

**Silver Salt Enabled H/D Exchange at β Position of Thiophene Rings: Synthesis of Fully Deuterated Thiophene derivatives**

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COMMUNICATION

Silver Salt Enabled H/D Exchange at β Position of Thiophene Rings: Synthesis of Fully Deuterated Thiophene derivatives

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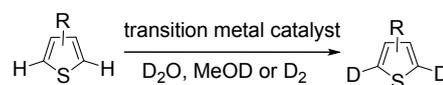
Fei-Fei Sheng, En-Ci Li, Jing-Wen Bai, Cai-Xia Wang, Guang-Qi Hu, Kai-Hui Liu, Zheng-Yi Sun, Kang Shen and Hong-Hai Zhang*^a

We disclose a silver catalyzed H/D exchange reaction, which can introduce deuterium atom at β position of thiophene rings without the assistance of any coordinating groups. The advantages of this reaction include operation in the open air, usage of D_2O as deuterium source, good tolerance to a range of functional groups and obtaining high atom% deuterium incorporation. In addition, this H/D exchange reaction is employed for direct deuteration of thiophene based monomer, which is usually prepared in multistep synthesis from expensive deuterated starting materials.

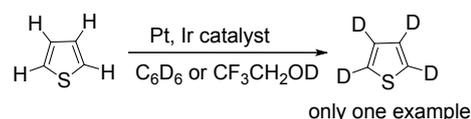
Selective hydrogen isotope exchange (HIE) is one of the most desirable methods for preparation of deuterium labeled molecules to eliminate additional steps associated with the traditional methodologies and recently attracted much more attentions.¹ During the past decades, the strategy with the use of directing groups containing N or O atoms to coordinate with a metal catalyst was commonly required to facilitate H/D exchange process.² Thus, many transition metal complexes, including Ir,³ Pd,⁴ Ru,⁵ Rh,⁶ were adopted for HIE and became the prevalent catalyst for synthesis of deuterated compounds. However, the extra synthetic steps to incorporate the directing groups limited the source of starting materials and their further applications. Achieving selective HIE of substrates without directing groups is one of the approaches to solve this problem, thus, many efforts have been made in this field. Pioneering studies from Chirik and coworkers described an iron complex catalyzed HIE reaction to afford deuterated arenes with steric controlled site-selectivity, which enabled selective deuteration of many arenes without directing groups.⁷ Then, selective H/D exchange of N-containing arenes has been separately achieved with ruthenium or nickel complex as catalyst in Chirik and

Pieters group.⁸ The H/D exchange of five-membered heteroarenes at the most active position with silver and ruthenium complex as catalyst has also been disclosed by several groups including us.⁹ In addition, halogenated arenes are also demonstrated to be good substrates for selective H/D exchange process with silver complex as catalyst in our group.¹⁰ While significant progress has been made in this field, the development of H/D exchange on (hetero)arenes without directing groups is still at an infant stage.

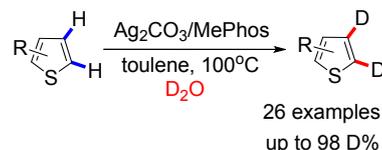
Reported H/D exchange of thiophenes at 2-position:



Reported H/D exchange for fully deuterated thiophenes:



This work:



Scheme 1. Transition metal catalyzed H/D exchange reaction for synthesis of deuterated thiophene derivatives

Thiophene is one of the most common structure motifs in drug molecules and functional materials.¹¹ Thus, developing novel methods for selective H/D exchange of thiophene derivatives become increasingly important, which are applied to modulate the properties of thiophene-containing functional molecules. The reported H/D exchange reaction of thiophenes always provides α -deuterated thiophenes, due to its higher reactivity of C-H bond.^{10,12} However, the thiophene structures in drug molecules and

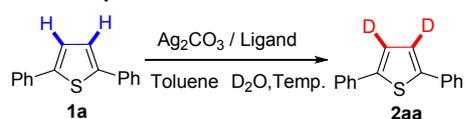
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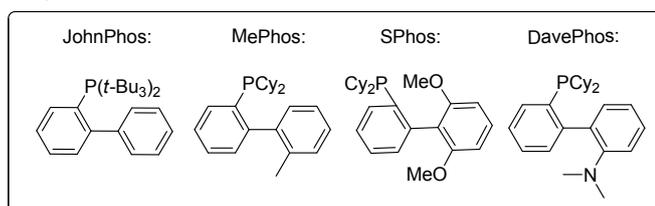
functional materials commonly contain functional groups at α position and are unable to be deuterated.¹³ Accordingly, the methods which can incorporate deuterium at β position of thiophenes should be more attractive, albeit rarely reported. In 2011, Grubbs and coworkers reported one example of H/D exchange reaction for synthesis of fully deuterated thiophenes with iridium complex as catalyst and C_6D_6 as deuterium source.¹⁴ Synthesis of fully deuterated thiophene is also achieved by a platinum catalyzed H/D exchange process.¹⁵ However, the unsubstituted thiophene is the only example in these cases. Herein, following our research interest on developing novel methods for synthesis of deuterated compounds,¹⁶ we disclose a general method to incorporate deuterium atoms at β position of thiophenes via a silver catalyzed H/D exchange reaction with D_2O as deuterium source.¹⁷

Table 1. Reaction Optimization



Entry ^a	Ligand	Deuterium Source	Temp.	D incorporation (%) ^b
1	Ph ₃ P	D ₂ O (20 eq.)	60°C	14
2	<i>o</i> -tol ₃ P	D ₂ O (20 eq.)	60°C	16
3	<i>p</i> -tol ₃ P	D ₂ O (20 eq.)	60°C	18
4	<i>t</i> -Bu ₃ P	D ₂ O (20 eq.)	60°C	18
5	JohnPhos	D ₂ O (20 eq.)	60°C	26
6	Cy ₃ P	D ₂ O (20 eq.)	60°C	37
7	MePhos	D ₂ O (20 eq.)	60°C	44
8	DavePhos	D ₂ O (20 eq.)	60°C	40
9	SPhos	D ₂ O (20 eq.)	60°C	22
10	MePhos	D ₂ O (20 eq.)	80°C	45
11	MePhos	D ₂ O (20 eq.)	100°C	73
12	MePhos	D ₂ O (10 eq.)	100°C	70
13	MePhos	D ₂ O (30 eq.)	100°C	85
14	MePhos	D ₂ O (40 eq.)	100°C	92
15 ^c	MePhos	D ₂ O (40 eq.)	100°C	10
16	MePhos	CDCl ₃ (40 eq.)	100°C	20
17	MePhos	DMSO- <i>d</i> ₆ (40 eq.)	100°C	33

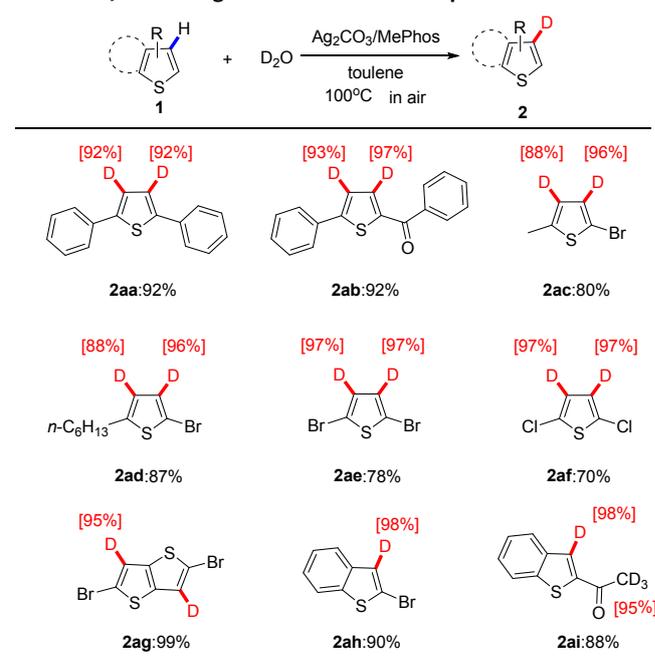
a. The reaction was conducted on 1 mmol of **1a**, D₂O, 0.5 mmol of Ag₂CO₃, 0.5 mmol of ligand in toluene, 12 hours. b. Determined by GC-MS. c. 0.1 mmol of Ag₂CO₃ and 0.1 mmol of MePhos was used



H/D exchange at β position of thiophenes was examined with 2,5-diphenylthiophene as model substrate, because it is a common structure motif in many functional materials. As shown in Table 1, we first investigated the influence of ligands, which have been demonstrated to play an important role in silver mediated H/D process.¹⁰ After thoroughly screening the ligands, we found several of them have positive effect on H/D exchange process, affording products with moderate level of deuterium incorporation (entries 1-9, Table 1). Among all the ligands, MePhos showed the best

result, giving the product with 44% deuterium incorporation (entry 7, Table 1). The ¹H NMR spectrum analysis of isolated products showed deuterium were selectively introduced at β position of thiophene ring and no deuteration was observed at phenyl rings. The atom% of deuterium incorporation can be further increased by conducting the reaction at higher temperature (entries 10-11, Table 1). When the reaction was conducted at 100°C, the product with 73% deuterium incorporation was observed. The attempt to further increase the atom% of deuterium incorporation was made by varying the amount of heavy water (entries 12-14, Table 1). The products with higher level of deuterium incorporation were obtained by using more heavy water. The best result of 92% deuterium incorporation was achieved with the use of 40 equivalent of heavy water. When 0.1 equivalent of Ag₂CO₃ and MePhos was used, the reaction afforded products with only 10% deuterium incorporation (entry 15, Table 1). Other deuterium source like CDCl₃ and DMSO-*d*₆ failed to give the product with high level of deuterium incorporation (entries 16-17, Table 1). These results indicated the β position of thiophene can be activated by silver salt, when α position of thiophene was blocked. Therefore, the optimal condition was established with Ag₂CO₃/MePhos as catalyst and 40 equivalent of heavy water as deuterium source at 100°C.

Table 2. H/D exchange of α -substituted thiophenes^a

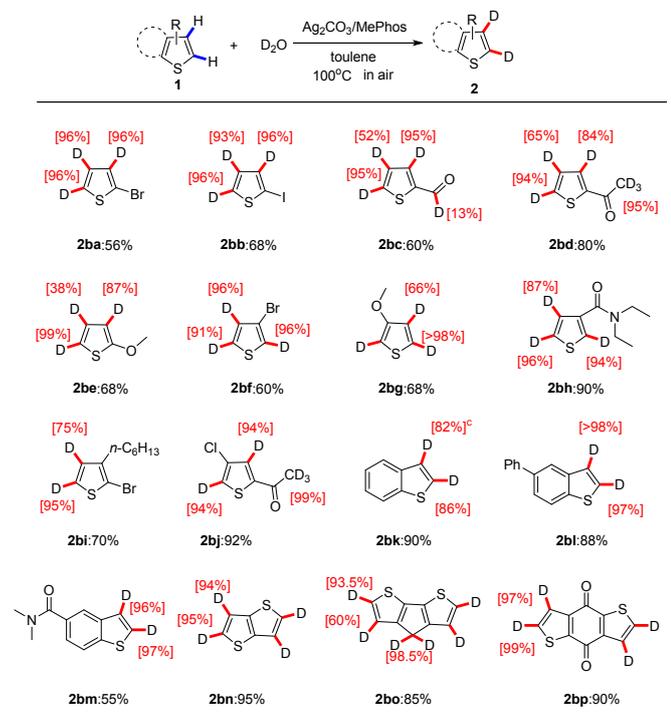


a. The reaction was conducted on 1 mmol of **1**, 40 mmol of D₂O, 0.5 mmol of Ag₂CO₃, 0.5 mmol of MePhos in toluene (5 mL) at 100°C, 12 hours.

With the optimized condition in hand, the substrate scope for HIE was next explored (Table 2). The reaction performed smoothly with α -substituted thiophenes as starting materials (**2aa–2af**), giving the products with high level of deuterium incorporation (88% - 97%). It is worthy to note C-Br and C-Cl bond were compatible with the reaction condition, which can be easily converted to other functional groups. The deuterium labeled bromothiophene or chlorothiophene were difficult to access by other transition metal catalyzed H/D exchange reaction, due to their high potential for oxidative addition reaction. In addition, deuterated 2,5-dibromo-1,4-dithiapentene, which is a common structure motif in many

functional materials, can be easily prepared with high atom% deuterium incorporation under the optimized condition (**2ag**). Moreover, H/D exchange of benzothiophene was also tested and deuterium atom was selectively introduced at β position of thiophene ring (**2ah**, **2ai**). In the case of **2ai**, over 95% deuterium incorporation at methyl group of 2-acetylbenzothiophene was observed, which indicated that Ag_2CO_3 is able to promote H/D exchange of the activated $\text{C}(\text{sp}^3)\text{-H}$ bonds next to carbonyl group.

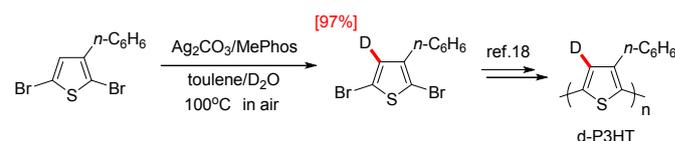
Table 3. Synthesis of Fully Deuterated Thiophenes Derivatives^a



a. The reaction was conducted on 1 mmol of **1**, 40 mmol of D_2O , 0.5 mmol of Ag_2CO_3 , 0.5 mmol of MePhos in toluene (5 mL) at 100°C , 12 hours.

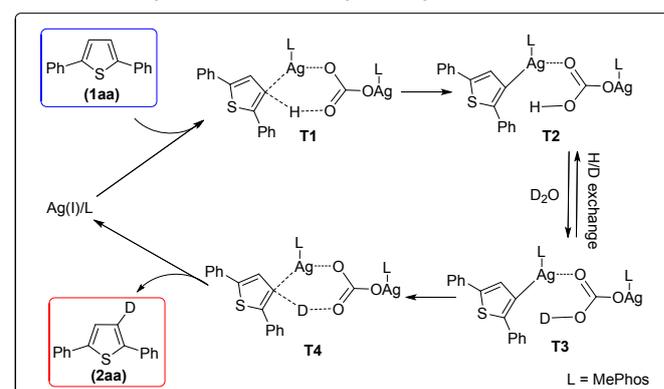
As shown in Table 3, when thiophenes containing one substitute at α position were employed as starting materials, fully deuterated thiophenes can be obtained with moderate to high atom% of deuterium incorporation. The reaction was tolerant to a good range of functional groups including halogen, amide, carbonyl, methoxyl and alkyl groups. The H/D exchange process of compounds **2bc-2be** obviously showed site selectivity towards α position, indicating the higher reactivity of C-H bond at α position of thiophenes. Thiophenes with substitute at β position are also good substrates for H/D exchange, affording products with 66%-98% deuterium incorporation. The use of multisubstituted thiophenes **2bl** and **2bj** as starting materials led to deuteration occurring at all C-H bonds of thiophene ring. In addition, H/D exchange of benzothiophene derivatives was performed smoothly under the optimized condition, affording products with high atom% deuterium incorporation at both α and β positions of thiophene rings. It is worthy to note that deuteration of 1,4-thiophthene, 4H-cyclopenta[2,1-b:3,4-b']dithiophene and benzo[1,2-b:4,5-b']dithiophene-4,8-dione, some important structure motifs in conjugated polymers for high performance organic solar cells, afforded fully deuterated products with 94% to 99% deuterium incorporation (**2bn-2bp**). These deuterated thiophene derivatives may serve as novel building blocks for synthesis of functional materials.

Scheme 2. Direct deuteration of monomer



To further demonstrate the utility of this H/D exchange reaction, direct deuteration of 2,5-dibromo-3-hexylthiophene has been performed under the optimized condition. 2,5-dibromo-3-hexylthiophene is the monomer for polythiophene, which is recognized as an important photoelectronic material. The reported method for preparation of deuterated 2,5-dibromo-3-hexylthiophene contains alkylation and bromination of commercial expensive fully deuterated 3-bromothiophene.¹⁸ By using our method, deuterated 2,5-dibromo-3-hexylthiophene can be prepared in just one step from the corresponding non-deuterated monomer. We also proposed a mechanistic pathway for this H/D exchange process. The phosphine ligand coordinated silver salt promoted C-H bond cleavage of **1aa**, which was followed by H/D exchange between intermediate T2 and heavy water to produce deuterated intermediate T3. Finally, deuterated thiophene (**2aa**) will generate from transformation of deuterium to aryl ring and release of silver salt.

Scheme 3. Proposed mechanistic pathway



In summary, we have developed an efficient method to incorporate deuterium atoms into β position of thiophene rings. The combination of silver carbonate and MePhos was identified as the catalyst for this H/D exchange reaction. A good range of functional groups were compatible to the reaction condition. The fully deuterated thiophene derivatives with high atom% deuterium incorporation could be easily prepared following the optimized condition. Furthermore, this protocol can be applied in the late-stage deuteration of complicated thiophene derivatives, which may find application at developing novel functional materials and exploring deuterium effect. Further extension of the substrate scope beyond thiophene derivatives is now under investigation in our laboratory.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

- 1 For selected reviews of H/D exchange, see: (a) J. Atzrodt, V. Derdau, W. J. Kerr and M. Reid, C-H Functionalization for Hydrogen Isotope Exchange. *Angew. Chem. Int. Ed.*, 2018, **57**, 3022; (b) J. Atzrodt, V. Derdau, T. Fey and J. Zimmermann, The Renaissance of H/D Exchange. *Angew. Chem. Int. Ed.*, 2007, **46**, 7744.
- 2 (a) W. J. Kerr, G. J. Knox and L. C. Paterson, Recent Advances in Iridium(I) Catalysis Towards Directed Hydrogen Isotope Exchange. *J. Label. Compd. Radiopharm.*, 2020, **63**, 281; (b) W. J. S. Lockley and J. R. Heys, Metal-Catalysed Hydrogen Isotope Exchange Labelling: a Brief Overview. *J. Label Compd. Radiopharm.*, 2010, **53**, 635.
- 3 (a) M. Valero, T. Kruissink, J. Blass, R. Weck, S. Gussregen, A. T. Plowright and V. Derdau, C-H-Functionalization-Prediction of Selectivity in Iridium(I) Catalyzed Hydrogen Isotope Exchange Competition Reactions. *Angew. Chem. Int. Ed.*, 2020, **59**, 5626; (b) W. Liu, L. Cao, Z. Zhang, G. Zhang, S. Huang, L. Huang, P. Zhao and X. Yan, Mesoionic Carbene-Iridium Complex Catalyzed *Ortho*-Selective Hydrogen Isotope Exchange of Anilines with High Functional Group Tolerance. *Org. Lett.*, 2020, **22**, 2210; (c) W. J. Kerr, D. M. Lindsay, M. Reid, J. Atzrodt, V. Derdau, P. Rojahn and R. Weck, Iridium-Catalysed *ortho*-H/D and -H/T Exchange under Basic Conditions: C-H Activation of Unprotected Tetrazoles. *Chem. Commun.*, 2016, **52**, 6669.
- 4 (a) H. Xu, M. Liu, L. L. Li, Y. F. Cao, J. Q. Yu and H. X. Dai, Palladium-Catalyzed Remote meta-C-H Bond Deuteration of Arenes Using a Pyridine Template. *Org. Lett.*, 2019, **21**, 4887; (b) D. Zhao, H. Luo, B. Chen, W. Chen, G. Zhang and Y. Yu, Palladium-Catalyzed H/D Exchange Reaction with 8-Aminoquinoline as the Directing Group: Access to *ortho*-Selective Deuterated Aromatic Acids and β -Selective Deuterated Aliphatic Acid. *J. Org. Chem.*, 2018, **83**, 7860; (c) S. Ma, G. Villa, P. S. Thuy-Boun, A. Homs and J. Q. Yu, Palladium-Catalyzed *ortho*-Selective C-H Deuteration of Arenes: Evidence for Superior Reactivity of Weakly Coordinated. *Angew. Chem. Int. Ed.*, 2014, **53**, 734.
- 5 (a) V. Müller, R. Weck, V. Derdau and L. Ackermann, Ruthenium(II)-Catalyzed Hydrogen Isotope Exchange of Pharmaceutical Drugs by C-H Deuteration and C-H Tritiation. *ChemCatChem*, 2020, **12**, 100; (b) L.-L. Zhao, W. Liu, Z. Zhang, H. Zhao, Q. Wang and X. Yan, Ruthenium-Catalyzed *Ortho* and Meta-H/D Exchange of Arenes. *Org. Lett.*, 2019, **21**, 10023; (c) P. Eisele, F. Ullwer, S. Scholz and B. Plietker, Mild, Selective Ru-Catalyzed Deuteration Using D₂O as a Deuterium Source. *Chem. Eur. J.*, 2019, **25**, 16550; (d) L. Piola, J. A. Fernandez-Salas, S. Manzini and S. P. Nolan, Regioselective Ruthenium Catalyzed H-D Exchange Using D₂O as the Deuterium Source. *Org. Biomol. Chem.*, 2014, **12**, 8683.
- 6 (a) A. L. Garreau, H. Zhou and M. C. Young, A Protocol for the *Ortho*-Deuteration of Acidic Aromatic Compounds in D₂O Catalyzed by Cationic Rh(III). *Org. Lett.*, 2019, **21**, 7044; (b) S. Chen, G. Song and X. Li, Chelation-Assisted Rhodium Hydride-Catalyzed Regioselective H/D Exchange in Arenes. *Tetrahedron Lett.*, 2008, **49**, 6929.
- 7 R. P. Yu, D. Hesk, N. Rivera, I. Pelczar and P. J. Chirik, Iron-Catalysed Tritiation of Pharmaceuticals. *Science*, 2016, **529**, 195.
- 8 (a) C. Zarate, H. Yang, M. J. Bezdek, D. Hesk and P. J. Chirik, Ni(I)-X Complexes Bearing a Bulky -Diimine Ligand: Synthesis, Structure and Superior Catalytic Performance in the Hydrogen Isotope Exchange in Pharmaceuticals. *J. Am. Chem. Soc.*, 2019, **141**, 5034; (b) A. Palazzolo, S. Feuillastre, V. Pferfer, S. Garcia-Argote, D. Bouzouita, S. Tricard, C. Chollet, E. Marcon, D. A. Buisson, S. Cholet, F. Fenaille, G. Lippens and B. Chaudret, G. Pieters, Efficient Access to Deuterated and Tritiated Nucleobase Pharmaceuticals and Oligonucleotides using Hydrogen-Isotope Exchange. *Angew. Chem. Int. Ed.*, 2019, **58**, 4891; (c) H. Yang, C. Zarate, W. N. Palmer, N. Rivera, D. Hesk and P. J. Chirik, Site-Selective Nickel-Catalyzed Hydrogen Isotope Exchange in *N*-Heterocycles and Its Application to the Tritiation of Pharmaceuticals. *ACS Catal.*, 2018, **8**, 10210.
- 9 (a) A. Tlahuext-Aca and J. F. Hartwig, Site-Selective Silver-Catalyzed C-H Bond Deuteration of Five-Membered Aromatic Heterocycles and Pharmaceuticals. *ACS Catal.*, 2021, **11**, 1119; (b) E. C. Li, G. Q. Hu, Y. X. Zhu, H. H. Zhang, K. Shen, X. C. Hang, C. Zhang and W. Huang, Ag₂CO₃-Catalyzed H/D Exchange of Five-Membered Heteroarenes at Ambient Temperature. *Org. Lett.*, 2019, **21**, 6745.
- 10 (a) G. Q. Hu, J. W. Bai, E. C. Li, K. H. Liu, F. F. Sheng and H. H. Zhang, Synthesis of Multideuterated (Hetero)aryl Bromides by Ag(I)-Catalyzed H/D Exchange. *Org. Lett.*, 2021, **23**, 1554; (b) G. Q. Hu, E. C. Li, H. H. Zhang and W. Huang, Ag(I)-Mediated Hydrogen Isotope Exchange of Mono-Fluorinated (Hetero)arenes. *Org. Biomol. Chem.*, 2020, **18**, 6627.
- 11 (a) R. C. So and A. C. Carreon-Aok, Molecular Design, Synthetic Strategies, and Application of Cationic Polythiophenes. *Chem. Rev.*, 2019, **21**, 11442; (b) Y. Zhu, E. L. Romero, X. Ren, A. J. Sanca, C. Du, C. Liu, Z. A. Karim, F. Z. Alshbool, F. T. Khasawneh, J. Zhou, D. Zhong and B. Geng, Clopidogrel as a donor probe and thioenol derivatives as flexible promoieties for enabling H₂S biomedicine. *Nature Commun.*, 2018, **9**, 3952; (c) T. P. Kaloni, P. K. Giesbrecht, G. Schreckenbach and M. S. Freund, Polythiophene: From Fundamental Perspectives to Applications. *Chem. Mater.*, 2017, **29**, 10248.
- 12 (a) V. Salamanca and A. C. Albeniz, Deuterium Exchange between Arenes and Deuterated Solvents in the Absence of a Transition Metal: Synthesis of D-Labeled Fluoroarenes. *Eur. J. Org. Chem.*, 2020, **20**, 3206; (b) K. Chernichenko, M. Lindqvist, B. Kotai, M. Nieger, K. Sorochkina, I. Papai and T. Repo, Metal-Free sp²-C-H Borylation as a Common Reactivity Pattern of Frustrated 2-Aminophenylboranes. *J. Am. Chem. Soc.*, 2016, **138**, 4860.
- 13 (a) S. Cardoza, M. K. Shrivash, P. Das and V. Tandon, Strategic Advances in Sequential C-Arylations of Heteroarenes. *J. Org. Chem.*, 2021, **86**, 1330-1356; (b) H. H. Zhang, C. Ma, P. V. Bonnesen, J. Zhu, B. G. Sumpter, J. M. Y. Carrillo, P. Yin, Y. Wang, A. P. Li and K. Hong, Helical Poly(5-alkyl-2,3-thiophene)s: Controlled Synthesis and Structure Characterization. *Macromolecules*, 2016, **49**, 4691; (c) T. Bura, T. Blaskovits and M. Leclerc, Direct (Hetero)arylation Polymerization: Trends and Perspectives. *J. Am. Chem. Soc.*, 2016, **138**, 10056; (d) D. Lapointe, T. Markiewicz, C. J. Whipp, A. Toderian and K. Fagnou, Predictable and Site-Selective Functionalization of Poly(hetero)arene Compounds by Palladium Catalysis. *J. Org. Chem.*, 2011, **76**, 749.
- 14 V. M. Iluc, A. Fedorov and R. H. Grubbs, H/D Exchange Processes Catalyzed by an Iridium-Pincer Complex. *Organometallics*, 2012, **31**, 39.
- 15 M. Kramer, D. Watts and A. N. Vedernikov, Catalytic Deuteration of C(sp²)-H Bonds of Substituted (Hetero)arenes in a Pt(II) CNN-Pincer Complex/2,2,2-Trifluoroethanol-*d*₁ System: Effect of Substituents on the Reaction Rate and Selectivity. *Organometallics*, 2020, **39**, 4102.
- 16 (a) D. C. Wu, J. W. Bai, L. Guo, G. Q. Hu, K. H. Liu, F. F. Sheng, H. H. Zhang, Z. Y. Sun, K. Shen and X. Liu, A Practical and Efficient Method for Late-Stage Deuteration of Terminal Alkynes with Silver Salt as Catalyst. *Tetrahedron Lett.*, 2021, **66**, 152807; (b) L. Guo, C. Xu, D. C. Wu, G. Q. Hu, H. H. Zhang, K. Hong, S. Chen and X. Liu, Cascade alkylation and deuteration with aryl iodides via Pd/norbornene catalysis: an efficient method for the synthesis of congested deuterium-labeled arenes. *Chem. Commun.*, 2019, **55**, 8567; (c) H. H.

- Zhang, P. V. Bonnesen and K. Hong, Palladium-catalyzed Br/D exchange of arenes: selective deuterium incorporation with versatile functional group tolerance and high efficiency. *Org. Chem. Front.*, 2015, **2**, 1071.
- 17 For selective reference for silver catalysed C-H functionalization, please see: (a) D. Whitaker, J. Bures, I. Larrosa, Ag(I)-Catalyzed C-H Activation: The Role of the Ag(I) Salt in Pd/Ag-Mediated C-H Arylation of Electron-Deficient Arenes. *J. Am. Chem. Soc.*, 2016, **138**, 8384; (b) C. Colletto, A. Panigrahi, J. Fernandez-Casado, I. Larrosa, Ag(I)-C-H Activation Enables Near-Room-Temperature Direct α -Arylation of Benzo[b]thiophenes. *J. Am. Chem. Soc.*, 2018, **140**, 9638; (c) S. Lee, J. F. Hartwig, Palladium-Catalyzed, Site-Selective Direct Allylation of Aryl C-H Bonds by Silver-Mediated C-H Activation: A Synthetic and Mechanistic Investigation. *J. Am. Chem. Soc.*, 2016, **138**, 15278; (d) M. D. Lotz, N. M. Camasso, A. J. Canty, M. S. Sanford, Role of Silver Salts in Palladium-Catalyzed Arene and Heteroarene C-H Functionalization Reactions. *Organometallics*, 2017, **36**, 165; (e) M. Lee, Y. K. Hwang, J. Kwak, Ag(I)-Catalyzed C-H Carboxylation of Thiophene Derivatives. *Organometallics*, 2021, **40**, 3136.
- 18 M. Shao, J. Keum, J. Chen, Y. He, W. Chen, J. F. Browning, J. Jakowski, B. G. Sumpter, L. N. Ivanov, Y. Z. Ma, C. M. Rouleau, S. C. Smith, D. B. Geohegan, K. Hong and K. Xiao, The Isotopic Effects of Deuteration on Optoelectronic Properties of Conducting Polymers. *Nature Comm.*, 2014, **5**, 3180.