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Reductive Lithiation in the Absence of Aromatic Electron Carriers. A Steric Effect Manifested on the Surface of Lithium Metal Leads to a Difference in Relative Reactivity Depending on Whether the Aromatic Electron Carrier Is Present or Absent

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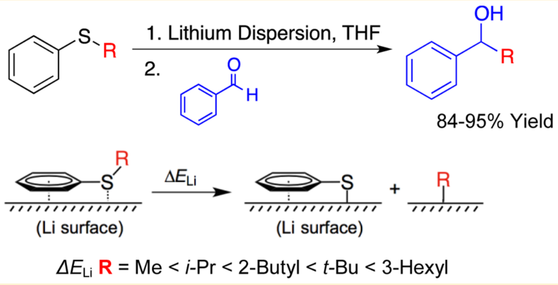
Supporting Information

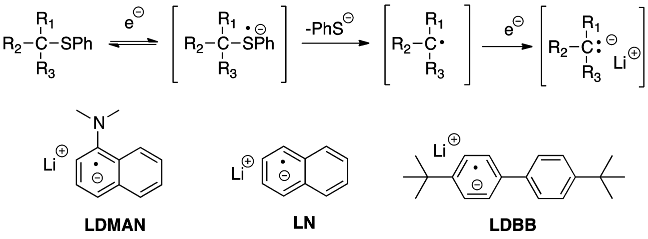
ABSTRACT: One of the most widely used methods of preparation of organolithium compounds is by the reductive lithiation of alkyl phenyl thioethers or, usually less conveniently, alkyl halides with either aromatic radical-anions of lithium or lithium metal in the presence of an aromatic electron-transfer catalyst. Here we present results showing that lithium dispersion can achieve reductive lithiation in the absence of the electron-transfer agent. This procedure is more efficient, and surprisingly, the order of reactivity of substrates is reversed depending on whether the electron-transfer agent is present or absent. For example, in the presence of a preformed radical-anion, *tert*-butyl phenyl sulfide cleaves significantly faster than methyl phenyl sulfide, whereas in the absence of the radical-anion, it is just the opposite. Density functional theory calculations reveal that the exothermicity of the cleavage of the C−S bond in alkyl phenyl thioethers on the lithium surface is dependent on the size of the alkyl group, the smaller the alkyl group the greater the exothermicity. The increased reactivity is attributed to the smaller steric repulsion between the alkyl group and the lithium surface. The methodology includes, but may not be limited to, the lithium dispersion reductive lithiation of phenyl thioethers, alkyl chlorides, acrolein diethyl acetal, and isochroman.



INTRODUCTION

One of the most versatile methods known for generating organolithiums is by the reductive lithiation of phenyl thioethers, the replacement of a C−S bond with a C−Li bond, using aromatic radical-anions as the source of the electron (Scheme 1).[1−4] Aromatic radical-anions including: lithium naphthalenide (LN), lithium 1-(*N*,*N*-dimethylamino)-naphthalenide (LDMAN), and lithium *p*,*p*′-di-*tert*-butylbiphenylide (LDBB) are currently in use. The superiority of alkyl phenyl thioethers as substrates for reductive lithiation arises from their almost unique ease of construction as well as the ability of the phenylthio group to enter a molecule as a nucleophile, electrophile, or radical.[5]

Scheme 1. Reductive Lithiation of Phenyl Thioethers with Aromatic Radical-Anions



Because LDMAN decomposes to 1-lithionaphthalene above −45 °C,[6] a ‘catalytic method’, which employs a catalytic amount of the aromatic hydrocarbon rather than a stoichiometric amount of the aromatic radical-anion, was devised in this laboratory.[7] This allowed higher temperatures to be used without destroying the LDMAN intermediate. More recently, Yus and co-workers performed the catalytic reductive lithiation of some alkyl chlorides and alkyl phenyl sulfides,[8] in which a solution of the substrate to be reduced is mixed with 1−5 mol% of the aromatic hydrocarbon, usually *p*,*p*′-di-*tert*-butyl biphenyl (DBB)[9−11] and a large excess of specially prepared lithium powder.[12] Furthermore, Yus has claimed, in a number of his papers, that the catalytic aromatic method, in which the radical-anion is continually generated and rapidly destroyed by electron transfer to the substrate,[5] is far more powerful than the use of a stoichiometric amount of preformed aromatic radical-anion.[9] This claim was tested in a number of cases, and in all but one case the opposite was found, namely that the preformed radical-anion method was superior to the catalytic method.[5]

The one case in which Yus's contention proved to be correct was the reductive cleavage of *N*-phenylaziridine (**1**). He reported that the three-membered ring can be opened by

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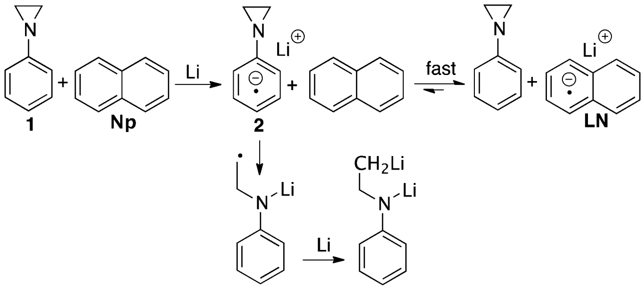
excess Li metal with a catalytic amount of naphthalene in 93% yield at −78 °C.[13] The Cohen lab found that the reductive lithiation of **1** with LN did not cause the desired cleavage at the temperature and time reported.[5] A possible explanation of this result, shown in Scheme 2, is that the transfer of an electron from the lithium to naphthalene (Np) occurs more slowly than the transfer of an electron to **1**. However, in the presence of Np, the resulting radical-anion (**2**) of *N*-phenylaziridine can transfer an electron to the Np to generate the more thermodynamically stable radical-anion, LN.[5] Thus, **2** is the kinetic product of electron transfer from lithium, but LN is the thermodynamic radical-anion and Np acts as an inhibitor rather than a catalyst. Experimentally, it was demonstrated that naphthalene is indeed an inhibitor in this case.[5]

Scheme 2. Proposed Mechanistic Explanation for the Catalytic Method of Reductive Lithiation of *N*-phenylaziridine



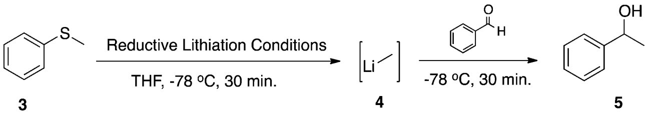
The reason that **1** accepts an electron from lithium more rapidly than Np is unknown; however, this finding is consistent with 1-(*N*,*N*-dimethylamino)-naphthalene (DMAN) forming LDMAN at −45 °C, faster than the formation of LN at room temperature.[5] The amino group may complex with a lithium cation, which increases the electrophilicity of the ring as well as the electron-donating power of the metal surface. Therefore, an electron would be transferred more rapidly to the π system of the aromatic.[5] Because *N*-phenylaziridine acquires an electron from Li metal faster than Np does and the resulting radical-anion can transfer the electron rapidly to Np, **1** "catalyzes" the formation of LN; however, **2** is unstable and easily undergoes ring opening at −78 °C.[14]

Thus, the commercially available and more stable analogue, *N*,*N*-dimethylaniline (DMA), was tested as an electron-transfer reagent on the reasonable assumption that its radical-anion would also form very rapidly but would not readily decompose. While we were disappointed to find that DMA did not behave as a catalyst for reductive lithiation, when lithium dispersion is the source of Li metal,[15] it was unexpectedly discovered that many compounds commonly used to generate organolithiums could actually be reductively lithiated in the absence of an aromatic electron-transfer reagent under the right conditions and the selectivity is just the opposite of that of the preformed radical-anion method. Phenyl thioethers with smaller alkyl groups were found to react significantly faster with lithium dispersion. Density functional theory (DFT) calculations were performed to investigate the origin of the steric effect.

■ RESULTS AND DISCUSSION

Attempted DMA-Catalyzed Reductive Lithiation. In order to properly assess its ability to promote the transfer of an electron from lithium to a substrate, DMA was compared to the well-known reductive lithiation catalyst, DBB, as well as the preformed radical-anion method with LDBB. Lithium dispersion (25 wt% in mineral oil) containing 0.1% sodium was used as the lithium metal source in the following reductive lithiations. An important advantage of this dispersion is that it can be weighed and transferred to the designated flask open to the air without the lithium reacting. The mineral oil that coats the lithium metal can then be removed under argon by rinsing with hexanes so that the lithium remains unreacted under argon until the solvent and the substrate are added. Lithium dispersion alone, without an aromatic electron carrier, was used as the control. The reductive lithiation of methyl phenyl sulfide (**3**) was studied, and the methyllithium intermediate (**4**) was trapped with benzaldehyde to form the isolable alcohol product, 1-phenylethanol (**5**, Table 1). Surprisingly, the lithium dispersion reductive lithiation of **3** (Table 1, entry 4) produced **5** in a yield comparable to those achieved via the preformed radical-anion (Table 1, entry 1) and catalytic (Table 1, entries 2 and 3) reductive lithiation methods.

Table 1. Catalytic, Preformed Radical-Anion, and Lithium Dispersion Methods of Reductive Lithiation of Methyl Phenyl Sulfide

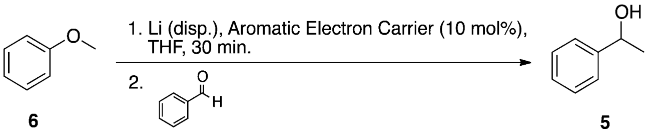


entry	conditions	yield (%)[a]
1	LDBB	79
2	Li (disp., 2.4 equiv), DMA (10 mol%)	77
3	Li (disp., 2.4 equiv), DBB (10 mol%)	74
4	Li (disp., 2.4 equiv)	73

[a]Isolated yield of **5** after chromatography purification.

Since **3** reacted with lithium dispersion both in the presence and absence of an aromatic electron carrier, the role of DMA could not be determined. There were two factors to be measured occurring in one reaction pot, the noncatalyzed and catalyzed reductive lithiation, which may be happening simultaneously or affecting one another. Therefore, the DMA catalyzed reductive lithiation of anisole (**6**), which does not readily undergo reductive lithiation in the absence of an aromatic electron carrier,[5] was investigated (Table 2). DBB and DMAN successfully catalyzed the reductive lithiation of **6** at 0 °C (Table 2, entries 1 and 2); however, in the presence of DMA, no cleavage product was formed, even after 24 h at room

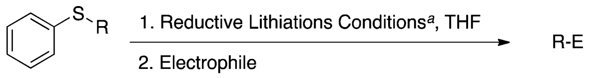
Table 2. Catalytic Method of Reductive Lithiation of Anisole



entry	temp. (°C)	aromatic electron carrier	yield (%)[a]
1	0	DBB	59
2	0	DMAN	66
3	0	DMA	0[b]
4	rt	DMA	0[b,c]

[a]Isolated yield of **5** after chromatography purification. [b]Trace amounts of phenol detected in crude ^{1}HNMR. [c]After 24 h.

Table 3. Reductive Lithiation of Phenyl Thioethers Using Lithium Dispersion and Some Comparisons with the Use of Granular Lithium and DBB Catalysis



3, 7, 8, 9 **5, 14, 15, 16**

entry	SM	R	temp. (°C)	time (min.)	method[a]	E	product (%)[b]
1	**3**	CH_3	0	15	A	C_6H_5CHOH	**5** (95)
2	**3**	CH_3	−78	60	A	C_6H_5CHOH	**5** (95)
3	**3**	CH_3	−78	150	B	$\overline{(CH_2)_5C}OH$	(92)[c]
4	**3**	CH_3	−78	60	C	C_6H_5CHOH	**5** (88)
5	**7**	$CH(CH_3)_2$	−78	90	A	C_6H_5CHOH	**14** (87)
6	**7**	$CH(CH_3)_2$	−78	90	C	C_6H_5CHOH	**14** (87)
7	**8**	$(CH_2)_3CH{=}CH_2$	0	15	A	C_6H_5CHOH	**15** (80)
8	**8**	$(CH_2)_3CH{=}CH_2$	−78	60	A	C_6H_5CHOH	**15** (83)
9	**8**	$(CH_2)_3CH{=}CH_2$	−78	60	D	C_6H_5CHOH	**15** (77)
10	**8**	$(CH_2)_3CH{=}CH_2$	−78	10	E	H	**8** (11)
11	**8**	$(CH_2)_3CH{=}CH_2$	−78	10	F	H	**8** (10)
12	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	0	15	A	C_6H_5CHOH	**16** (88)
13	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	0	30	G	$c\text{-}C_6H_{11}CHOH$	(63)[d]
14	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	−45	60	A	C_6H_5CHOH	**16** (88)
15	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	−78	60	A	C_6H_5CHOH	**16** (84)
16	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	−78	60	C	C_6H_5CHOH	**16** (86)
17	**9**	$\overline{C{=}CH(CH_2)_3CH_2}$	−78	60	D	C_6H_5CHOH	**16** (64)

[a] Method A: Li (disp.); benzaldehyde. Method B: Li powder, Np (1 mol%); cyclohexanone.[8] Method C: Li (disp.), DBB (10 mol%); benzaldehyde. Method D: Li granular; benzaldehyde. Method E: Li (disp.); H_2O. Method F: Li (disp.), DBB (10 mol%); H_2O. Method G: LN; cyclohexanecarboxaldehyde.[21] [b] Product and isolated yield after chromatography purification. [c] Ref 8. [d] Ref 21.

temperature (Table 2, entries 3 and 4). With these results, it was concluded that DMA does not catalyze the reductive lithiation of either **3** or **6**, and therefore, may not be an effective electron-transfer promoter when lithium dispersion is the source of Li metal.

Reductive Lithiation of Phenyl Thioethers. In order to gain a preliminary understanding of the scope of the lithium dispersion reductive lithiation of phenyl thioethers and to optimize conditions, four substrates, which had previously undergone either catalytic or preformed radical-anion reductive lithiation, were surveyed. The phenyl thioethers, including: isopropyl phenyl sulfide (**7**),[16] 5-(phenylthio)-1-pentene (**8**),[17] 1-(phenylthio)-1-cyclohexene (**9**),[18] *tert*-butyl phenyl sulfide (**10**),[19] 2-(phenylthio)-butane (**11**),[20] 3-(phenylthio)-hexane (**12**),[20] and cyclooctyl phenyl sulfide (**13**),[20] were synthesized following the literature protocols. Unlike Yus's procedure, which generally uses a large excess of lithium, prepared in a special apparatus[12] not generally available in synthetic laboratories, the procedure developed here uses a slight stoichiometric excess (2.4 equiv) of the lithium dispersion.

Excellent yields of the corresponding benzyl alcohol products were obtained after the organolithium intermediates were captured with benzaldehyde (80−95% yield) (Table 3). With optimum conditions developed, the significance of DBB in the reductive lithiation of phenyl thioethers was determined. As shown in Table 3 (entries 4, 6, and 16), DBB did not affect the isolated yield under identical reaction conditions. Furthermore, less time was required for the lithium dispersion reductive lithiation of **3** and **9** in comparison to the catalytic and preformed radical-anion reductive lithiations of these substrates at the same temperature (Table 3, entries 2, 3, 12, and 13).[8,21] Lastly, similar amounts of unreacted starting material **8** were recovered, in both the presence and absence of DBB (Table 3, entries 10 and 11), after the organolithium intermediate was quenched with water. Thus, it was determined that DBB does not catalyze the reductive lithiation of phenyl thioethers when lithium dispersion is the Li metal source.

In order to determine if commercially available granular lithium behaved in a manner similar to that of lithium dispersion, the Li source was changed to granular lithium (0.5% sodium), which presumably has less surface area due to the large chunks of granular metal. The granular lithium reductive lithiation of **8** and **9** produced a slightly lower isolated yield (Table 3, entries 9 and 17), despite the granular lithium having five times the amount of sodium compared to the lithium dispersion.[22] Thus, the increase in the surface area of the Li metal, from the granular to the dispersion, apparently somewhat enhances the rate of reductive lithiation.

The finding that phenyl thioethers were reductively lithiated by lithium metal with no aromatic catalyst present was surprising. In the past, with very few exceptions, the overwhelming number of reductive lithiations of phenyl thioethers have been performed in the presence of either preformed aromatic radical-anions or an aromatic catalyst that was thought to act as an electron carrier. The only exceptions of which we are aware of are the findings of Screttas et al. that a few phenyl thioethers can be reductively lithiated by a substantial excess of specially prepared lithium dispersion alone[1] and that allylic phenyl thioethers can be reductively lithiated under highly unusual conditions, that is with an excess of lithium chips in solutions of diethyl ether, rather than the standard THF, at ice bath temperature.[23]

In Table 3, overall yields were used to compare the efficacy of the procedures for different substrates. In order to gain an

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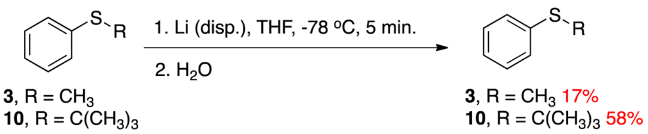
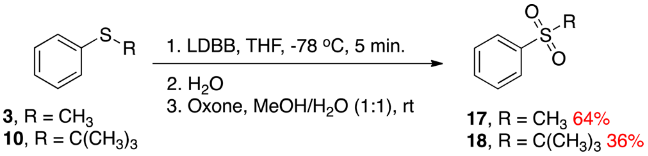
understanding of the relative rates of cleavage of two different substrates, **3** and **10**, the yields of the unreacted starting materials after a 5 min reductive lithiation were determined. As shown in Scheme 3, **3** cleaves significantly faster than **10** rather than slower, as would be predicted for the preformed radical-anion method.[3a,g] The relative reactivity is reversed in going from the preformed radical-anion method (Scheme 4) to the lithium dispersion method (Scheme 3). Thus, the preformed radical-anion method of reductive lithiation must be fundamentally different from the lithium dispersion method.

Scheme 3. Lithium Dispersion Reductive Lithiation of 3 and 10[a]



[a]The % of recovered starting material after chromatography purification.

Scheme 4. Preformed Radical-Anion Reductive Lithiation of 3 and 10[a]

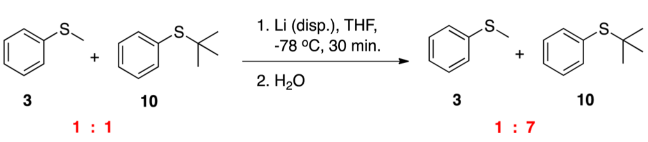


[a]The % of isolated sulfone after chromatography purification.

Under the preformed radical-anion method with LDBB (Scheme 4), the unreacted starting material was oxidized to a sulfone[24] in order to facilitate separation from DBB via column chromatography. Thus, as expected, **10** cleaved more rapidly than **3**.

Further evidence includes the lithium dispersion reductive lithiation of a 1:1 mixture of **3** and **10** being selective for methyl phenyl sulfide, resulting in a 1:7 ratio of recovered starting material (Scheme 5). The reversal in reactivity in the presence and absence of the electron-transfer agent is truly remarkable.

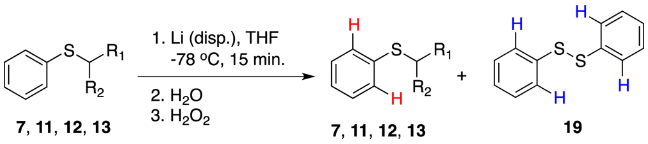
Scheme 5. Selective Reductive Lithiation of 3[a]



[a]Ratio of recovered starting material determined from ^{1}HNMR.

In order to determine if this unique finding results from an electronic effect or a steric effect, the relative rates of reductive lithiation of secondary alkyl phenyl sulfides, increasing in bulkiness, were compared. Four substrates were individually reductively lithiated with lithium dispersion, and the lithium thiophenoxide products were oxidized to diphenyl disulfide (**19**) (Table 4). The ratio of the starting material (SM) to **19** was determined by comparing the ratio of the *ortho* aromatic protons of each product in the crude ^{1}HNMR spectrum. The result is that the rate is very sensitive to steric effects; an increase in bulkiness of the alkyl group led to a sharp increase in unreacted starting material. This thus is a steric effect rather than an electronic effect.

Table 4. Lithium Dispersion Reductive Lithiation of Secondary Alkyl Phenyl Sulfides

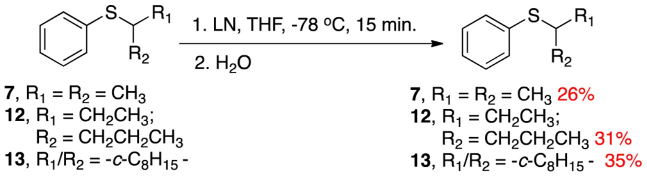


Entry	SM	R_1	R_2	SM (H) : 19 (H)[a]
1	**7**	CH_3	CH_3	3:1
2	**11**	CH_3	CH_2CH_3	8:1
3	**12**	CH_2CH_3	$CH_2CH_2CH_3$	34:1
4	**13**	-*c*-C_8C_{15}-		36:1

[a]Ratio determined from crude ^{1}HNMR.

The preformed radical-anion reductive lithiation of some of these substrates was performed in order to determine whether there are similar or different steric effects on the rate of reductive lithiation when compared to the lithium dispersion method. The ratio of the starting material to **19** could not be determined by ^{1}HNMR due to overlap of the aromatic protons with Np; therefore, the unreacted starting material was isolated. As shown in Scheme 6, compounds **7**, **12**, and **13** have similar rates of cleavage under the preformed radical-anion reaction conditions. There was little to no discrepancy observed in the percentages of the unreacted SM (Scheme 6) in comparison to the considerable difference observed in the ratios of the SM to **19** in Table 4.

Scheme 6. Preformed Radical-Anion Reductive Lithiation of Secondary Alkyl Phenyl Sulfides[a]

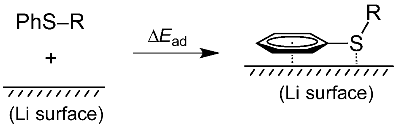


[a]The % of recovered starting material after chromatography purification.

Computational Studies of C–S Bond Cleavage of Alkyl Phenyl Sulfides on the Lithium Surface. This is one of those rare circumstances in which one discovers completely unexpected chemical results that, without theoretical calculations, are quite inexplicable. The reductive lithiation of alkyl phenyl sulfides with lithium dispersion is expected to occur through the dissociative adsorption mechanism on the lithium surface. This process involves molecular adsorption of the alkyl phenyl sulfide on the lithium surface, followed by C–S bond cleavage to form a thiophenoxyl radical and an alkyl radical adsorbed on the lithium surface. The carbon–halogen bond dissociative adsorption of alkyl halides on magnesium, aluminum, and various transition-metal surfaces have been investigated in detail experimentally and computationally.[25,26] Interestingly, the carbon–halogen bond cleavage is generally promoted by substrates with longer or bulkier alkyl chains,[27] which is opposite to the reactivity trend observed in the reductive lithiation of alkyl phenyl sulfides with lithium dispersion. The increased reactivity of bulky alkyl halides on metal surface was attributed to the greater molecular adsorption energy of the longer-chain alkyl halides, while the rate of the subsequent C-X bond cleavage step was found to be independent of alkyl chain length.[28] To investigate the steric effects of alkyl substituents on the reactivity of alkyl phenyl sulfide C−S bond cleavage on lithium surface, density functional theory (DFT) calculations were performed to evaluate the dissociative adsorption of substrates with different alkyl groups (**3**, **7**, **10**, **11**, and **12**).

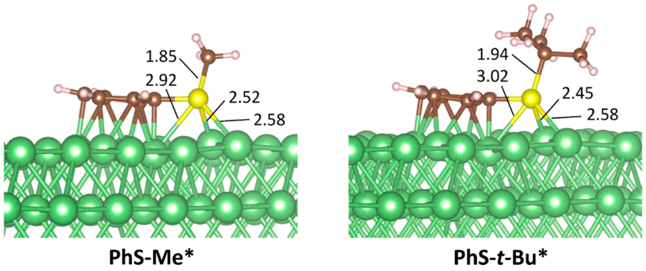
We first computed the molecular adsorption energies (ΔE_{ad}) of alkyl phenyl sulfides on the lithium surface (Table 5). The adsorption energies of the sulfides are surprisingly similar regardless of the very different size of the alkyl groups. The small effects of the alkyl group on the adsorption energies are attributed to the adsorbed geometry of the substrate on the surface. In all complexes, the substrate binds with the phenyl group and the sulfur atom parallel to the surface, while the alkyl group stands upright, pointing away from the surface (Figure 1). In contrast, based on previous reports,[27b] the alkyl chain in adsorbed alkyl halide complexes binds to the metal surface and thus has much more significant effects on the adsorption energies. The lack of correlation between the computed adsorption energy and reactivity suggests the cleavage rate does not depend on the substrate adsorption step. As a result, the reaction energies of the C−S bond cleavage on the surface of lithium were computed to investigate the reactivity trend in this step. Previous studies have demonstrated the reactivity of carbon−heteroatom bond cleavage on metal surface follows the Brønsted−Evans−Polanyi relationship, i.e., the reactivity depends linearly on the reaction energy of bond cleavage.[29]

Table 5. Substrate Adsorption Energy on Li Surface



entry	substrate	substrate on Li (110) Surface (*)[a]	ΔE_{ad} (kcal/mol)
1	**3**	PhS-Me + * → PhS-Me*	−12.0
2	**7**	PhS-*i*-Pr + * → PhS-*i*-Pr*	−15.5
3	**11**	PhS-2-butyl + * → PhS-2-butyl*	−14.4
4	**12**	PhS-3-hexyl + * → PhS-3-hexyl*	−15.1
5	**10**	PhS-*t*-Bu + * → PhS-*t*-Bu*	−15.1
6	**6**	PhO-Me + * → PhO-Me*	−6.3

[a] All calculations were performed with the PBE functional in CP2K/Quickstep.[30] Li (110) surface was modeled using five atomic layers with a $p(5 \times 5)$ supercell.

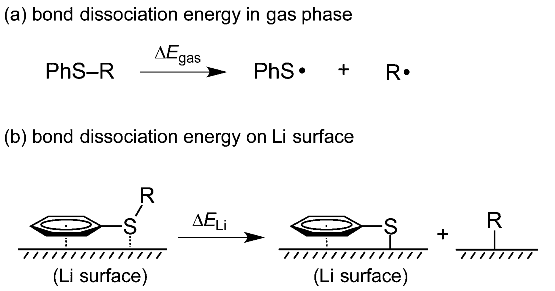


PhS-Me* **PhS-*t*-Bu***

Figure 1. Adsorption geometries of methyl phenyl sulfide (**3**) and *tert*-butyl phenyl sulfide (**10**) on Li(110) surface.

The computed C−S bond dissociation energies in the gas phase (ΔE_{gas}) and on the Li surface (ΔE_{Li}, i.e., the reaction energy of the adsorbed alkyl phenyl sulfide on the Li surface to form a thiophenoxyl radical and an alkyl radical bound to the Li surface) are shown in Table 6. The C−S bond cleavage on the Li surface is found to be exothermic, and the exothermicity parallels the reactivity trend. The reaction with **3** is the most favorable thermodynamically, although the PhS-Me bond is the strongest in terms of gas phase bond dissociation energies (Table 6, entry 1). The bulkier alkyl groups, **10** and **12**, result in much less exothermic C−S bond cleavage on the Li surface (Table 6, entries 4 and 5). The unfavorable steric interaction between the bulky alkyl groups and the surface is evident from the elongation of the Li−C distance of the adsorbed R−Li complexes in going from the methyl group to the larger *tert*-butyl group (Figure 2).

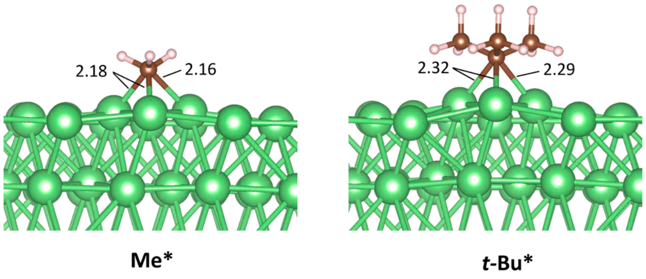
Table 6. Calculated C−S Bond Dissociation Energies[a]



entry	substrate	R	ΔE_{gas} (kcal/mol)	ΔE_{Li} (kcal/mol)[b]	d(Li−C) (Å)[c]
1	**3**	Me	68.1	−38.0	2.17
2	**7**	*i*-Pr	60.2	−27.1	2.24
3	**11**	2-butyl	60.7	−26.4	2.26
4	**12**	3-hexyl	60.7	−24.5	2.28
5	**10**	*t*-Bu	57.1	−24.8	2.31

[a] All calculations were performed with the PBE functional in CP2K/Quickstep.[30] Li (110) surface was modeled using five atomic layers with a $p(5 \times 5)$ supercell. [b] The dissociative adsorption energy is the energy difference between adsorbed PhS and R groups on the Li surface and the adsorbed substrate and Li surface. See equation (b). [c] Average distance of three shortest Li−C bonds in adsorbed alkyl radical complex.

The origin of the more favorable C−S bond dissociation with smaller alkyl groups is attributed to the stronger binding of the sterically less hindered alkyl radical to the Li surface.[31] According to Table 7, the adsorption of the methyl radical on Li is the most exothermic, and the adsorption energy decreases as the bulkiness of the alkyl group increases. Again,



Me* ***t*-Bu***

Figure 2. Adsorption geometries of Me and *t*-Bu radicals on Li(110) surface.

Table 7. Calculated Radical Adsorption Energies

entry	substrate	radical adsorption on Li surface (*)[a]	ΔE_{ad} (kcal/mol)
1	**3**	Me$^{\bullet}$ + * → Me*	−45.4
2	**7**	*i*-Pr$^{\bullet}$ + * → *i*-Pr*	−30.2
3	**11**	2-butyl$^{\bullet}$ + * → 2-butyl*	−28.9
4	**12**	3-hexyl$^{\bullet}$ + * → 3-hexyl*	−27.7
5	**10**	*t*-Bu$^{\bullet}$ + * → *t*-Bu*	−24.3

[a] Li (110) surface modeled by five atomic layers with a p(5 × 5) supercell.

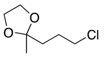
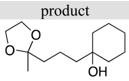
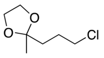
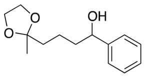
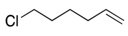
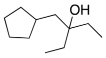
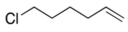
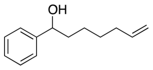
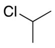
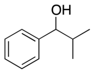
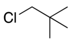
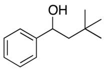
an electronic explanation, rather than a steric one, is quite unlikely since there is not a noticeable difference in the adsorption energies between the secondary radicals (Table 7, entries 2−4). Although experimental studies on lithium surfaces are rare, calorimetry and DFT studies about alkyl adsorption on Pt reveal that, similar to the reaction with Li, the methyl radical was found to adsorb much more strongly than the *tert*-butyl radical on the Pt surface.[32]

In summary, the DFT calculations indicate that the relative rates of cleavage of the phenyl thioethers are controlled by the steric repulsions between the alkyl group and the lithium surface in the adsorbed alkyl radical complex.

Reductive Lithiation of Additional Substrates. In order to determine if other functional groups behaved in a manner similar to that of the phenyl thioether, that is accept an electron from lithium metal in the absence of an aromatic electron-transfer reagent, the lithium dispersion method of reductive lithiation of some diverse substrates, which have previously undergone either catalytic or preformed radical-anion reductive lithiation, was investigated. The importance of the lithium dispersion methodology is currently demonstrated in the industrial production of commercially available organolithium reagents. This procedure involves the exothermic reaction of the alkyl chloride with lithium dispersion (0.5−2% Na) in the desired hydrocarbon solvent.[22]

Yus and co-workers have performed a large number of catalyzed lithiation reactions of alkyl chlorides.[8,33] In two of their blank reactions, in the absence of an aromatic electron carrier, the lithiation of different alkyl chlorides resulted in one failed reaction, with 2-(3-chloropropyl)-2-methyl-1,3-dioxolane (**20**) (Table 8, entry 1),[8] and one successful reaction, with 6-chloro-1-hexene (**21**) (Table 8, entry 3).[33d] In order to determine if **20** could be lithiated under our lithium dispersion conditions, we treated this substrate with lithium dispersion, also at −78 °C. As a result, the corresponding alcohol product **24** was successfully obtained, in half the amount of time, after capturing the organolithium intermediate with benzaldehyde (entry 2).

Table 8. Reductive Lithiation of Alkyl Chlorides

entry	alkyl chloride	temp. (°C)	time (min.)	product	% Yield[a]
1	 **20**	-78	240		0[b]
2	 **20**	-78	120	 **24**	85
3	 **21**	-30	50		83[c]
4	 **21**	-45	60	 **25**	78
5	 **22**	-45	30	 **14**	79
6	 **23**	-45	30	 **26**	99

[a] Isolated yield after chromatography purification. [b] Ref 8. [c] Ref 33d.

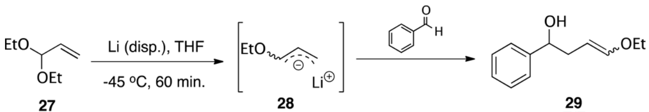
Unlike the cyclopentyl product that Yus isolated (entry 3), our reductive lithiation of **21** gave no rearranged product (entry 4). In the process of C−S bond cleavage on the Li surface, no free alkyl radical is formed. The large adsorption energies (Table 7) suggest the alkyl group remains strongly adsorbed on the surface. Furthermore, the short C−Li distance in the adsorbed complexes (Figure 2) indicates bonding interaction with the radical carbon, which will likely prevent the radical cyclization to form the cyclopentylmethyl radical. The lithium dispersion method of reductive lithiation of isopropyl chloride (**22**) and neopentyl chloride (**23**) provided excellent yields of the corresponding alcohol products, **14** and **26**, after the organolithium intermediates were trapped with benzaldehyde (Table 8, entries 5 and 6). It is probably safe to assume that the reductive lithiation of alkyl chlorides, like that of phenyl thioethers, is general in the absence of added aromatic electron carriers under our very mild conditions.

A 2006 report of the reductive cleavage of anisole (**6**) at the alkyl C−O bond, at 0 °C indicated that using 14 equiv of Li but no DBB gave no product.[5] When this result was repeated with our lithium dispersion method, no cleavage product was formed. This result was puzzling because the bond dissociation energy values for the homolytic cleavage of the methyl-heteroatom bond of anisole (65.7 kcal/mol) and of methyl phenyl sulfide (66.7 kcal/mol) are close in energy.[34] Therefore, under the same reductive lithiation conditions, the rate at which the methyl radical is formed from each compound should be similar.

Calculations reveal that the adsorption energy of **6** onto the surface of lithium is significantly less exothermic than the adsorption energies of alkyl phenyl sulfides (Table 5, entry 6). The more favorable adsorption energies of the alkyl phenyl sulfides compared to anisole are presumably due to the greater polarizability of sulfur compared to oxygen. Since previous studies indicated stronger substrate adsorption promotes carbon−halogen bond cleavage,[27] the much greater molecular adsorption energies of phenyl thioethers compared to anisole are expected to contribute to their reactivity on the lithium surface in the absence of an aromatic electron carrier.

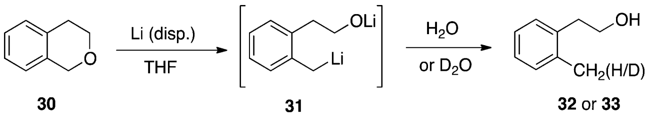
In that same 2006 report, Cohen and co-workers performed the aromatic radical-anion reductive cleavage of acrolein diethyl acetal (**27**).[5,35] When **27** was subjected to the lithium dispersion method conditions developed in our work, the reductive cleavage occurred smoothly at −45 °C to provide a 68% yield of **29** in a *Z*/*E* ratio of 7:1 (Scheme 7). This yield closely matches that obtained from the LDBB reductive cleavage of **27** after 90 min at −50 °C.[5] Our yield of **29** surpasses the 34% yield obtained with Yus's catalytic method in which a 4-fold excess of lithium and Barbier conditions were employed.[36]

Scheme 7. Reductive Lithiation of Acrolein Diethyl Acetal



In 1995, Yus and co-workers reported that isochroman (**30**) can be converted into lithium 2-(2-lithiomethylphenyl)-ethanolate (**31**) via the reductive ring-opening by an excess of lithium powder (20 molar) and a catalytic amount of DBB (Table 9, entries 1 and 3).[37] Furthermore, the claim is made that in the absence of the DBB, lithiation times were longer (ca. 3 h), and yields were considerably lower.[37] When **30** was subjected to our lithium dispersion conditions, 2-(2-methylphenyl)ethanol (**32**) was isolated in excellent yields at both 0 °C and −78 °C (Table 9, entries 2 and 5). The formation of **31** was confirmed by quenching the reaction mixture with D_2O (entry 4) to obtain 2-(2-deuteriomethylphenyl)ethanol (**33**). Thus, only 2.4 mol equiv of lithium dispersion was necessary to achieve similar yields as Yus et al., even at lower temperatures.

Table 9. Reductive Lithiation of Isochroman



entry	temp. (°C)	time (min.)	product	% yield[a]
1	20	45	H (**32**)	89[b]
2	0	30	H (**32**)	78
3	20	45	D (**33**)	86[b]
4	0	30	D (**33**)	70
5	−78	120	H (**32**)	99

[a] Isolated yield after chromatography purification. [b] Ref 37.

■ CONCLUSION

Many reductive lithiations, previously thought to be possible only in the presence of aromatic electron-transfer reagents, can be performed by the use of lithium metal alone with no electron-transfer reagent present when lithium dispersion is the Li metal source. Furthermore, the absence of preformed radical-anions can completely change and even reverse the selectivity of reduction of different but very similar substrates. Phenyl thioethers with smaller alkyl groups are much more reactive than those with bulkier substituents. This is highly unusual and probably unprecedented.

DFT calculations reveal that the key step of alkyl phenyl sulfide cleavage on the lithium surface involves the formation of a thiophenoxyl and an alkyl radical adsorbed on the surface. Sterically less hindered alkyl radicals bind to the surface more strongly and thus lead to more exothermic cleavage of the alkyl phenyl sulfide. To the best of our knowledge, the work presented here is the first example where this steric effect controls the selectivity in reductive lithiation reactions. The methodology developed in this work includes, but may not be limited to, the reductive lithiation of phenyl thioethers, alkyl chlorides, acrolein diethyl acetal, and isochroman.

■ EXPERIMENTAL SECTION

General Methods. All reactions were carried out under a positive pressure of dry argon gas in oven-dried (120 °C) flasks, and standard precautions against moisture were taken. A dry ice/acetone bath was used to obtain −78 °C, an ice-water bath was used to obtain 0 °C, and a dry ice/acetonitrile bath was used to obtain −45 °C. Flash chromatography (low pressure) was performed with either silica gel (32−63 μm) or aluminum oxide, activated basic or neutral. Thin-layer chromatography (TLC) was performed on glass supported (0.25 mm) silica plates. Visualization of TLC plates was accomplished with one or more of the following: 254 nm UV light, aqueous solution of $KMnO_4$. Commercial solvents and reagents were used as received with the following exceptions: tetrahydrofuran (THF) was distilled over sodium metal in the presence of benzophenone as indicator, hexanes was freshly distilled over CaH_2, and benzaldehyde was washed with saturated $NaHCO_{3(aq)}$, extracted with diethyl ether, and vacuum distilled (∼20 mmHg).[38] Lithium dispersion (25 wt% in mineral oil) was commercially available from a chemical supplier. Toward the end of the work described here, the chemical supplier discontinued offering lithium dispersion; however, recipes for its preparation are available.[39] Furthermore, as described here, granular lithium, commercially available from a chemical supplier, is only slightly less effective than the dispersion. ^{1}H and ^{13}C NMR operated at 300 or 400 MHz for ^{1}H and 75 MHz for ^{13}C at 22 °C unless otherwise noted. Chemical shift data are reported in units of δ (ppm) relative to internal standard TMS (set to 0 ppm). Chemical shifts for ^{13}C are referenced to the central peak of the $CHCl_3$ triplet (set to 77.0 ppm). Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), pent (pentet), m (multiplet), and br (broad). Coupling constants, *J*, are reported in Hz.

Phenyl Thioethers. *Isopropyl Phenyl Sulfide (**7**).* A round-bottom flask was charged with water (45 mL) and NaOH (1.75 g, 43.8 mmol). Thiophenol (4.0 mL, 39 mmol) was added dropwise to the solution. The reaction mixture was stirred for 30 min to ensure the complete formation of sodium thiophenoxide. Isopropyl iodide (4.0 mL, 40 mmol) in ethanol (7 mL) was added slowly at room temperature. The resulting reaction mixture was stirred at the same temperature for 24 h. The product was extracted with dichloromethane, and the combined organic extracts were washed with 1 M $NaOH_{(aq)}$ followed by water. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude colorless oil **7** was used without purification (4.91 g, 80% yield). ^{1}HNMR ($CDCl_3$) δ (ppm): 7.39 (d, *J* = 8.0 Hz, 2H), 7.28, (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 3.36 (septet, *J* = 6.7 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 6H); ^{13}CNMR ($CDCl_3$) δ (ppm): 135.5, 131.9, 128.7, 126.6, 38.2, 23.1. These NMR data compare well with the literature values.[16]

*5-(Phenylthio)-1-pentene (**8**).* A 100 mL round-bottom flask was charged with water (45 mL) and NaOH (1.7 g, 45 mmol). Thiophenol (4.3 g, 39 mmol) was added dropwise to the solution. The reaction mixture was stirred for 30 min to ensure the complete formation of sodium thiophenoxide. 5-Bromo-1-pentene (3.7 mL, 31 mmol) in ethanol (6 mL) was added slowly at room temperature. The resulting reaction mixture was stirred at the same temperature for 24 h. The product was extracted with dichloromethane, and the combined organic extracts were washed twice with 1 M $NaOH_{(aq)}$ followed by water. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude colorless oil **8** was used without purification (6.0 g, 99% yield). ^{1}HNMR ($CDCl_3$) δ (ppm): 7.32 (d, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 5.78 (ddt, *J* = 6.8, 3.6, 3.4 Hz, 1H), 5.05−4.97 (m, 2H), 2.92 (t, *J* = 7.2 Hz, 2H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.74 (pentet, *J* = 7.2 Hz, 2H); ^{13}CNMR ($CDCl_3$) δ (ppm): 137.6, 136.7, 129.1, 128.9, 125.8, 115.4, 33.0, 32.7, 28.3. These NMR data compare well with the literature values.[17]

*1-(Phenylthio)-1-cyclohexene (**9**).* Thiophenol (2.0 mL, 20 mmol), cyclohexanone (2.1 mL, 20 mmol), Montmorillonite K10 (4.0 g), and toluene (200 mL) were added under argon to a 250 mL three neck round-bottom flask equipped with a Dean−Stark trap and condenser. The light-beige slurry was heated at reflux for a 6 h period and then was cooled to ambient temperature and was filtered. The filter pad was washed with toluene, and the filtrate was washed twice with 1 M $NaOH_{(aq)}$ followed by water. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (100% hexanes) afforded pure product **9** (2.8 g, 72% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.31−7.23 (m, 4H), 7.17−7.14 (m, 1H), 6.06 (s, 1H), 2.13(m, 4H), 1.62 (dd, *J* = 20.4, 3.8 Hz, 4H); ^{13}CNMR ($CDCl_3$) δ (ppm): 135.2, 132.7, 131.3, 130.0, 128.8, 126.2, 29.9, 26.7, 23.6, 21.6. These NMR data compare well with the literature values.[18]

*tert-Butyl Phenyl Sulfide (**10**).* A mixture of indium powder (1.0 g, 8.7 mmol), diphenyl disulfide (1.9 g, 8.7 mmol), and *tert*-butyl bromide (2.0 mL, 18 mmol) in dichloromethane (50 mL) was heated at reflux for 2 h under argon. The reaction mixture was cooled to room temperature and then was then quenched with 1 M $HCl_{(aq)}$. The product was extracted with dichloromethane, and the combined organic extracts were washed twice with 1 M $NaOH_{(aq)}$ followed by water. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to afford **10** (2.1 g, 72% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.53−7.52 (m, 2H), 7.36−7.29 (m, 3H), 1.29 (s, 9H); ^{13}CNMR ($CDCl_3$) δ (ppm): 137.4, 132.7, 128.6, 128.4, 45.8, 31.0. These NMR data compare well with the literature values.[19]

*2-(Phenylthio)-butane (**11**).* Sodium hydride (60 wt% in mineral oil, 0.60 g, 15 mmol) was charged to a 3-neck 25 mL round-bottom flask equipped with a condenser. The sodium hydride was washed with hexanes. DMF (5 mL) was added, and the reaction mixture was stirred at room temperature. Thiophenol (1.0 mL, 9.8 mmol) was added dropwise to the reaction mixture followed by 2-bromobutane (0.70 mL, 6.4 mmol). The reaction mixture was stirred at approximately 80 °C for 2 h under argon and then was cooled to room temperature and quenched with water. The product was extracted with hexanes, and the combined organic extracts were washed twice with 1 M $NaOH_{(aq)}$ followed by H_2O. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on basic alumina (100% hexanes) afforded pure product **11** (0.95 g, 89% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.36 (dd, *J* = 5.1, 2.2 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 3.13 (sextet, *J* = 6.6 Hz, 1H), 1.71−1.42 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}CNMR ($CDCl_3$) δ (ppm): 135.6, 131.9, 128.7, 126.6, 44.9, 29.5, 20.5, 11.4. These NMR data compare well with the literature values.[20]

*3-(Phenylthio)-hexane (**12**).* Sodium hydride (60 wt% in mineral oil, 1.2 g, 30 mmol) was charged to a three-neck 25 mL round-bottom flask equipped with a condenser. The sodium hydride was washed with hexanes. DMF (10 mL) was added, and the reaction mixture was stirred at room temperature. Thiophenol (2.0 mL, 19.6 mmol) was added dropwise to the reaction mixture followed by 3-bromohexane (1.8 mL, 12.8 mmol). The reaction mixture was stirred at 100 °C for 2 h under argon and then was cooled to room temperature and quenched with water. The product was extracted with hexanes, and the combined organic extracts were washed twice with 1 M $NaOH_{(aq)}$ followed by H_2O. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on basic alumina (100% hexanes) afforded pure product **12** (2.4 g, 99% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.36 (d, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 2H), 7.14−7.09 (m, 1H), 3.01 (pent, *J* = 6.2 Hz, 1H), 1.63−1.41 (m, 6H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 6.9 Hz); ^{13}CNMR ($CDCl_3$) δ (ppm): 136.0, 131.8, 128.7, 126.4, 50.4, 36.2, 27.3, 20.1, 14.0, 11.1; IR (thin film) 3073 (s); 2959 (m); 2930 (m); 2872 (m); 1584 (s); 1477 (s); 1459 (s); 1439 (s); 1378 (s); 1091 (s); 1025 (s); 740 (m); 692 (m) cm^{-1}; TOF MS (ES$^+$) calcd for $C_{12}H_{18}S$ 194.1129; found 194.1126.

*Cyclooctyl Phenyl Sulfide (**13**).* Sodium hydride (60 wt% in mineral oil, 0.7 g, 15 mmol) was charged to a 3-neck 25 mL round-bottom flask equipped with a condenser. The sodium hydride was washed with hexanes. DMF (5 mL) was added, and the reaction mixture was stirred at room temperature. Thiophenol (1.10 mL, 10.8 mmol) was added dropwise to the reaction mixture followed by cyclooctyl bromide (1.0 g, 5.2 mmol). The reaction mixture was stirred at 100 °C for 3 h under argon and then was cooled to room temperature and quenched with water. The product was extracted with hexanes, and the combined organic extracts were washed twice with 1 M $NaOH_{(aq)}$ followed by H_2O. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on basic alumina (100% hexanes) afforded pure product **13** (0.81 g, 52% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.37 (dd, *J* = 7.2, 0.8 Hz, 2H), 7.27 (dd, *J* = 5.6, 1.6 Hz, 2H), 7.19 (td, *J* = 5.2, 1.2 Hz, 1H), 3.43−3.36 (m, 1H), 2.00−1.93 (m, 2H), 1.79−1.50 (m, 12H); ^{13}CNMR ($CDCl_3$) δ (ppm): 136.3, 131.5, 128.9, 126.5, 47.8, 32.1, 27.3 26.0, 25.3. These NMR data compare well with the literature values.[20]

Catalytic and Lithium Dispersion Reductive Lithiation of Methyl Phenyl Sulfide (3) (Table 1). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was then cooled to −78 °C, and THF (1 mL) was added. A solution of the electron-transfer catalyst (DBB or DMA, 0.10 mmol) in THF (0.5 mL) was added dropwise to the flask. Immediately following was the dropwise addition of a solution of methyl phenyl sulfide, **3** (0.11 mL, 1.0 mmol) in THF (0.5 mL). The reaction mixture was stirred at −78 °C for 30 min. Benzaldehyde (0.12 mL, 1.2 mmol) was added dropwise, and the reaction mixture was stirred at −78 °C for 30 min. The reaction was then quenched with water, and the product was extracted with diethyl ether. For the DMA catalyst, the combined organic extracts were washed with 1% $HCl_{(aq)}$ (5 mL), and the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded 1-phenylethanol (**5**) as a light-yellow oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.33−7.27 (m, 4H), 7.26−7.22 (m, 1H), 4.82 (q, *J* = 6.4 Hz, 1 H), 2.37 (br, 1H), 1.44 (d, *J* = 6.4 Hz, 3H); ^{13}CNMR ($CDCl_3$) δ (ppm): 146.0, 128.4, 127.3, 125.5, 70.2, 25.2. These NMR data compare well with the literature values.[5]

LDBB Reductive Lithiation of Methyl Phenyl Sulfide (3) (Table 1). A 25 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. THF (3 mL) was added, and the mixture was stirred at room temperature. A solution of DBB (0.64 g, 2.7 mmol) in THF (2 mL) was added to the flask, and the reaction mixture was stirred at room temperature for 5 min and then was cooled to 0 °C. The reaction mixture was stirred at 0 °C for 5 h and then was cooled to −78 °C. A solution of methyl phenyl sulfide, **3** (0.11 mL, 1.0 mmol) in THF (0.5 mL) was added dropwise, and the reaction mixture was stirred at −78 °C for 30 min. Benzaldehyde (0.12 mL, 1.2 mmol) was added dropwise, and the reaction mixture was stirred at −78 °C for 30 min. The reaction was then quenched with water, and the product was extracted with diethyl ether. The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **5** (96 mg, 79% yield).

Catalytic Method of Reductive Lithiation of Anisole (6) (Table 2). An oven-dried 25 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (220 mg, 7.9 mmol). The lithium was washed three times with hexanes (3 mL) and once with THF (3 mL) under argon. The lithium was then cooled to 0 °C, and THF (2.5 mL) was added followed by a solution of DBB (98 mg, 0.37 mmol) in THF (0.5 mL). Anisole, **6** (0.40 mL, 3.7 mmol), was added dropwise, and the reaction proceeded for 30 min at 0 °C and then was cooled to −45 °C. Benzaldehyde (0.46 mL, 4.5 mmol) was added dropwise, and the mixture was stirred for an additional 15 min at −45 °C and then was quenched with water. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **5** (0.26 g, 59% yield).

Under the same conditions but with 10 mol% of DMAN (63 mg, 0.37 mmol) afforded the title compound **5** (0.30 g, 66% yield).

Under the same conditions but with 10 mol% of DMA (45 mg, 0.37 mmol) afforded no product.

Under the same conditions but with 10 mol% of DMA (45 mg, 0.37 mmol) at room temperature for 24 h afforded no product.

Reductive Lithiation of (3), (7), (8), and (9) with Lithium Dispersion (Table 3, Method A). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.13 g, 4.8 mmol). The lithium was washed three times with hexanes (3 mL) and once with THF (3 mL) under argon. The lithium was cooled (see Table 3, Method A), and THF (3.5 mL) was added. A solution of methyl phenyl sulfide, **3** (0.25 g, 2.0 mmol) in THF (0.5 mL) was then added dropwise. The reaction mixture was stirred for the allotted amount of time, and then benzaldehyde (0.24 mL, 2.4 mmol) was added dropwise. The reaction mixture was warmed to room temperature and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **5**.

*2-Methyl-1-phenylpropan-1-ol (**14**).* The same procedure as that for **3** with isopropyl phenyl sulfide, **7** (0.30 g, 2.0 mmol) in place of methyl phenyl sulfide, afforded the title compound **14** as a light-yellow oil. ^{1}HNMR (CDCl$_3$) δ (ppm): 7.33−7.23 (m, 5H), 4.31 (d, J = 6.8 Hz, 1H), 2.08 (br, 1H), 1.93 (sextet, J = 6.8 Hz, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 7.2 Hz, 3H); ^{13}CNMR (CDCl$_3$) δ (ppm): 143.6, 128.0, 127.2, 126.5, 79.8, 35.1, 18.9, 18.2. These NMR data compare well with the literature values.[40]

1-Phenylhex-5-en-1-ol (15). The same procedure as that for **3** with 5-(phenylthio)-1-pentene, **8** (0.36 g, 2.0 mmol) in place of methyl phenyl sulfide, afforded the title compound **15** as a light-yellow oil. TOF MS (ES$^+$) calcd for $C_{12}H_{15}O$ 175.1123; found 175.1114; ^{1}HNMR (CDCl$_3$) δ (ppm): 7.34−7.23 (m, 5H), 5.77 (ddd, J = 6.5, 3.6, 3.2 Hz, 1H), 5.00−4.92 (m, 2H), 4.64−4.61 (m, 1H), 2.08 (br, 1H), 2.06, (q, J = 7.2 Hz, 2H), 1.82−1.65 (m, 2H), 1.54−1.32 (m, 2H); ^{13}CNMR (CDCl$_3$) δ (ppm): 145.0, 138.7, 128.5, 127.5, 126.0, 114.8, 74.5, 38.5, 33.7, 25.2. These NMR data compare well with the literature values.[41]

1-(1′-Cyclohexenyl)-1-phenylmethanol (16). The same procedure as that for **3** with 1-(phenylthio)-1-cyclohexene, **9** (0.38 g, 2.0 mmol) in place of methyl phenyl sulfide, afforded the title compound **16** as a light-yellow oil. TOF MS (ES$^+$) calcd for $C_{13}H_{15}O$ 187.1123; found 187.1143; ^{1}HNMR (CDCl$_3$) δ (ppm): 7.32−7.23 (m, 5H), 5.82−5.77 (m, 1H), 5.03 (s, 1H), 2.17 (br, 1H), 2.06 (m, 2H), 1.89 (d, J = 16 Hz, 1H), 1.73 (d, J = 16 Hz, 1H), 1.54 (m, 4H); ^{13}CNMR (CDCl$_3$) δ (ppm): 142.6, 139.6, 128.2, 127.3, 126.3, 123.5, 78.3, 25.0, 24.0, 22.5, 22.4. These NMR data compare well with the literature values.[42]

DBB Catalyzed Reductive Lithiation of (3), (7), and (9) (Table 3, Method C). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.13 g, 4.8 mmol). The lithium was washed three times with hexanes (3 mL) and once with THF (3 mL) under argon. The lithium was cooled to −78 °C and THF (3 mL) was added. A solution DBB (53 mg, 0.20 mmol) in THF (0.5 mL) was added to the flask followed by the dropwise addition of methyl phenyl sulfide, **3** (0.25 g, 2.0 mmol) in THF (0.5 mL). The reaction mixture was stirred for 60 min, and then benzaldehyde (0.24 mL, 2.4 mmol) was added dropwise. The reaction mixture was warmed to room temperature and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **5** (0.22 g, 88% yield).

2-Methyl-1-phenylpropan-1-ol (14). The same procedure as that for **3** with isopropyl phenyl sulfide, **7** (0.30 g, 2.0 mmol) in place of methyl phenyl sulfide and a reaction time of 90 min, afforded the title compound **14** (0.26 g, 87% yield).

1-(1′-Cyclohexenyl)-1-phenylmethanol (16). The same procedure as that for **3** with 1-(phenylthio)-1-cyclohexene, **9** (0.38 g, 2.0 mmol) in place of methyl phenyl sulfide, afforded the title compound **16** (0.32 g, 86% yield).

Reductive Lithiation of (8) and (9) with Granular Lithium (Table 3, Method D). A 10 mL round-bottom flask was charged with granular lithium (34 mg, 4.8 mmol) and THF (3.5 mL) under argon. The flask was cooled to −78 °C, and then a solution of the 5-(phenylthio)-1-pentene, **8** (0.36 g, 2.0 mmol) in THF (0.5 mL) was added dropwise. The reaction mixture was stirred for 60 min, and then benzaldehyde (0.24 mL, 2.4 mmol) was added dropwise. The reaction mixture was warmed to room temperature and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **15** (0.27 g, 77% yield).

1-(1′-Cyclohexenyl)-1-phenylmethanol (16). The same procedure as that for **8** with 1-(phenylthio)-1-cyclohexene, **9** (0.38 g, 2.0 mmol) in place of 5-(phenylthio)-1-pentene, afforded the title compound **16** (0.24 g, 64% yield).

Reductive Lithiation of (8) in the Presence and Absence of DBB (Table 3, Methods E and F). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to −78 °C and THF (1 mL) was added. A solution DBB (27 mg, 0.10 mmol) in THF (0.5 mL) was added to the flask followed by the dropwise addition of 5-(phenylthio)-1-pentene, **8** (0.18 g, 1.0 mmol) in THF (0.5 mL). The reaction mixture was stirred for 10 min at −78 °C and then was quenched with water. The mixture was extracted with diethyl ether, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (100% hexanes) led to recovered starting material **8**.

Reductive Lithiation of (3) and (10) with Lithium Dispersion (Scheme 3). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (33 mg, 1.2 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to −78 °C and THF (1.5 mL) was added. A solution of methyl phenyl sulfide, **3** (62 mg, 0.50 mmol) in THF (0.5 mL) was added dropwise. The reaction mixture was stirred for 5 min at −78 °C and then was quenched with H$_2$O. The product was extracted with hexanes, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (100% hexanes) led to recovered starting material **3** (11 mg, 17%).

tert-Butyl Phenyl Sulfide (10). The same procedure as that for **3** with *tert*-butyl phenyl sulfide (83 mg, 0.50 mmol) in place of methyl phenyl sulfide, led to recovered starting material **10** (48 mg, 58%).

LDBB Reductive Lithiation of (3) and (10): (Scheme 4). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (33 mg, 1.2 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. THF (2 mL) was added, and the mixture was stirred at room temperature. A solution of DBB (0.36 g, 1.4 mmol) in THF (0.5 mL) was added to the flask, and the reaction mixture was stirred at room temperature for 5 min and then was cooled to 0 °C. The reaction mixture was stirred at 0 °C for 5 h and then was cooled to −78 °C. A solution of methyl phenyl sulfide, **3** (62 mg, 0.50 mmol) in THF (0.5 mL) was added dropwise, and the reaction mixture was stirred 5 min at −78 °C and then was quenched with H$_2$O. The product was extracted with hexanes, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. To the crude reaction mixture a 1:1 solution of H$_2$O/MeOH (5 mL) was added followed by oxone (0.92 g, 1.5 mmol). The reaction mixture was stirred overnight at room temperature. The product was extracted with diethyl ether, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (Et$_2$O/hexanes) afforded methyl phenyl sulfone (**17**) (50 mg, 64% yield) as a colorless oil. ^{1}HNMR (CDCl$_3$) δ (ppm): 7.95 (d, J = 7.2 Hz, 2H), 7.67 (t, J = 7.2 Hz, 1H), 7.58 (t, J = 7.2 Hz, 2H), 3.06 (s, 3H); ^{13}CNMR (CDCl$_3$) δ (ppm): 140.6, 133.6, 129.3, 127.2, 44.4. These NMR data compare well with the literature values.[43]

tert-Butyl Phenyl Sulfone (18). The same procedure as that for **3** with *tert*-butyl phenyl sulfide, **10** (83 mg, 0.50 mmol) in place of methyl phenyl sulfide, afforded the title compound **18** (36 mg, 36% yield) as a colorless oil. ^{1}HNMR (CDCl$_3$) δ (ppm): 7.89 (d, J = 7.5 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.56 (t, J = 7.2 Hz, 2H), 1.34 (s, 9H); ^{13}CNMR (CDCl$_3$) δ (ppm): 135.4, 133.5, 130.4, 128.6, 59.8, 23.6. These NMR data compare well with the literature values.[44]

Reductive Lithiation of (3) in the Presence of (10) (Scheme 5). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (33 mg, 1.2 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to −78 °C, and THF (1.5 mL) was added. A solution of methyl phenyl sulfide, **3** (62 mg, 0.50 mmol) and *tert*-butyl phenyl sulfide, **10** (83 mg, 0.50 mmol) in THF (0.5 mL) was added dropwise. The reaction mixture was stirred for 30 min at −78 °C and then was quenched with H$_2$O. The product was extracted with hexanes, and the combined organic extracts were dried over MgSO$_4$ and concentrated *in vacuo*. ^{1}HNMR ratio of **3** to **10** as 1:7.

Reductive Lithiation of (7), (11), (12), and (13) with Lithium Dispersion (Table 4). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to −78 °C and THF (1.5 mL) was added. A solution of isopropyl phenyl sulfide, **7**

(0.15 g, 1.0 mmol) in THF (0.5 mL) was then added dropwise. The reaction mixture was stirred for 15 min, then H_2O (5 mL) was added slowly, and the reaction mixture was warmed to room temperature. Hydrogen peroxide (30 wt%, 9.8 M, 0.10 mL) was added dropwise, and the reaction mixture was stirred overnight at room temperature. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. ^{1}HNMR provided a ratio of the isopropyl phenyl sulfide (**7**) starting material to the diphenyl disulfide product (**19**) as 3:1. ^{1}HNMR (**19**) ($CDCl_3$) δ (ppm): 7.49 (d, J = 7.2 Hz, 4H), 7.28 (t, J = 7.2 Hz, 4H), 7.20 (t, J = 7.2 Hz, 2H).

*2-(Phenylthio)-butane (**11**).* The same procedure as that for **7** with 2-(phenylthio)-butane (0.17 g, 1.0 mmol) in place of isopropyl phenyl sulfide gave a crude ^{1}HNMR ratio of **11** to **19** as 8:1.

*3-(Phenylthio)-hexane (**12**).* The same procedure as that for **7** with 3-(phenylthio)-hexane (0.19 g, 1.0 mmol) in place of isopropyl phenyl sulfide gave a crude ^{1}HNMR ratio of **12** to **19** as 34:1.

*Cyclooctyl Phenyl Sulfide (**13**).* The same procedure as that for **7** with cyclooctyl phenyl sulfide (0.22 g, 1.0 mmol) in place of isopropyl phenyl sulfide gave a crude ^{1}HNMR ratio of **13** to **19** as 36:1.

LN Reductive Lithiation of (7), (12), and (13) (Scheme 6). A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (33 mg, 1.2 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. THF (1.5 mL) was added to the flask followed by a solution of naphthalene (0.17 g, 1.3 mmol) in THF (1 mL), and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of isopropyl phenyl sulfide, **7** (76 mg, 0.50 mmol) in THF (0.25 mL) was added dropwise. The reaction mixture was stirred for 15 min at −78 °C and then was quenched with H_2O. The product was extracted with hexanes, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (100% hexanes) led to recovered starting material **7** (16 mg, 26%).

*3-(Phenylthio)-hexane (**12**).* The same procedure as that for **7** with 3-(phenylthio)-hexane (97 mg, 0.50 mmol) in place of isopropyl phenyl sulfide led to recovered starting material **12** (30 mg, 31%).

*Cyclooctyl Phenyl Sulfide (**13**).* The same procedure as that for **7** with cyclooctyl phenyl sulfide (0.11 g, 0.50 mmol) in place of isopropyl phenyl sulfide led to recovered starting material **13** (39 mg, 35%).

*2-(4-Hydroxy-4-phenylbutyl)-2-methyl-1,3-dioxolane (**24**).* A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to −78 °C, and THF (1.5 mL) was added. A solution of 2-(3-chloropropyl)-2-methyl-1,3-dioxolane, **20** (0.16 g, 1.0 mmol) in THF (0.5 mL) was added dropwise, and the reaction mixture was stirred for 2 h. Benzaldehyde (0.12 mL, 1.2 mmol) was added dropwise, and the reaction mixture was stirred for an additional hour at −78 °C and then was quenched with water. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **24** (0.20 g, 85% yield) as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.35−7.29 (m, 5H), 4.66 (m, 1H), 3.90 (d, J = 4.8 Hz, 4H), 2.50 (br, 1H), 1.79−1.41 (m, 6H), 1.30 (s, 3H); ^{13}CNMR ($CDCl_3$) δ (ppm): 144.8, 128.3, 127.4, 125.8, 110.0, 74.3, 64.5, 39.1, 38.7, 23.6, 20.3. These NMR data compare well with the literature values.[45]

*1-Phenylhept-6-en-1-ol (**25**).* A 25 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.23 g, 8.2 mmol). The lithium was washed three times with hexanes (5 mL) and once with THF (5 mL) under argon. The lithium was cooled to −45 °C, and THF (5 mL) was added. 6-Chloro-1-hexene, **21** (0.50 mL, 3.8 mmol) was then added dropwise, and the reaction mixture was stirred for 60 min. Benzaldehyde (0.46 mL, 4.5 mmol) was added dropwise, and the reaction mixture was warmed to room temperature and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **25** (0.56 g, 78% yield) as a light-yellow oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.32−7.24 (m, 5H), 5.78 (ddt, J = 6.8, 3.6, 3.2 Hz, 1H), 5.00−4.91 (m, 2H), 4.64 (t, J = 6.8 Hz, 1H), 2.03 (d, J = 6.8 Hz, 2H), 1.95 (br, 1H), 1.83−1.6.5 (m, 2H), 1.42−1.28 (m, 4H); ^{13}CNMR ($CDCl_3$) δ (ppm): 144.9, 138.9, 128.4, 127.5, 125.9, 114.4, 74.6, 38.9. 33.7, 28.8, 25.3. These NMR data compare well with the literature values.[46]

*2-Methyl-1-phenylpropan-1-ol (**14**).* Reductive lithiation of isopropyl chloride (**22**) with lithium dispersion (Table 8, entry 4). A 25 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.34 g, 12.2 mmol). The lithium was washed three times with hexanes (5 mL) and once with THF (5 mL) under argon. The lithium was cooled to −45 °C, and THF (5 mL) was added. Isopropyl chloride, **22** (0.50 mL, 5.5 mmol) was then added dropwise, and the reaction mixture was stirred for 30 min. Benzaldehyde (0.67 mL, 6.6 mmol) was added dropwise, and the reaction mixture was stirred for an additional 30 min at −45 °C and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **14** (0.65 g, 79% yield).

*3,3-Dimethyl-1-phenylbutan-1-ol (**26**).* A 25 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.25 g, 9.0 mmol). The lithium was washed three times with hexanes (5 mL) and once with THF (5 mL) under argon. The lithium was cooled to −45 °C, and THF (5 mL) was added. Neopentyl chloride, **23** (0.50 mL, 4.1 mmol) was then added dropwise, and the reaction mixture was stirred for 30 min. Benzaldehyde (0.50 mL, 4.9 mmol) was added dropwise, and the reaction mixture was stirred for an additional 30 min at −45 °C and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **26** (0.72 g, 99% yield) as a light-yellow oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.32−7.31 (m, 4H), 7.28−7.22 (m, 1H), 4.78 (d, J = 5.2 Hz, 1H), 1.88 (br, 1H), 1.73 (dd, J = 8.4, 6 Hz, 1H), 1.58 (dd, J = 11.2, 3.4 Hz, 1H), 0.98 (s, 9H); ^{13}CNMR ($CDCl_3$) δ (ppm): 146.4, 128.4, 127.2, 125.7, 72.4, 52.8, 30.4, 30.1. These NMR data compare well with the literature values.[47]

*4-Ethoxy-1-phenylbut-3-en-1-ol (**29**).* A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (0.13 g, 4.8 mmol). The lithium was washed three times with hexanes (3 mL) and once with THF (3 mL) under argon. The lithium was cooled to −45 °C, and THF (3.5 mL) was added. A solution of the acrolein diethyl acetal, **27** (0.30 mL, 2.0 mmol) in THF (0.5 mL) was then added dropwise. The reaction mixture was at −45 °C stirred for 60 min, and then benzaldehyde (0.24 mL, 2.4 mmol) was added dropwise. The reaction mixture was warmed to room temperature and then was quenched with water in an ice-water bath. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **29** (0.26 g, 68% yield, Z/E ≈ 7:1) as a light-yellow oil. *E*- and *Z*-isomers could not be separated. The following data concern the mixture of these two compounds: IR (thin film) 3429, 3031, 2977, 2925, 1664, 1494, 1453, 1382, 1305, 1247, 1192, 1040, 984, 759, 701 cm^{-1}; TOF MS (EI$^+$) calcd for $C_{12}H_{15}O_2$ 191.1072; found 191.1057.

Z-Isomer: ^{1}HNMR ($CDCl_3$) δ (ppm): 7.38−7.30 (m, 5H), 6.08 (d, J = 6.3 Hz, 1H), 4.72 (dd, J = 5.1, 2.4 Hz, 1H), 4.38 (dd, J = 7.2, 6.6 Hz, 1H), 3.78 (q, J = 7.0 Hz, 2H), 2.62−2.50 (m, 2H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}CNMR ($CDCl_3$) δ (ppm): 146.6, 144.2, 127.9, 126.9, 125.7, 101.6, 73.7, 67.5, 33.9, 15.0.

E-Isomer: ^{1}HNMR ($CDCl_3$) δ (ppm): 7.38−7.30 (m, 5H), 6.30 (d, J = 12.6 Hz, 1H), 4.61 (dd, J = 5.1, 2.4 Hz, 1H), 4.38 (dd, J = 7.2, 6.6 Hz, 1H), 3.69 (q, J = 7.0 Hz, 2H), 2.47−2.27 (m, 2H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}CNMR ($CDCl_3$) δ (ppm): 148.4, 144.9, 128.0, 127.1, 125.7, 98.8, 73.7, 64.5, 37.8, 14.5.

*2-(2-Methylphenyl)ethanol (**32**).* A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled (see Table 9), and THF (1.5 mL) was added. A solution of isochroman, **30**, (0.13 g, 1.0 mmol) in THF (0.5 mL) was then added dropwise. The reaction mixture was stirred for the allotted amount of time and then was quenched with water. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **32** as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.14 (m, 4H), 3.80 (t, J = 7.0 Hz, 2H), 2.88 (t, J = 6.8 Hz, 2H), 2.32 (s, 3H), 1.79 (br, 1H); ^{13}CNMR ($CDCl_3$) δ (ppm): 136.5, 136.5, 130.4, 129.7, 126.6, 126.0, 62.6, 36.4, 19.5. These NMR data compare well with the literature values.[37]

*2-(2-Deuteriomethylphenyl)ethanol (**33**).* A 10 mL round-bottom flask was charged with 25 wt% lithium dispersion in mineral oil (67 mg, 2.4 mmol). The lithium was washed three times with hexanes (2 mL) and once with THF (2 mL) under argon. The lithium was cooled to 0 °C, and THF (1.5 mL) was added. A solution of isochroman, **30**, (0.13 g, 1.0 mmol) in THF (0.5 mL) was then added dropwise. The reaction mixture was stirred for 30 min and then was quenched with D_2O. The product was extracted with diethyl ether, and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography on silica gel (EtOAc/hexanes) afforded **33** as a colorless oil. ^{1}HNMR ($CDCl_3$) δ (ppm): 7.20 (m, 4H), 3.85 (t, J = 6.8 Hz, 2H), 2.93 (t, J = 6.8 Hz, 2H), 2.37 (d, J = 5.2 Hz, 2H), 2.05 (br, 1H); ^{13}CNMR ($CDCl_3$) δ (ppm): 136.4, 130.3, 129.5, 126.5, 126.0, 62.5, 36.3, 19.1 (t, J = 19.5 Hz). These NMR data compare well with the literature values.[37]

Computational Details (Tables 5−7). The DFT calculations were carried out using the spin-polarized, gradient-corrected density functional PBE as implemented in CP2K/Quickstep.[30] A double-ζ DZVP Gaussian basis set[30c] was employed, and an auxiliary plane wave basis of 400 Ry energy cutoff was used to expend the densities. The core electrons are represented by analytic Goedecker−Teter−Hutter pseudopotentials[30d,e] with 1, 3, 4, and 6 valence electrons for H, Li, C, and S (or O), respectively. The Γ-point approximation was employed for Brillouin zone integration. Li(110) was chosen as the Li metal surface, because it is the most stable among low index crystal planes.[48] Previous DFT calculations indicated Li(100), Li(110), and Li(111) surfaces behave the same in the adsorption with an ionic-liquid crystal.[49] The Li(110) surface was modeled using a five-layer slab, with a $p(5 \times 5)$ unit cell in the lateral directions and a vacuum of 15 Å between slabs. The upper three layers were allowed to relax, and the atoms in the bottom two layers were fixed at the bulk positions. Isolated gas-phase molecules were optimized in a (20 × 20 × 20 Å) unit cell.

We have performed test calculations to evaluate whether using dispersion correction will affect the computed bond dissociation energies. The C−S bond dissociation energies of alkyl phenyl sulfide substrates **3** and **10** in gas phase (ΔE_{gas}) and on the lithium surface (ΔE_{Li}) were computed using the DFT-D3 dispersion corrections (see Supporting Information).[50] The computed dissociation energies on lithium surface are very similar using the two different methods. This suggests dispersion interactions have small effects on the exothermicity of the C−S bond cleavage.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01136.

Spectral characterization data and computational details (PDF)

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Notes

The authors declare no competing financial interest.

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