HETEROCYCLES, Vol. 104, No. 4, 2022, pp. 655 - 666. © 2022 The Japan Institute of Heterocyclic Chemistry
Received, 11th December, 2021, Accepted, 24th January, 2022, Published online, 31st January, 2022
DOI: 10.3987/COM-21-14611

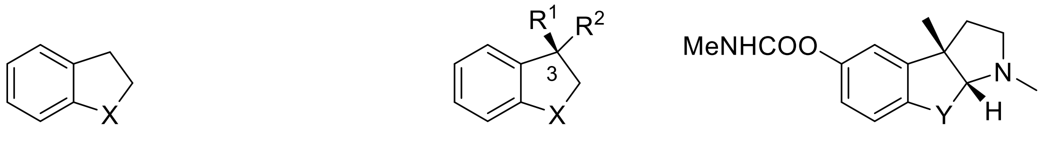
PREPARATION OF 2,3-DIHYDROBENZO[*b*]THIOPHENE BEARING BENZYLIC QUATERNARY CARBON BY PALLADIUM-CATALYZED CASCADE REACTION

Yosuke Hosoya, Honoka Yasukochi, Kota Mizoguchi, and Masahisa Nakada*

Department of Chemistry and Biochemistry, Faculty of Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan; E-mail: mnakada@waseda.jp

Abstract – A palladium-catalyzed cascade reaction for preparing 2,3-dihydrobenzo[*b*]thiophenes and the corresponding 1,1-dioxides bearing the C3 benzylic quaternary carbon is described. This cascade reaction involves the oxidative addition of aryl iodide to Pd(0) to form a σ-aryl palladium intermediate, insertion of the internal alkene into the σ-aryl palladium intermediate to form a σ-alkyl palladium intermediate with concomitant formation of a heterocyclic ring bearing a benzylic all-carbon quaternary stereogenic center, which undergoes transmetalation with a TIPS ether of thiol, and finally, reductive elimination to afford the product. The use of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) under previously optimized conditions is key to achieving a high yield.

2,3-Dihydrobenzo[*b*]thiophene (Figure 1) has continued to the attention of synthetic chemists owing to the bioactive derivatives of this compound.



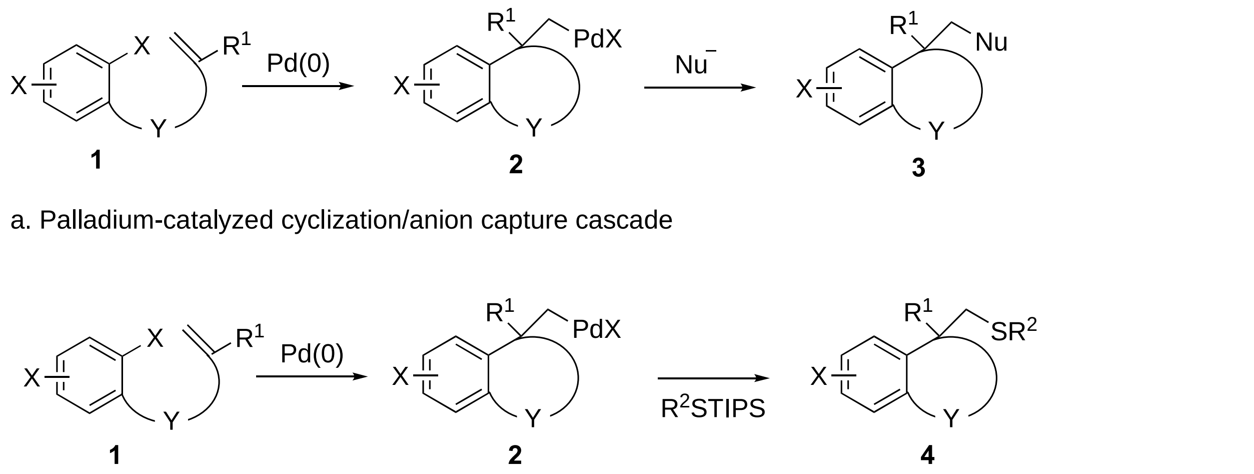
2,3-Dihydrobenzo[*b*]thiophene (X = S)
2,3-Dihydrobenzo[*b*]thiophene 1,1-dioxide (X = SO_2)
I (R^1 = R^2 = alkyl)
II (Y = S)
(–)-physostigmine (Y = NMe)

Figure 1. Structures of 2,3-dihydrobenzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide, compounds **I**, **II**, and (–)-physostigmine

For example, a raloxifene analog that exhibits selective estrogen receptor modulator activity,[1] NSC-380292, which is a potential HIV-1 reverse transcriptase inhibitor,[2] and compounds that strongly inhibit both adenosine 5´-diphosphate- and collagen-induced platelet aggregation[3] all include 2,3-dihydrobenzo[*b*]thiophene in their structures. Moreover, a variety of bioactive derivatives of 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide have also been reported.[4]

To the best of our knowledge, naturally occurring 2,3-dihydrobenzo[*b*]thiophene derivatives bearing two alkyl groups at the C3 position, such as structure **I** (Figure 1), which has an all-carbon quaternary stereogenic center, have never been reported. However, a number of bioactive derivatives with structure **I** have been synthesized. For example, compound **II**, which is a sulfur analog of physostigmine with bioactivity comparable to that of physostigmine, but with an enhanced safety profile, was reported by Takamura and co-workers.[5] Thus, structure **I** is an important scaffold for bioactive compounds; hence, the development of protocols for synthesizing structure **I** is important.

Indoline is an aza-analogue of 2,3-dihydrobenzo[*b*]thiophene and has been recognized as a biologically important privileged scaffold because it is found in various bioactive natural products. Hence, its synthesis has been reported by many research groups. However, indolines bearing two alkyl groups at the C3 position, which are incorporated into the structure of various bioactive natural products, for example, physostigmine (Figure 1), pose synthetic challenges because the construction of an all-carbon quaternary stereogenic center is a synthetically formidable task.



a. Palladium-catalyzed cyclization/anion capture cascade

b. Palladium-catalyzed carbothiolation with R^2STIPS (Y = N, O, C) reported by us.[10] TIPS: triisopropylsilyl.

Scheme 1. Palladium-catalyzed cascade reactions

Recently, cascade reactions have attracted the attention of synthetic chemists because they enable the successive formation of new bonds, which is advantageous for the efficient construction of complex structures. Moreover, cascade reactions reduce the time and labor required for the requisite transformations, and also reduce waste output and the use of energy and resources.

Palladium-catalyzed reactions are efficient and useful because they comprise successive elementary reactions, where the reactive palladium species formed in the catalytic cycle can be used for subsequent reactions in a cascade manner. For example, an aryl-Pd(II) intermediate, which is derived from the oxidative addition of compound **1** to Pd(0) (Scheme 1a), undergoes alkene insertion to afford σ-alkyl palladium intermediate **2** with forming an all-carbon quaternary stereogenic center. Intermediate **2** does not undergo β–elimination because it lacks a β-hydrogen, but **2** reacts with a nucleophile to afford **3**.

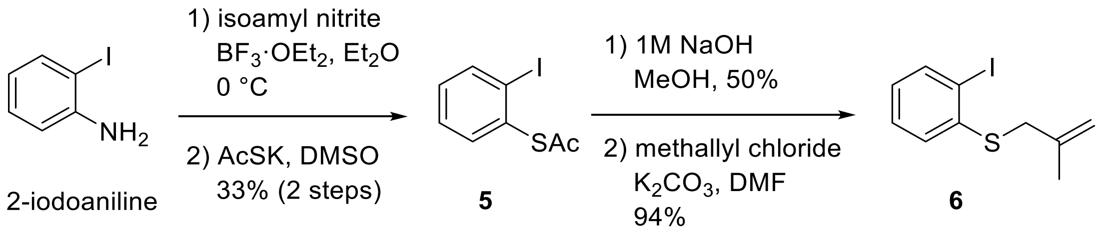
The reactions of σ-alkyl palladium intermediate **2** with a nucleophile,[6] bis(pinacolate)diboron,[7] hexamethyldisilane, hexamethyldistannane,[8] and diethyl H-phosphonate,[9] which afford the corresponding alkyl pinacol borane, silane, stannane, and phosphonate, respectively, have been reported.

Recently, we reported the palladium-catalyzed carbothiolation reaction of **1** to afford **4** via the interaction of in situ formed σ-alkyl palladium intermediate **2** with a TIPS ether derivative of alkane or arylthiol (Scheme 1b).[10] This cascade reaction is the first example in which a σ-alkyl palladium intermediate is used to form various alkyl aryl and dialkyl sulfides with an all-carbon quaternary stereogenic center. Thus, a variety of alkyl aryl and dialkyl sulfide derivatives of chromane, 2,3-dihydrobenzofuran, 2,3,4,5-tetrahydrobenzo[*b*]oxepine, 1,2,3,4-tetrahydronaphthalene, indoline, and indolin-2-one with an all-carbon quaternary stereogenic center have been successfully prepared using this protocol. In these reactions, Cs_2CO_3, (IPr)Pd(allyl)Cl, and a TIPS ether derivative of thiol in toluene are used to form the desired product in high yield.

In the previous studies, it was found that the palladium-catalyzed carbothiolation reaction is sensitive to the purity of the TIPS thioether, possibly because the crude TIPS thioether contains thiol or some unidentified compounds, including sulfur, which could deactivate the used catalyst. Hence, our interest is in preparing organosulfur compounds such as 2,3-dihydrobenzo[*b*]thiophene by the palladium-catalyzed carbothiolation reaction developed in our group because this reaction has never been reported, but also because it would shed light on the limitations of the carbothiolation reaction.

Herein, the palladium-catalyzed carbothiolation reaction of sulfur-tethered substrates is investigated, demonstrating that a new carbon-sulfur bond is successfully formed with generating an all-carbon quaternary stereogenic center, affording alkyl aryl and dialkyl sulfides.

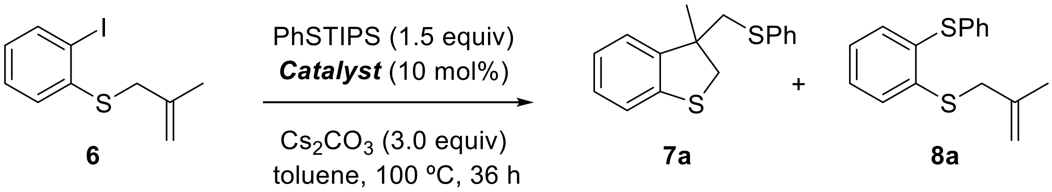
Aryl iodide **6** (Scheme 2) was selected as a model compound for optimizing the conditions of the palladium-catalyzed carbothiolation reaction. Compound **6** was readily prepared from 2-iodoaniline. Diazotization of 2-iodoaniline and subsequent reaction with potassium thioacetate afforded compound **5**, which was then hydrolyzed with 1 M NaOH/methanol, followed by methallylation of the resultant thiol to give compound **6**.



Scheme 2. Preparation of compound **6**. AcSK: potassium thioacetate

The carbothiolation reaction of compound **6** was first carried out under the optimized conditions reported previously for the carbothiolation reaction. Thus, compound **6** was treated with PhSTIPS (1.5 equiv) and Cs_2CO_3 (3.0 equiv) in the presence of a catalytic amount of (IPr)Pd(allyl)Cl (10 mol%) in toluene at 100 °C (Table 1, entry 1). Interestingly, a mixture of **7a** and **8a** (**7a**/**8a** = 64/36) was formed in 36% combined yield and 39% of **6** was recovered.[11]

Table 1. Optimization of palladium catalyst for the carbothiolation reaction of **6**



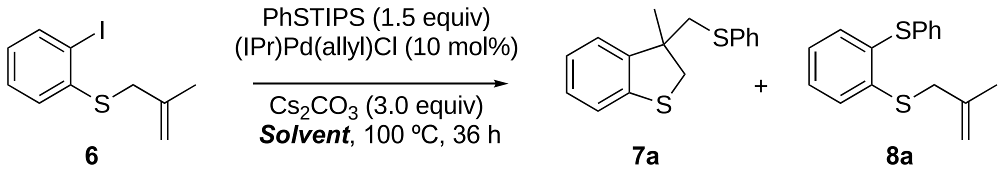
Entry	Catalyst	Yield (%)[a,b]	Ratio (**7a**/**8a**)[c]
1	**(IPr)Pd(allyl)Cl**	**36**	**64/36**
2	Pd_2dba_3, PPh_3 (20 mol%)	15	0/100
3	Pd_2dba_3, Sphos (20 mol%)	5	24/76
4	Pd_2dba_3, Xantphos	45	44/56
5	Pd_2dba_3, dppf	13	0/100
6	$Pd(PPh_3)_4$	48	19/81

[a]Isolated yield of a mixture of **7a** and **8a**. [b]Low conversion was observed in all entries. [c]Ratio determined by ^{1}H-NMR.

The reduced yield (Table 1, entry 1) prompted us to investigate the reaction conditions for compound **6**. First, the catalysts were screened. The reaction with Pd_2dba_3 (5 mol%) and PPh_3 (20 mol%) afforded only

8a (Table 1, entry 2), and the use of Sphos gave a mixture of **7a** and **8a** (**7a**/**8a** = 24/76) in only 5% combined yield (Table 1, entry 3). The bidentate ligand Xantphos (Table 1, entry 4) afforded a mixture of **7a** and **8a** in 45% yield, but the ratio of **7a**/**8a** was unsatisfactory. The use of dppf (Table 1, entry 5) resulted in almost the same yield and **7a**/**8a** ratio as those in entry 2, and the use of $Pd(PPh_3)_4$ afforded the products in 48% yield, but the ratio of **7a**/**8a** was 19/81 (Table 1, entry 6). The results in Table 1 indicate that (IPr)Pd(allyl)Cl is the most suitable catalyst for the carbothiolation reaction of **6**.

Table 2. Optimization of solvent for the carbothiolation reaction of **6**



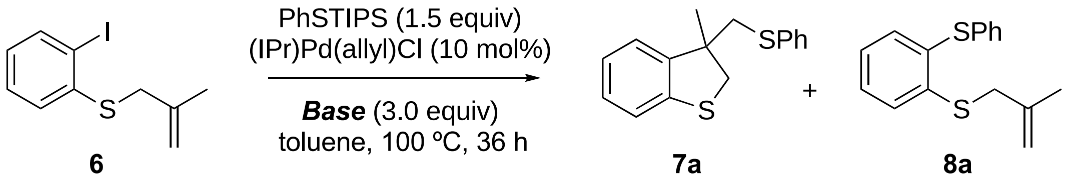
Entry	Solvent	Yield (%)^a	Ratio (**7a**/**8a**)^b
1	**toluene**	**36**^{c}	**64/36**
2	benzene^d	36^c	47/53
3	THF^e	0^f	–
4	MeCN^d	0^g	–
5	DMSO	0^h	–
6	NMP	0^h	–

^{a}Isolated yield of a mixture of **7a** and **8a**. ^{b}Ratio determined by ^{1}H-NMR. ^{c}Low conversion was observed. ^{d}Reaction at 80 ºC. ^{e}Reaction at 65 ºC. ^{f}No reaction even after 36 h. ^{g}A large amount of **6** remained and some unidentified by-products were formed. ^{h}Only decomposition was observed.

A suitable solvent for the palladium-catalyzed carbothiolation reaction of **6** (Table 2) was also examined. The carbothiolation reaction of **6** in benzene afforded a mixture of **7a** and **8a** in 36% combined yield (Table 2, entry 1), which is comparable to the yield obtained in in entry 1. However, the ratios of **7a** and **8a** were inferior to those in entry 1. Interestingly, the reactions in other solvents, such as tetrahydrofuran (THF; Table 2, entry 3), MeCN (Table 2, entry 4), dimethyl sulfoxide (DMSO; Table 2, entry 5), and *N*-methylpyrrolidone (NMP; Table 2, entry 6), did not afford the products. Thus, the reaction in THF did not proceed even after 36 h and the use of MeCN resulted in almost no reaction with forming some unidentified by-products. Only decomposition of **6** was observed in the reactions using DMSO or NMP.

The reason for the solvent effect on the palladium-catalyzed carbothiolation reaction of **6** (Table 2) has not yet been clarified; however, toluene was found to be the most suitable solvent for the reaction of **6**.

Table 3. Optimization of base for the carbothiolation reaction of **6**

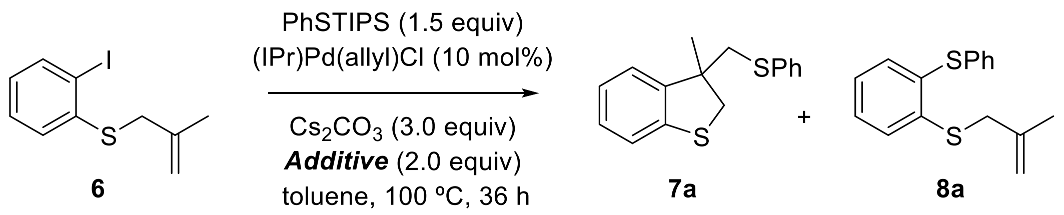


Entry	Base	Yield (%)^{a}	Ratio (**7a**/**8a**)^{b}
1	**Cs_2CO_3**	**36**	**64/36**
2	Li_2CO_3	4	34/66
3	Na_2CO_3	8	29/71
4	K_2CO_3	19	69/31
5	Ag_2CO_3	7	2/98
6	CsF	28	66/34
7	K_3PO_4	14	100/0
8	Et_3N	0	–

^{a}Isolated yield of a mixture of **7a** and **8a**. ^{b}Ratio determined by ^{1}H-NMR.

The base (Table 3) for the carbothiolation reaction of **6** was re-examined, using toluene as the solvent. Metal carbonates such as lithium carbonate (Table 3, entry 2), sodium carbonate (Table 3, entry 3), potassium carbonate (Table 3, entry 4), and silver carbonate (Table 3, entry 5) were examined for the carbothiolation reaction of **6**. However, although the ratio of **7a**/**8a** increased from 64/36 to 69/31 when potassium carbonate was used, none of the yields in entries 2-5 exceeded the yield in entry 1. The use of cesium fluoride (Table 3, entry 6) resulted in a comparable ratio of **7a**/**8a**, but did not improve the yield. The carbothiolation reaction of **6** using potassium phosphate (Table 3, entry 7) afforded **7a** without the formation of **8a**; however, the yield of **7a** was low. The reaction with triethylamine (Table 3, entry 8) did not afford the desired products. Therefore, cesium carbonate was found to be the most suitable base for the carbothiolation reaction of **6**.

Table 4. Optimization of additive for the carbothiolation reaction of **6**



Entry	Additive	Yield (%)[a]	Ratio (**7a**/**8a**)[b]
1	-	36	64/36
2	TBAC	0	–
3	TMSCl	80	65/35
4	TBSCl	14[c]	94/6
5	**BSA**	**96**	**97/3**
6	BTBSA	85	97/3
7	MSTFA	68	91/9
8	BSU	82	83/17
9	HMDS	17[d]	96/4
10	2-methyl-2-oxazoline	11	75/25

[a]Isolated yield of a mixture of **7a** and **8a**. [b]Ratio determined by ^{1}H-NMR. [c]86% of **6** remained. [d]46% of **6** remained and many by-products were observed on the TLC.

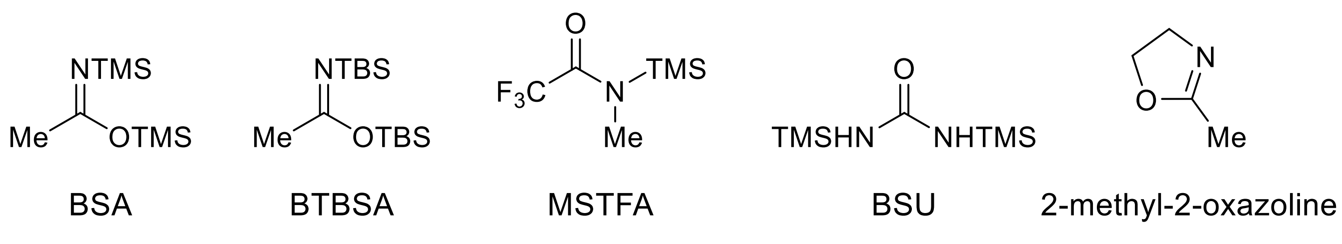
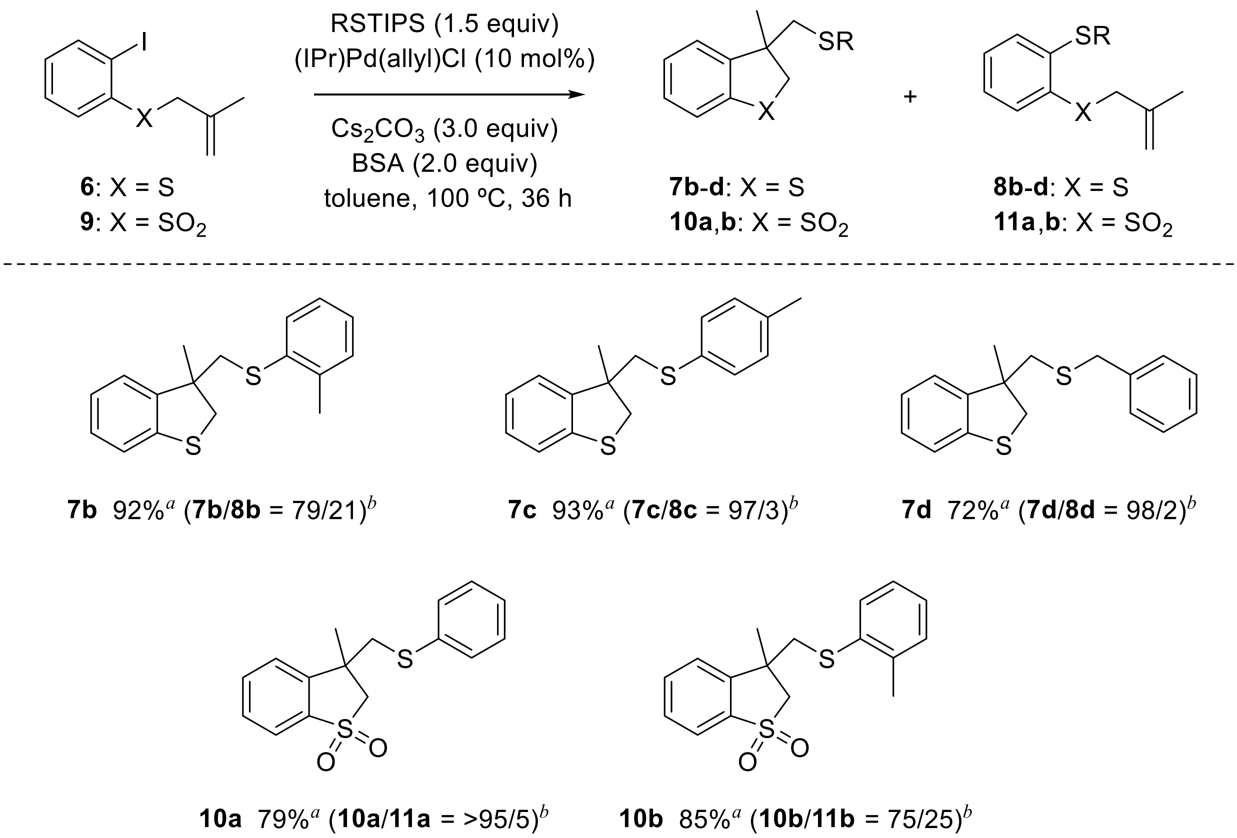


Figure 2. Structures of BSA, BTBSA, MSTFA, BSU, and 2-methyl-2-oxazoline

As shown in Tables 1-3, changing the catalyst, solvent, and base did not increase the yield and the ratio of **7a/8a** in the carbothiolation reaction of **6**; therefore, additives were investigated (Table 4). A phase transfer catalyst has been reported to enhance the Heck reaction;[12] hence, the reaction of **6** was conducted in the presence of tetrabutylammonium chloride (TBAC) (Table 4, entry 2). However, no reactions were observed.

In our previous work, it was observed that the carbothiolation reaction was very sensitive to thiol and impurities containing sulfur atoms.[10] Indeed, we reported that the carbothiolation reaction was retarded by thiols and it was found that repeating purification of PhSTIPS by silica gel column chromatography improved the yield. Since substrate **6** has been prepared, **6** was suspected to include impurities containing sulfur atoms while **6** was purified by silica gel column chromatography. Hence, we examined the carbothiolation reaction of **6** in the presence of a silylating reagent to scavenge impurities including thiol.

First, the reaction of **6** was carried out in the presence of trimethylsilyl chloride (TMSCl) (Table 4, entry 3). Gratifyingly, the use of TMSCl (2.0 equiv) improved the yield to 80%, while the ratio of **7a/8a** was the same as that in entry 1. Two equivalent of a silylating reagent was used to ensure the effect owing to its high volatility. Use of *tert*-butyldimethylsilyl chloride (TBSCl) (Table 4, entry 4) resulted in low yield while the ratio of **7a/8a** was improved. Hence, other silylating reagents were screened, and it was found that the use of 2.0 equiv of *N*,*O*-bis(trimethylsilyl)acetamide (BSA), which is frequently used for preparing samples for gas chromatography analysis, largely improved the yield (96%) as well as the ratio of **7a/8a** (97/3) (Table 4, entry 5). *N*,*O*-Bis(*tert*-butyldimethylsilyl)acetamide (BTBSA) was also effective but the yield was 85% (Table 4, entry 6). Suspecting that BSA and BTBSA may coordinate to palladium to change its catalytic activity, other silylating reagents were tested. *N*-Methyl-*N*-trimethylsilyltrifluoroacetamide (MSTFA) (Table 4, entry 7) and *N*-bis(trimethylsilyl)urea (BSU) (Table 4, entry 8) were effective, too, while the yield and the ratio of **7a/8a** did not exceed those in the reaction using BSA. A commonly used silylating reagent, 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (Table 4, entry 9), was not effective probably because it is base and could reduce the catalytic activity of palladium by the strong coordination. The reaction with 2-methyl-2-oxazoline (Table 4, entry 10), which can coordinate to palladium, afforded the products, but the yield was low. The results in Table 4 suggest that silylating reagents scavenge impurities, including thiol, to retain the catalytic activity of palladium, and BSA was found to be the best additive for the carbothiolation reaction of **6**.



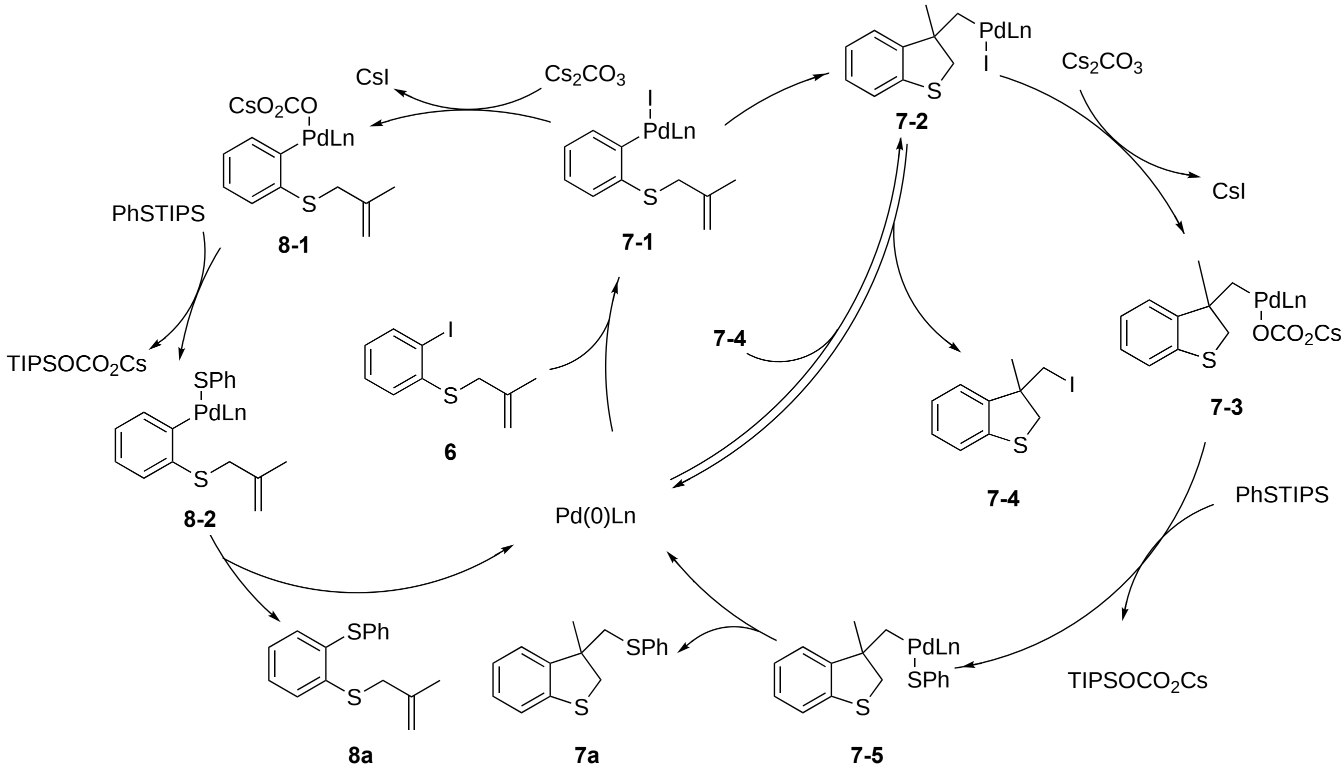
[a]Isolated yield of a mixture of products. [b]Ratio determined by ^{1}H-NMR.

Scheme 3. Products prepared by the palladium-catalyzed carbothiolations of **6** and **9**

Under the optimized reaction conditions, the carbothiolation reactions of **6** with some TIPS thioethers were examined (Scheme 3). The reaction with the TIPS thioether of *o*-methylthiophenol afforded **7b** in 92% combined yield (**7b**/**8b** = 79/21). The reduced yield and ratio of **7b**/**8b** compared with those of the reaction using PhSTIPS could be attributed to the steric hindrance induced by the *o*-methyl group of the TIPS thioether. The reaction of the TIPS thioether of *p*-methylthiophenol proceeded without the steric problem, to afford **7c** in 93% combined yield (**7c**/**8c** = 97/3). The reaction of the TIPS thioether of benzylthiol afforded dialkyl sulfide **7d** in 72% combined yield (**7d**/**8d** = 98/2).

The carbothiolation reaction of sulfone **9**, which is derived from sulfide **6**, was also investigated. The reaction of **9** with PhSTIPS under the optimized reaction conditions afforded **10a** exclusively in 79% combined yield (**10a**/**11a** = >95/5), while the reaction with the TIPS thioether of *o*-methylthiophenol afforded **10b** in 85% combined yield (**10b**/**11b** = 75/25). The reduced yield and the ratio of the products are consistent with those observed in the reactions of **6** with TIPS thioethers of thiophenol and *o*-methyl-thiophenol.

The successful carbothiolation reaction of sulfone **9** revealed that it is beneficial for the synthesis of a variety of bioactive derivatives of 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide (Figure 1) bearing an all-carbon quaternary stereogenic center at the C3 benzylic position.



Scheme 4. Plausible mechanism for the palladium-catalyzed carbothiolation of **6** with PhSTIPS

The proposed catalytic cycle for the reaction of **6** with PhSTIPS is shown in Scheme 4. This palladium-catalyzed reaction involves the formation of σ-alkyl palladium intermediates. The oxidative addition of **6** to Pd(0) generated the σ-aryl palladium intermediate **7-1**, followed by alkene insertion to afford the σ-alkyl palladium intermediate **7-2**. The reaction of iodide **7-4** with Pd(0) could regenerate **7-2**. Intermediate **7-2** did not undergoes β–elimination because it lacks a β–hydrogen. Subsequent reaction of **7-2** with Cs_2CO_3 afforded **7-3**, which underwent transmetalation with PhSTIPS to give **7-5** owing to the high affinity of the oxygen for the silicon atoms. Finally, the reductive elimination of **7-5** delivered product **7a** with concomitant regeneration of Pd(0). σ-Aryl palladium intermediate **7-1** could also react with Cs_2CO_3 to afford **8-1**, which underwent transmetalation with PhSTIPS to give **8-2**, and reductive elimination afforded product **8a** with concomitant regeneration of Pd(0), but this pathway depends on the additive used.

In conclusion, a palladium-catalyzed cascade reaction to form 2,3-dihydrobenzo[*b*]thiophenes and the corresponding 1,1-dioxides bearing C3 benzylic quaternary carbons was developed. This cascade reaction involves the formation of a σ-aryl palladium intermediate by the oxidative addition of aryl iodide to Pd(0), insertion of the internal alkene into the σ-aryl palladium intermediate to afford a σ-alkyl palladium intermediate having a carbocyclic ring with a benzylic all-carbon quaternary stereogenic center; subsequent transmetalation with TIPS thioether and reductive elimination afford the product. In addition to the use of Cs_2CO_3, (IPr)Pd(allyl)Cl, and a TIPS ether derivative of thiol, the use of BSA as an additive is key to attaining a high yield. It has been suggested that BSA preserves the catalytic activity of palladium; hence, BSA should be useful for other palladium-catalyzed reactions that are retarded by sulfur impurities.

ACKNOWLEDGEMENTS

We acknowledge supports of the Materials Characterization Central Laboratory, Waseda University, for characterization of new compounds. This work was financially supported in part by JSPS KAKENHI Grant Number JP19H02725 and a Waseda University Grant for Special Research Projects.

SUPPORTING INFORMATION

The supporting information includes experimental information and ^{1}H and ^{13}C NMR, IR, and HRMS data for all new compounds. The data associated with this article can be found, in the online version, at URL: https://www.heterocycles.jp/newlibrary/downloads/PDFsi/27546/104/4

REFERENCES AND NOTES

1. A. L. Glasebrook, J. W. Misner, G. A. Stephenson, and C. R. Schmid, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1137.
2. K. Krajewski, Y. Zhang, D. Parrish, J. Deschamps, P. P. Rollera, and V. K. Pathakb, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 3034.
3. K. Kikugawa and M. Ichino, *Chem. Pharm. Bull.*, 1973, **21**, 1151.
4. (a) M. Saitou, H. Sekiguchi, and S. Ogawa, WO 2000020408, 2000; (b) M. Saitou, H. Sekiguchi, and S. Ogawa, WO 2000069853, 2000; (c) L. Aigars, L. Gundars, K. Ivars, B. Daniel, F. Paul, and K. Nagma, WO 2008142376, 2008; (d) R. G. Hall, O. Loiseleur, J. Pabba, S. Pal, A. Jeanguenat, A. Edmunds, and A. Stoller, WO 2009010260, 2009; (e) F. Wendelin, G. Heiner, T. Stefan, and E. Ralf, WO 2011107494, 2011; (f) A. Edmunds, M. Mghlebach, A. Stoller, O. Loiseleur, A. Buchholz, O. F. Hueter, A. Bigot, R. G. Hall, D. Emery, P. Jung, L. Lu, Y. Wu, and R. Chen, WO 2015000715, 2015; (g) D. Dixon, J. Grina, J. A. Josey, J. P. Rizzi, S. T. Schlachter, E. M. Wallace, B. Wang, P. Wehn, R. Xu, and H. Yang, WO 2015095048, 2015; (h) P. Wehn and P. Yang, US 20160362390, 2016.

5. M. An-naka, K. Yasuda, M. Yamada, A. Kawai, N. Takamura, S. Sugasawa, Y. Matsuoka, H. Iwata, and T. Fukushima, *Heterocycles*, 1994, **39**, 251.
6. For selected reviews, see: (a) Y. Ping, Y. Li, J. Zhu, and W. Kong, *Angew. Chem. Int. Ed.*, 2019, **58**, 1562; (b) J. Muzart, *Tetrahedron*, 2013, **69**, 6735; (c) J. E. M. N. Klein and R. J. K. Taylor, *Eur. J. Org. Chem.*, 2011, 6821; (d) T. Vlaar, E. Ruijter, and R. V. A. Orru, *Adv. Synth. Catal.*, 2011, **353**, 809; (e) G. Poli, G. Giambastiani, and A. Heumann, *Tetrahedron*, 2000, **56**, 5959; (f) R. Grigg and V. Sridharan, *J. Organomet. Chem.*, 1999, **576**, 65.
7. (a) D. D. Vachhani, H. H. Butani, N. Sharma, U. C. K. Bhoya, A. K. Shah, and E. V. Van der Eycken, *Chem. Commun.*, 2015, **51**, 14862; (b) F. Wei, L. Wei, L. Zhou, C.-H. Tung, Y. Ma, and Z. Xu, *Asian J. Org. Chem.*, 2016, **5**, 971.
8. (a) A. Lu, X. Ji, B. Zhou, Z. Wu, and Y. Zhang, *Angew. Chem. Int. Ed.*, 2018, **57**, 3233; (b) G. Xiao, L. Chen, G. Deng, J. Liu, and Y. Liang, *Tetrahedron Lett.*, 2018, **59**, 1836.
9. Y. Hong, W. Liu, M. Dong, X. Chen, T. Xu, P. Tian, and X. Tong, *Org. Lett.*, 2019, **21**, 5742.
10. Y. Hosoya, I. Kobayashi, K. Mizoguchi, and M. Nakada, *Org. Lett.*, 2019, **21**, 8280.
11. In our previous studies on the palladium-catalyzed carbothiolations that form cyclic compounds other than 2,3-dihydrobenzo[*b*]thiophenes and the corresponding 1,1-dioxides, major by-products were not aryl sulfides such as **8a** but alkyl iodides. It is speculated that these differences could be ascribed to the rate of cyclization. Namely, the formation of aryl sulfides could be faster when the cyclization is slow. In the case of compound **6**, internal coordination of a sulfur atom in **6** could stabilize the aryl palladium intermediate to retard the cyclization. On the other hand, in the case of compound **9**, the strain in the transition state which derived from the sulfone moiety could retard the cyclization.
12. T. Jeffery, *Tetrahedron*, 1996, **52**, 10113.