Tetrahedron Letters xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Anion binding by *tert*-butanesulfinamide based phenol receptors

Ye-Ye Shen [a,†], Yao Li [a,†], Bin Wang [b,*], Xin Li [a,*]

[a] State Key Laboratory of Elemento-Organic Chemistry, Collaborative Innovation Center of Chemical Science and Engineering, Department of Chemistry, Nankai University, Tianjin 300071, PR China
[b] Tianjin Key Laboratory of Structure and Performance for Functional Molecule, College of Chemistry, Tianjin Normal University, Tianjin 300387, PR China

ARTICLE INFO

Article history:
Received 21 October 2015
Revised 9 December 2015
Accepted 23 December 2015
Available online xxxx

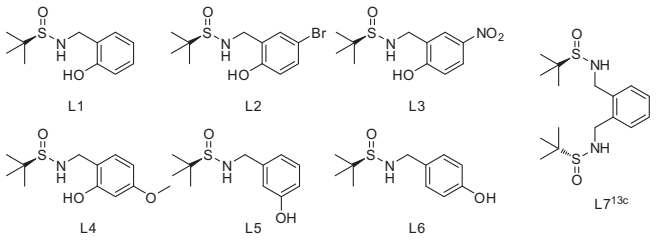
Keywords:
tert-Butanesulfinamide
Phenol
Anion recognition
Hydrogen-bond donor
O–H group

ABSTRACT

A series of *tert*-butanesulfinamide type compounds, which were decorated with phenol receptors, were found to recognize chlorine ion, nitrate ion, and acetate ion by ^{1}H NMR titration experiments. The results indicated that the interaction between subject molecule and anion was enhanced with the increase of the acidity of the phenolic O–H group. Furthermore, the *tert*-butyl group seemed to play a role in the anion recognition.

Anions, such as chloride, nitrate, acetate, phosphate, and sulfate ion, play important roles in the areas of biological, medical, environmental, and life science.[1] In general, the functions of anions are achieved by recognition between a substrate and anion. Therefore, the study of the recognition of anions has moved on from being an area solely of academic interest to a fundamental pillar of supramolecular chemistry and attracted great attention.[2] Furthermore, the anion recognition has also been used to develop a very efficient organocatalytic strategy, ie anion-binding catalysis, which realized a number of challenge organic transformations.[3] As is known, featuring the molecular complementarity of the two partners, highly specific anion binding may occur through a series of multifarious noncovalent interactions, such as electrostatic, hydrophobic, hydrogen-bonding, and anion-interactions.[4] Based on the various associative interactions, plenty of subject molecules have been designed and synthesized for the application in anion recognition, transport, sensing, and extraction.[5] Among them, hydrogen bond type compounds, by virtue of their diversity and modification of structure and convenient synthesis, have become the most widely studied anion receptors.[6] As a result, traditional receptors containing N–H groups, such as amide, sulfonamide, urea, thiourea, and pyrrole, have been extensively employed.[7] Recently, some new fashioned hydrogen bond donors, such as squaramides and aliphatic polyols, have also been developed as efficient anion receptors.[8] It is worth mentioning that the studied hydrogen bond sources of the aforementioned anion receptors are mostly N–H groups. Relative fewer examples of the anion receptors bearing phenolic hydroxyl groups were reported.[9] In fact, in nature, multiple hydrogen bonds using both N–H and O–H donors were verified responsible for the anion recognition and transport process.[10] Therefore, designing a new kind of receptors, especially cooperative with N–H and O–H functional groups, which have great ability of recognizing biologically important anions, is still a formidable challenge and highly desirable.

tert-Butanesulfinamide, which was developed by Ellman and coworkers, has been widely used as a chiral auxiliary in asymmetric synthesis.[11] Recently, chiral sulfinamide based organocatalysts have been reported for a series of important asymmetric transformations.[12,13] However, unlike sulfonamides, sulfinamide based



Scheme 1. Structure of the receptors.

* Corresponding authors.
E-mail addresses: hxxywangb@mail.tjnu.edu.cn (B. Wang), xin_li@nankai.edu.cn (X. Li).
† These authors contribute the same to this work.

http://dx.doi.org/10.1016/j.tetlet.2015.12.090
0040-4039/

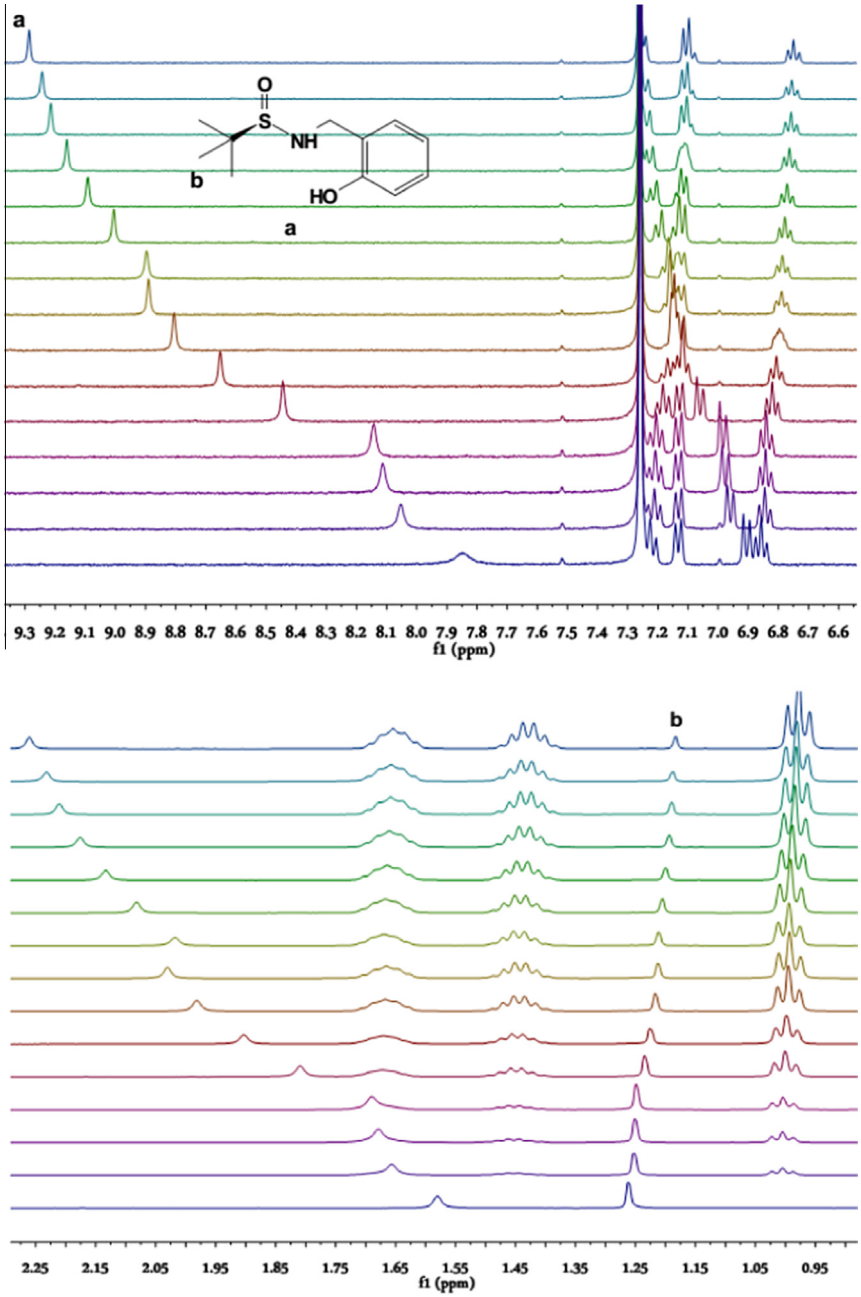


Figure 1. Stack plot of ^{1}H NMR spectra (400 MHz, $CDCl_3$) of receptor **L1** (5×10^{-3} M) upon addition of Cl^- ($(Bu_4N)Cl$).

Table 1
Association constants ($K_{a(1:1)}$) of receptors with various anions in $CDCl_3$

	Cl^-	NO_3^-	AcO^-
L1	44.3 ± 2.1[a]	15.2 ± 1.0[a]	47.2 ± 2.1[b]
L2	85.3 ± 3.6[a]	78.3 ± 4.8[b]	298.0 ± 10.4[b]
L3	697.5 ± 37.1[b]	81.2 ± 5.9[a]	—
L4	41.4 ± 0.8[a]	18.0 ± 1.3[a]	108.0 ± 2.9[b]
L5	65.9 ± 6.8[b]	36.9 ± 2.7[b]	184.2 ± 10.0[b]
L6	95.8 ± 9.0[b]	40.0 ± 2.4[b]	346.0 ± 41.3[b]
L7	<10	<10	<10

[a] The association constants were determined by the chemical shift of proton of phenolic hydroxyl.
[b] The association constants were determined by the chemical shift of aromatic proton.

receptors have not been used in anion recognition. Herein, *tert*-butanesulfinamide based phenols, which had been used as chiral Lewis base catalysts in reduction of aromatic ketimines,[13a] were chosen as cooperative body of N–H and O–H donors to examine their anion recognition ability.

Six target compounds (Scheme 1) were prepared from salicylaldehyde and *tert*-butanesulfinamide in two steps following the reported procedures.[13a] Furthermore, disulfinyl compound **L7**,[13d] which had double sulfinamide symmetrical structure, was also prepared to investigate its anion binding ability (Scheme 1).

Initially, we investigated a range of potential guest anions by **L1**. ^{1}H NMR experiment of a 1:1 mixture of **L1** and several anions was performed to examine the binding abilities. Since **L1** showed poor binding ability with the less basic anions (Br^-, I^-), we mainly tested the binding behavior of chlorine ion (Cl^-), nitrate ion

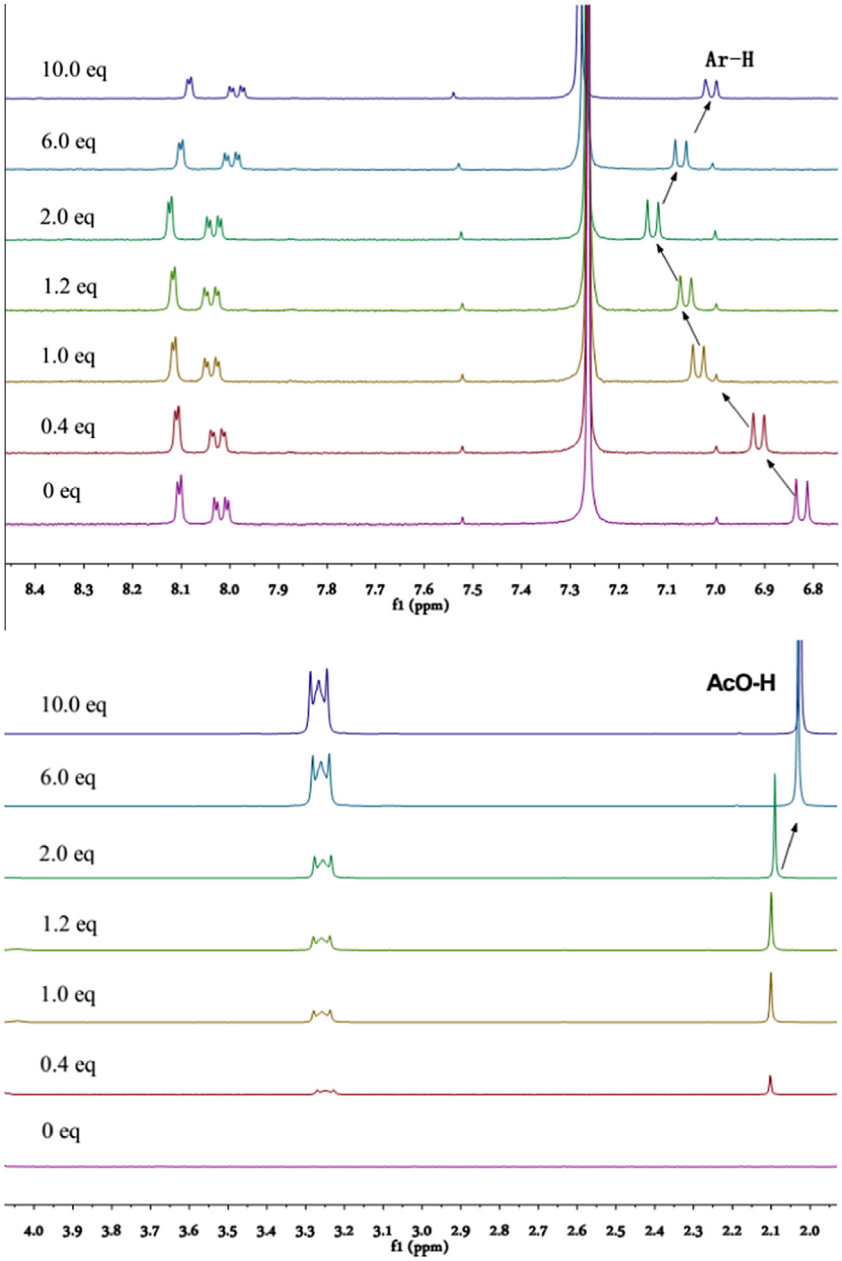


Figure 2. Stack plot of ^{1}H NMR spectra (400 MHz, $CDCl_3$) of receptor **L3** upon addition of AcO^-. Ratio of concentration [AcO^-]/[**L3**] is shown above.

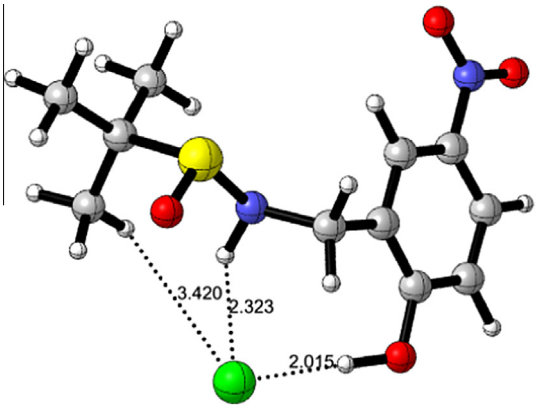


Figure 3. Optimized geometry of **L3** and chloride complex in $CHCl_3$ calculated with the M06-2x/6-311+G(d,p) (SMD) method.

(NO_3^-), and acetate ion (AcO^-) in this work. As shown in Figure 1, the O–H of **L1** had an obvious downfield shift from 7.843 ppm to 9.605 ppm. This result indicated that the O–H had a strong interaction with Cl^-. Meanwhile, the aromatic proton of **L1** at around 7 ppm had some shifts, which illustrated that the aromatic proton also participated in Cl^- binding. Unexpectedly, the proton of the *tert*-butyl group at 1.262 ppm shifted upfield a little bit. It seemed that the C–H of the *tert*-butyl group played a small role in the process of anion recognition as a potential weak hydrogen bond donor. All the evidences showed that **L1** and Cl^- had multiple hydrogen bond interactions.

We then examined the titrations of other receptors (**L2**–**L7**) and different anions (Cl^-, NO_3^- and AcO^-). The binding affinity was indicated by the changes of the chemical shifts of the proton of the phenolic hydroxyl group or aromatic proton. And the binding affinity data are summarized in Table 1. All the titration curves of receptors to anions give the best fit for the 1:1 binding

Please cite this article in press as: Shen, Y.-Y.; et al. *Tetrahedron Lett.* (2015), http://dx.doi.org/10.1016/j.tetlet.2015.12.090

model in agreement with Job's plot shown in the Supporting information.

Among the examined three anions, NO_3^- showed the weakest binding interactions with all the receptors. This maybe due to that the basicity of NO_3^- is too weak. On the opposite, the AcO^-, which had higher basicity, showed the strongest interactions with the examined receptors. As for different receptors, **L2** and **L3**, which were substituted with electron withdrawing groups, they had stronger binding affinity with all the three anions. As for receptor **L4**, which substituted with a methoxy group, exhibited a slightly stronger binding affinity than **L1**. Next, the effect of the different position of the phenolic hydroxyl group on the anion recognition was investigated. As shown in Table 1, the order of binding ability of anion interaction was **L6** > **L5** > **L1**. The different hindrance caused by the position of O–H, which affected the interaction between the anion and the aromatic proton of receptors, was suspected to induce the observed diversity of affinity data. It is noteworthy that the interaction of **L7** and anions, even with AcO^-, was very weak, which could not get the binding affinity data via ^1H NMR titration. This fact illustrated that the hydroxyl group played an important role in current studied anion interaction mode.

On careful examination of the experiment, we found that the titration of the **L3** and anions was a clear color change process, in which the solution of the mixture of **L3** and anions in $CDCl_3$ changed from light yellow to deep yellow along with the increase of the anion concentration. This interesting phenomenon indicated that we can monitor the recognition of anion by **L3** via a visual observation.

As for the ^1H NMR titration of AcO^- in **L3**, the chemical shift of Ar–H appeared at 6.831 ppm and showed a significant downfield shift upon the addition of AcO^-. However, the trend changed from downfield shift into upfield shift accompanied with excessive addition of AcO^-. Simultaneously, the chemical shift of the proton of AcO^- suddenly changed from 2.102 ppm to 2.025 ppm (Fig. 2), which meant that the AcO^- had already become AcOH. UV–vis experiment in $CHCl_3$ was then conducted. During the titration of **L3** with Cl^-, NO_3^-, and AcO^- by UV–vis, spectral change was observed only upon addition of AcO^-. A new band at around 425 nm, which was the same as the absorbance band obtained when strong base tetrabutylammonium hydroxide (TBAOH) was added into **L3**, was observed. And from the UV–vis titration spectra of **L3** with AcO^-, we also found that the deprotonation happened at the start of titration.[14] The aforementioned evidences revealed a fact that a typical Brønsted acid–base reaction should be happen between **L3** and AcO^-. Moreover, corresponding pK_a values of AcOH (12.6) and *p*-nitrophenol (10.8) can reasonably explain the experimental observation.[15]

To further explore the interaction modes of the complex, the geometry of the receptor **L3** and chloride complex was optimized with the M06-2X/6-311+G(d,p) (SMD) method.[16,17] As illustrated in Figure 3, the distances between the Cl^- and the O–H proton and the N–H proton are 2.015 and 2.323 Å, respectively. These distances are distinctly smaller than the sum (2.86–3 Å) of the van der Waals radii of hydrogen and Cl^-,[18] thereby indicating the formation of hydrogen bond. It should be noted that the distance between the Cl^- and the C–H proton of the *tert*-butyl group is 3.420 Å. The distance is a little longer than the 3 Å, indicating the possible weak interaction of C–H···Cl.

In summary, we have found that *tert*-butanesulfinamide based phenols can act as receptors recognizing Cl^-, NO_3^-, and AcO^- through ^1H NMR titration experiment. The information of the relationship between the structure of acceptors (or anions) and recognition capability was discussed, which was helpful for the future design of efficient *tert*-butanesulfinamide phenol type anion receptors. To our knowledge, this is the first example of *tert*-butanesulfinamide derived anion receptors.

Acknowledgments

The project was supported by 973 Program (2012CB821600), NSFC (21390400, 21421062, 21172112 and 21172118) and the "111" project (B06005) of the Ministry of Education of China.

Supplementary data

Supplementary data (experimental procedures, analysis data of new compounds, NMR spectra and titrations data) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.12.090.

References and notes

1. (a) Christianson, D. W.; Lipscomb, W. N. *Acc. Chem. Res.* **1989**, *22*, 62; (b) Berg, J. M. *Acc. Chem. Res.* **1995**, *28*, 14.
2. (a) Gale, P. A.; Quesada, R. *Coord. Chem. Rev.* **2006**, *250*, 3219; (b) Steed, J. W. *Chem. Soc. Rev.* **2009**, *38*, 506; (c) Yang, Z.-P.; Zhang, K.; Gong, F.-B.; Li, S.-Y.; Chen, J.; Ma, J.-S.; Sobenina, L. N.; Mikhaleva, A. I.; Trofimov, B. A.; Yang, G. Q. *J. Photochem. Photobiol., A* **2011**, *217*, 29; (d) Bao, X.-P.; Zhou, Y.-H. *Sens. Actuators, B* **2010**, *147*, 434; (e) Evans, N.; Beer, H. P. D. *Angew. Chem., Int. Ed.* **2014**, *53*, 11716; (f) Busschaert, N.; Caltagirone, C.; Rossom, W. V.; Gale, P. A. *Chem. Rev.* **2015**, *115*, 8038.
3. (a) Zhang, Z.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187; (b) Beckendorf, S.; Asmus, S.; Mancheño, O. G. *ChemCatChem* **2012**, *4*, 926; (c) Brak, K.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2013**, *52*, 534; (d) Mahlau, M.; List, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 518; (e) Seidel, D. *Synlett* **2014**, 783.
4. Gale, P. A.; Busschaert, N.; Haynes, C. J. E.; Karagiannidis, L. E.; Kirby, I. L. *Chem. Soc. Rev.* **2014**, *43*, 205.
5. (a) Gale, P. A. *Acc. Chem. Res.* **2011**, *44*, 216; (b) Kruppa, M.; König, B. *Chem. Rev.* **2006**, *106*, 3520; (c) Giese, M.; Albrecht, M.; Rissanen, K. *Chem. Rev.* **2015**, *115*, 8867; (d) Liu, Y.-Z.; Yuan, K.; Lv, L.-L.; Zhu, Y.-C.; Yuan, Z. *J. Phys. Chem. A* **2015**, *119*, 5842; (e) Yuan, Z.; Liang, F. *Curr. Org. Chem.* **2014**, *18*, 2016.
6. (a) Davis, A. P.; Joos, J.-B. *Coord. Chem. Rev.* **2003**, *240*, 143; (b) Li, F.; Gan, Q.; Xue, L.; Wang, Z.-M.; Jiang, H. *Tetrahedron Lett.* **2009**, *50*, 2367.
7. For selected examples: (a) Klare, H.; Hanft, S.; Neudçrfl, J. M.; Schlçrer, N. E.; Griesbeck, A.; Goldfuss, B. *Chem. Eur. J.* **2014**, *20*, 11847; (b) Amendola, V.; Fabbrizzi, L.; Mosca, L. *Chem. Soc. Rev.* **2010**, *39*, 3889; (c) Hoque, M. N.; Gogoi, A.; Das, G. *Dalton Trans.* **2015**, *44*, 15220; (d) Bernier, N.; Carvalho, S.; Li, F.; Delgado, R.; Félix, V. *J. Org. Chem.* **2009**, *74*, 4819; (e) Pinter, T.; Jana, S.; Courtemanche, R. J. M.; Hof, F. *J. Org. Chem.* **2011**, *76*, 3733; (f) Alliband, A.; Meece, F. A.; Jayasinghe, C.; Burns, D. H. *J. Org. Chem.* **2013**, *78*, 356; (g) Ema, T.; Okuda, K.; Watanabe, S.; Yamasaki, T.; Minami, T. *Org. Lett.* **2014**, *16*, 1302; (h) Wienkers, M.; Ramos, J.; Jemal, H.; Cardenas, C.; Wiget, P.; Nelson, A.; Free, S.; Wu, J.; Roach, R.; Vulcan, M.; Waynant, K.; Fort, K.; Vladimirova, A.; Sun, J.; Hunt, S. E.; Rudkevich, D. M.; Starnes, S. D. *Org. Lett.* **2012**, *14*, 1370; (i) Ghule, N. V.; Bhosale, S. V.; Bhosale, S. V. *RSC Adv.* **2014**, *4*, 27112.
8. (a) Edwards, S. J.; Valkenier, H.; Busschaert, N.; Gale, P. A.; Davis, A. P. *Angew. Chem., Int. Ed.* **2015**, *54*, 4592; (b) Jin, C.; Zhang, M.; Wu, L.; Guan, Y.; Pan, Y.; Jiang, J.; Lin, C.; Wang, L. *Chem. Commun.* **2013**, 2025; (c) Elmes, R. B. P.; Yuen, K. K. Y.; Jolliffe, K. A. *Chem. Eur. J.* **2014**, *20*, 7373; (d) Shokri, A.; Schmidt, J.; Wang, X.-B.; Kass, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 16944; (e) Gaeta, C.; Sala, C.; Sala, P. D.; Margarucci, L.; Casapullo, A.; Neri, P. *J. Org. Chem.* **2014**, *79*, 3704; (f) Samet, M.; Danesh-Yazdi, M.; Fattahi, A.; Kass, S. R. *J. Org. Chem.* **2015**, *80*, 1130; (g) Martínez-Aguirre, M. A.; Yatsimirsky, A. K. *J. Org. Chem.* **2015**, *80*, 4985; (h) Wang, X.; Feng, L.; Zhang, L. *Sens. Actuators, B* **2015**, *208*, 588; (i) Shokri, A.; Wang, X.-B.; Kass, S. R. *J. Am. Chem. Soc.* **2013**, *135*, 9525.
9. (a) Wei, G.-N.; Zhang, J.-L.; Jia, C.; Fan, W.-Z.; Lin, L.-R. *Spectrochim. Acta Part A* **2014**, *128*, 168; (b) Sato, T.; Ito, K. *J. Incl. Phenom. Macrocycl. Chem.* **2013**, *77*, 385; (c) Staffilani, M.; Hancock, K. S. B.; Steed, J. W.; Holman, K. T.; Atwood, J. L.; Juneja, R. K.; Burkhalter, R. S. *J. Am. Chem. Soc.* **1997**, *119*, 6324; (d) Fegade, U.; Sahoo, S. K.; Singh, A.; Mahulikar, P.; Attarde, S.; Singh, N.; Kuwar, A. *RSC Adv.* **2014**, *4*, 15288; (e) Isaad, J.; Salaün, F. *Sens. Actuators, B* **2011**, *157*, 26; (f) Schmidt, E. V. J.; Wang, X.-B.; Kass, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 18534.
10. (a) Wang, Y.; Zhao, Q.; Zang, L.; Liang, C.; Jiang, S. *Dyes Pigm.* **2015**, *123*, 166; (b) Yong, X.; Su, M.; Wan, W.; You, W.; Lu, X.; Qu, J.; Liu, R. *New J. Chem.* **2013**, *37*, 1591; (c) Stoikov, I. I.; Yantemirova, A. A.; Nosov, R. V.; Rizvanov, I. K.; Julmetov, A. R.; Klochkov, V. V.; Antipin, I. S.; Konovalova, A. I.; Zharov, I. *Org. Biomol. Chem.* **2011**, *9*, 3225; (d) Xu, L.; Li, Y.; Yu, Y.; Liu, T.; Cheng, S.; Liu, H.; Li, Y.-L. *Org. Biomol. Chem.* **2012**, *10*, 4375; (e) Shokri, A.; Deng, S. H. M.; Wang, X.-B.; Kass, S. R. *Org. Chem. Front.* **2014**, *1*, 54; (f) Guo, L.; Wang, Q.-L.; Jiang, Q.-Q.; Jiang, Q.-J.; Jiang, Y.-B. *J. Org. Chem.* **2007**, *72*, 9947.
11. (a) Liu, G.; Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1997**, *119*, 9913; (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984; (c) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600.
12. For highlight of chiral sulfinamides as organocatalysts, see: Diner, P.; Sadhukhan, A.; Blomkvist, B. *ChemCatChem* **2014**, *6*, 3063.
13. (a) Pei, D.; Wang, Z.; Wei, S.; Zhang, Y.; Sun, J. *Org. Lett.* **2006**, *8*, 5913; (b) Robak, M. T.; Trincado, M.; Ellman, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 15110; (c) Pei, D.; Zhang, Y.; Wei, S.-Y.; Wang, M.; Sun, J. *Adv. Synth. Catal.* **2008**, *350*, 619;

(d) Wang, C.; Wu, X.; Zhou, L.; Sun, J. *Chem. Eur. J.* **2008**, *14*, 8789; (e) Kimmel, K. L.; Robak, M. T.; Ellman, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 8754; (f) Xu, H.; Zuend, S. J.; Woll, M. G.; Tao, Y.; Jacobsen, E. N. *Science* **2010**, *327*, 986; (g) Beck, E. M.; Hyde, A. M.; Jacobsen, E. N. *Org. Lett.* **2011**, *13*, 4260; (h) Kimmel, K. L.; Weaver, J. D.; Ellman, J. A. *Chem. Sci.* **2012**, *3*, 121; (i) Kimmel, K. L.; Weaver, J. D.; Lee, M.; Ellman, J. A. *J. Am. Chem. Soc.* **2012**, *134*, 9058; (j) Saravanan, S.; Khan, N.-U. H.; Kureshy, R. I.; Abdi, S. H. R.; Bajaj, H. C. *ACS Catal.* **2013**, *3*, 2873; (k) Kumar, M.; Kureshy, R. I.; Saravanan, S.; Verma, S.; Jakhar, A.; Khan, N. H.; Abdi, S. H. R.; Bajaj, H. C. *Org. Lett.* **2014**, *16*, 2798; (l) Wan, W.; Gao, W.; Ma, G.-B.; Ma, L.; Wang, F.; Wang, J.; Jiang, H. Z.; Zhu, S.-Z.; Hao, J. *RSC Adv.* **2014**, *4*, 26563; (m) Wang, C.; Wu, X.-J.; Zhou, L.; Sun, J. *Org. Biomol. Chem.* **2015**, *13*, 577.

14. For details see the Supporting information.
15. Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.
16. Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157.
17. Frisch, M. J. et al *Gaussian 09, Revision B.01*; Gaussian: Wallingford, CT, 2009.
18. Batsanov, S. S. *Inorg. Mater.* **2001**, *37*, 871.

Please cite this article in press as: Shen, Y.-Y.; et al. *Tetrahedron Lett.* (2015), http://dx.doi.org/10.1016/j.tetlet.2015.12.090