in an aggregate state.[11] Liu's group originally proposed a kind of chiral amino acid-based lipid, which could self-assemble to form an organogel composed of helicoid nanotubes.[12] Moreover, they used this gel to build some CPL systems commendably.[13] Inspired by their study, we tried to take advantage of this chiral amino acid-based lipid to construct a reaction-based chiral probe through covalently linking it to an activatable chromophore. Here, a phenothiazine derivative was chosen as the candidate because phenothiazine not only exhibits pretty good absorption and emission properties, but can also be used to detect ClO^- through the oxidation of the sulfur atom bridge.[5] In this work, we report first the design and synthesis of a reaction-based CPL sensor, PTZ-D, to monitor hypochlorite ion (ClO^-) with switchable CPL signals (Fig. 1).

The synthesis and characterization of PTZ-D and its enantiomer PTZ-L are described in the ESI.† In general, chiral glutamic

[a] *Cancer Centre and Centre of Reproduction, Development and Aging, Faculty of Health Sciences, University of Macau, Macau SAR, China. E-mail: xuanjunzhang@um.edu.mo*

[b] *State Key Laboratory of Luminescent Materials and Devices, South China University of Technology, Guangzhou 510640, China*

† Electronic supplementary information (ESI) available: Synthesis, experimental details, NMR spectra and MS spectra. See DOI: 10.1039/c9cc05245c

‡ These authors contributed equally.

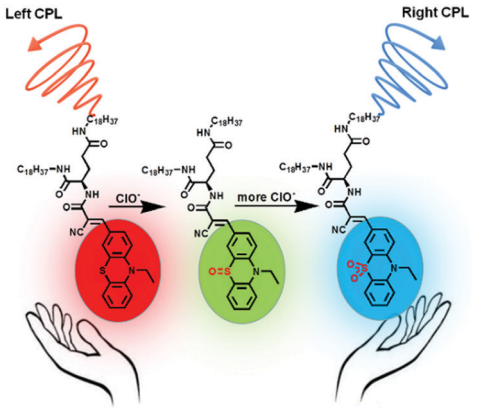

Fig. 1 Chemical structure of PTZ-D and the proposed switchable CPL mechanism towards ClO^-.

acid-based lipids were synthesized through an amide condensation reaction between glutamic acid and octadecylamine. Then a phenothiazine derivative with a carboxyl group was linked to the glutamic acid-based lipids to obtain the probes.

Firstly, the selectivity of PTZ-D toward different ROS/RNS (Reactive Oxygen Species/Reactive Nitrogen Species), including $ONOO^-$, NO, H_2O_2, TBHP (*tert*-butyl hydroperoxide), GSH (glutathione), L-Cys (L-cysteine), $^{\bullet}OH$ and ClO^- was assessed (Fig. 2a). PTZ-D exhibited highly specific selectivity towards ClO^- compared with other ROS/RNS. To investigate the sensing mechanism, titration experiments of PTZ-D (10 μM) were conducted in a $CH_3CN/CHCl_3$ (3/1, vol/vol) mixed solvent. Upon addition of ClO^- from 0 to 80 μM, the two absorption bands at 313 nm and 428 nm decreased gradually with an emerging peak at 375 nm (Fig. 2b). The fluorescence band intensity at 625 nm decreased and that at 498 nm increased gradually with the increase in concentration of ClO^- (Fig. 2c). Then, we studied the changes in the time-dependent fluorescence intensity of PTZ-D (10 μM) in the presence of 10 equivalents of ClO^-. As shown in Fig. 2d, PTZ-D showed a fast response to ClO^- in $CH_3CN/CHCl_3$ (3/1, vol/vol) of about 210 s. The reaction mechanism of phenothiazine-based probes towards hypochlorite was investigated clearly by our group in previous reports.[5a,14] According to the mechanism, the sulfur atom on the phenothiazine moiety was oxidized to sulfoxide first, and then to sulphone with more hypochlorite.

Since the probe has a chiral center, the chirality was first characterized by circular dichroism (CD) spectroscopy (Fig. 2e). PTZ-D showed a negative Cotton effect at 438 nm, and a positive Cotton effect at 313 nm, which was in accordance with the regions of its UV/vis absorption peaks. PTZ-L showed a mirror-imaged CD signal with PTZ-D. The probe PTZ-D was further found to change the CD intensity with addition of ClO^- from 0 to 90 μM (Fig. 2f). The negative Cotton effect at 438 nm in PTZ-D decreased gradually at first, and then turned into a positive Cotton effect with continuous addition of ClO^-. This is an interesting reversing phenomenon in agreement with that reported by our group previously.[5a] The formation of sulfur–oxygen bonds led to a change in the dihedral angle in the

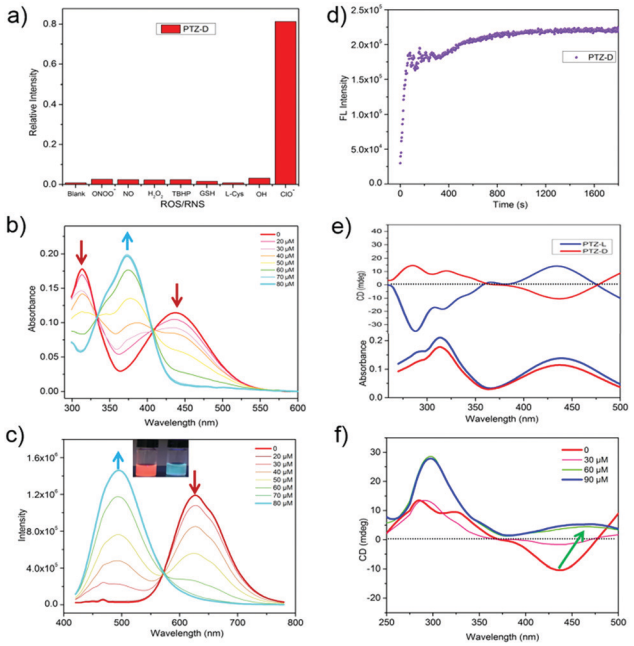

Fig. 2 (a) Relative fluorescence intensities of PTZ-D (10 μM) treated with various ROS and RNS in 0.05 M PBS/DMF (7/3, vol/vol) at pH 7.4 for 60 min. $ONOO^-$: 50 μM NaONOO; NO: 50 μM; H_2O_2: 50 μM; TBHP: 50 μM; GSH: 50 μM; L-Cys: 50 μM; $^{\bullet}OH$: 50 μM + 50 μM ferrous ammonium sulfate; ClO^-: 50 μM NaClO. (b) UV/vis absorption spectral changes of PTZ-D (10 μM) after reaction with different concentrations of ClO^- (0–80 μM) in $CH_3CN/CHCl_3$ (3/1, vol/vol) for 30 min. (c) Fluorescence spectral changes of PTZ-D (10 μM) responding to absorption under the same conditions. (d) Time-dependent fluorescence intensity changes of PTZ-D (10 μM) in the presence of 10 equiv. ClO^- in $CH_3CN/CHCl_3$ (3/1, vol/vol) for 30 min. The fluorescence intensity point was recorded every 5 s (λ_{ex} = 410 nm, λ_{em} = 498 nm). (e) CD (top) and UV/vis spectra (bottom) of PTZ-L (10 μM) and PTZ-D (10 μM) in $CH_3CN/CHCl_3$ (3/1, vol/vol). (f) CD spectral change of PTZ-D after reaction with different concentrations of ClO^-. All optical measurements were taken in quartz cuvettes (1 cm × 1 cm, 3 mL).

phenothiazine moiety, which was responsible for the CD signal reversal.[5a,15]

Due to the presence of a donor chromophore, ethyl-substituted phenothiazine, conjugated with a universal gelator moiety *N*,*N*′-bis(octadecyl)-D(L)-glutamic diamide, PTZ-D and PTZ-L displayed excellent gel ability in the $CHCl_3/CH_3CN$ (3/1, vol/vol) mixed solvent when its concentration increased to 8 mM.

To verify the gel structure, we determined the morphology of the PTZ-D gel by scanning electron microscopy (SEM). As shown in Fig. 3a, PTZ-D gel formed a visible left-handed helicoid structure. The SEM observation indicated that the molecular

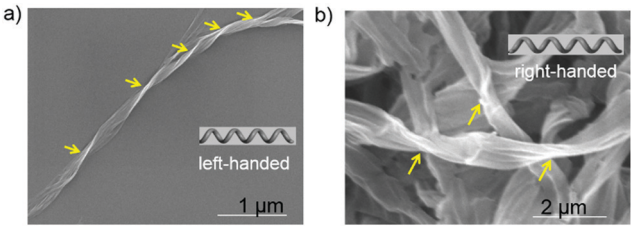

Fig. 3 SEM images of xerogel made from (a) PTZ-D and (b) PTZ-D + ClO^-.

chirality was transferred to the self-assembled structure during the formation of the gel. After interaction with ClO^-, it could be observed from Fig. 3b that the renewed structure of PTZ-D gel did not show a left-handed nanohelix but displayed a weak right-handed one. This reversing phenomenon was consistent with the result observed in the CD spectra mentioned above.

Subsequently, we investigated the CPL of PTZ-D gel and PTZ-L gel (Fig. 4a). CPL signals with different chiralities and emissions at 610 nm could be observed. The g_{lum} value was about 1.68×10^{-3} and -1.78×10^{-3} at 610 nm for PTZ-L and PTZ-D gel, respectively (Fig. 4b), comparable to other organic self-assembly systems.[9,16]

Then we studied the feasibility of PTZ-D gel to monitor ClO^-. At first, with addition of ClO^-, the negative CPL signal of PTZ-D gel decreased gradually. Then the signal reversed to positive and increased gradually with addition of an increasing volume of NaClO (Fig. 4c). Additionally, the reversed signals obtained in the CD and CPL spectra both showed a red-shift phenomenon, which was also observed in other phenothiazine-based systems.[5] It has been proved that the supramolecular chirality mainly depends on self-assembly rather than the individual molecular chirality, and hydrogen bonds and steric hindrance are crucial factors for the CPL inversion.[17] It was not hard to conclude that the CPL reversion of PTZ-D resulted from the incorporation of oxygen atoms and the change of stereoscopic configuration of the phenothiazine moiety. The introduction of oxygen atoms might affect the molecular π–π stacking and provide new intermolecular interaction such as hydrogen bonds between PTZ-D and PTZ-D, which changed the stack mode and the orientation of amide groups during the gelation process. Thus, the combination of the stereoscopic configuration change and new intermolecular interaction generation transformed the supramolecular chirality from left-handed to right-handed.

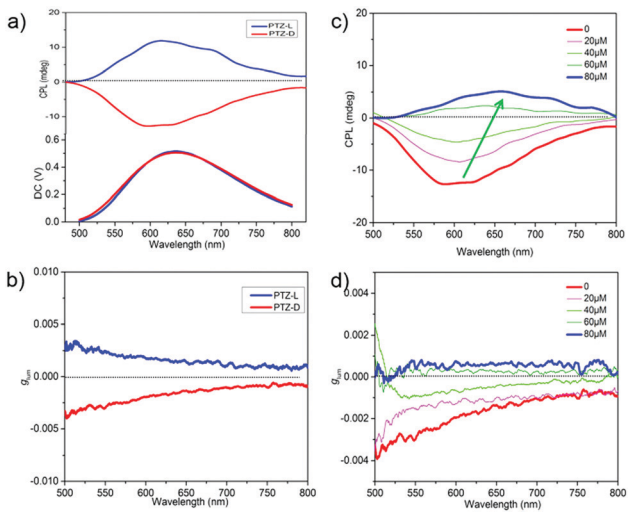

Fig. 4 (a) CPL spectra of PTZ-L and PTZ-D gel. The DC value in the bottom spectrum stands for fluorescence intensity. (b) g_{lum} of PTZ-L and PTZ-D gel *versus* wavelength curves. (c) CPL spectral change and (d) g_{lum} change of PTZ-D gel in the presence of different amounts of ClO^- (λ_{ex} = 410 nm).

In conclusion, we have demonstrated a useful strategy to construct a reaction-based probe to monitor ClO^- with switchable CPL signals for the first time. Through covalently linking a chiral amphiphilic lipid to a hypochlorite-triggerable phenothiazine moiety, the chirality of amino acid was transferred to the self-assembly organogel with distinct CPL emission. The self-assembled organogel showed switchable CPL sensing towards ClO^-. The strategy presented in this work is anticipated to broaden the insights to develop more efficient reaction-based chiroptical probes with highly specific and sensitive CPL signals towards various achiral and chiral targets in living bodies, foods and environments.

This work was funded by the Science and Technology Development Fund, Macau SAR (File No.: 082/2016/A2 and 019/2017/AMJ) and the Research Grant of University of Macau under grant no.: MYRG2016-00058-FHS and MYRG2017-00066-FHS.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 L. You, D. Zha and E. V. Anslyn, *Chem. Rev.*, 2015, **115**, 7840–7892.
2 (*a*) Y. Yang, R. C. da Costa, M. J. Fuchter and A. J. Campbell, *Nat. Photonics*, 2013, **7**, 634–638; (*b*) Y. Yang, B. Rice, X. Shi, J. R. Brandt, O. C. da Costa, G. J. Hedley, O. M. Smilgies, J. M. Frost, D. W. Samuel, A. O. Roza, E. R. Johnson, O. E. Jelfs, O. Nelson, A. J. Campbell and M. J. Fuchter, *ACS Nano*, 2017, **11**, 8329–8338; (*c*) X. Shang, I. Song, H. Ohtsu, Y. H. Lee, T. Zhao, T. Kojima, J. H. Jung, M. Kawano and J. H. Oh, *Adv. Mater.*, 2017, **29**, 1605828.
3 (*a*) G. Albano, M. Lissia, G. Pescitelli, L. A. Aronica and L. Di Bari, *Mater. Chem. Front.*, 2017, **1**, 2047–2056; (*b*) G. Albano, F. Salerno, L. Portus, W. Porzio, L. A. Aronica and L. Di Bari, *ChemNanoMat*, 2018, **4**, 1059–1070.
4 (*a*) G. A. Hembury, V. V. Borovkov and Y. Inoue, *Chem. Rev.*, 2008, **108**, 1–73; (*b*) L. You, J. S. Berman and E. V. Anslyn, *Nat. Chem.*, 2011, **3**, 943–948; (*c*) J. Gong, P. Sun, N. Jiang, R. Riccio, G. Lauro, G. Bifulco, T.-J. Li, W. H. Gerwick and W. Zhang, *Org. Lett.*, 2014, **16**, 2224–2227; (*d*) J. Gong, A. Ju, D. Zhou, D. Li, W. Zhou, W. Geng, B. Li, L. Li, Y. Liu and Y. He, *Molecules*, 2015, **20**, 683–692; (*e*) L.-E. Guo, Y. Hong, S.-Y. Zhang, M. Zhang, X.-S. Yan, J.-L. Cao, Z. Li, T. D. James and Y.-B. Jiang, *J. Org. Chem.*, 2018, **83**, 15128–15135; (*f*) R.-J. Li, J. J. Holstein, W. G. Hiller, J. Andréasson and G. H. Clever, *J. Am. Chem. Soc.*, 2019, **141**, 2097–2103; (*g*) Z. A. De los Santos, C. C. Lynch and C. Wolf, *Angew. Chem., Int. Ed.*, 2019, **58**, 1198–1202.
5 (*a*) J. Tan, C. Wang, H. K. Lao, W. Wang, G. Feng, D. Yuan, C. Wu and X. Zhang, *Chem. Commun.*, 2019, **55**, 7438–7441; (*b*) H. Xiao, K. Xin, H. Dou, G. Yin, Y. Quan and R. Wang, *Chem. Commun.*, 2015, **51**, 1442–1445; (*c*) D. Soni, N. Duvva, D. Badgurjar, T. K. Roy, S. Nimesh, G. Arya, L. Giribabu and R. Chitta, *Chem. – Asian J.*, 2018, **13**, 1594–1608.
6 (*a*) E. M. Sánchez-Carnerero, F. Moreno, B. L. Maroto, A. R. Agarrabeitia, M. J. Ortiz, B. G. Vo, G. Muller and S. d. l. Moya, *J. Am. Chem. Soc.*, 2014, **136**, 3346–3349; (*b*) S. Zhang, Y. Wang, F. Meng, C. Dai, Y. Cheng and C. Zhu, *Chem. Commun.*, 2015, **51**, 9014–9017.
7 (*a*) N. Çoruh, G. L. Hilmes and J. P. Riehl, *J. Lumin.*, 1988, **40**, 227–228; (*b*) C. P. Montgomery, E. J. New, D. Parker and R. D. Peacock, *Chem. Commun.*, 2008, 4261–4263; (*c*) J. Yuasa, T. Ohno, H. Tsumatori, R. Shiba, H. Kamikubo, M. Kataoka, Y. Hasegawa and T. Kawai, *Chem. Commun.*, 2013, **49**, 4604–4606; (*d*) K. Okutani, K. Nozaki and M. Iwamura, *Inorg. Chem.*, 2014, **53**, 5527–5537; (*e*) Q. Jin, S. Chen, H. Jiang, Y. Wang, L. Zhang and M. Liu, *Langmuir*, 2018, **34**, 14402–14409; (*f*) H. Isla, N. Saleh, J. K. Ou-Yang, K. Dhbaibi, M. Jean, M. Dziurka, L. Favereau, N. Vanthuyne, L. Toupet, B. Jamoussi, M. Srebro-Hooper and J. Crassous, *J. Org. Chem.*, 2019, **84**, 5383–5393; (*g*) A. Homberg, E. Brun, F. Zinna,

S. Pascal, M. Górecki, L. Monnier, C. Besnard, G. Pescitelli, L. D. Bari and J. Lacour, *Chem. Sci.*, 2018, **9**, 7043–7052; (*h*) P. Reiné, J. Justicia, S. P. Morcillo, S. Abbate, B. Vaz, M. Ribagorda, Á. Orte, L. Álvarez de Cienfuegos, G. Longhi, A. G. Campaña, D. Miguel and J. M. Cuerva, *J. Org. Chem.*, 2018, **83**, 4455–4463.

8 Y. Hashimoto, T. Nakashima, D. Shimizu and T. Kawai, *Chem. Commun.*, 2016, **52**, 5171–5174.

9 S. Ito, K. Ikeda, S. Nakanishi, Y. Imai and M. Asami, *Chem. Commun.*, 2017, **53**, 6323–6326.

10 E. M. Sánchez-Carnerero, A. R. Agarrabeitia, F. Moreno, B. L. Maroto, G. Muller, M. J. Ortiz and S. de la Moya, *Chem. – Eur. J.*, 2015, **21**, 13488–13500.

11 J. Kumar, T. Nakashima, H. Tsumatori and T. Kawai, *J. Phys. Chem. Lett.*, 2014, **5**, 316–321.

12 X. Zhu, Y. Li, P. Duan and M. Liu, *Chem. – Eur. J.*, 2010, **16**, 8034–8040.

13 (*a*) D. Yang, P. Duan, L. Zhang and M. Liu, *Nat. Commun.*, 2017, **8**, 15727; (*b*) D. Yang, P. Duan and M. Liu, *Angew. Chem., Int. Ed.*, 2018, **130**, 9501–9505; (*c*) Y. Li and M. Liu, *Chem. Commun.*, 2008, 5571–5573.

14 S. Wang, B. Zhang, W. Wang, G. Feng, D. Yuan and X. Zhang, *Chem. – Eur. J.*, 2018, **24**, 8157–8166.

15 (*a*) M. Okazaki, T. Mizusawa, K. Nakabayashi, M. Yamashita, N. Tajima, T. Harada, M. Fujiki and Y. Imai, *J. Photochem. Photobiol., A*, 2016, **331**, 115–119; (*b*) T. Kimoto, N. Tajima, M. Fujiki and Y. Imai, *Chem. – Asian J.*, 2012, **7**, 2836–2841.

16 J. Kumar, T. Nakashima and T. Kawai, *J. Phys. Chem. Lett.*, 2015, **6**, 3445–3452.

17 F. Wang, W. Ji, P. Yang and C.-L. Feng, *ACS Nano*, 2019, **13**, 7281–7290.