Review

Sulfonium-aided coupling of aromatic rings via sigmatropic rearrangement

By Hideki YORIMITSU[*1,†] and Gregory J. P. PERRY[*1]

(Edited by Keisuke SUZUKI, M.J.A.)

Abstract: Biaryl synthesis continues to occupy a central role in chemical synthesis. From blockbuster drug molecules to organic electronics, biaryls present numerous possibilities and new applications continue to emerge. Transition-metal-catalyzed coupling reactions represent the gold standard for biaryl synthesis and the mechanistic steps, such as reductive elimination, are well established. Developing routes that exploit alternative mechanistic scenarios could give unprecedented biaryl structures and expand the portfolio of biaryl applications. We have developed metal-free C–H/C–H couplings of aryl sulfoxides with phenols to afford 2-hydroxy-2′-sulfanylbiaryls. This cascade strategy consists of an interrupted Pummerer reaction and [3,3] sigmatropic rearrangement. Our method enables the synthesis of intriguing aromatic molecules, including oligoarenes, enantioenriched dihetero[8]helicenes, and polyfluorobiaryls. From our successes in aryl sulfoxide/phenol couplings and a deeper understanding of sigmatropic rearrangements for biaryl synthesis, we have established related methods, such as aryl sulfoxide/aniline and aryl iodane/phenol couplings. Overall, our fundamental interests in underexplored reaction mechanisms have led to various methods for accessing important biaryl architectures.

Keywords: sulfur, interrupted Pummerer reaction, sigmatropic rearrangement, biaryl, C–H/C–H coupling

1. Introduction

As the biaryl skeleton is structurally rigid, yet electronically flexible and peripherally modifiable, it occupies a central position in the design and synthesis of electronically and structurally tunable molecules. Needless to say, transition-metal-catalyzed cross-coupling reactions have been widely used to reliably prepare biaryls (Scheme 1).[1),2)] Recently, catalytic direct C–H arylation reactions have been established as a more atom- and step-economical alternative.[3)–5)] In both methods, the key intermediate is a transition
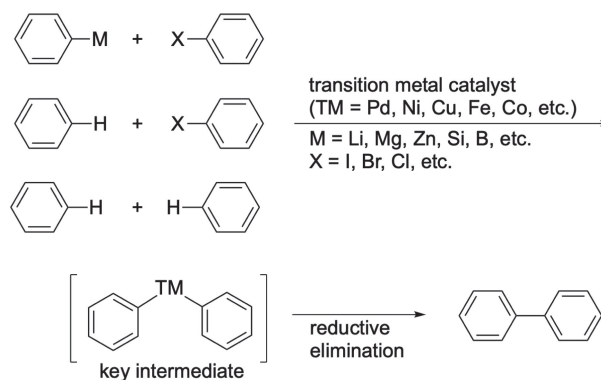
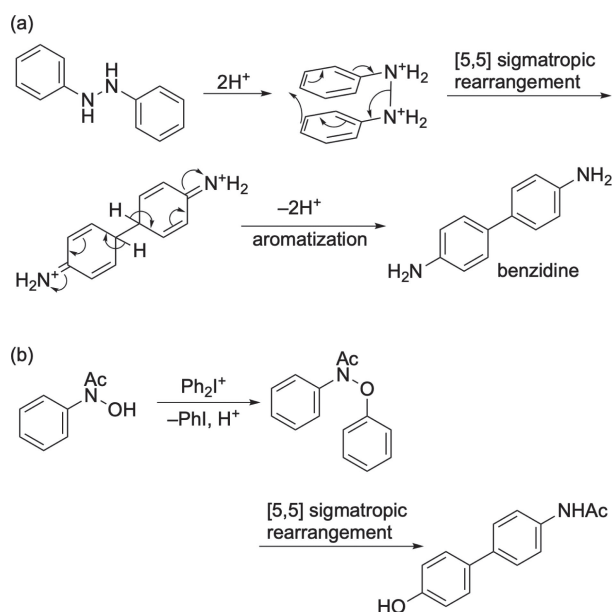Scheme 1. Transition-metal-catalyzed coupling through reductive elimination.

metal complex bearing two aryl groups on the metal center, from which reductive elimination provides the desired biaryl.

Despite extensive studies, these catalytic methods for the synthesis of biaryls are not universal. For example, there remain several classes of substituted

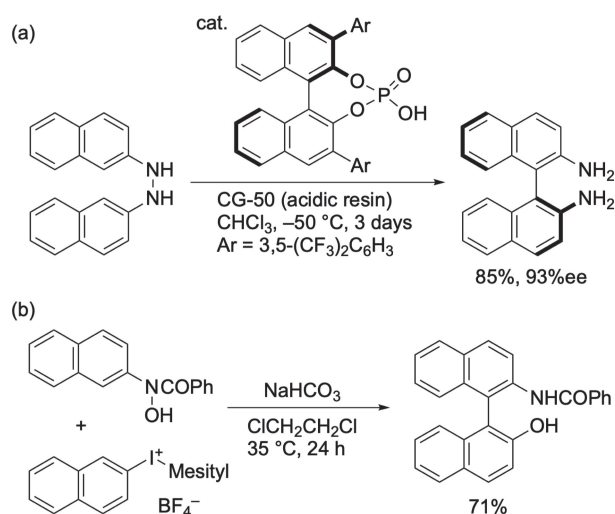 [*1] Department of Chemistry, Graduate School of Science, Kyoto University, Kyoto, Japan.

  [†] Correspondence should be addressed to: H. Yorimitsu, Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan (e-mail: yori@kuchem.kyoto-u.ac.jp).

  Non-standard abbreviation list: An: *p*-methoxybenzenesulfonyl; Boc: *t*-butoxycarbonyl; Bpin: pinacolatoboryl; HMDS: hexamethyldisilazide; KDM: ketene dithioacetal monoxide; LDA: lithium diisopropylamide; *m*CPBA: *m*-chloroperbenzoic acid; Tf: trifluoromethanesulfonyl; Ts: *p*-toluenesulfonyl.

Scheme 2. (a) Benzidine rearrangement and (b) its *N,O* variant.

Scheme 3. Syntheses of axially chiral binaphthyls through benzidine-type rearrangement. (a) Enantioselective synthesis of 2,2′-diaminobinaphthyl by List.[14] (b) Synthesis of 2-amino-2′-hydroxybinaphthyl by Gao.[17]

biaryls that are not easily accessible by current catalytic methods. Such limitations mostly originate from the difficulty in generating the key diaryl transition metal complex, for example due to steric hindrance around the metal center or poor regioselectivity of metalation. Thus, developing new methods for the construction of biaryls based on different reaction mechanisms without recourse to the biaryl-forming reductive elimination is highly sought after.[6)–8)]

We would like to draw your attention to the benzidine rearrangement (Scheme 2a).[9),10)] This 150-year-old reaction represents the isomerization of *N,N′*-diphenylhydrazine (hydrazobenzene) under acidic conditions into 4,4′-diaminobiphenyl (benzidine) via a protonation-induced sigmatropic rearrangement. Its N–O analogues, *N,O*-diphenylhydroxylamine derivatives, also undergo similar rearrangement (Scheme 2b).[11),12)] By looking at these classical reactions from the viewpoint of modern organic chemistry, we become aware of the following interesting features. (1) This unique C–C bond-forming event accompanies dearomatization of both the benzene rings, which is made possible through cleavage of the weak N–N or N–O bond. (2) The transformations are regarded as a formal dehydrogenative C–H/C–H coupling, which proceeds with high regioselectivity controlled by [5,5] sigmatropic rearrangement. (3) The products naturally have two heteroatom substituents that stem from the tether.

Similarly, [3,3] sigmatropic rearrangement gives 2,2′-disubstituted biaryls that are often useful synthetic intermediates. As an elegant recent example, Kürti[13] and List[14] independently reported in 2013 enantioselective benzidine rearrangement of hydrazonaphthalene by using an Akiyama-Terada catalyst, which affords 2,2′-diaminobinaphthyl, a privileged motif for axially chiral catalysts (Scheme 3a). Similarly, Kürti/Gao[15)–17)] and Li/Tan[18] reported the coupling reaction of *N*-naphthylhydroxylamine with naphthyliodonium salts to synthesize racemic 2-amino-2′-hydroxybinaphthyl via sigmatropic rearrangement of *in situ* generated *N,O*-dinaphthylhydroxylamine (Scheme 3b). Currently, the construction of biaryl skeletons via sigmatropic rearrangement is attracting increased attention.

Such couplings to prepare biaryls via sigmatropic rearrangement is distinct from transition-metal-catalyzed coupling and hence intriguing. However, significant progress is needed to establish it as a truly useful strategy for biaryl synthesis. For example, these reports suffer from several limitations. (1) There are only a few methods to prepare the precursors for the rearrangement. (2) The available tethers between the two aromatic rings are limited to an N–N or N–O bond.

Since 2005, we have been interested in chemical transformations that utilize the unique reactivity of organosulfur compounds. During our study,[19),20)] we developed a new method for the synthesis of biaryls

via sigmatropic rearrangement of sulfur-tethered intermediates. Here we summarize our progress regarding this new sulfur-based method,[21] together with related work by others, after briefly detailing how our idea for sulfonium-aided biaryl synthesis was evolved in our laboratory in the next section.

2. Discovery of a cascade of interrupted Pummerer reaction and sigmatropic rearrangement

It was when we had been exploring the use of ketene dithioacetal monoxides (KDMs) for extended Pummerer reactions[22)–32)] that we accidentally realized the sigmatropic rearrangement of sulfur-tethered intermediates. As described in Scheme 4, treatment of KDM **1** with trifluoromethanesulfonic anhydride (Tf_2O, $Tf = CF_3SO_2$) results in activation of the sulfoxide moiety of **1**. Typically, a nucleophile (Nu^-) would then attack at the distant exocyclic vinylic carbon of the sulfonium cation **2** (an additive Pummerer reaction) to yield intermediate **3** and eventually ketene dithioacetal product **4**, a useful disubstituted ketene equivalent.

By considering the importance of allylic groups in organic synthesis, we tested allylic silane **5** as the
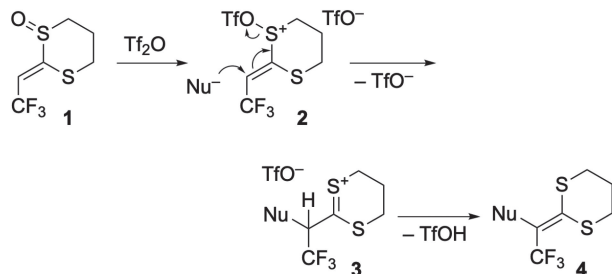
nucleophile (Scheme 5)[33] and encountered a totally unexpected result: The reaction exclusively afforded the linear product **6** via a formal α-attack, without forming the branched product **7**, the regioselectivity of which is opposite to the γ-attack that the Hosomi–Sakurai reactions always undertake. We considered that the following rationalizes the abnormal regioselectivity: The activated sulfonium cation **2** reacts with allylic silane **5** in a normal Hosomi–Sakurai fashion. However, the nucleophilic attack does not occur at the exocyclic vinylic carbon of **2** but at the cationic sulfur atom to yield allyl vinyl sulfonium intermediate **8** (an interrupted Pummerer reaction). The intermediate **8** then undergoes charge-accelerated sigmatropic rearrangement[34] at room temperature very smoothly to deliver the linear product **6** after the final deprotonation. We realized that such a cascade of interrupted Pummerer reaction and [3,3] sigmatropic rearrangement would provide unusual reactivity/selectivity and thus great possibilities in organic synthesis and started pursuing new transformations utilizing this cascade. It is worth noting that our work on the allylation of ketene dithioacetal monoxides inspired others to develop related interesting allylation and propargylation processes of aryl sulfoxides.[35)–38)]
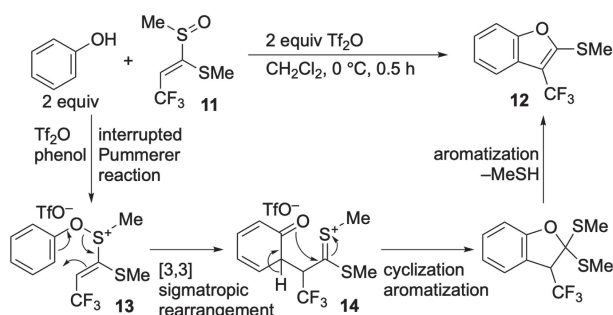
For example, instead of allylic silanes, ketones are suitable nucleophiles for the cascade reaction (Scheme 6).[39] Sulfonium cation **2** undergoes nucleophilic attack of the carbonyl oxygen at the cationic sulfur atom to yield **9**, which rearranges to make a carbon–carbon bond between the α position of the ketone and the exocyclic vinylic carbon. The initial product **10** is a 2-trifluoromethyl-1,4-dicarbonyl equivalent that can be easily converted to the corresponding 3-trifluoromethylheteroles by Paal–Knorr-type transformations. This report was followed by interesting reports by others using aryl

Scheme 4.   Typically conceived mechanism of functionalization of KDM **1** at the β position.
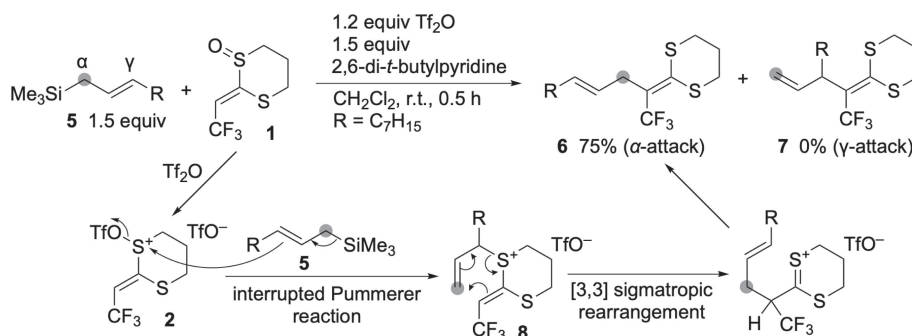
Scheme 5.   Discovery of a cascade of interrupted Pummerer reaction and [3,3] sigmatropic rearrangement.
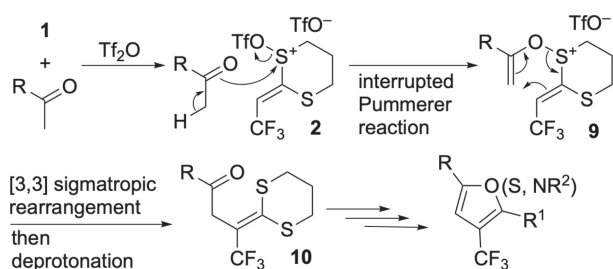
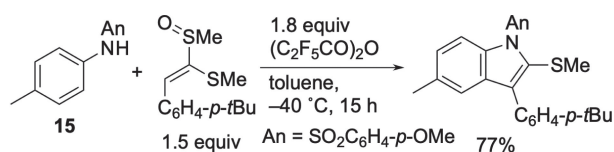Scheme 6. α-Functionalization of ketones for the synthesis of 3-trifluoromethylheteroles.

Scheme 7. Annulation between phenol and alkenyl sulfoxide into benzofuran.

Scheme 8. Annulation between N-sulfonylaniline and KDM into indole.

Scheme 9. Formation of biaryl via a cascade of interrupted Pummerer reaction and [3,3] sigmatropic rearrangement.

sulfoxides instead of KDMs to develop transition metal-free α-arylation of carbonyls.[40)–42)]
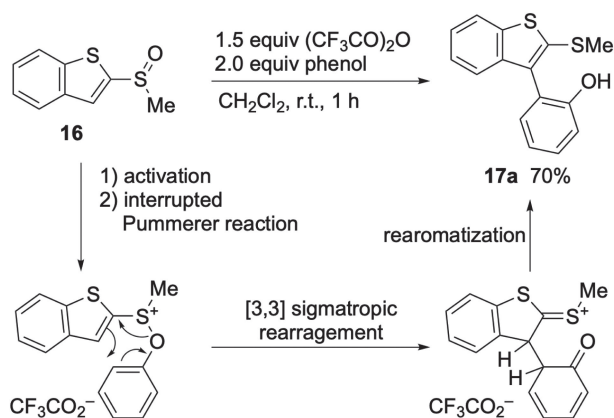
Another notable example is the reaction of phenols with alkenyl sulfoxides such as KDM **11** to yield benzofuran **12** (Scheme 7).[43)–47)] As phenol is a tautomer of 2,4-cyclohexadienone, similarly to Scheme 6, phenol interrupts the sulfonium intermediate from **11** to yield **13**. Interestingly, subsequent [3,3] sigmatropic rearrangement occurs with concomitant dearomatization at or below room temperature to form a C–C bond at the *ortho* position of phenol. Cyclization and global aromatization of intermediate **14** provided **12**. This sulfonium-aided annulation reaction is operationally very simple, proceeding by an addition of anhydride to a mixture of phenol and alkenyl sulfoxide. The reaction has a wide substrate scope, even N-sulfonylanilines such as **15** can be used to prepare indoles (Scheme 8).[48)] This beautiful cascade process reminds us of the Fischer indole synthesis.

3. Synthesis of biaryls from phenols and aryl sulfoxides via sigmatropic rearrangement of sulfonium intermediates

We then envisioned using aromatic sulfoxides as unsaturated sulfoxides instead of alkenyl sulfoxides.

To our delight, treatment of phenol and 2-benzothienyl sulfoxide **16** with trifluoroacetic anhydride provided biaryl **17a** in high yield with exclusive regioselectivity (Scheme 9).[49)] The reaction should proceed in a similar fashion to Scheme 7. After formation of the phenoxy-substituted sulfonium intermediate by an interrupted Pummerer reaction, [3,3] sigmatropic rearrangement takes place with concomitant dearomatization of both the aromatic rings to form a C–C bond between the *ortho* position of phenol and the 3 position of **16**. Subsequent rearomatization of both the rings furnishes **17a**. Other regioisomers were not observed, which suggests the reaction is not a simple Friedel–Crafts-type electrophilic aromatic substitution of phenol.

A series of aromatic sulfoxides were found to participate in the synthesis of biaryls (Scheme 10). Other five-membered heteroaromatic sulfoxides participated to yield **17b–f**. 2-Benzothienyl 4-tolyl sulfoxide reacted selectively on the less aromatic and more electron-rich benzothiophene ring to yield **17c** exclusively. The reaction of 2-naphthyl sulfoxide with 2-naphthol afforded 1,1′-binaphthyl **17g** in high yield. However, the reaction of phenyl sulfoxide with 2-naphthol afforded the expected product **17h** in low yield in a complex product mixture. In contrast, electron-rich 3,5-dimethoxyphenyl sulfoxide is a good
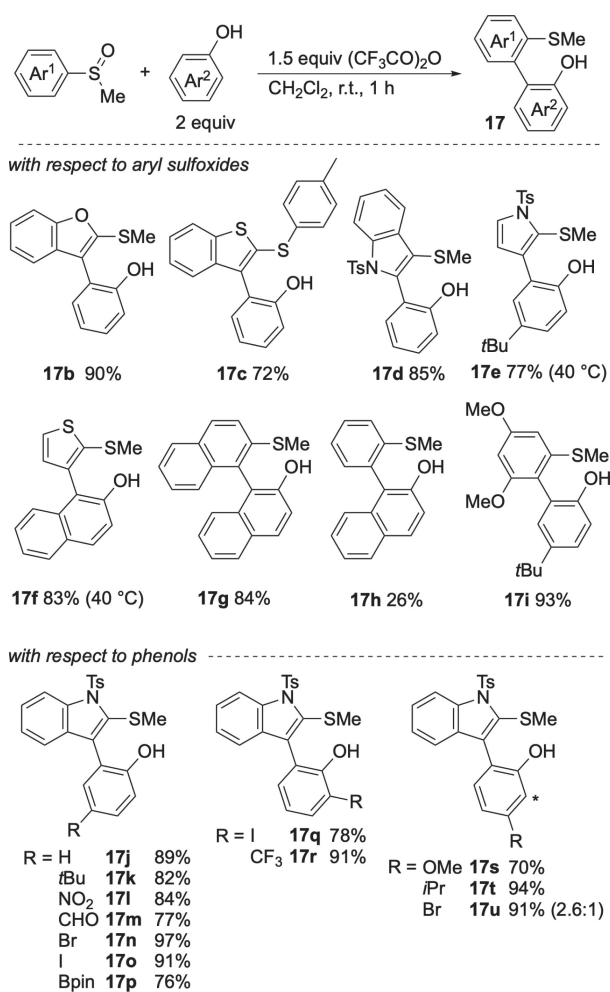
Scheme 10. Scope of the biaryl synthesis. Compound **17u** was obtained as a 2.6:1 mixture of regioisomers and the asterisk (*) in **17u** indicates the position where the C–C bond formation occurred in the minor isomer.

substrate to yield **17i** in excellent yield. These electronic effects provide important information on the detailed nature of the sigmatropic rearrangement (vide infra).

The scope with respect to phenols is wide as shown in Scheme 10. Functional groups such as iodo in **17o** and **17q** and pinacolatoboryl in **17p** survived under the conditions, which is in sharp contrast to transition-metal-catalyzed coupling reactions. Arylation of 3- or 2-substituted phenols occurred at the less hindered 6 positions to afford **17q–u** with exclusive or high regioselectivity. These regioselectivities strongly suggest again that the reactions proceeded not via Friedel–Crafts-type electrophilic aromatic substitution of phenols but via the sigmatropic rearrangement of sulfonium-tethered intermediates.

Interestingly, the reaction of 2,6-dimethylphenol resulted in the preferential arylation at the 3 position of 2,6-dimethylphenol to yield biaryl **18** with high regioselectivity (Scheme 11). By following a similar mechanism to that shown in Scheme 9, the sterically encumbered interrupted intermediate **19** is formed and undergoes [3,3] sigmatropic rearrangement to yield **20**, despite the presence of the methyl group. The benzothiophene skeleton should be easily regenerated, but the cyclohexadienone would fail to aromatize. Instead, the trifluoroacetic acid that is generated *in situ* would protonate cyclohexadienone **21** to induce 1,2-shift of the benzothienyl group, which followed by deprotonation furnishes **18**.

It is worth noting that Procter reported a similar method detailing the reaction of *in situ* generated benzothiophene *S*-oxides with phenols and trifluoroacetic anhydride to give the phenol and benzothiophene coupled products linked at their ortho and 3 positions, respectively (Scheme 12).[30),50)–55)]
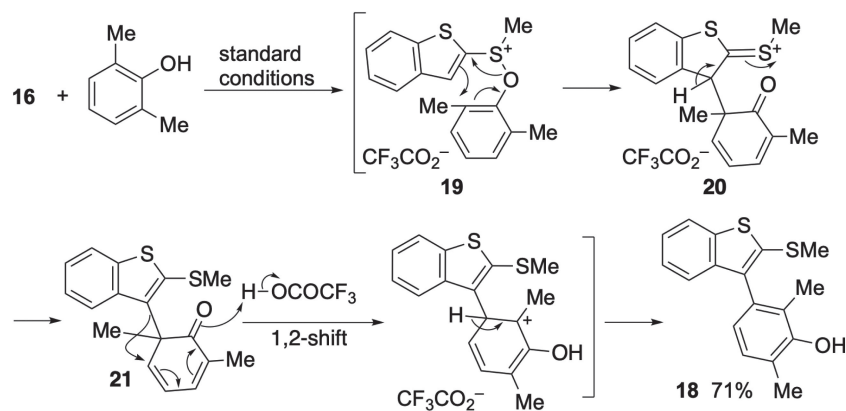
Scheme 11. Arylation of 2,6-dimethylphenol at the 3 position.
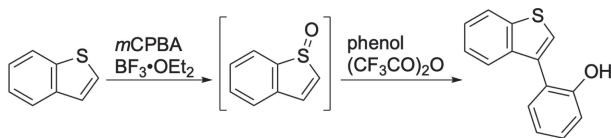
Scheme 12. Arylation of benzothiophene at the 3 position by Procter.[50]

This new sulfonium-aided coupling of two arenes is mechanistically totally different from the conventional transition-metal-catalyzed coupling reactions. Although similar benzidine rearrangements have been extensively investigated, they remain mechanistically obscure. In light of the importance of such coupling reactions via sigmatropic rearrangement, we investigated the mechanism of our sulfonium-aided coupling experimentally and computationally.[56] For clarity, here we mainly discuss computationally obtained reaction pathways (Fig. 1) without detailing experimental results that coincide with the computational results.

As we expected, the reaction was found to proceed via an interrupted Pummerer reaction followed by sigmatropic rearrangement. Interestingly, activation of sulfoxide **16** and the subsequent interrupted Pummerer reaction of the resulting sulfurane **INT1** with phenol to yield **INT2** were calculated to be reversible. The transition state of the interrupted Pummerer reaction **TS1** was found to be six-membered and cyclic, wherein the S–OPh-bond formation and deprotonation by the CF_3CO_2 unit occurs in a concerted way. From **INT2**, the rate-determining sigmatropic rearrangement proceeds via a boat-like transition state **TS2** with an activation free energy of 20.3 kcal/mol. The rate-determining step is supported by the fact that **INT2** was observable by ^{1}H NMR experiments. The subsequent two tautomerization processes are both kinetically and thermodynamically facile.

Detailed analysis of the intrinsic reaction coordinate (IRC) of the sigmatropic rearrangement revealed the apparent asynchronous nature of the concerted rearrangement. As shown in Fig. 2a, the sigmatropic rearrangement shows a nearly flat region in energy (deep blue solid line) before **TS2**. The root mean squared (RMS) gradient (red dotted line) clearly shows a trough around the flat region, which indicates the existence of a "hidden intermediate". This asynchronous nature is also observed in the bond lengths of the cleaving S–O bond and the developing C–C bond (Fig. 2b). The S–O bond cleavage takes place at the early stage of the

sigmatropic rearrangement with the C–C bond underdeveloped, and the C–C bond formation follows to reach **TS2** and then **INT3**.

In the reaction of an electron-deficient phenol, the "hidden intermediate" was not observed and the sigmatropic rearrangement is synchronous. In contrast, in the reaction of an electron-rich phenol, the "hidden intermediate" is not hidden any more and was computationally obtained as an energy minimum (Fig. 3). The Wiberg bond indexes (WBI) of the cleaving S–O bond and the developing C–C bond in the emerging intermediate **INTπ** are 0.07 and 0.06, respectively, which suggests the benzothiophene and phenoxy units are not connected through apparent σ bonds and that **INTπ** can be regarded as a π-complex. The changes of the natural population analysis (NPA) charge distribution during the sigmatropic rearrangement indicates the following: Initially, the methylsulfanylbenzothiophene part and the phenoxy part have positive (+1.27) and negative (−0.39) NPA charges, respectively. As the reaction proceeds, the electron density moves to the benzothienyl part (reaching +0.72 at **INTπ**) from the phenoxy part (reaching +0.26 at **INTπ**). From **INTπ**, nucleophilic attack by the benzothienyl unit onto the electron-deficient phenoxy moiety (phenoxonium) occurs to form the C–C bond of **INT3′** and yield the cationic thionium (+0.92) and almost neutral cyclohexadienone (+0.06). Thus, when comparing the formation of products **17h** and **17i**, the positive effect of methoxy substituents in **17i** can be explained as an increase in electron density on the sulfoxide unit, which facilitates smoother nucleophilic attack. This detailed analysis of the sigmatropic rearrangement is highly informative for the design and realization of new efficient coupling reactions of two arenes.

4. Application of the new biaryl synthesis

With a new unique method for regioselectively coupling aryl sulfoxides and phenols in hand, we explored applications that highlight the advantages over transition-metal-catalyzed coupling reactions.

4.1. Synthesis of oligoaryls via repetitive couplings. Oligoaryls represent an important class of organic frameworks and are used as functional core structures for biological and materials applications. In order to synthesize well-designed oligoaryls, stepwise elongation via iterative cross-coupling has been regarded as a powerful and reliable methodology.[57] In particular, the utilization of on/off-switchable difunctional coupling partners has occu-
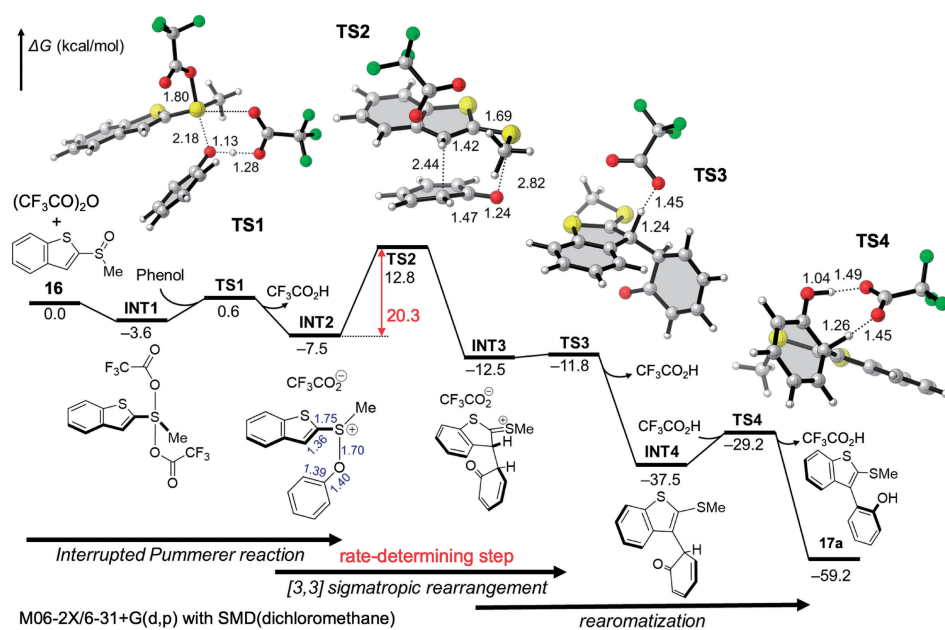
Fig. 1.   Energy diagram of the whole process of the reaction of **16** with phenol. Structures of transition states are shown by ball and stick model, with representative bond lengths in angstrom (Å).
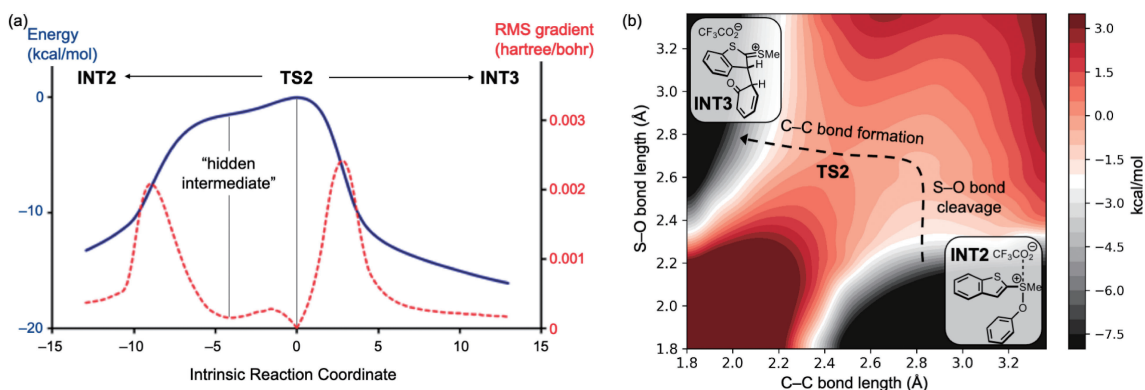

Fig. 2.   (a) IRC pathway from **TS2**. (b) Potential energy surface around **TS2**.
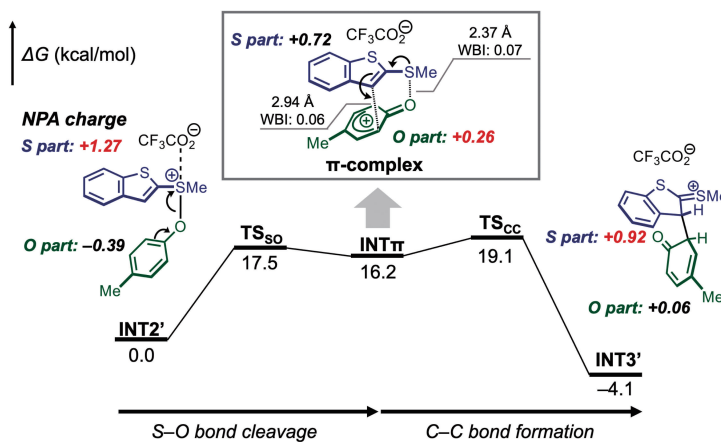

Fig. 3.   Stepwise rearrangement in the reaction of **16** with electron-rich *p*-cresol.

Phenolic OH as on/off-switchable unit by Hamilton and Manabe

On/off-switchable arylboron and -silane reagents

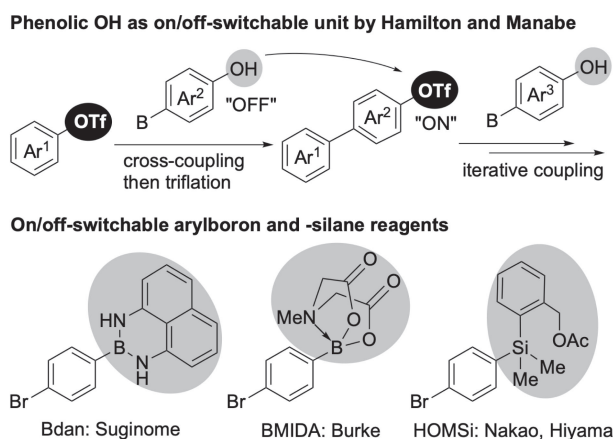Bdan: Suginome   BMIDA: Burke   HOMSi: Nakao, Hiyama

Fig. 4.   On/off-switchable units for iterative cross-coupling.

pied a central position to this end, as exemplified in Fig. 4 by the pioneering work using an OH/OTf switch by Hamilton[58] and Manabe[59] and by elaborate work concerning on/off organometallic switches by Suginome (Bdan),[60] Burke (BMIDA),[61] and Nakao/Hiyama (HOMSi).[62]

With this in mind, we envisioned that our coupling of aryl sulfoxide with phenols is applicable to metal-free iterative synthesis of oligoaryls.[63] Two-fold arylation of aryl sulfoxide **22** with two different naphthols is exemplified in Scheme 13. Of note, concomitant with the coupling, the sulfinyl moiety is reduced to the sulfanyl group which is "off" and no longer able to promote the dehydrogenative coupling with phenols, thus preventing unwanted polymerizations. The resulting aryl sulfides **23** can be readily switched "on" through oxidation to the corresponding sulfoxide **24**, which consists of two diastereomers that have axial chirality in the biaryl motif and central chirality at the sulfur atom. Another dehydrogenative coupling is possible for the synthesis of teraryl **25**, which consists of two diastereomers that have two stereogenic axes in the skeleton. It is worth stating that this switching 'on' and 'off' of reactivity

by sulfur oxidation was also recognized and exploited by Procter and his team.[64]

4.2. Synthesis of heterohelicenes. Our method always provides biaryls bearing an ortho-hydroxy group on one aromatic ring and an ortho-methylsulfanyl group on the other aromatic ring. Utilizing these two functional groups in proximity, one can envision synthesizing π-extended heteroles via intramolecular cyclization. We have indeed achieved systematic syntheses of a series of enantio-merically pure dihetero[8]helicenes.[65] This presents a unique route to heterohelicenes, which have attracted attention because of their intriguing helical π-conjugated systems and resulting chiral optical properties.[66],[67]

The synthetic scheme starts with assembling a common synthetic intermediate **27** from bissulfinyl-naphthalene **26** and 2 equivalents of 2-naphthol through our method (Scheme 14a). It is worth noting that the reaction proceeds with high efficiency and *anti* selectivity even though **27** has a highly crowded ternaphthyl motif, which highlights a clear advantage of our method. Optical resolution of **27** was facile to obtain pure material of both enantiomers of **27** on multi-gram scales.

The situation is set for systematic syntheses of enantiomerically pure dihetero[8]helicenes (Scheme 14b). After oxidation of (S_a,S_a)-**27**, disulfone (S_a,S_a)-**28** underwent two-fold S_NAr cyclization using the sulfur functionality as a leaving group to yield dioxa[8]helicene (P)-**29O**. Alternatively, E2 elimination of (S_a,S_a)-**27** to yield bisthiol **30** and subsequent ring-closing condensation with triflic acid afforded (P)-**29S**. These cyclization reactions took place with excellent axial-to-helical chirality conversion, especially in the room temperature synthesis of (P)-**29S**. Dithia[8]helicene (P)-**29S** was oxidized to the corresponding tetraoxide **29SO$_2$** quantitatively, which was further transformed into the nitrogen and the carbon analogs by replacing the two endocyclic SO_2 units via S_NAr-based aromatic
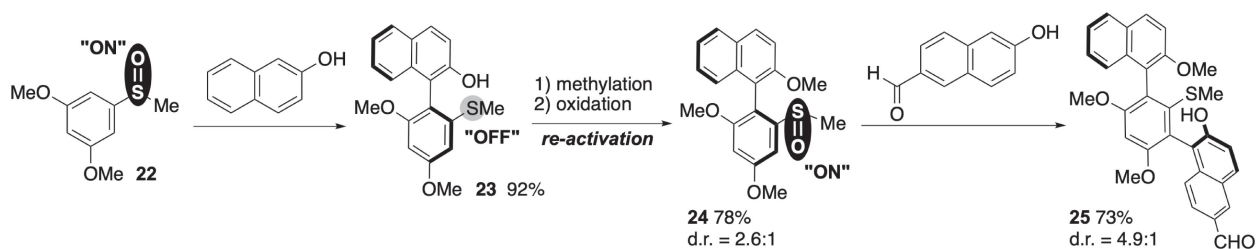
Scheme 13.   Sulfoxide-based iterative couplings.
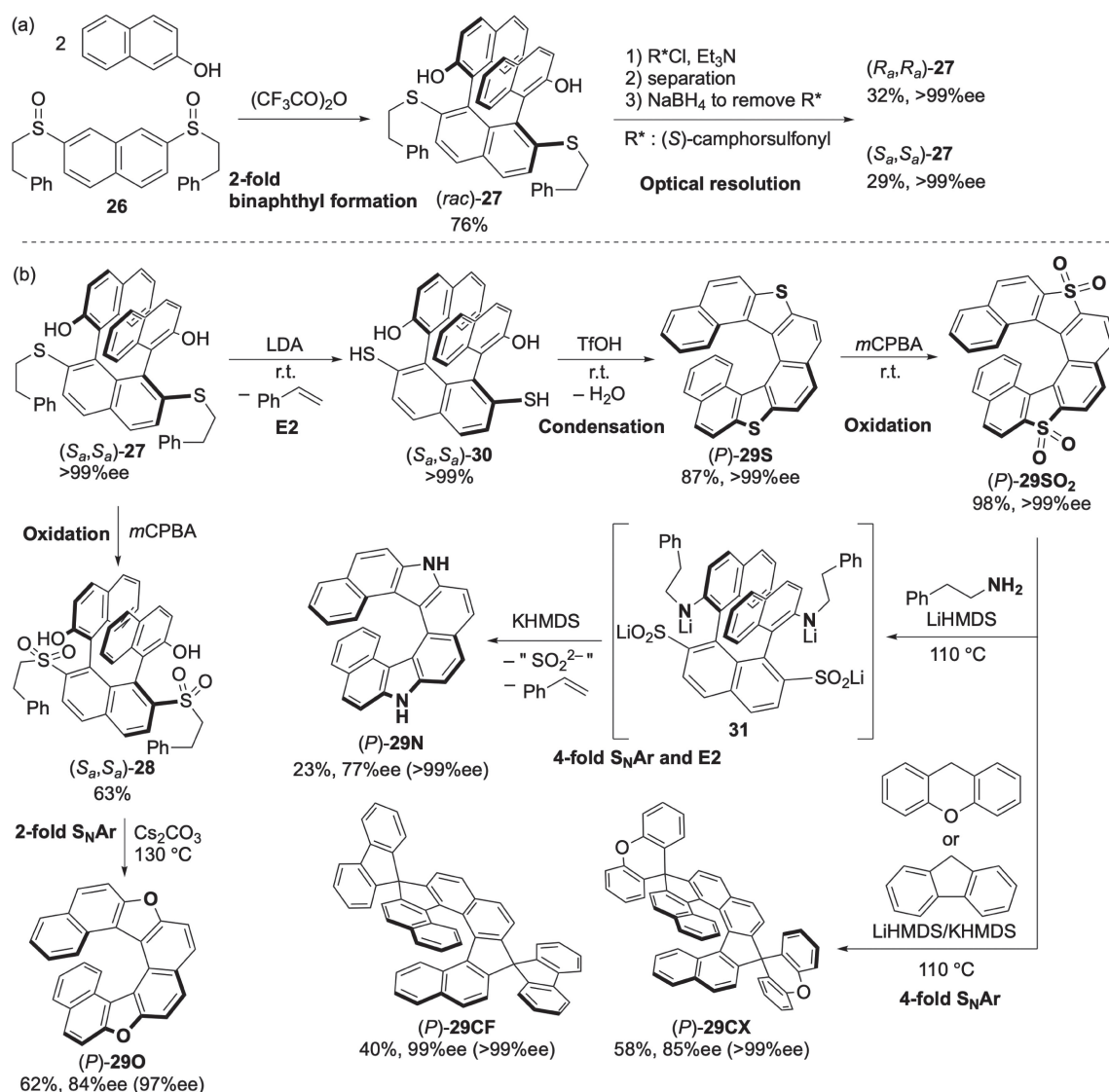
Scheme 14. Synthesis of a series of (P)-dihetero[8]helicenes. (a) Synthesis of enantiopure common intermediate (S_a,S_a)-27. (b) Construction of helicenes from (S_a,S_a)-27. The synthesis of the (M) isomer is omitted for clarity. Values of ee after recrystallization are in parentheses.

metamorphosis.[68],[69] Diaza[8]helicene (P)-29N was synthesized by treatment of (P)-29SO₂ with 2-phenylethylamine under strongly basic conditions. This reaction proceeded via an S_NAr-based replacement of the SO₂ units to give intermediate 31 followed by E2 elimination to furnish (P)-29N.[70],[71] A slight decrease in the optical purity of 29N to 77%ee was observed during the substitution because of the high reaction temperature (110 °C). In a similar fashion, xanthene and fluorene served as carbon nucleophiles for the endocyclic substitution reaction[72] to yield (P)-29CX and (P)-29CF. For

all the heterohelicenes, recrystallization provided the enantiomerically pure (P) isomers. Notably, the enantiomers of all the heterohelicenes were obtained from a common precursor (S_a,S_a)-27. Analogously, the (M)-heterohelicene isomers can be obtained in similar yields and enantioselectivities from (R_a,R_a)-27 by following the same synthetic pathways.

We thus succeeded in the syntheses of a series of enantiomerically pure dihetero[8]helicenes with extremely high efficiency. The efficient construction of this library allowed us to comprehensively and systematically evaluate the chemical and photo-

physical properties of the series of dihetero[8]-helicenes. Several comments are worth noting. 1) The kinetic studies for racemization dynamics revealed that the dihetero[8]helicene skeleton is fixed due to the rigid 5-membered rings and exhibits unexpectedly higher thermal conformational stability in comparison with carbo[8]helicene that shows larger overlap between the terminal edges. This observation offers a seemingly contradictory viewpoint in designing helicenes: introduction of a smaller 5-membered heterole ring to stabilize helicity. 2) Spirocyclic **29CX** and **29CF** were found to exhibit by far the highest fluorescence quantum yields of 62% and 66%, respectively. In addition, **29CF** was found to emit blue fluorescence in the solid state ($\Phi_F = 40\%$). 3) **29O** and **29N** show both high fluorescence efficiency ($\Phi_F = 39\%$ and 13%) and dissymmetric factors of fluorescence $|g_{lum}|$ (6.1×10^{-3} for **29O** and 9.5×10^{-3} for **29N**) among reported helicenes.[73] Thus, the potential utility of our systematic synthetic strategy will be applicable to efficient generations of chemical libraries of π-extended compounds to find 'hit' molecules as well as to accelerate the progress of the chemistry of heterohelicenes.

4.3. Synthesis of fluorinated arenes via defluorinative strategy. Organofluorine compounds are widely used in pharmaceutical, agrochemical, and material science and vastly related industrial applications. Development of methods for the synthesis of fluorinated compounds has been an important topic in organic synthesis. While introduction of a fluorine atom to a molecule is a straightforward and conventional method, the recent increase in the availability of polyfluorinated compounds pose questions about developing selective and controlled defluorinative transformations.[74),75] However, this new contrasting methodology remains underdeveloped in many aspects such as regioselectivity and mono/di/tri-defluorination selectivity.

In analogy to the reaction of 2,6-dimethylphenol in Scheme 11, we investigated the use of 2,6-difluorophenol for our Pummerer chemistry (Scheme 15).[76),77] The reaction with **16** should provide dearomatized intermediate **33**, which then undergoes reductive defluorination by means of zinc in the same pot to recover aromaticity and to afford monofluorobiaryl **32a**. This defluorinative transformation accommodates a broad range of polyfluorophenols including heptafluoro-2-naphthol and heteroaryl sulfoxides (Scheme 16). The biaryl bond formations took place exclusively at the ortho
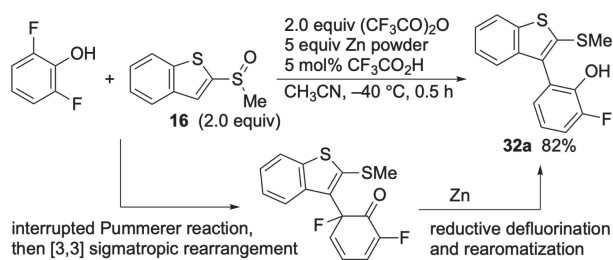

Scheme 15.   Defluorinative synthesis of biaryls from 2,6-difluorophenol and benzothienyl sulfoxide with the aid of zinc as a reducing agent.
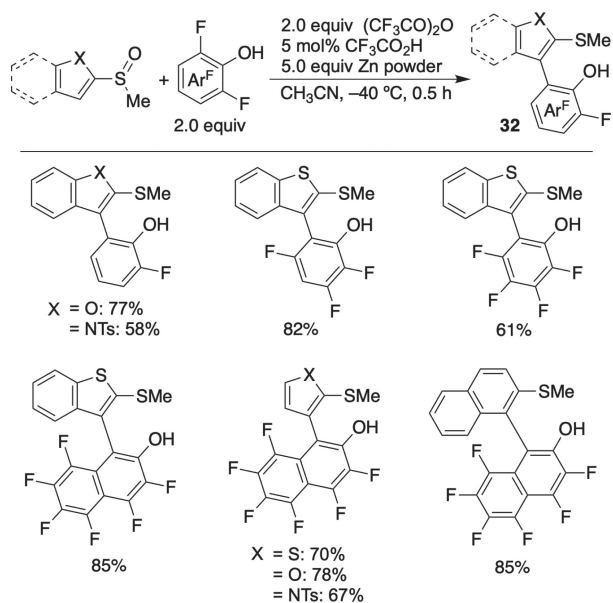

Scheme 16.   Defluorinative synthesis of biaryls from polyfluorophenols and heteroaryl sulfoxide.

position of the phenols and selectively removed only one fluorine atom. On a negative note, simple phenyl sulfoxide is not a suitable substrate because of the stronger aromaticity of the phenyl ring. The chemistry is applicable to the synthesis of a fluorinated analog of Maxipost (BMS-204352), a competent potassium channel modulator (Scheme 17). Indolyl sulfoxide **35**, prepared from commercially available **34**, reacted with 4-chloro-2,6-difluorophenol to afford **36** in high yield. Methylation of the phenolic hydroxy group, Boc deprotection, and electrophilic fluorination with Selectfluor culminates in the synthesis of the fluorinated analog.

We also focused on the usefulness of dearomatized intermediates such as **33** as building blocks for the synthesis of multi-substituted phenols.[77] In the
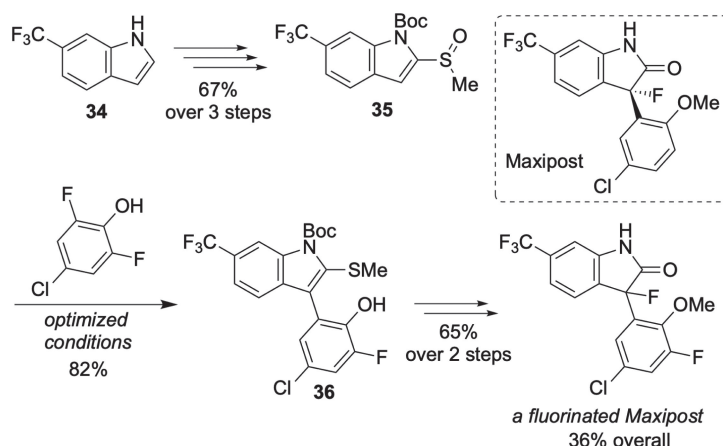
Scheme 17. Synthesis of a fluorinated analog of Maxipost.
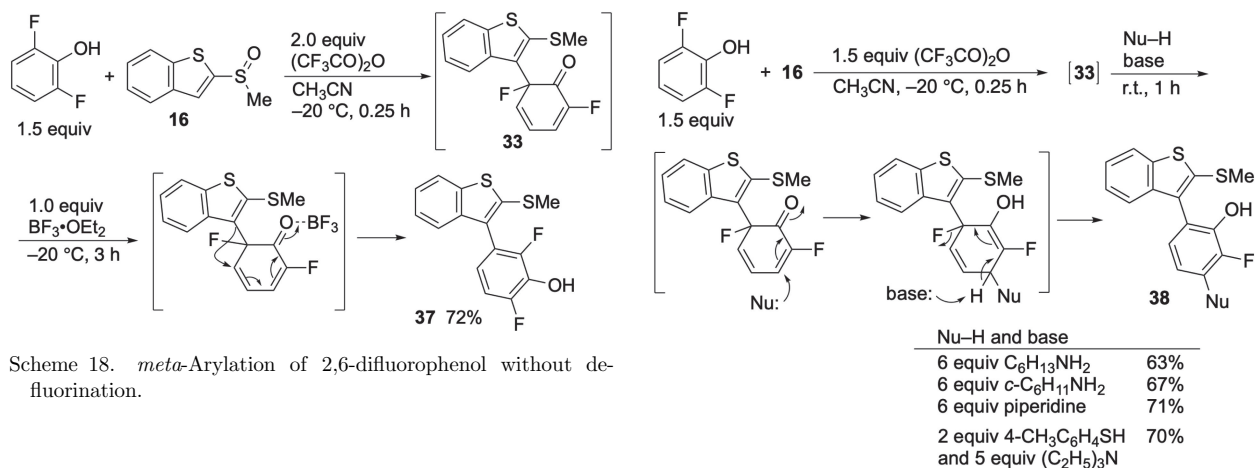
Scheme 18. *meta*-Arylation of 2,6-difluorophenol without defluorination.

Scheme 19. Nucleophilic *meta*-amination and thiolation of 2,6-difluorophenol with *ortho*-defluorinative arylation.

absence of zinc powder, the reaction of 2,6-difluorophenol produces **33** in the reaction flask. The subsequent addition of BF$_3$·OEt$_2$ induces acid-mediated 1,2-shift of the benzothienyl unit as shown in Scheme 11 to result in the *meta*-substituted 2,6-difluorophenol **37** without defluorination (Scheme 18). Instead of treatment with acid, treatment of **33** with a nucleophile triggers 1,4-addition onto the cyclohexadienone skeleton. Then, elimination of HF and concomitant aromatization yields monofluorophenol **38** bearing the nucleophilic unit at the *meta* position (Scheme 19).[78]

5. Variations of the synthesis of 2-hydroxy-2′-sulfanylbiphenyls

In the previous sections, the reactions of phenols via the transient formation of S–O bonds were discussed. If one can use different combinations of heteroatom linkers, biaryl synthesis based on sigmatropic rearrangement becomes a more popular synthetic strategy.

5.1. Synthesis of 2-amino-2′-sulfanylbiphenyls.
We used a simple aniline instead of phenols and tried reactions with trifluoroacetic anhydride as an activator under similar conditions. However, trifluoroacetylation of highly nucleophilic aniline took place exclusively and activation of sulfoxide did not occur. Interestingly, triflic anhydride Tf$_2$O was found to react preferentially with sulfoxide leading to an interrupted Pummerer reaction (Scheme 20).[79] Unfortunately, another problem arose from the high stability of sulfyliminium intermediate **39**; no sigmatropic rearrangement took place because the cationic charge on the sulfur is shared with the neighboring nitrogen. We thus envisioned that protonation of **39** would form dicationic intermediate **40**, which was expected to undergo sigmatropic rearrangement. This was indeed the case, and treatment of **39** with
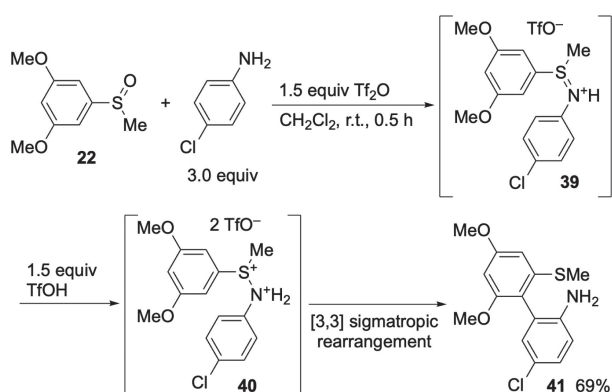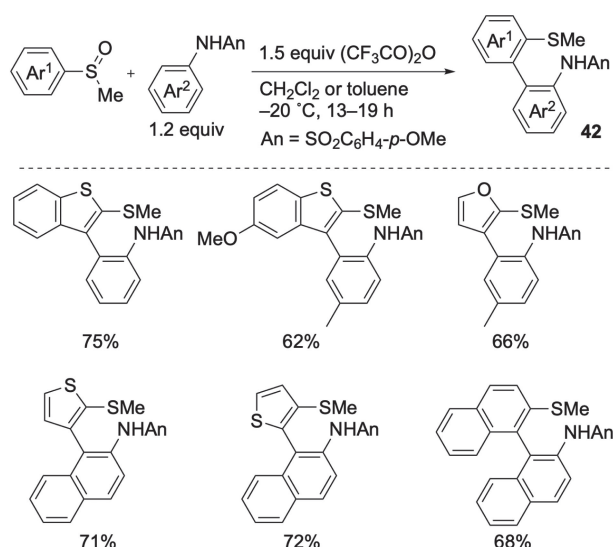
Scheme 20. Biaryl synthesis from aryl sulfoxide and aniline via dicationic intermediate.
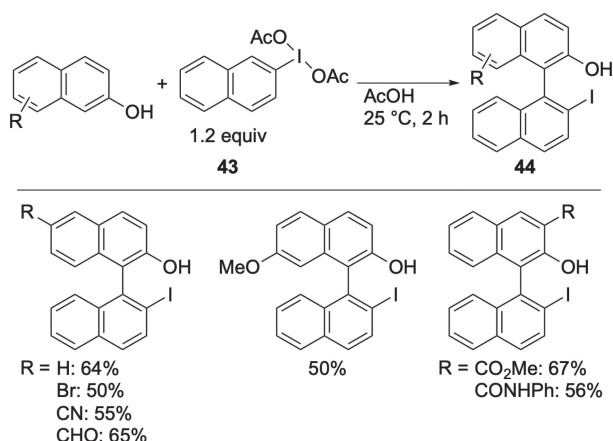

Scheme 21. Biaryl synthesis from aryl sulfoxides and sulfoanilides.

Scheme 22. Binaphthyl synthesis from 2-iodonaphthanlene diacetate and 2-naphthols.

TfOH yielded 2-amino-2′-sulfanylbiaryl **41** in good yield.

One drawback of the reaction of unprotected anilines is its limited scope. To achieve a more general method, we investigated the effect of protecting groups on the aniline substrates. Electron-withdrawing protecting groups on the nitrogen should impart several favorable features, for example, reduce the nucleophilicity of the nitrogen to avoid direct reaction with anhydride, increase the acidity of the N–H unit to construct an S–N bond by concerted deprotonation (Fig. 1, from **INT1** to **INT2**), and weaken the S–N bond in the precursor to charge-accelerated sigmatropic rearrangement. After the screening of electron-withdrawing groups, sulfonyl groups were found to participate in the biaryl formation efficiently (similar to the indole synthesis in Scheme 8), and p-methoxybenzenesulfonyl group showed the best performance among those tested (Scheme 21).[80] While the scope of the reactions is not so wide as in the case of phenols, a range of heteroaryl sulfoxides and naphthyl sulfoxides reacted to yield sulfonylaminobiaryls **42**.

5.2. Synthesis of 2-hydroxy-2′-iodobinaphthyls. We also sought sulfur-free surrogates of aryl sulfoxides for biaryl synthesis. Considering the similarity in structure and reactivity,[26),81)] we focused on hypervalent iodine compounds. However, because trivalent iodine compounds are strong oxidants, we naturally suffered from oxidative side reactions of phenols. After extensive screening, we found that 2-naphthols are suitable for the coupling and that treatment with 2-iodonaphthalene diacetate (**43**) in acetic acid yielded 2-hydroxy-2′-iodobinaphthyls **44** (Scheme 22).[82)] Furthermore, iodoarene diacetate can be generated *in situ* and used without isolation;

iodobenzene **45** was treated sequentially with *m*CPBA and 2-naphthol to afford biaryl **47** via **46** (Scheme 23).

6. Conclusion

Transition metal-catalyzed cross-coupling is currently considered the first choice in the synthesis of biaryls. The key step in this process is the reductive elimination of two aryl ligands on the transition metal center. In contrast, our biaryl synthesis totally differs from catalytic cross-coupling in terms of the reaction mechanism and reaction scope. By transiently connecting two aryl groups with a heteroatom–heteroatom linker, sigmatropic
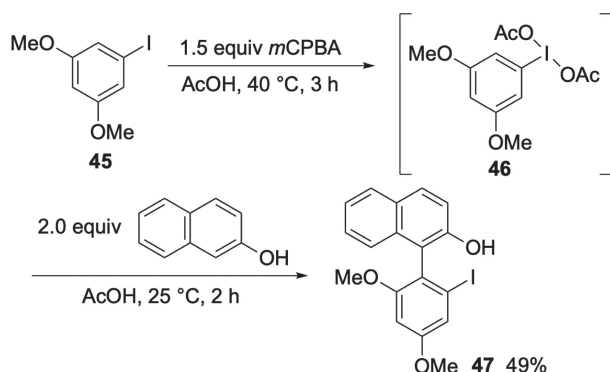
Scheme 23.   Biaryl synthesis from iodoarene diacetate generated *in situ.*

rearrangements can be harnessed to construct biaryls. Remarkably, the aromaticity of both aryl rings is lost during the sigmatropic rearrangement, though this aromaticity is regained upon formation of the final product. Our method has provided access to biaryls that are difficult to synthesize via conventional methods. We have demonstrated the power of our methods by using them to access important compound classes, such as oligoarenes, drug candidates, atropisomers and heterohelicenes. Considering the future of biaryl skeletons, we hope that new methods to prepare biaryls by underexplored mechanisms will be discovered.[83]

Acknowledgment

References

1)   Hassan, J., Sévignon, M., Gozzi, C., Schulz, E. and Lemaire, M. (2002) Aryl-aryl bond formation one century after the discovery of the Ullmann reaction. Chem. Rev. **102**, 1359–1470.

2)   Suzuki, A. (2002) The Suzuki reaction with arylboron compounds in arene chemistry. *In* Modern Arene Chemistry (ed. Astruc, D.). Wiley-VCH, Weinheim, pp. 53–106.

3)   Alberico, D., Scott, M.E. and Lautens, M. (2007) Aryl-aryl bond formation by transition-metal-catalyzed direct arylation. Chem. Rev. **107**, 174–238.

4)   Ackermann, L., Vincente, R. and Kapdi, A.R. (2009) Transition-metal-catalyzed direct arylation of (hetero)arenes by C–H bond cleavage. Angew. Chem. Int. Ed. **48**, 9792–9826.

5)   Miura, M., Satoh, T. and Hirano, K. (2014) Development of direct aromatic coupling reactions by transition-metal catalysis. Bull. Chem. Soc. Jpn. **87**, 751–764.

6)   Sun, C.-L. and Shi, Z.-J. (2014) Transition-metal-free coupling reactions. Chem. Rev. **114**, 9219–9280.

7)   Rossi, R., Lessi, M., Manzini, C., Marianetti, G. and Bellina, F. (2015) Transition metal-free direct C–H (hetero)arylation of heteroarenes: a sustainable methodology to access (hetero)aryl-substituted heteroarenes. Adv. Synth. Catal. **357**, 3777–3814.

8)   Uçar, S. and Daştan, A. (2021) Recent advances in the transition-metal-free arylation of heteroarenes. Synthesis **53**, 4353–4374.

9)   Hofmann, A.W. (1863) Notes of researches on the polyammonias, No. XXIII.—hydrazobenzol, a new compound isomeric with benzidine. Proc. R. Soc. Lond. **12**, 576–578.

10)   Banthorpe, D.V., Hughes, E.D. and Ingold, C. (1964) Mechanism of benzidine and semidine rearrangements. Part XV. A Collective Discussion. J. Chem. Soc. 2864–2901.

11)   Cox, J.R. Jr. and Dunn, M.F. (1963) The chemistry of O,N-diarylhydroxylamines – I. Tetrahedron Lett. **4**, 985–989.

12)   Sheradsky, T. and Salemnick, G. (1971) The benzidine-like rearrangement of N,O-diarylhydroxylamines. Tetrahedron Lett. **12**, 645–648.

13)   Li, G.-Q., Gao, H., Keene, C., Devonas, M., Ess, D.H. and Kürti, L. (2013) Organocatalytic aryl–aryl bond formation: an atroposelective [3,3]-rearrangement approach to BINAM derivatives. J. Am. Chem. Soc. **135**, 7414–7417.

14)   De, C.K., Pesciaioli, F. and List, B. (2013) Catalytic asymmetric benzidine rearrangement. Angew. Chem. Int. Ed. **52**, 9293–9295.

15)   Gao, H., Ess, D.H., Yousufuddin, M. and Kürti, L. (2013) Transition-metal-free direct arylation: synthesis of halogenated 2-amino-2′-hydroxy-1,1′-biaryls and mechanism by DFT calculations. J. Am. Chem. Soc. **135**, 7086–7089.

16)   Guo, L., Liu, F., Wang, L., Yuan, H., Feng, L., Kürti, L. *et al.* (2019) Cascade approach to highly functionalized biaryls by a nucleophilic aromatic substitution with arylhydroxylamines. Org. Lett. **21**, 2894–2898.

17)   Yuan, H., Du, Y., Liu, F., Guo, L., Sun, Q., Feng, L. *et al.* (2020) Tandem approach to NOBIN analogues from arylhydroxylamines and diaryliodonium salts via [3,3]-sigmatropic rearrangement. Chem. Commun. **56**, 8226–8229.

18)   Zhang, J.-W., Qi, L.-W., Li, S., Xiang, S.-H. and Tan, B. (2020) Direct construction of NOBINs via domino arylation and sigmatropic rearrangement reactions. Chin. J. Chem. **38**, 1503–1514.

19)   Yorimitsu, H. (2013) Synthesis of heteroaromatic compounds by newly extended Pummerer reac-

tions. J. Synth. Org. Chem. Jpn. **71**, 341–354.

20) Yorimitsu, H. (2017) Cascades of interrupted Pummerer reaction-sigmatropic rearrangement. Chem. Rec. **17**, 1156–1167.

21) Yanagi, T. and Yorimitsu, H. (2021) Recent development of biaryl synthesis through sigmatropic rearrangements. J. Synth. Org. Chem. Jpn. **79**, 427–438.

22) Bur, S.K. and Padwa, A. (2004) The Pummerer reaction: methodology and strategy for the synthesis of heterocyclic compounds. Chem. Rev. **104**, 2401–2432.

23) Feldman, K.S. (2006) Modern Pummerer-type reactions. Tetrahedron **62**, 5003–5034.

24) Akai, S. and Kita, Y. (2007) Recent advances in Pummerer reactions. Top. Curr. Chem. **274**, 35–76.

25) Smith, L.H.S., Coote, S.C., Sneddon, H.F. and Procter, D.J. (2010) Beyond the Pummerer reaction: recent developments in thionium ion chemistry. Angew. Chem. Int. Ed. **49**, 5832–5844.

26) Shafir, A. (2016) The emergence of sulfoxide and iodonio-based redox arylation as a synthetic tool. Tetrahedron Lett. **57**, 2673–2682.

27) Pulis, A.P. and Procter, D.J. (2016) C–H coupling reactions directed by sulfoxides: teaching an old functional group new tricks. Angew. Chem. Int. Ed. **55**, 9842–9860.

28) Yanagi, T., Nogi, K. and Yorimitsu, H. (2018) Recent development of ortho-C–H functionalization of aryl sulfoxides through [3,3] sigmatropic rearrangement. Tetrahedron Lett. **59**, 2951–2959.

29) Kaiser, D., Klose, I., Oost, R., Neuhaus, J. and Maulide, N. (2019) Bond-forming and -breaking reactions at sulfur (IV): sulfoxides, sulfonium salts, sulfur ylides, and sulfinate salts. Chem. Rev. **119**, 8701–8780.

30) He, Z., Pulis, A.P., Perry, G.J.P. and Procter, D.J. (2019) Pummerer chemistry of benzothiophene S-oxides: metal-free alkylation and arylation of benzothiophenes. Phosphorus Sulfur Silicon Relat. Elem. **194**, 669–677.

31) Zhang, L., Hu, M. and Peng, B. (2019) [3,3]- and [5,5]-Sigmatropic rearrangements of aryl sulfoxides using an 'assembly/deprotonation' technology. Synlett **30**, 2203–2208.

32) Higuchi, K. and Tayu, M. (2021) The interrupted Pummerer reaction: design of sulfoxides and their utility in organic synthesis. Heterocycles **102**, 783–824.

33) Yoshida, S., Yorimitsu, H. and Oshima, K. (2009) 2-(2,2,2-Trifluoroethylidene)-1,3-dithiane monoxide as a trifluoromethylketene equivalent. Org. Lett. **11**, 2185–2188.

34) Huang, X., Klimczyk, S. and Maulide, N. (2012) Charge-accelerated sulfonium [3,3]-sigmatropic rearrangements. Synthesis **44**, 175–183.

35) Eberhart, A.J., Imbriglio, J.E. and Procter, D.J. (2011) Nucleophilic ortho allylation of aryl and heteroaryl sulfoxides. Org. Lett. **13**, 5882–5885.

36) Eberhart, A.J. and Procter, D.J. (2013) Nucleophilic ortho-propargylation of aryl sulfoxides: an inter-

rupted Pummerer/allenyl thio-claisen rearrangement sequence. Angew. Chem. Int. Ed. **52**, 4008–4011.

37) Eberhart, A.J., Cicoira, C. and Procter, D.J. (2013) Nucleophilic ortho-allylation of pyrroles and pyrazoles: an accelerated Pummerer/thio-claisen rearrangement sequence. Org. Lett. **15**, 3994–3997.

38) Eberhart, A.J., Shrives, H.J., Álvarez, E., Carrër, A., Zhang, Y. and Procter, D.J. (2015) Sulfoxide-directed metal-free ortho-propargylation of aromatics and heteroaromatics. Chem. Eur. J. **21**, 7428–7434.

39) Kobatake, T., Yoshida, S., Yorimitsu, H. and Oshima, K. (2010) Reaction of 2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide with ketones under Pummerer conditions and its application to the synthesis of trifluoromethyl-substituted five-membered heteroaromatics. Angew. Chem. Int. Ed. **49**, 2340–2343.

40) Huang, X. and Maulide, N. (2011) Sulfoxide-mediated α-arylation of carbonyl compounds. J. Am. Chem. Soc. **133**, 8510–8513.

41) Huang, X., Patil, M., Farès, C., Thiel, W. and Maulide, N. (2013) Sulfur(IV)-mediated transformations: from ylide transfer to metal-free arylation of carbonyl compounds. J. Am. Chem. Soc. **135**, 7312–7323.

42) Shang, L., Chang, Y., Luo, F., He, J.-N., Huang, X., Zhang, L. et al. (2017) Redox-neutral α-arylation of alkyl nitriles with aryl sulfoxides: a rapid electrophilic rearrangement. J. Am. Chem. Soc. **139**, 4211–4217.

43) Kobatake, T., Fujino, D., Yoshida, S., Yorimitsu, H. and Oshima, K. (2010) Synthesis of 3-trifluoromethylbenzo[b]furans from phenols via direct ortho functionalization by extended Pummerer reaction. J. Am. Chem. Soc. **132**, 11838–11840.

44) Ookubo, Y., Wakamiya, A., Yorimitsu, H. and Osuka, A. (2012) Synthesis of a library of fluorescent 2-aryl-3-trifluoromethylnaphthofurans from naphthols by using a sequential Pummerer annulation/cross-coupling strategy and their photophysical properties. Chem. Eur. J. **18**, 12690–12697.

45) Murakami, K., Yorimitsu, H. and Osuka, K. (2014) Practical, modular, and general synthesis of benzofurans through extended Pummerer annulation/cross-coupling strategy. Angew. Chem. Int. Ed. **53**, 7510–7513.

46) Murakami, K., Yorimitsu, H. and Osuka, K. (2014) Two-step, practical, and diversity-oriented synthesis of multisubstituted benzofurans from phenols through Pummerer annulation followed by cross-coupling. Bull. Chem. Soc. Jpn. **87**, 1349–1366.

47) Hori, M., Yanagi, T., Murakami, K., Nogi, K. and Yorimitsu, H. (2019) Annulative synthesis of benzofurans from general alkenyl sulfoxides and phenols via Pummerer/sigmatropic cascade. Bull. Chem. Soc. Jpn. **92**, 302–311.

48) Kinoshita, J., Baralle, A., Yoshida, A., Yanagi, T., Nogi, K. and Yorimitsu, H. (2020) A route to indoles via modified Fischer indole intermediates

from sulfonanilides and ketene dithioacetal monoxides. Asian J. Org. Chem. **9**, 1655–1659.

49) Yanagi, T., Otsuka, S., Kasuga, Y., Fujimoto, K., Murakami, K., Nogi, K. *et al.* (2016) Metal-free approach to biaryls from phenols and aryl sulfoxides by temporarily sulfur-tethered regioselective C–H/C–H coupling. J. Am. Chem. Soc. **138**, 14582–14585.

50) Shrives, H.J., Fernández-Salas, J.A., Hedtke, C., Pulis, A.P. and Procter, D.J. (2017) Regioselective synthesis of C3 alkylated and arylated benzothiophenes. Nat. Commun. **8**, 14801.

51) Yang, K., Pulis, A.P., Perry, G.J.P. and Procter, D.J. (2018) Transition-metal-free synthesis of C3-arylated benzofurans from benzothiophenes and phenols. Org. Lett. **20**, 7498–7503.

52) He, Z., Shrives, H.J., Fernández-Salas, J.A., Abengózar, A., Neufeld, J., Yang, K. *et al.* (2018) Synthesis of C2 substituted benzothiophenes via an interrupted Pummerer/[3,3]-sigmatropic/1,2-migration cascade of benzothiophene *S*-oxides. Angew. Chem. Int. Ed. **57**, 5759–5764.

53) He, Z., Biremond, T., Perry, G.J.P. and Procter, D.J. (2018) *Para*-coupling of phenols with C2/C3-substituted benzothiophene *S*-oxides. Tetrahedron **76**, 131315.

54) He, Z., Pulis, A.P. and Procter, D.J. (2019) The interrupted Pummerer reaction in a sulfoxide-catalyzed oxidative coupling of 2-naphthols. Angew. Chem. Int. Ed. **58**, 7813–7817.

55) He, Z., Perry, G.J.P. and Procter, D.J. (2020) Sulfoxide-mediated oxidative cross-coupling of phenols. Chem. Sci. **11**, 2001–2005.

56) Yanagi, T. and Yorimitsu, H. (2021) Mechanistic investigation of a synthetic route to biaryls by the sigmatropic rearrangement of arylsulfonium species. Chem. Eur. J. **27**, 13450–13456.

57) Lehmann, J.W., Blair, D.J. and Burke, M.D. (2018) Towards the generalized iterative synthesis of small molecules. Nat. Rev. Chem. **2**, 0115.

58) Ernst, J.T., Kutzki, O., Debnath, A.K., Jiang, S., Lu, H. and Hamilton, A.D. (2002) Design of a protein surface antagonist based on α-helix mimicry: inhibition of gp41 assembly and viral fusion. Angew. Chem. Int. Ed. **41**, 278–281.

59) Ishikawa, S. and Manabe, K. (2006) Repetitive two-step method for oligoarene synthesis through rapid cross-coupling of hydroxyphenylboronic acids and anhydrides. Chem. Lett. **35**, 164–165.

60) Noguchi, H., Hojo, K. and Suginome, M. (2007) Boron-masking strategy for the selective synthesis of oligoarenes via iterative Suzuki–Miyaura coupling. J. Am. Chem. Soc. **129**, 758–759.

61) Li, J., Grillo, A.S. and Burke, M.D. (2015) From synthesis to function via iterative assembly of *N*-methyliminodiacetic acid boronate building blocks. Acc. Chem. Res. **48**, 2297–2307.

62) Nakao, Y., Chen, J., Tanaka, M. and Hiyama, T. (2007) A silicon-based approach to oligoarenes by iterative cross-coupling reactions of halogenated organo[(2-hydroxymethyl)phenyl]dimethylsilanes. J. Am. Chem. Soc. **129**, 11694–11695.

63) Yanagi, T., Nogi, K. and Yorimitsu, H. (2020) Sulfoxide-directed iterative assembly into oligoarenes. Synlett **31**, 153–157.

64) Eberhart, A.J., Shrives, H., Zhang, Y., Carrër, A., Parry, A.V.S., Tate, D.J. *et al.* (2016) Sulfoxide-directed metal-free cross-couplings in the expedient synthesis of benzothiophene-based components of materials. Chem. Sci. **7**, 1281–1285.

65) Yanagi, T., Tanaka, T. and Yorimitsu, H. (2021) Asymmetric systematic synthesis, structures, and (chir)optical properties of a series of dihetero[8]-helicenes. Chem. Sci. **12**, 2784–2793.

66) Dhbaibi, K., Favereau, L. and Crassous, J. (2019) Enantioenriched helicenes and helicenoids containing main-group elements (B, Si, N, P). Chem. Rev. **119**, 8846–8953.

67) Jakubec, M. and Storch, J. (2020) Recent advances in functionalizations of helicene backbone. J. Org. Chem. **85**, 13415–13428.

68) Yorimitsu, H., Vasu, D., Bhanuchandra, M., Murakami, K. and Osuka, A. (2016) Aromatic metamorphosis of dibenzothiophenes. Synlett **27**, 1765–1774.

69) Nogi, K. and Yorimitsu, H. (2017) Aromatic metamorphosis: conversion of an aromatic skeleton into a different ring system. Chem. Commun. **53**, 4055–4065.

70) Bhanuchandra, M., Murakami, K., Vasu, D., Yorimitsu, H. and Osuka, A. (2015) Transition-metal-free synthesis of carbazoles and indoles by an S_NAr-based "aromatic metamorphosis" of thiaarenes. Angew. Chem. Int. Ed. **54**, 10234–10238.

71) Kaga, A., Nogi, K. and Yorimitsu, H. (2019) Synthesis of *N*-alkyl and *N*-H carbazoles via S_NAr-based aminations of dibenzothiophene dioxides. Chem. Eur. J. **25**, 14780–14784.

72) Bhanuchandra, M., Yorimitsu, H. and Osuka, A. (2016) Synthesis of spirocyclic diarylfluorenes by one-pot twofold S_NAr reactions of diaryl sulfones with diarylmethanes. Org. Lett. **18**, 384–387.

73) Zhao, W.-L., Li, M., Lu, H.-Y. and Chen, C.-F. (2019) Advances in helicene derivatives with circularly polarized luminescence. Chem. Commun. **55**, 13793–13803.

74) Amii, H. and Uneyama, K. (2009) C–F bond activation in organic synthesis. Chem. Rev. **109**, 2119–2183.

75) Liu, C. and Zhang, B. (2016) Facile access to fluoroaromatic molecules by transition-metal-free C–F bond cleavage of polyfluoroarenes: an efficient, green, and sustainable protocol. Chem. Rec. **16**, 667–687.

76) Okamoto, K., Nogi, K., Shimokawa, J. and Yorimitsu, H. (2020) C–F arylation of polyfluorophenols by means of sigmatropic dearomatization/defluorination sequence. Chem. Eur. J. **26**, 5615–5618.

77) Okamoto, K., Hori, M., Yanagi, T., Murakami, K., Nogi, K. and Yorimitsu, H. (2018) Sigmatropic dearomatization/defluorination strategy for C–F transformation: synthesis of fluorinated benzofurans from polyfluorophenols. Angew. Chem. Int.

Ed. **57**, 14230–14234.

78) Okamoto, K., Nogi, K. and Yorimitsu, H. (2020) Regioselective difunctionalization of 2,6-difluorophenols triggered by sigmatropic dearomatization. Org. Lett. **22**, 5540–5544.

79) Yanagi, T., Nogi, K. and Yorimitsu, H. (2020) Construction of biaryls from aryl sulfoxides and anilines by means of a sigmatropic rearrangement. Chem. Eur. J. **26**, 783–787.

80) Yoshida, A., Okamoto, K., Yanagi, T., Nogi, K. and Yorimitsu, H. (2020) Metal-free synthesis of biaryls from aryl sulfoxides and sulfonanilides via sigmatropic rearrangement. Tetrahedron **76**, 131232.

81) Chen, W.W., Cuenca, A.B. and Shafir, A. (2019) The power of iodane-guided C–H coupling: a group-

transfer strategy in which a halogen works for its money. Angew. Chem. Int. Ed. **59**, 16294–16309.

82) Hori, M., Guo, J.-D., Yanagi, T., Nogi, K., Sasamori, T. and Yorimitsu, H. (2018) Sigmatropic rearrangements of hypervalent-iodine-tethered intermediates for the synthesis of biaryls. Angew. Chem. Int. Ed. **57**, 4663–4667.

83) Perry, G.J.P. and Yorimitsu, H. (2022) Sulfur(IV) in transition-metal-free cross-couplings for biaryl synthesis. ACS Sustainable Chem. Eng. **10**, 2569–2586.

Profile

Hideki Yorimitsu was born in Kochi Prefecture, Japan, in 1975 and graduated from the Faculty of Engineering, Kyoto University in 1997. He obtained his Ph.D. in 2002 from Kyoto University under the tutelage of Professor Koichiro Oshima by engaging in research on synthetic radical reactions in aqueous media. He then served as a JSPS postdoctoral fellow with Professor Eiichi Nakamura at the Department of Chemistry, the University of Tokyo, where he worked on the synthesis of ^{15}O-labeled 2-deoxyglucose of 2-min half-life for PET imaging as well as chemical modifications of nanocarbons. Subsequently, he became Assistant Professor (2003) and Associate Professor (2008) in the Graduate School of Engineering, Kyoto University. In 2009, he moved to the Graduate School of Science, Kyoto University, where he was promoted to Full Professor in 2015. He was Project Leader of ACT-C (2012–2018) and is currently Project Leader of CREST (since 2019), supported by Japan Science and Technology Agency. He received the Chemical Society of Japan Award for Young Chemists in 2009, the Young Scientists' Prize from MEXT in 2011, the Mukaiyama Award in 2016, the Negishi Award in 2018, the JSPS Prize in 2020, and the Japan Academy Medal in 2020. His research has always focused on the development of new organic transformations in order to create new molecules, phenomena, and concepts. Currently, he is interested in electron injection into unsaturated molecules to generate and use the resulting carbanion species for modern organic synthesis, in addition to sulfur-aided organic synthesis.

Profile

Gregory J. P. Perry received his Master of Chemistry from the University of Liverpool (U.K.) in 2012. During his undergraduate studies, he carried out research under the supervision of Professor P. Andrew Evans. He then joined the group of Professor Igor Larrosa and was awarded his Ph.D. from the University of Manchester (U.K.) in 2016. His doctoral studies focused on the development of decarboxylative and C–H transformations for organic synthesis. In 2017, he moved to Professor Kenichiro Itami's group at the Institute of Transformative Bio-Molecules, Nagoya University (Japan) where he worked on the preparation of small molecules for chemical biology. Greg then moved back to the University of Manchester (U.K.) in 2018 as a Lecturer in Organic Chemistry. During this time, he worked within the group of Professor David J. Procter whilst developing his own research themes. In 2021, Greg was awarded a JSPS Postdoctoral Fellowship to continue his research within the group of Professor Hideki Yorimitsu at Kyoto University (Japan). His current research interests include the application of sulfur (VI) compounds (*e.g.*, sulfonamides, sulfones) in synthesis and the carboxylation/decarboxylation of organic molecules.