Article

Aryl Silyl Ethers Enable Preferential Ar−O bond Cleavage in Reductive Generation of Aryllithium Species

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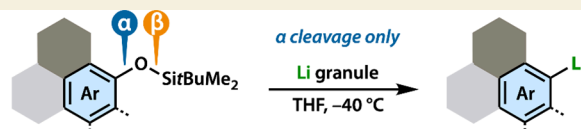
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ABSTRACT: Two-electron transfer to haloarenes constitutes one of the most reliable synthetic methodologies for the generation of aryllithiums. In addition to the conventional halides, readily available aryl ethers can function as potent substrates. However, it is known that the reductive cleavage of alkoxides is plagued by insufficient selectivity concerning the cleaving bond adjacent to the ether oxygen, resulting in decreased reliability of these alkoxyarene substrates. In the present study, we discovered that naphthalenes bearing readily installable *tert*-butyldimethylsilyl ethers undergo two-electron reduction with lithium metal, resulting in lithiation at the position of the original siloxy group. DFT calculations elucidated the rationale for the change in selectivity upon incorporation of the siloxy group. Our results underscore the practical utility of a siloxy group as a leaving group for reductive transformations involving electron transfer.

[Naphthalene or Larger Aryls] [Di-lithiation in One Pot]
[Various Electrophiles] [DFT Rationale for α-Selective Cleavage]

KEYWORDS: *aryllithium, electron transfer, silyl ether, silicon, lithium, alkali metal reduction*

INTRODUCTION

Aryllithiums are indispensable synthetic reagents that underpin the evolution of contemporary synthetic organic chemistry. These species serve as either nucleophiles or bases for the synthesis of a wide range of organic and organometallic compounds. Common preparative methods for aryllithiums necessitate aryl halide as a substrate, which employs either two-electron reduction of aryl halides or a halogen−lithium exchange reaction.[1−7] Despite the recognized utility of this exchanging technique, substrate halides are often costly or synthetically difficult to access, necessitating a reliable alternative method for the preparation of aryllithiums from more readily available substrates. A relatively overlooked and potent candidate is the wide range of phenol derivatives, which have unique synthetic and commercial accessibility that differs from aryl halides. It is therefore advantageous to develop a method for the precise and predictable conversion of phenolic substrates to aryllithiums via a deoxygenative transformation.

Aryl alkyl ethers are known to be reduced by lithium metal (Figure 1A).[8] The reduction of the substrate is followed by the cleavage of either of the two bonds adjacent to the oxygen atom; one leading to the formation of lithium alkoxide and an aryllithium (α cleavage), while the other leads to LiOAr accompanied by the formation of alkyllithium (β cleavage). The ratio between these two reactions is known to vary depending on the solvent and the type of alkyl substituents.[8−14] For example, both α and β cleavage occur in THF or DME, whereas α cleavage tends to be favored in heptane albeit with a significantly slower reaction rate. Consequently, the synthetic chemist's toolbox still lacks transformations that can selectively generate reactive aryllithium species from readily accessible aryl ether derivatives.

We have recently reported that silyl enolates can be converted to alkenyllithium species via electron transfer from lithium arenides provided that an aryl group is conjugated to the silyl enolate (Figure 1B).[15] This result suggests the unique and potential utility of the siloxy group as a leaving group for reductive transformations. Our hypothesis is that employing a siloxy group also modifies the bond dissociation energy, which could offer a potential solution to the issue of unintentional β-cleavage of aryl alkyl ethers during the reductive transformation of aryl alkyl ethers. Herein, we demonstrate the synthesis of aryllithium species using a siloxy group as the leaving group based on the sequential one-electron transfers from lithium metal to the arene moiety (Figure 1C). Owing to the higher dissociation energy of a Si−O bond (128 kcal/mol)[16] compared to a C−O bond (57 ± 2 kcal/mol)[17] as well as the lower pK_a of silanol species than carbinols,[18] the cleavage of the Si−O bond is expected to be minimized.
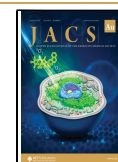
Consequently, the reaction of naphthyl silyl ether selectively accelerates the cleavage of the C−O bond, culminating in the formation of the siloxide anion and aryllithium species, which can react with various electrophiles.

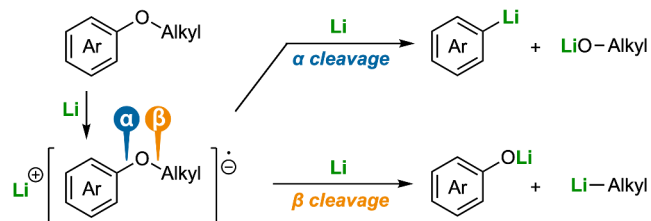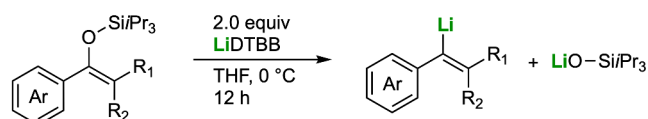**A. Two Possibilities for C–O Cleavage of Aryl Alkyl Ethers with Lithium Metal**

B. Reduction of Silyl Enolates with Lithium Arenide Forms Alkenyllithium.[15]

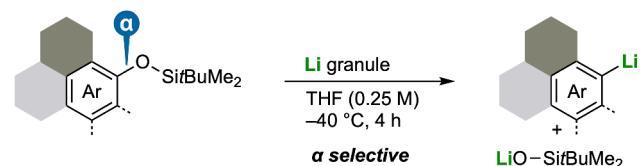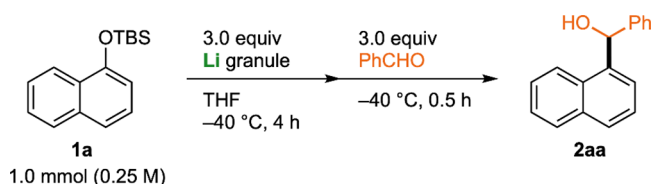**C. Selective Ether Cleavage of Siloxy Arenes with Lithium [This Work]**

Figure 1. Overview of the current study.

RESULTS AND DISCUSSION

Table 1 delineates our optimization of the reaction conditions. The initial optimization was carried out using *tert*-butyldime-

Table 1. Optimization of the Reaction Conditions

entry	deviations from conditions above	NMR yield (%)[a] 2aa		
1	none	82 (78)[b]		
2	Li powder instead of Li granule	82		
3	Na dispersion/LiI instead of Li granule	46[c]		
4	0 °C	65		
5	10 mmol scale	72 (67)[b]		

entry	functional group instead of TBS	NMR yield (%)[a]		
		2aa	1-naphthol	other
6	Si*i*Pr$_3$ (TIPS)	89	0	
7	Si*t*BuPh$_2$ (TBDPS)	68	0	
8	SiEt$_3$ (TES)	62	0	
9	SiMe$_3$ (TMS)	41	20[d]	[e]
10	Me	51	22	
11	Et	44	20	
12	Ts	0	60	
13	P(O)Ph$_2$	0	90	
14	P(O)(OEt)$_2$	0	0	[f]

[a]Yields were determined by ^{1}H NMR using mesitylene as an internal standard. [b]Isolated yield, [c]Naphthalene (39%) was observed. [d]Generated by intermolecular substitution on the TMS group. [e]1-Trimethylsilylnaphthalene (17%). [f]Naphthalene (30%).
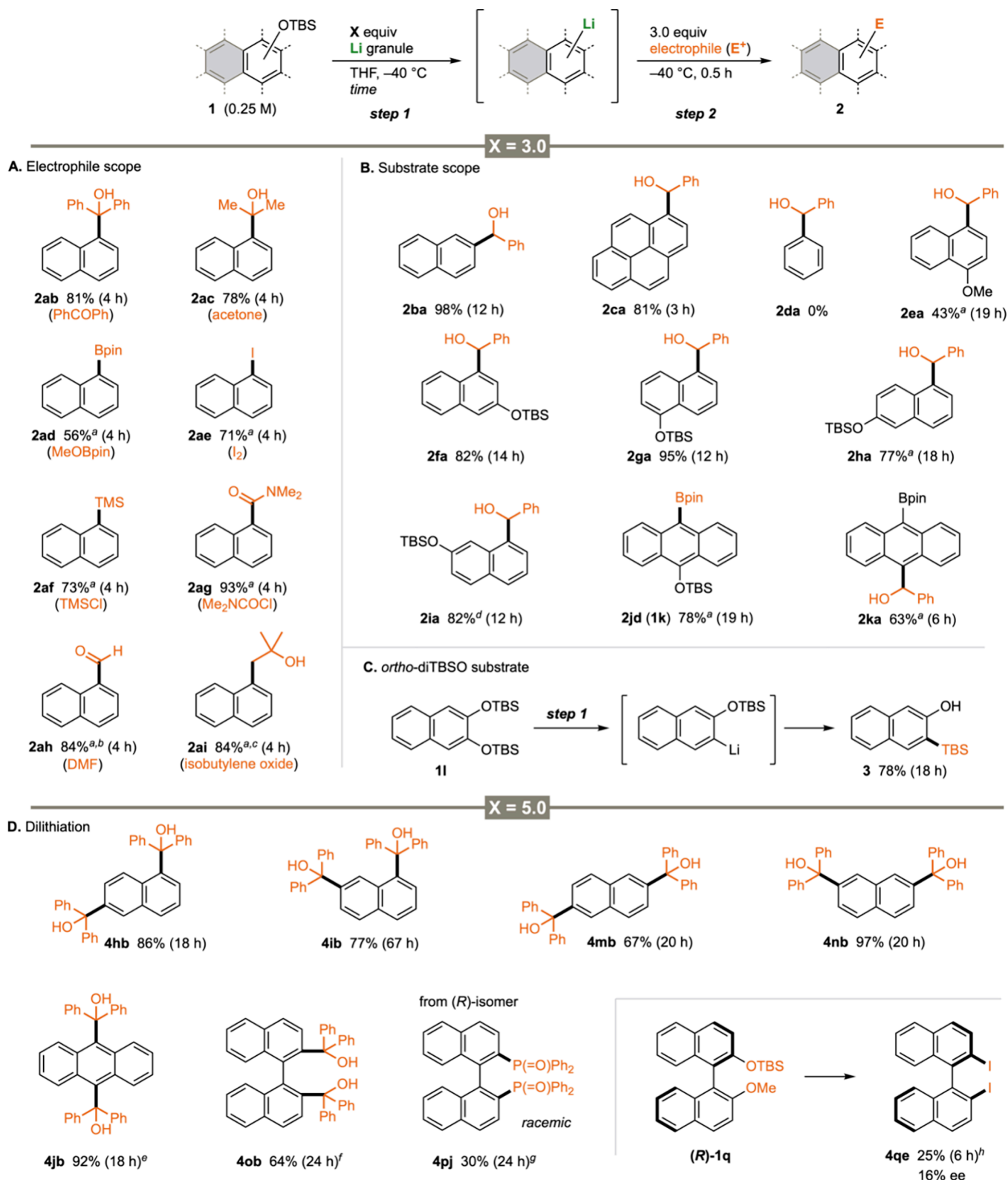
thylsilyl (TBS) ether of 1-naphthol **1a** as the substrate. Our standard conditions were devised as follows: **1a** (0.25 M), 3.0 equiv of Li granules in THF, 4 h, −40 °C. 1-Naphthyllithium species that formed was reacted with benzaldehyde at −40 °C for 0.5 h. The product **2aa** was obtained in 82% NMR and 78% isolated yields (entry 1). The reaction was also conducted with Li powder[19] as a substitute for Li granules in the same yield (entry 2). When a combination of sodium dispersion and LiI[20] was employed, the reaction proceeded moderately to give **2aa** in a reduced yield of 46% with concomitant formation of naphthalene, probably the protonation product of highly reactive naphthylsodium (entry 3). An increase in the reaction temperature to 0 °C resulted in a decreased yield (65%) (entry 4). The reaction could be scaled up to a 10 mmol scale to give the product in 72% yield (67% isolated) (entry 5).

Functional groups other than the TBS group were also investigated. The TIPS group yielded better results in the case of 1-naphthol, but due to the inefficiency of some substrates in preparation, it was not finally selected for subsequent study (entry 6). The yields from the TBDPS or TES ethers decreased to 68% and 62%, respectively (entries 7 and 8). The yield from the TMS ether (41%) declined significantly, partly due to the intermolecular transfer of the silyl group from the substrate silyl ether **1a** upon interaction with the in situ generated aryllithium, as confirmed by the formation of 1-trimethylsilylnaphthalene (17%) (entry 9). In the case of a methyl group instead of a silyl group, the selectivity of the C−O bond cleavage diminished, as documented in the literature.[8] Expected product **2aa** was obtained in 51% yield, while 1-naphthol was obtained as a byproduct in 22% yield (entry 10). 1-Ethoxynaphthalene has been reported to increase the selectivity toward the formation of aryllithium species.[8] However, in our experiments, this substrate exhibited selectivity similar to that of the methoxy substrate (entry 11). When a *p*-tosyl group (entry 12) or diphenylphosphinyl group (entry 13) was utilized, only 1-naphthol was observed due to the propensity to form the sulfinate radical or phosphinyl radical. The substrate with a diethoxyphosphoryl group (entry 14) demonstrated the synthesis of naphthalene (30%), while the desired product **2aa** was not detected. The result suggests protonation of the aryllithium intermediate possibly via E2 elimination at the ethoxyphosphate moiety. Based on the considerations above, the conditions of entry 1 were deemed optimal.

A study of generality with respect to electrophiles is presented in Scheme 1A. The naphthyllithium species prepared from **1b** were subjected to treatment with different electrophiles. Benzophenone and acetone gave high yields of the adducts **2ab** (81%) and **2ac** (78%), respectively. Boron functional groups can be incorporated to form **2ad** in 56% yield by utilizing MeOBpin. Iodo (**2ae**, 71%), trimethylsilyl (**2af**, 73%), dimethylcarbamoyl (**2ag**, 93%), and formyl (**2ah**, 84%) groups can also be introduced with high yields. The ring-opening reaction of isobutylene oxide delivered an alkyl group to give **2ai** in 84% yield.

The substrate scope with respect to the structures of the siloxyarene was examined (Scheme 1B). 2-Naphthyl group underwent a similar lithiation to afford **2ba** in 98% yield, albeit at a slower rate than the 1-naphthyl group. The 1-pyrenyl substrate also reacted smoothly and gave product **2ca** in 81% yield. The reductive transformation of phenyl substrate (*O*-TBS phenol) to **2da** did not proceed under these conditions, and the starting material was fully recovered. Even at elevated

Scheme 1. Reaction Scope with Respect to Electrophiles and Aromatic Moieties

A. Electrophile scope

2ab 81% (4 h) (PhCOPh)

2ac 78% (4 h) (acetone)

2ad 56%[a] (4 h) (MeOBpin)

2ae 71%[a] (4 h) (I₂)

2af 73%[a] (4 h) (TMSCl)

2ag 93%[a] (4 h) (Me₂NCOCl)

2ah 84%[a,b] (4 h) (DMF)

2ai 84%[a,c] (4 h) (isobutylene oxide)

B. Substrate scope

2ba 98% (12 h)

2ca 81% (3 h)

2da 0%

2ea 43%[a] (19 h)

2fa 82% (14 h)

2ga 95% (12 h)

2ha 77%[a] (18 h)

2ia 82%[d] (12 h)

2jd (1k) 78%[a] (19 h)

2ka 63%[a] (6 h)

C. ortho-diTBSO substrate

3 78% (18 h)

D. Dilithiation

4hb 86% (18 h)

4ib 77% (67 h)

4mb 67% (20 h)

4nb 97% (20 h)

4jb 92% (18 h)[e]

4ob 64% (24 h)[f]

from (R)-isomer

4pj 30% (24 h)[g] racemic

(R)-1q

4qe 25% (6 h)[h] 16% ee

[a]Step 1: 2.2 equiv Li granule. [b]Step 2: −78 °C to rt, 10 min. [c]Step 2: −40 °C to rt, 1 h. [d]Step 1: 2.2 equiv Li granule, −20 °C, step 2: −20 °C. [e]Step 1: 4.2 equiv Li granule. [f]Step 2: −40 °C to rt, 1 h. [g]Step 1: 4.2 equiv Li granule, step 2: 9.2 equiv Ph₂P(O)Cl, −40 °C to rt, 2 h. [h]Step 1: 4.2 equiv Li granule, step 2: 6.0 equiv I₂, −40 °C, 3 h.

temperature (0 °C), only partial intractable decomposition was observed. This result was easily understood by considering the difficulty of electron transfer to the monocyclic benzene

derivatives compared to the facile formation of lithium naphthalenide from lithium metal and naphthalene. From the substrate where both methoxy and siloxy were present as *para-*
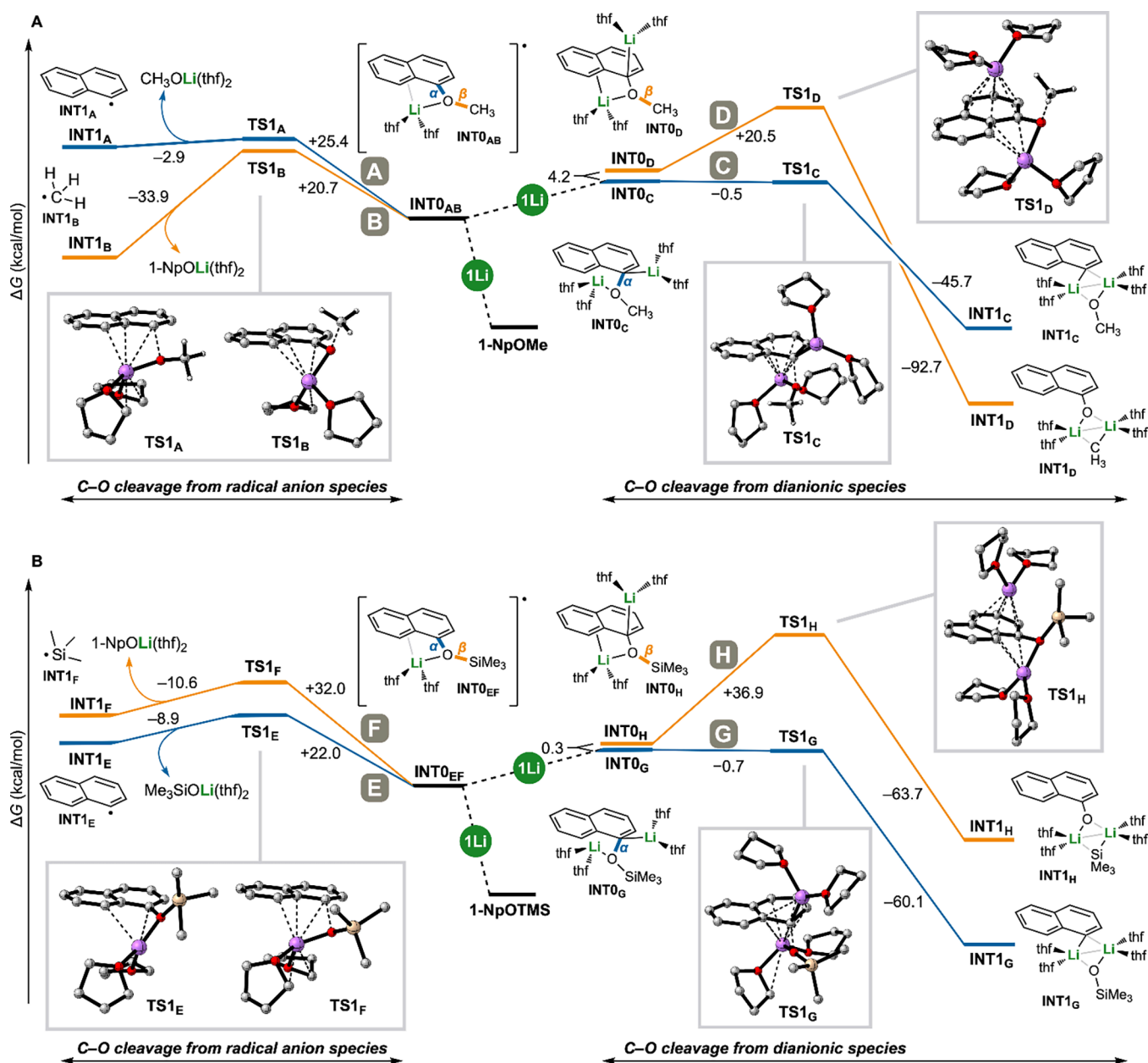
Figure 2. (A) Energy profile for α cleavage (blue) and β cleavage (orange) of 1-trimethylsiloxy naphthalene (**1-NpOTMS**) through the radical anion species (left) from **INT0$_{AB}$** and the dianion species (right) from **INT0$_E$** or **INT0$_F$** at the (U)ωB97X-D/def2-TZVPP/SMD (THF)// (U)ωB97X-D/def2-SVP level of theory at 233.15 K. (B) Energy profile for α cleavage (blue) and β cleavage (orange) of 1-methoxy naphthalene (**1-NpOMe**) through the radical anion species (left) from **INT0$_{CD}$** and the dianion species (right) from **INT0$_G$** or **INT0$_H$** at the (U)ωB97X-D/ def2-TZVPP/SMD (THF)//(U)ωB97X-D/def2-SVP level of theory at 233.15 K. The Gibbs free energy of **INT0$_C$** is higher than that of **TS1$_C$**. As these reversals may seem contradictory, the electronic energy of **INT0$_C$** is lower than that of **TS1$_C$** on the potential energy surface. IRC calculations also confirmed that **TS1$_C$** connects to **INT0$_C$**. The same is true for the relationship between **INT0$_G$** and **TS1$_G$**.

substituents, only the siloxy group reacted and gave product **2ea** in a moderate yield, leaving the methoxy residue intact. For a 1,*n*-disubstituted system (*n* = 3, 5, 6, and 7), position 1 was inclined to react faster. Thus, the 1,3-disubstituted substrate reacted initially at position 1 to afford **2fa** (82%). The reaction of 1,5- and 1,6-disubstituted substrates both proceeded selectively at position 1 to yield **2ga** (95%) and **2ha** (77%). The reaction of the 1,7-disubstituted substrate was sluggish under the same conditions, necessitating step 1 at −20 °C and yielding the 1-substituted **2ia** in 82% yield.

From the 9,10-disubstituted anthracene, it was found that Bpin could be introduced by the selective conversion of only

one of the TBSO groups to give **2jd** in 78% yield. This product could be further elaborated in a similar manner while preserving the Bpin functional group intact to the corresponding aryllithium, eventually reacting with benzaldehyde to yield **2ka** in 63% yield. From the 2,3-disubstituted substrate **1l**, the reaction proceeded through an intermediary aryllithium to undergo the migration of the TBS group from the adjacent TBSO to give **3** in 78% yield (Scheme 1C).

It was also discovered that the dilithiated intermediate could be prepared by the successive conversion of the two TBSO groups with 5.0 equiv of lithium granule (Scheme 1D). The 1,6-, 1,7-, 2,6-, and 2,7-disubstituted substrates were converted

to the dilithiated intermediate, which indeed reacted with benzophenone and gave the corresponding doubly functionalized products **4hb**, **4ib**, **4mb**, and **4nb** in high yields. The 9,10-disubstituted anthracene was also instantaneously transformed, reacted with benzophenone, and gave product **4jb** in 92% yields. The bis-TBS ether of BINOL was converted to the dilithiated form to react in a similar manner to yield **4ob**. From (R)-BINOL derivative (R)-**1p**, with the use of an excess amount of diphenylphosphoryl chloride as an electrophile, the reaction proceeded to give BINAP dioxide **4pj**, which was found to have lost its optical activity and was obtained as a racemate. Therefore, the faster formation of dilithium binaphthyl species and their rapid capture by the more reactive electrophile were investigated. We had already noticed that additives such as TMEDA did not improve the rate and yield of the reaction. Also, stepwise functionalization was not possible due to the faster reaction of the second siloxy group once the first siloxy group was lithiated. Finally, it was found that monomethyl mono-TBS ether **1q** was more rapidly reduced than **1p** to the dilithiated species, which immediately reacted with the more reactive iodine as an electrophile. The resulting diiodobinaphtyl **4qe** was found to retain only reduced chirality (16% ee). These results corroborate the presence of a nonbulky intermediate that allows the rotation of the biaryl axis during the reductive transformation.

To elucidate the key mechanism behind the selectivity of the α and β cleavage, DFT calculations were performed (Figure. 2). The experimental results revealed that a siloxynaphthalene predominantly undergoes α cleavage by selective elimination of the siloxy group, whereas a methoxynaphthalene results in a mixture of both α and β cleavages (Table 1, entry 10). Our aim is to elucidate this shift in the mode of cleavage by the substituent variation. We initially focused on the reductive transformation of 1-methoxynaphthalene. The reaction mechanism of alkali-mediated reductive C−O bond cleavage seems to be rather controversial in the literature. In the early studies, the reductive bond cleavage was considered to proceed via a dianionic intermediate.[9,12,21] Another plausible mechanistic postulation was a fragmentation of a one-electron-reduced radical anion intermediate that was also strongly supported by the experimental identification of bond cleavage in the electrochemical study.[8,13,22,23] Several studies have suggested that neither the dianion nor the radical anion should be ignored as intermediates for C−O bond cleavage.[11,24] In this scenario, the proportion of the two mechanisms is expected to vary, depending on the reaction conditions. Our attempt was to determine which mechanistic pathway is more realistic. We have computationally modeled the monolithium radical anion or dilithium dianion species, where one lithium cation bears two THF molecules. The methyl group was chosen as a model alkyl group, and the TMS group was chosen as a model silyl group because of the calculation cost while disregarding the lability of the TMS group to nucleophiles (Table 1, entry 9). C−O bond cleavage was hypothesized to yield a lithium alkoxide/silanolate, concomitant with either an aryllithium or an aryl/alkyl/silyl radical to be further reduced by lithium.

Before investigating the reductive cleavage of a siloxynaphthalene, we studied the reaction profile of the reduction of methoxynaphthalene (Figure 2A). For the reaction of the 1-methoxynaphthalene radical anion **INT0$_{AB}$**, the $\Delta G^{\ddagger}$ (20.7 kcal/mol) for pathway B via **TS1$_B$**, leading to a methyl radical **INT1$_B$** and a lithium naphthoxide, is significantly lower than the $\Delta G^{\ddagger}$ (25.4 kcal/mol) for pathway A via **TS1$_A$**, leading to a

naphthyl radical **INT1$_A$** and a lithium methoxide. Given these computational results, one would expect the selective formation of 1-naphthol. However, the experimental data showed only a 20% yield of 1-naphthol, accompanied by the concomitant formation of product **2aa** in a 51% yield (Table 1, entry 10). Consequently, pathway B does not provide an explanation for the experimental result on its own. Consequently, we investigated an alternative reaction mechanism to assess the bond cleavage following a two-electron reduction, which is known to generate dianionic species from parent naphthalene.[25] We computationally searched for transition states and their corresponding reaction pathways via bond cleavage from the dianionic species. The results showed that pathway D via **TS1$_D$** for the elimination of a methyllithium from dianionic species **INT0$_D$** presents a high barrier ($\Delta G^{\ddagger}$ = 20.5 kcal/mol) for the formation of methyllithium **INT1$_D$**. Conversely, pathway C via **TS1$_C$** for the elimination of naphthyllithium **INT1$_C$** from dianionic species **INT0$_C$** was found to be virtually barrierless. As **INT0$_C$** is energetically more favorable than **INT0$_D$**, with minimal structural and energy differences between **INT0$_C$** and **INT0$_D$**, these intermediates were considered capable of facilitating structural interconversions with each other, thereby allowing the evaluation of the $\Delta\Delta G^{\ddagger}$ value between pathways C and D. Thus, pathway C is supported over pathway D. These results illustrate a contrasting result depending on the intermediate species generated from 1-methoxynaphthalene. If the reaction proceeds from radical anion **INT0$_{AB}$**, the reaction exclusively favors the β cleavage via pathway B to provide a naphthol. If the reaction proceeds from dianion **INT0$_C$**, the reaction would favor the α cleavage via pathway C to generate naphtyllithium species. The experimental result that shows a ca. 5:2 mixture upon reduction of 1-methoxynaphthalene cannot be thoroughly explained by either pathway B from the radical anion or pathway C from the dianion. Thus, both the radical anion intermediate and the dianion intermediate appear to contribute synergistically to the reductive cleavage of 1-methoxynaphthalene.

Next, the reduction of 1-siloxynaphthalene was investigated (Figure 2B). The results revealed that pathway F ($\Delta G^{\ddagger}$ = 32.0 kcal/mol), which starts from siloxynaphthalene **INT0$_F$** to produce silyl radical **INT1$_F$** and a lithium naphthoxide via **TS1$_F$**, has a significantly higher activation energy than pathway E ($\Delta G^{\ddagger}$ = 22.0 kcal/mol), which produces naphthyl radical **INT1$_E$** and a lithium silanolate via **TS1$_E$**. The naphthyl radical would be rapidly reduced by an electron from lithium to form naphthyllithium. Thus, the pathway F to the formation of a silyl radical via the O−Si bond cleavage is expected to be unfeasible. The formation of naphthol was not actually observed in any of the experiments except in the case of Table 1 entry 9, which used a labile TMS group. The computational search was continued for the reaction pathways by bond cleavage from the siloxynaphthalene dianionic species. The results indicated that pathway H ($\Delta G^{\ddagger}$ = 36.9 kcal/mol) via **TS1$_H$**, which generates a trimethylsilyllithium **INT1$_H$** from the dianionic species **INT0$_H$**, has extremely high barriers. In contrast, pathway G via **TS1$_G$** for the elimination of naphthyllithium **INT1$_G$** from the dianionic species **INT0$_G$** was found to be barrierless, as was pathway C. Both the preferred pathways for 1-siloxy naphthalene, pathway E from the radical anion and pathway G from the dianion, were confirmed to favor the formation of naphthyllithium species. Considering that pathway E has a relatively high activation

energy ($\Delta G^{\ddagger}$ = 22.0 kcal/mol) to proceed at -40 °C, it is suggested that pathway G is not negligible in our reductive formation of aryllithium species from 1-siloxynaphthalene, although the ratio of the contributions from both pathways remains unclear. The above discussion of computational chemistry highlights the reason for the high selectivity of the α cleavage to generate aryllithium species via the metal reduction of siloxynaphthalenes.

■ CONCLUSIONS

A new method has been developed that allows the selective lithiation by simply applying lithium metal to a TBS ether of naphthalene or larger aryls. The resulting aryllithium species was found to retain the expected reactivity with a wide range of electrophiles. Substrates with two siloxy groups were converted to the monolithiated or dilithiated intermediates, depending on the amount of lithium metal added. Compared to the case of alkoxy leaving groups, where both bonds on the oxygen may cleave to give a product mixture, the present method uses silyl ethers as substrates and simplifies the reaction course, thereby maximizing the utility of the conversion. By using computational chemistry to assess the propensity of C–O bond cleavage from radical anion and dianionic intermediates, the mechanism behind the high selectivity from aryl silyl ether is rationalized by illustrating the favored Ar–O cleavage both from radical anion and dianionic species, in contrast to the aryl methyl ether which was revealed to favor different pathways for bond cleavage from each species.

■ METHODS

General Procedure for Preparation of Siloxynaphthalene (GP1)

The synthesis of 1-(*tert*-butyldimethylsiloxy)pyrene (**1c**) is representative. A 30 mL two-necked flask was charged under a nitrogen atmosphere with 1-hydroxypyrene (874 mg, 4.00 mmol), imidazole (411 mg, 6.03 mmol), and DMF (8.0 mL). After cooling the mixture to 0 °C, *tert*-butyldimethylsilyl chloride (739 mg, 4.90 mmol) was added to the flask in one portion at the same temperature, and the resulting mixture was allowed to warm to room temperature. After 18 h, the reaction mixture was poured into a separatory funnel with Et$_2$O (20 mL) and water (40 mL) and partitioned. The organic phase was collected, and the aqueous phase was extracted with Et$_2$O (20 mL × 2). The combined organic layer was washed with water (10 mL) and brine (10 mL), dried over Na$_2$SO$_4$ (ca. 10 g), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane as an eluent to give **1c** (1.26 g, 3.79 mmol, 95%) as a white solid.

General Procedure for Lithiation of Aryl Silyl Ethers and the Subsequent Reaction with Electrophiles (GP2)

An oven-dried 20 mL Schlenk tube was charged with Li granule (20.2 mg, 2.91 mmol) and THF (4.0 mL). The mixture was stirred at room temperature for 5 min at -40 °C, and aryl silyl ether **1a** (251 mg, 0.970 mmol) was added to the tube in one portion. The resulting suspension was stirred at -40 °C for 4 h. Benzaldehyde (0.30 mL, 3.0 mmol) was then added to the tube as an electrophile, and the reaction mixture was stirred at -40 °C for an additional 30 min. The reaction mixture was quenched with saturated aqueous NH$_4$Cl solution (1 mL). The mixture was poured into a separatory funnel with Et$_2$O (10 mL) and water (20 mL) and partitioned. The organic phase was collected, and the aqueous phase was extracted with Et$_2$O (10 mL × 2). The combined organic layer was washed with brine (10 mL) and Na$_2$SO$_4$ (ca. 10 g), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane/EtOAc = 50/1 to 10/1) and GPC (eluent: CHCl$_3$) provided **2aa** (176 mg, 0.754 mmol, 78%) as a colorless sticky oil.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.4c00448.

> Experimental procedures, computational data, and characterization and spectral data for new compounds (PDF)

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Author Contributions

D.A. formal analysis, investigation, methodology, and writing−review & editing; **Z.Z.** formal analysis, investigation; **F.T.** formal analysis, investigation, methodology, and writing−review & editing; **H. S.** conceptualization, formal analysis, investigation, methodology, project administration, supervision, and writing−review & editing; **J.S.** conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing original draft, and writing−review & editing; **H.Y.** conceptualization, funding acquisition, project administration, supervision, and writing−review & editing.

Notes

The authors declare no competing financial interest.

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