Cumyl Phenyl Sulfide Forms Bicumyl Instead of Cumyllithium Upon Reductive Lithiation. Thiophenoxide as a Leaving Group in Nucleophilic Substitution by SET

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Abstract: Upon reduction with aromatic radical-anions, cumyl phenyl sulfide (1_S) yields mainly bicumyl (2) rather than the expected cumyllithium (3), despite a literature report, herein revealed to be in error, that anion 3 is produced. Related examples from the literature are compiled. A suggested mechanism involves a single electron transfer from the generated cumyllithium (3) to the cumyl phenyl sulfide (1_S) leading to thiophenoxide anion and two cumyl radicals, which mainly couple in a solvent cage. Such a thiophenoxide displacement by anion 3 has been demonstrated experimentally. Para *tert*-butyl groups, either on the phenyl or cumyl ring, increase the ratio of the cumyllithium to the bicumyl, presumably by sterically inhibiting the pi complexation thought to be necessary for electron transfer. © 1997 Elsevier Science Ltd.

INTRODUCTION

In this paper, we present our own results and tie together a number of isolated but obviously related literature reports concerning mostly failed attempts to prepare cumyllithium (3) and closely related benzyllithiums.

We and others have demonstrated in a multitude of cases that reductive lithiation of alkyl phenyl sulfides with aromatic radical-anions is an extremely general and useful method of producing alkyllithiums.[1,2,3] Furthermore, there is an excellent correlation between the ease of the reaction and the stability of the corresponding alkyl radical which is believed to be an intermediate produced in the rate-determining step.[1,4] We were therefore surprised that our attempt to prepare anion 3 by reductive lithiation of cumyl phenyl sulfide (1_S) with the aromatic radical-anions lithium 4,4'-di-*tert*-butylbiphenylide (LDBB),[5] naphthalenide (LN), or 1-(dimethylamino)naphthalenide (LDMAN)[1] failed to give usable yields, producing instead bicumyl (2) in good yield. Our result was particularly confusing because this very reductive lithiation was reported to be successful in one of the earliest reports of this method of generation of organolithiums.[3] It has now been found that this report was in error and that bicumyl was the actual product.[6,7] When our work, described below, was nearly complete, we discovered a paper that describes a similar result during an attempt to prepare 1-phenylcyclohexyllithium.[8] A very recent paper reports that an attempt to generate 3 by reductive lithiation of cumyl phenyl selenide (1_{Se}), using lithium naphthalenide, also failed, producing mainly 2 instead.[9] Finally, in a very revealing paper, Clarembeau and Krief reported that bicumyl (2) also results from attempts to prepare cumyllithium (3) by the reaction of selenide (1_{Se}) with *n*-butyllithium.[10]
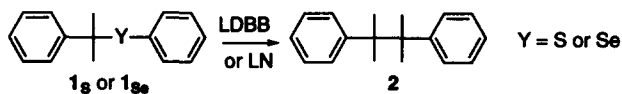
In a conceivable mechanism for the cumyl couplings observed during the reductive lithiations, the resonance stabilized, and therefore long-lived, cumyl radical intermediate (5) is able to resist accepting an electron from the radical-anion reducing agent long enough to couple with an identical radical. However, this mechanism is rendered questionable not only because it requires an encounter of radicals that are reduced to anions, probably with extreme rapidity,[11,12] by aromatic radical anion reducing agents but by the coupling that occurs upon treatment of cumyl phenyl selenide with butyllithium,[10] a reaction that is unlikely to involve radical intermediates.[13] Furthermore, benzyl halides, as well as other alkyl halides often yield similar coupling products upon treatment with aromatic radical-anions, including lithium naphthalenide,[14] and there is extensive evidence that the coupling products are not generated by coupling of the radicals generated during the reduction with the aromatic radical-anion.[11,15] These couplings have been shown to occur by the displacement of halide ion from the substrate by the carbanion that is the reduction product of the intermediate radical.

It is likely that the explanation for the couplings that are observed in the reductive lithiations of sulfide 1_S and selenide 1_{Se} and in the selenium-lithium exchange is that the anion 3 that is produced in all of these processes is capable of executing a displacement of the thiophenoxide group of the substrate. Given the extreme steric crowding in the vicinity of the carbon atom undergoing the exchange of groups, the mechanism of this displacement clearly can not be S_N2. There has been extensive study of a class of displacements of halide ions at saturated carbon atoms by carbanions that are thought to proceed in a stepwise manner by single electron transfer (SET) from the anion to the alkyl halide.[16,17] This process results in the conversion of the anion to a radical and, upon acquisition of the electron, the alkyl halide either forms a radical-anion or decomposes in a concerted manner to another radical and a halide ion (dissociative electron transfer).[16b] If the new radical-anion decomposes to a radical and a halide ion before the original radical can diffuse away from it or if the electron transfer is dissociative, the two radicals are formed in a solvent cage and can combine to form the product (radical pair mechanism). This pathway appears to be a major mechanism in the Wurtz-type coupling reactions between organolithiums and certain alkyl halides.[18] If, on the other hand, the two radicals are not produced in a cage, they are often capable of reacting with the carbanion at an extremely high rate (thought to approach the diffusion controlled limit),[19] to produce a delocalized radical-anion. The latter yields product when it donates an electron to the alkyl halide substrate ($S_{RN}1$ chain mechanism[20]).

If thiophenoxide ion could behave as a leaving group in such a SET reaction, Scheme 1 (radical pair mechanism) and/or Scheme 2 (chain mechanism) could account for the results.[21] It is thus suggested that electron transfer to sulfide 1_S occurs competitively from cumyllithium (3) and from the aromatic radical-anion reducing agent. The greater the ratio of reducing agent to the sulfide substrate the greater the yield ratio of organolithium to coupling product is expected; this is just what was observed in the attempted preparation of 1-phenylcyclohexyllithium by reductive lithiation.[8] Analogous sequences could also account for the bicumyl (2) generated in the reactions of selenide 1_{Se} with aromatic-radical anions[9] and with butyllithium.[10] There is indeed at least one case of thiophenoxide as a leaving group in a SET reaction; it was observed in the reaction of carbonyl-stabilized anions with p-nitrocumyl phenyl sulfide.[22] In the latter cases, the anion is a weak electron

donor and the *p*-nitrocumyl group is a strong electron acceptor. On the other hand, in Schemes 1 and 2, the anion is a powerful electron donor and the cumyl phenyl sulfide (1_S) is a weak electron acceptor.
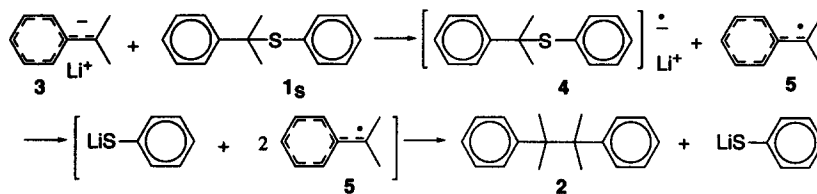
Scheme 1
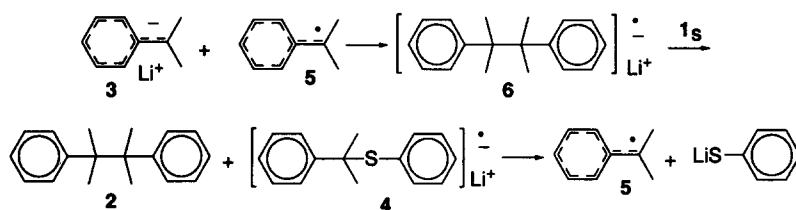
Scheme 2

As implied above, the intermediate **4** is not obligatory since the electron transfer could be a dissociative process as it is in the case of many alkyl halides.[16b] Electrochemical studies on benzyl phenyl sulfides indicate that the corresponding radical-anions are extremely short-lived intermediates.[4] The two extra methyl groups present in **4** would be expected to destabilize the radical-anion **4** and to stabilize the radical **5** so that it is likely that either **4** is not generated as an intermediate or that if it is, it fragments with great rapidity to lithium thiophenoxide and **5**. This is just the situation that favors the production of radical pairs in a solvent cage as the proximate products of the SET process such as that shown in Scheme 1.[23]

The geminate nature of the coupling in the radical pair shown is Scheme 1 would assure that during the reductive lithiation, competition from reduction of the cumyl radicals **5** by the radical-anion reducing agent would be insignificant. However, radical-pair separation as well as any portion of a SET process that does involve the radical-anion **4** as a discrete intermediate would produce free cumyl radicals (**5**) capable of such reduction or of combining with the anion **3** to produce the radical anion **6** of bicumyl (**2**) and thus to initiate the chain process. The chain mechanism in Scheme 2, which is closely analogous to the $S_{RN}1$ mechanism,[20] is the explanation given for the coupling observed in the attempted generation of 1-phenylcyclohexyllithium from 1-phenylcyclohexyl phenyl sulfide.[8]
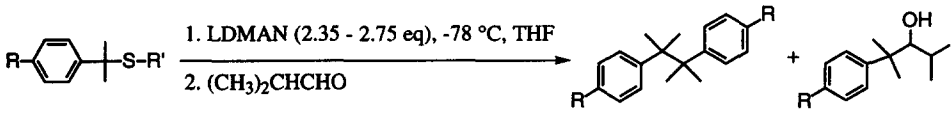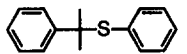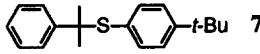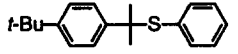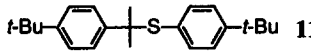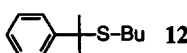
It seems likely that the main route to the couplings occurs according to Scheme 1 since, as discussed above, the lifetime of the radical-anion **4** should be negligible. Our working hypothesis was that the reason that such coupling occurs in the case of sulfide 1_S and selenide 1_{Se} and very few other cases[24] is that the cumyllithium (**3**) is an effective electron donor to the substrate because it can transfer an electron while undergoing pi-pi interaction with either of the rings of the substrate.[25,26] Whereas steric hindrance has been used to inhibit concerted S_N2 reactions in order to favor single electron transfer (SET) induced nucleophilic

substitutions,[16a] we now reveal experiments in which the SET mechanism itself is apparently inhibited by steric congestion, albeit at a site remote from the position of the substitution. The para *tert*-butyl group was used in each ring of cumyl phenyl sulfide as a group expected to decrease pi complexation, and therefore electron transfer, due to steric hindrance, as well as to serve as a labeling group. There are some literature reports of diminished pi complex constants due to steric hindrance.[27] The decrease in electron transfer was expected to manifest itself as an increase in the ratio of production of the cumyllithium to that of the bicumyl .

RESULTS AND DISCUSSION

The yields of the bicumyls **2** and **9** and of the alcohols **6** and **10**, resulting from the reaction of isobutyraldehyde with the anions, generated from the reductive lithiation of sulfide **1s** and its analogues, **7, 8,** and **11**, substituted at the para position of each and both rings with *tert*-butyl groups, are shown in Table 1. The overwhelming product from unsubstituted cumyl phenyl sulfide (**1s**) is bicumyl (**2**). A *tert*-butyl group on the phenyl ring attached to sulfur increases the ratio of production of cumyllithium (**3**) to that of bicumyl (**2**) by a factor of 2. When the bulky substituent is placed instead on the cumyl ring, anion **14** becomes the major product, the yield ratio having increased by a factor of 10 compared to that from sulfide **1s**. When *tert*-butyl groups are placed on both rings, the bicumyl **9** becomes a minor product. Finally, when cumyl *n*-butyl sulfide (**12**) is used, a good yield of anion **3** and only a very minor amount of **2** is generated.

Table 1. Yields of Bicumyls and Trapping Products of Cumyllithiums with Isobutyraldehyde in the Reductive Lithiation of Substituted and Unsubstituted Cumyl Phenyl Sulfides with LDMAN

1s	**2** R = H 74%	**6** R = H 13%
7	**2** R = H 70%	**6** R = H 22%
8	**9** R = *t*-Bu 29%	**10** R = *t*-Bu 50%
11	**9** R = *t*-Bu 19%	**10** R = *t*-Bu 66%
12	**2** R = H 7%	**6** R = H 76%

The fact that substitution of a *tert*-butyl group on the phenyl ring attached to sulfur increases the ratio of cumyllithium (**3**) to bicumyl (**2**) produced makes it appear likely that at least some of the electron transfer from the carbanion to the substrate occurs in a complex between the cumyl anion and the phenyl ring attached to sulfur. There should be modest steric hindrance to such electron transfer due to the *tert*-butyl group on the

phenylthio ring. It is not surprising that the experiment in which the *p-tert*-butyl group is on the cumyl ring causes a far larger effect, which is attributed to the considerable steric hindrance that the *p-tert*-butylcumyllithium (**14**) would encounter in pi complexing with an aromatic ring of the substrate due to the large groups at the 1 and 4 positions. Assuming, as above, that some of the electron transfer occurs when the cumyl group pi complexes with the phenylthio group, one would expect the greatest effect when both rings are substituted with *tert*-butyl groups since both aromatic rings in the pi-complex are appended to large substituents; this is precisely what is observed.

The minor amount of coupling that is observed when the aryl group attached to the sulfur atom is replaced by an alkyl group (**12**; last entry in Table 1) is consistent with a significant degree of electron transfer occurring in a pi-complex between the anion and the phenyl group attached to sulfur. However, an equally plausible explanation is that the radical anion (analogous to **4**), generated when sulfide **12** receives an electron from anion **3**, has a significantly longer lifetime than **4**, due to its poorer leaving group. As a result, the two cumyl radicals (**5**) would not be produced in a solvent cage and each would be converted to anions by reduction from the radical-anion reducing agent LDMAN. Krief[9] found a similar phenomenon upon reductive lithiation of 1-phenylethyl phenyl selenide and 1-phenylethyl methyl selenide; the former gave substantial coupling while the latter gave mainly organolithium.

It is asserted above that the main route to bicumyl (**2**) is the geminate recombination pathway shown in Scheme 1. The results in Table 1 provide some evidence that the radical chain mechanism (Scheme 2) is not the main route to bicumyl **2** during the reductive lithiation.[28] The finding that a substituent on the phenylthio ring influences the ratio of reduction to coupling (compare the behavior of **1s** and **7** in Table 1) upon treatment with a radical-anion reducing agent is incompatible with a competition between reduction of the radical **5** by aromatic radical-anion LDMAN and attack of that radical on cumyllithium **3** (Scheme 2) because the leaving group is no longer present at the time that this competition is manifested.

Having in hand a high-yield method of generating cumyllithium (**3**), we were now able to test a key concept of our hypothesis, namely that **3** is able to react with cumyl phenyl sulfide (**1s**) to produce bicumyl (**2**). The anion **3** was generated from cumyl *n*-butyl sulfide (**12**) by reductive lithiation with LDMAN as in Table 1. We chose to use *p-tert*-butylcumyl phenyl sulfide (**8**) as the target of attack of **3** in order to be able to differentiate the bicumyl type product **13** arising by the displacement reaction from the small amount of **2** produced in the reductive lithiation experiment in which the anion **3** is generated (Table 1, last entry).

$$(1)$$
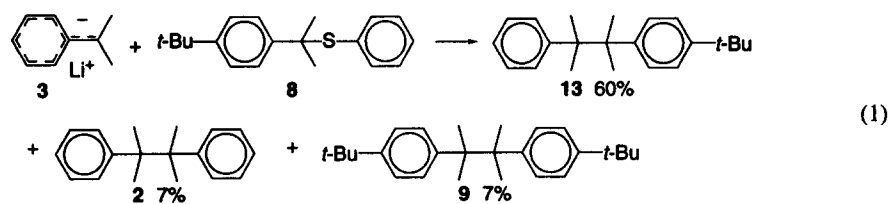
A smooth displacement did indeed occur producing mainly (60% yield) the mixed bicumyl **13** (eq 1). Only very small amounts of bicumyl (**2**) and the symmetrically substituted bicumyl **9** were produced.[29a] The ratio of **13**:**2**:**9** was 9:2:1; however, it can be calculated that one half of bicumyl (**2**) was generated in the original reductive lithiation of sulfide **12**, so that the ratio of bicumyls produced in the displacement reaction

shown in eq 1 is 9:1:1. Thus the postulated displacement is indeed capable of occurring. It is not surprising that equal amounts of **2** and **9** are produced since that is required by the stoichiometry in view of the equal quantities of cumyl and *p-tert*-butylcumyl groups that are introduced into the reaction mixture.

The production of a small amount of 4,4'-di-*tert*-butylbicumyl (**9**) in the reaction of cumyllithium (**3**) with *p-tert*-butylcumyl phenyl sulfide (**8**) must mean that radicals that escape from the solvent cage are not only capable of forming a C-C bond upon reaction with the anion as in Scheme 2 but, during an encounter with the same anion, an electron transfer can also occur (eq 2).[29b,30] It would not be surprising if electron transfer were faster than bond formation, which occurs at the exceedingly crowded benzylic positions, since the electron transfer can presumably occur via pi-stacking. This electron transfer, of course, would only be discernible if some **14** and **5** were successful in escaping from each other before they establish a C-C bond. It is difficult to gauge the relative rate of such escape compared to that of bond formation.

$$\text{(2)}$$
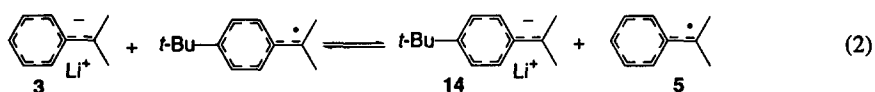
An interesting observation, which provides some evidence for the effect of steric hindrance on charge transfer interactions in aromatic systems, was made during the separation of **13, 2,** and **9**. The separation method was charge transfer chromatography using caffeine absorbed on silica gel.[31] The order of elution was **9, 13, 2,** just that expected if *tert*-butyl groups hinder pi-pi interactions. This order lends some credence to the hypothesis that *tert*-butyl groups hinder electron transfer from benzylic type anions to neutral aryl groups.

CONCLUSIONS

Contrary to a literature report, revealed herein to be in error, cumyl phenyl sulfide (**1S**) does not undergo reductive lithiation by aromatic radical anions to generate cumyllithium (**3**) under the usual conditions but instead it is converted mainly to bicumyl (**2**). This finding correlates well with a number of isolated literature reports which are shown to be related for the first time in the present report. An explanation that fits all of the facts is that anion **3**, produced in the reductive lithiation, is capable of efficiently displacing the thiophenoxide anion from sulfide **1S** in competition with the reductive lithiation. It appears likely that this process involves a single electron transfer from anion **3** to the sulfide **1S** leading mainly to a radical cage combination of the two cumyl radicals (**5**). The displacement process has been demonstrated by treating *p-tert*-butylcumyl phenyl sulfide (**8**) with anion **3** produced by reductive lithiation of cumyl *n*-butyl sulfide (**12**). A minor pathway in this displacement involves non-cage reactions between cumyl radicals and anions resulting either in electron transfer and/or in the production of a radical-anion adduct. An unusual aspect of the work is that steric hindrance in the form of *tert*-butyl groups retards the displacement reaction presumably by destabilizing the charge transfer complexes between anion **14** and the sulfides **8** and **11**. This work illustrates an advantage of using the thiophenoxide group as the leaving group in SET studies rather than halides, which are nearly always used, namely the ability to modify the leaving group for labeling or reactivity studies.

EXPERIMENTAL

All reactions were performed under an atmosphere of prepurified argon. A dry ice / acetone bath was used to obtain a temperature of -78 °C, and an ice bath was used to obtain 0 °C. Tetrahydrofuran (THF) was distilled over sodium benzophenone ketyl. ^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ on either a Bruker WH-300 or a Bruker AF-300 spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. Chemical shifts are reported in ppm relative to tetramethylsilane as $\delta = 0$ for ^{1}H NMR spectra or residual CHCl$_3$ as $\delta = 77.09$ for ^{13}C NMR spectra. Infrared spectra were recorded on an IR/32 FT-IR spectrometer and are reported in wave numbers (cm^{-1}). High resolution or CI mass spectra were recorded on a CH-5 double focusing Varian Mat mass spectrometer or on a VG 70-G mass spectrometer. Elemental analyses were conducted at Atlantic Microlabs, Norcross, GA. Silica gel 60 (40-60 μm, E. Merck) was used for flash column chromatography. Thin-layer chromatography was performed on glass supported 250 μm silica gel GF plates (Analtech). Visualization of TLC plates was accomplished with one or more of the following: 254 nm UV light; 7% phosphomolybdic acid in ethanol; 5% p-anisaldehyde in ethanol containing 5% sulfuric acid and a trace amount of acetic acid. Gas liquid chromatographic mass spectral (GC/MS) analyses were performed on a Hewlett Packard 5890 Series II gas chromatograph equipped with a 5970 mass selective detector.

2-Phenyl-2-(phenylsulfanyl)propane (1$_S$) was prepared according to the procedure of Guindon et al.[32] The general procedure is given in the description of the preparation of **7** below. The spectroscopic properties were identical to those reported.

2-(4-*tert*-Butyl-phenyl)-2-propanol (15) was synthesized from methyl 4-*tert*-butylbenzoate and methyl magnesium bromide by a procedure similar to that of Arnold et al.[33] The spectroscopic properties were identical to those reported.

2-Phenyl-2-(4-*tert*-butyl-phenylsulfanyl)propane (7). General Procedure for Preparation of 1$_S$, 7, 8, 11 and 12. To a solution of 2-phenyl-2-propanol (16) (3.0 g, 22 mmol) in 1,2-dichloroethane (30 mL) was added dry ZnI$_2$ (3.51 g, 11.0 mmol) and 4-*tert*-butyl-benzenethiol (4.38 g, 26.4 mmol). The mixture was stirred for 1 h at room temperature and diluted with methylene chloride (75 mL) and water (40 mL). The organic layer was washed with 1 N NaOH to remove excess benzenethiol (bleach test). The organic layer was dried over Na$_2$SO$_4$ and the solvent was removed by rotary evaporation. The crude product was purified by column chromatography over silica gel. Elution with 1% EtOAc / hexanes yielded sulfide **7** (5.2 g, 83%) as a white solid. IR (film) 3182, 2942, 1588, 1480, 1356, 1238, 1194, 1022, 762 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.4 (d, J = 7.6 Hz, 2H), 7.31 - 7.16 (m, 5H), 7.1 (d, J = 8.3 Hz, 2H), 1.68 (s, 6H), 1.27 (s, 9H); ^{13}C NMR (CDCl$_3$) δ 151.8, 146.6, 136.3, 129.5, 127.9, 126.6, 125.4, 50.9, 34.6, 31.3, 29.8. HRMS (EI) calcd for C$_{19}$H$_{24}$S (M$^+$) 284.1599, found 284.1589.

2-(4-*tert*-Butyl-phenyl)-2-(phenylsulfanyl)propane (8). According to the general procedure, 2-(4-*tert*-butyl-phenyl)-2-propanol (15) (2.0 g, 10 mmol) in 1,2-dichloroethane (22 mL) was treated with dry ZnI$_2$ (1.66 g, 5.20 mmol) and benzenethiol (1.3 mL, 13 mmol) and the product was purified by column chromatography over silica gel. Elution with 1% EtOAc / hexanes yielded sulfide **8** (2.8 g, 95%) as a colorless oil. IR (film) 3033, 2936, 1454, 1356, 1079, 1008, 824 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.36 - 7.23 (m, 5H), 7.18 - 7.15 (m, 4H), 1.67 (s, 6H), 1.31 (s, 9H); ^{13}C NMR (CDCl$_3$) δ 149.5, 143.2, 136.7, 133.1,

128.5, 128.2, 126.2, 124.8, 50.9, 34.4, 31.4, 29.7; HRMS (EI) calcd for $C_{19}H_{24}S$ (M$^+$) 284.1599, found 284.1609.

2-(4-*tert*-Butyl-phenyl)-2-(4-*tert*-butyl-phenylsulfanyl)propane (11). According to the general procedure 2-(4-*tert*-butyl-phenyl)-2-propanol (15) (1.5 g, 7.8 mmol) in 1,2-dichloroethane (20 mL) was treated with dry ZnI_2 (1.24 g, 3.88 mmol) and 4-*tert*-butyl-benzenethiol (1.6 g, 9.6 mmol) and the product was purified by column chromatography over silica gel. Elution with 1% EtOAc / hexanes yielded sulfide 11 (2.3 g, 87%) as a white solid. IR (film) 3050, 2923, 1584, 1453, 1354, 1261, 1103, 1080, 828 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.37 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.2 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 1.67 (s, 6H), 1.32 (s, 9H), 1.28 (s, 9H); ^{13}C NMR (CDCl$_3$) δ 151.6, 149.3, 143.3, 136.4, 129.8, 126.2, 125.3, 124.8, 50.6, 34.6, 34.4, 31.4, 31.3, 29.8; HRMS (EI) calcd for $C_{23}H_{32}S$ (M$^+$) 340.2225, found, 340.2236.

2-Phenyl-2-(butylsulfanyl)propane (12). According to the general procedure 2-phenyl-2-propanol (16) (3.0 g, 22 mmol) in 1,2-dichloroethane (30 mL) was treated with dry ZnI_2 (3.5 g, 11 mmol) and butanethiol (2.9 ml, 27 mmol) and the product was purified by column chromatography over silica gel. Elution with 1% EtOAc / hexanes yielded sulfide 12 (4.3 g, 94%) as a colorless oil. IR (film) 3066, 2946, 1533, 1462, 1127, 1092, 1024, 764 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ 7.53 (d, *J* = 7.9 Hz, 2H), 7.31 (dd, *J* = 7.2 Hz, 7.9 Hz, 2H), 7.19 (m, 1H), 2.2 (t, *J* = 7.2 Hz, 2H), 1.43 - 1.21 (m, 4H), 1.7 (s, 6H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 146.8, 128, 126.5, 126.3, 47.3, 31.25, 30.3, 29.1, 22.2, 13.7. HRMS (EI) calcd for $C_{13}H_{20}S$ (M$^+$) 208.1286, found, 208.1288.

Reductive Lithiation of 2-Phenyl-2-(phenylsulfanyl)propane (1$_S$). General Procedure for Reductive Lithiation of 1$_S$, 7, 8, 11 and 12. To a solution of LDMAN,[34] prepared from lithium ribbon (40.6 mg, 5.85 mmol) and *N,N*-dimethyl-1-naphthylamine (DMAN) (900 μL, 5.48 mmol), in THF (9 mL) was added at -78 °C a solution of 1$_S$ (534 mg, 2.34 mmol) in THF (5 mL) via cannula. The dark red solution was stirred at -78 °C for 10 min and isobutyraldehyde (315 μL, 3.47 mmol) was added dropwise. The reaction mixture was warmed to 0 °C over 1.5 h and quenched with water (1 mL). The organic layer was diluted with ether (60 mL), and washed successively with 10% HCl (2 x 25 mL) (to remove DMAN), water (15 mL), 1 N NaOH (20 mL) and brine. The organic layer was dried over $MgSO_4$ and the solvent was removed by rotary evaporation. The crude product was purified by column chromatography over silica gel. Elution with 1% EtOAc / hexanes yielded bicumyl 2 (205 mg, 74%) as a white solid. Further elution with 3% EtOAc / hexanes yielded alcohol 6 (60.5 mg, 13%) as a colorless oil. **2,3-Dimethyl-2,3-diphenylbutane (2)** ^{1}H NMR (CDCl$_3$) δ 7.22 - 7.12 (m, 6H), 7.1 - 7.02 (m, 4H), 1.31 (s, 12H); ^{13}C NMR (CDCl$_3$) δ 146.9, 128.7, 126.7, 125.5, 43.7, 25.3; the spectrum is identical to that reported.[35] **2,4-Dimethyl-2-phenyl-3-pentanol (6)** IR (film) 3478, 2946, 1489, 1381, 1017, 968, 760, 696 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.40 (d, *J* = 7.9 Hz, 2H), 7.32 (dd, *J* = 7.4 Hz, 7.9 Hz, 2H), 7.20 (m, 1H), 3.50 (d, *J* = 2.85 Hz, 1H), 1.78 (m, 1H), 1.36 (s, 6H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.70 (d, *J* = 6.75 Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 147.6, 128.2, 126.5, 126, 83.5, 43.2, 29.05, 25.75, 24.4, 23.6, 17.0; Anal. Calcd for $C_{10}H_{13}O$: C, 81.20; H, 10.48. Found: C, 81.12; H, 10.39.

Reductive Lithiation of 2-Phenyl-2-(4-*tert*-butyl-phenylsulfanyl)propane (7). The general procedure was used. The solution of LDMAN was prepared from lithium ribbon (38 mg, 5.5 mmol)

and DMAN (855 μL, 5.20 mmol); the other reactants were **7** (620 mg, 2.18 mmol) and isobutyraldehyde (238 μL, 2.62 mmol). The product was purified by column chromatography on silica gel. Elution with 1% EtOAc / hexanes yielded bicumyl **2** (182 mg, 70%) as a white solid. Further elution with 3% EtOAc / hexanes yielded alcohol **6** (92 mg, 22%) as a colorless oil.

Reductive Lithiation of 2-(4-*tert*-Butyl-phenyl)-2-(phenylsulfanyl)propane (8). The general procedure was used. The solution of LDMAN was prepared from lithium ribbon (37.5 mg, 5.40 mmol) and DMAN (835 μL, 5.08 mmol); the other reactants were **8** (613 mg, 2.16 mmol) and isobutyraldehyde (231 μL, 2.54 mmol). The product was purified by column chromatography on silica gel. Elution with 1% EtOAc / hexanes yielded bicumyl **9** (108 mg, 29%) as a white solid. Further elution with 3% EtOAc / hexanes yielded alcohol **10** (270 mg, 50%) as a colorless oil. **2,3-Bis-(4-*tert*-butyl-phenyl)-2,3-dimethylbutane (9)** ^{1}H NMR (CDCl$_3$) δ 7.18 (d, J = 8.5 Hz, 4H), 7.02 (d, J = 8.4 Hz, 4H), 1.31 (s, 18H), 1.28 (s, 12H); ^{13}C NMR (CDCl$_3$) δ 148.1, 143.9, 128.2, 123.5, 43.3, 34.25, 31.5, 25.2; CI MS using ammonia: C$_{26}$H$_{42}$N (M+NH$_4$)$^+$ = 368; the spectrum is identical to that reported.[36] **2-(4-*tert*-Butyl-phenyl)-2,4-dimethyl-3-pentanol (10)** IR (film) 3476, 2944, 1503, 1454.5, 1383, 1194, 1117, 1049, 968 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.31 (br s, 4H), 3.46 (d, J = 1.8 Hz, 1H), 1.83 (m, 1H), 1.35 (s, 6H), 1.31 (s, 9H), 0.88 (d, J = 6.9 Hz, 3H), 0.72 (d, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 148.8, 144.5, 126.2, 125.1, 83.6, 42.8, 34.3, 31.4, 28.95, 25.2, 24.8, 23.8, 17.0; Anal. Calcd for C$_{17}$H$_{28}$O: C, 82.20; H, 11.36. Found: C, 82.28; H, 11.34.

Reductive Lithiation of 2-(4-*tert*-Butyl-phenyl)-2-(4-*tert*-butyl-phenylsulfanyl)-propane (11). The general procedure was used. The solution of LDMAN was prepared from lithium ribbon (39 mg, 5.6 mmol) and DMAN (926 μL, 5.63 mmol); the other reactants were **11** (780 mg, 2.29 mmol) and isobutyraldehyde (256 μL, 2.82 mmol). The product was purified by column chromatography on silica gel. Elution with 1% EtOAc / hexanes yielded bicumyl **9** (78 mg, 19%) as a white solid. Further elution with 3% EtOAc / hexanes yielded alcohol **10** (373 mg, 66%) as a colorless oil.

Reductive Lithiation of 2-Phenyl-2-(butylsulfanyl)propane (12). The general procedure was used. The solution of LDMAN was prepared from lithium ribbon (50 mg, 7.2 mmol) and DMAN (1.2 mL, 7.3 mmol); the other reactants were **12** (550 mg, 2.64 mmol) and isobutyraldehyde (327 μL, 3.60 mmol). The product was purified by column chromatography on silica gel. Elution with 1% EtOAc / hexanes yielded bicumyl **2** (22 mg, 7%) as a white solid. Further elution with 3% EtOAc / hexanes yielded alcohol **6** (385 mg, 76%) as a colorless oil.

Reaction of Cumyllithium (3) with 2-(4-*tert*-Butyl-phenyl)-2-(phenylsulfanyl)propane (8). To a solution of LDMAN prepared by stirring lithium ribbon (18.9 mg, 2.72 mmol) and *N,N*-dimethyl-1-naphthylamine (DMAN) (404 μL, 2.46 mmol) in THF (8 mL) was added a solution of **12** (256 mg, 1.23 mmol) in THF (4 ml) at -78 °C via cannula. The resulting dark red solution was stirred for 10 min at -78 °C and a solution of **8** (349 mg, 1.23 mmol) in THF (3 ml) was cannulated into it. The mixture was stirred at -78 °C for 25 min and isobutyraldehyde (139 μL, 1.53 mmol) was added. The mixture was warmed to 0 °C over 1.5 h and the reaction was quenched with water (0.5 mL). The product was purified by column chromatography on silica gel. Elution with hexanes yielded a white solid (236 mg). GC/MS of this fraction showed the presence of a major peak corresponding to 2-(4-*tert*-butyl-phenyl)-2,3-dimethyl-3-phenylbutane (13) and smaller peaks

due to **2** and **9**. ^{1}H NMR analysis confirmed the ratio of **13, 2** and **9** to be **9:2:1**. Further elution with 1% EtOAc / hexanes yielded a (4:9) mixture of sulfides **12** and **8** (182 mg) as a colorless oil. The yield of **13** was thus calculated to be 60% based on recovered **12**. An analytically pure sample of **13** was obtained by subjecting the mixture of **2, 9** and **13** to charge transfer chromatography on silica gel containing 15% caffeine and eluting with hexanes. Compound **13** was found to elute after **9**, while **2** eluted last. **2-(4-*tert*-Butyl-phenyl)-2,3-dimethyl-3-phenylbutane (13)** ^{1}H NMR (CDCl$_3$) δ 7.22 - 7.13 (m, 5H), 7.11 - 7.06 (m, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 1.31 (s, 9H), 1.30 (s, 6H), 1.29 (s, 6H); ^{13}C NMR (CDCl$_3$) δ 148.2, 147.1, 143.7, 128.7, 128.2, 126.65, 125.4, 123.5, 43.8, 43.3, 34.3, 31.5, 25.3, 25.2; Anal. Calcd for C$_{22}$H$_{30}$: C, 89.73, H; 10.27. Found: C, 89.47; H, 10.36.

ACKNOWLEDGMENTS.

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