123811-73-4; **4e**, 79415-18-2; **4f**, 123811-74-5; **4g**, 123811-75-6; **4h**, 123811-76-7; **4i**, 89047-45-0; **5a**, 4043-87-2; BOC-**5a**, 98303-20-9; **5b**, 123878-70-6; **5c**, 123811-77-8; BOC-**5c**·DCHA, 123834-10-6; **5d**, 123878-71-7; BOC-**5d**, 123811-83-6; **5e**, 123811-78-9; BOC-**5e** (free acid), 123811-84-7; BOC-**5e**·DCHA, 123811-85-8; **5f**, 123811-79-0; **5g**, 123811-80-3; BOC-**5g**, 123811-86-9; **5h**, 123811-81-4; hexahydro-**5h**, 123811-89-2; **5i**, 123811-82-5; BOC-**5i**·DCHA, 123811-88-1.

Stereospecific Reductive Desulfurization of Vinyl Sulfoxides with *tert*-Butyllithium and an Internal Proton Source

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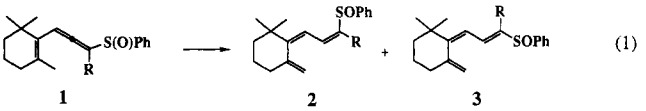
Trienyl and allenyl phenyl sulfoxides can be reduced stereospecifically with retention of configuration in good yields using *tert*-butyllithium with methanol (MeOH) as an internal (in situ) proton source. The method can be easily modified to give stereospecifically deuterium-labeled compounds. While simple monoene sulfoxides afford attenuated yields of reduced olefin, the method is useful for the reduction of the more sensitive and complex polyene sulfoxides as exemplified by the reduction of trienyl sulfoxides **2b**, **3b**, and **9** and allenyl sulfoxide **10** and by a brief review of additional examples which have emerged from this laboratory. That the reaction proceeds through the direct protonation of sulfurane intermediates such as **35** or **35'** is an attractive mechanistic hypothesis, but several other possibilities exist. A pathway involving a vinyllithium as a reactive intermediate is considered to be less likely.

Vinylallene sulfoxide **1** undergoes a facile sigmatropic [1,5]-hydrogen shift to afford triene sulfoxides **2** and **3** with the former *Z* sulfoxide predominating (eq 1).[1] The resulting triene sulfoxide necessarily has a (3*Z*)-1,3,5-hexatriene unit because of the intramolecular, cyclic nature of the process, but the ability of the phenylsulfinyl group to effect selective formation of geometric isomer **2** was unexpected. Nonetheless, this feature, in conjunction with the mild conditions required for the vinylallene variant[2] of the [1,5]-shift, was anticipated to be useful for polyene syntheses in general. The phenylsulfinyl group renders this route especially attractive because it represents a functional group which might be manipulated for further synthetic transformation. For example, if a vinyl sulfoxide could be converted stereospecifically to a vinyllithium compound, then the utility of this kind of substrate in synthesis could be greatly expanded.

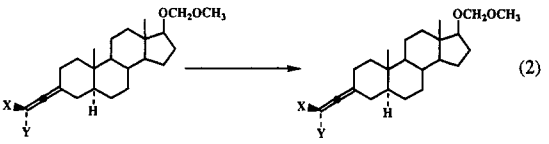


(1)

1 **2** **3**

a, R=H
b, R=CH_3

In earlier independent studies, Johnson and Durst reported the preparation of dialkyl sulfoxides, R'S(O)R, from aryl alkyl sulfoxides, ArS(O)R, by treatment with 4 equiv of the alkyllithium reagent R'Li at −78 °C.[3] It was suggested that the cleavage reaction proceeded by attack of R'Li on the sulfoxide in an S_N2-like fashion with expulsion of ArLi. Consistent with this hypothesis was the fact that essentially complete inversion of configuration at sulfur was observed (except in the case of *t*-BuLi). In a subsequent report, Neef and co-workers reported that allene sulfoxides could be desulfurized with retention of configuration in good yields with 4 equiv of CH_3Li (eq 2).[4] It was suggested that the reaction proceeded via formation of an allenyl anion, which was subsequently protonated.



(2)

4a, X = S(O)Ph; Y = CH_3
b, X = CH_3; Y = S(O)Ph

5a, X = H; Y = CH_3
b, X = CH_3; Y = H

Thus, based on these studies, it appeared feasible that formation of a vinyl anion (i.e., a vinyllithium species) could be achieved by reaction of a vinyl sulfoxide with excess RLi. In initial exploratory studies, we observed that treatment of **2b** with a variety of alkyllithium reagents in ether followed by proton quenching afforded a complex array of products and/or modest yields of triene **6a**. For example, when an ethereal solution of **2b** at −78 °C was treated with 3–4 equiv of *tert*-butyllithium in pentane followed by quenching with methanol, the hydrocarbon **6a** was obtained in only 47% yield at best. By contrast, it was serendipitously (but logically) discovered that when *tert*-butyllithium was added to an ethereal solution of **2b** containing methanol as an in situ proton source at −78 °C, the reduced hydrocarbon was obtained in significantly improved yields (72%) (eq 3). The observations that a deuterium label could be incorporated by simply employing methanol-d_1 (MeOD) as the in situ deuteron source and that an analogous transformation of **3b** to **8a** or **8b** (eq 4) render this procedure especially useful. From a mechanistic standpoint, it was particularly interesting of course that *tert*-butyllithium reacted with sulfoxide competitively with the proton source methanol. Accordingly,

(1) (a) Okamura, W. H.; Shen, G.-Y.; Tapia, R. *J. Am. Chem. Soc.* **1986**, *108*, 5018. (b) Shen, G.-Y.; Tapia, R.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 7499.

(2) Okamura, W. H. *Acc. Chem. Res.* **1983**, *16*, 81 and references therein.

(3) (a) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485. (b) Durst, T.; LeBelle, M. J.; Van den Elzen, R.; Tin, K.-C. *Can. J. Chem.* **1974**, *52*, 761.

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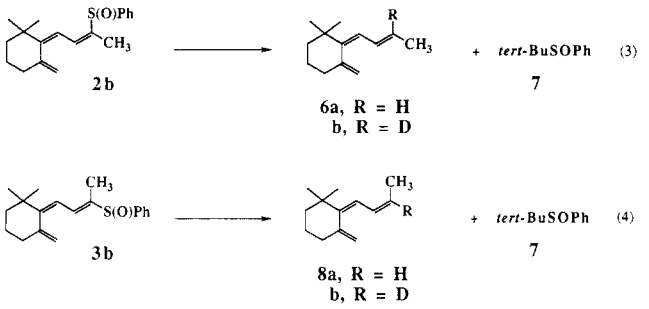
0022-3263/90/1955-0741$02.50/0

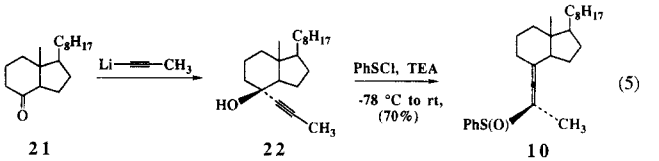


these initial findings prompted a closer examination of the process. Not only would this be useful synthetically, but there is the potential that a further study would lend insight into the mechanism of the reaction of vinyl sulfoxides with organometallic reagents. It is the purpose of this article to describe the full experimental details of the preliminary report[5] and also to report new experiments.

Results and Discussion

Preparation of Vinyl Sulfoxide Substrates. In order to better define the scope and limitations of this novel desulfurization reaction, a variety of cis and trans vinyl sulfoxides were studied (Chart I). Besides the sulfoxides **2a**, **2b**, **3a**, and **3b**, which were prepared as previously described,[1] the sulfoxides **9**, **10**,[6] and **11a–d** were also prepared. For the preparation of triene sulfoxide **9** (Scheme I), 3-heptyn-1-ol (**12**) was first isomerized with a solution of potassium aminopropylamide (KAPA) in 1-aminopropylamine (APA)[7] to afford **13**. Protection of **13** as the TBDMS (*tert*-butyldimethylsilyl) ether[8] followed by lithiation and addition of β-cyclocitral (**15**) afforded propargyl alcohol **16**. The latter was treated with *p*-chlorophenylsulfenyl chloride, and after the mixture was stirred at room temperature for a sufficient time to allow for the [2,3]- and [1,5]-sigmatropic shifts (via **17** and **18**), triene sulfoxides **19a** and **19b** (in a ratio of 10:1 by weight) were isolated.[1] The synthesis of **9** was completed by deprotection of major isomer **19a** with $(n\text{-Bu})_4NF$ followed by bromination.[9]

The allenyl sulfoxide **10** was prepared in two steps (eq 5) by addition of 1-lithiopropyne[10] to Grundmann's ketone **21**[11] to afford propargyl alcohol **22**, which was then treated with PhSCl to give the (*S*)-allene sulfoxide **10**.[6]



(5) Theobald, P. G; Okamura, W. H. *Tetrahedron Lett.* **1987**, *28*, 6565.
(6) (a) Haces, A.; van Kruchten, E. M. G. A.; Okamura, W. H. *Isr. J. Chem.* **1985**, *26*, 140. (b) See also, Haces, A.; van Kruchten, E. M. G. A.; Okamura, W. H. *Tetrahedron Lett.* **1982**, *23*, 2707.
(7) (a) Kimmel, T.; Becker, D. *J. Org. Chem.* **1984**, *49*, 2494. (b) Brown, C. A.; Yamashita, A. *J. Chem. Soc., Chem. Commun.* **1976**, 959. (c) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891. (d) Lindhoudt, J. C.; van Mourik, G. L.; Pabon, H. J. J. *Tetrahedron Lett.* **1976**, 2565. (e) Hommes, H.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1977**, *96*, 160. (f) Abrams, S. R. *Can. J. Chem.* **1984**, *62*, 1333. (g) Midland, M. M.; Halterman, R. L.; Brown, C. A.; Yamaichi, A. *Tetrahedron Lett.* **1981**, *22*, 4171.
(8) Corey, E. J.; Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190.
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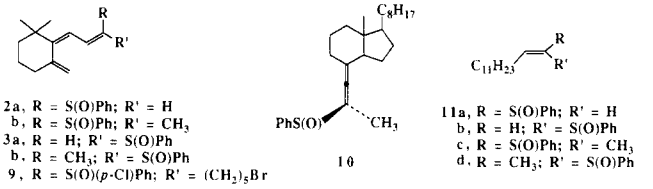
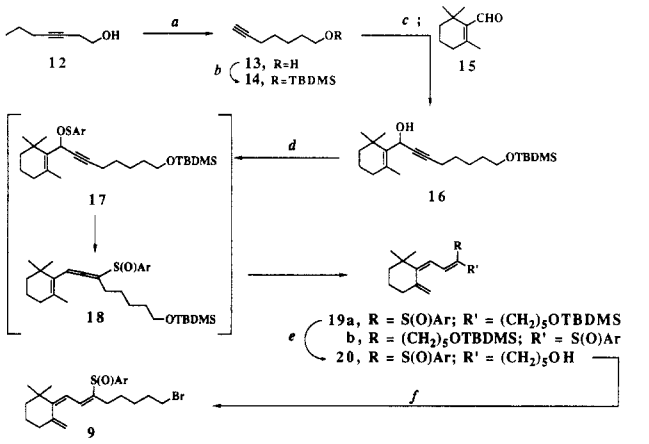
(10) Midland, M. M. *J. Org. Chem.* **1975**, *40*, 2250.
(11) (a) Condran, P., Jr.; Hammond, M. L.; Mouriño, A.; Okamura, W. H. *J. Am. Chem. Soc.* **1980**, *102*, 6259. (b) Inhoffen, H. H.; Quinkert, G.; Schutz, S.; Kampe, D.; Domagk, G. F. *Chem. Ber.* **1957**, *90*, 664.

Chart I

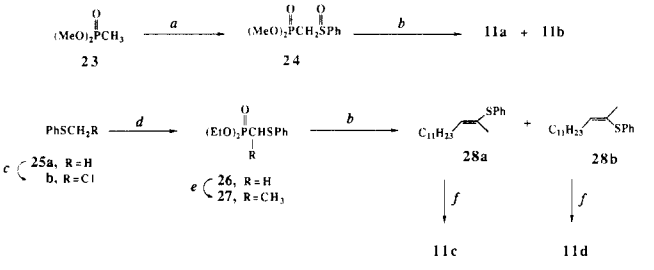


Scheme I[a]



[a] Reagents: (a) KAPA/APA (78%); (b) TBDMS-Cl, imidazole (85%); (c) *n*-BuLi and then **15** (78%); (d) *p*-ClPhSCl (ArSCl), TEA, −78 °C and then room temperature, 24 h (59%); (e) $(n\text{-Bu})_4NF$, THF (81%); (f) CBr_4, Ph_3P (85%).

Scheme II[a]



[a] Reagents: (a) *n*-BuLi; PhS(O)OMe (56%); (b) *n*-BuLi; dodecylaldehyde (93%, ~2:1 ratio of **11b** to **11a**; 70%, ~1:1 ratio of **28a** and **28b**); (c) NCS, CCl_4 (99%); (d) $(EtO)_3P$ (73%); (e) *n*-BuLi; MeI (75%); (f) MCPBA (**11c**, 98%; **11d**, 81%).

The four monoene sulfoxides **11a-d** were synthesized via Horner–Emmons–Wadsworth reaction of α-phosphoryl sulfoxides[12] or α-phosphoryl sulfides[13] with the appropriate carbonyl compound (Scheme II). For the vinyl sulfoxides **11a** and **11b**, dimethyl methylphosphonate (**23**) was lithiated followed by addition of methyl phenylsulfinate to afford sulfoxide **24**. To the lithio anion of **24** was added an excess of dodecylaldehyde to afford an isomeric mixture of (*E*)- and (*Z*)-tridecenes **11a** and **11b** (~1:2 ratio), which were then separated. For the preparation of **11c** and **11d**, *N*-chlorosuccinimide (NCS) was added to a solution of thioanisole (**25a**) in CCl_4[14] to afford **25b**, which was then reacted with triethyl phosphite to afford diethyl ((phenylthio)methyl)phosphonate (**26**). The latter was subjected to a lithiation–alkylation sequence to

(12) (a) Mikolajczyk, M.; Grzejszczak, S.; Zatorski, A. *J. Org. Chem.* **1975**, *40*, 1979. (b) Mikolajczyk, M.; Midura, W.; Grzejszczak, S.; Zatorski, A.; Chefczynska, A. *J. Org. Chem.* **1978**, *43*, 473. (c) Mikolajczyk, M.; Zatorski, A. *Synthesis* **1973**, 669.
(13) (a) Corey, E. J.; Shulman, J. I. *J. Org. Chem.* **1970**, *35*, 777. (b) Green, M. *J. Chem. Soc.* **1963**, 1324.
(14) Harada, T.; Karasawa, A.; Oku, A. *J. Org. Chem.* **1986**, *51*, 842.

Table I. Reduction of Vinyl Sulfoxides

entry	vinyl sulfoxide[a]	product(s)[b]	yield, %
1	**2b**	**6a**	72
2	**3b**	**8a**	70
3	**9**	**29**	70
4	**2a**	**30**	28
5	**3a**	**30**	19
6	**10**	**31a (31b)**	87 (**31a/31b** > 97/3)
7	**11a**	**32a**	28
8	**11b**	**32a**	57
9	**11c**	**32b (33)**	28 (29)
10	**11d**	**32c (33)**	52 (14)

[a] The structures of the substrates are shown in Chart I. [b] The product structures are shown in Chart II.

give **27**, and treatment of the α-lithio anion of **27** with dodecylaldehyde afforded an isomeric mixture of *trans*- and *cis*-vinyl sulfides **28a** and **28b**, respectively, in a ratio of ~1:1. The isomeric sulfides were separated and then oxidized separately with *m*-chloroperoxybenzoic acid (MCPBA) to the corresponding vinyl sulfoxides **11c** and **11d**.

Desulfurization of Vinyl Sulfoxides. For the reductive desulfurization of the vinyl sulfoxide substrates thus prepared, an optimized procedure as illustrated for **2b** involved the rapid addition of 4 equiv of *t*-BuLi (as a solution in pentane) to an ether solution of 1 molar equiv of vinyl sulfoxide **2b** (0.05 M) and 2.5 equiv of MeOH (or *s*-BuOH) at −78 °C. After 10 min at −78 °C, the reaction was post quenched at −78 °C by introduction of additional MeOH. After workup and chromatography, the hydrocarbon **6a** was obtained in good yields. The sulfur-containing byproduct was isolated and identified as *tert*-butyl phenyl sulfoxide (**7**).

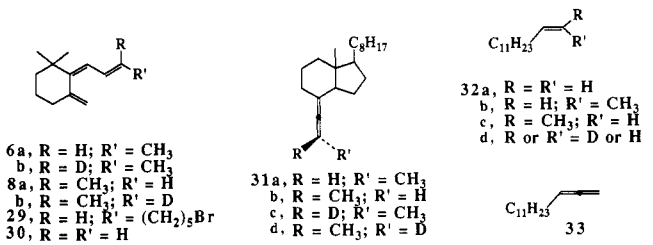
The results for a number of such reductions of triene sulfoxides, allene sulfoxides and monoene sulfoxides using the standard procedure just described (*t*-BuLi and an in situ proton source) are summarized in Table I. The stereospecific nature of the reduction is illustrated by a comparison of entries 1 and 2, which were described earlier in the introduction of this article.

As shown by entries 1–3 and 6, the most effective substrates for the reduction were trienes **2b**, **3b**, and **9** and also allene sulfoxide **10**, which all gave ≥70% yields of the reduced hydrocarbon products with the in situ proton quench method. As indicated above, the in situ quench significantly enhances the yield of the reduced product as contrasted to yields obtained using post quenching alone. It is most interesting that bromide **29** was obtained from **9** (entry 3) without reaction of the alkylbromide moiety, demonstrating that the reaction of *t*-BuLi with the sulfoxide moiety is faster than metal–halogen exchange.

It should be noted too that in these reductions, *tert*-butyl phenyl sulfoxide (**7**) was produced in amounts comparable to the reduced product isolated (e.g., **7** was obtained in 92–95% of the amount of **6b** isolated). While *tert*-butyl phenyl sulfoxide (**7**) was a product from the reductions carried out in ether as evidenced by its isolation and characterization, the byproduct from the reduction of **2b** in THF was *tert*-butylbenzene[15] along with hydrocarbon **6a**. Slightly better yields of **6a** were obtained (81%) under these conditions but due to their similar polarities on silica gel, an HPLC purification step was necessary to separate the desired product and *tert*-butylbenzene. Only minor amounts of **7** were produced in the reaction with

(15) The *tert*-butylbenzene which was not isolated in pure form was identified by comparison to the ^{1}H NMR spectrum of the known compound and also by GC/MS analysis of the mixture of **6b** and *tert*-butylbenzene.

Chart II



THF as the solvent as determined by examination of the ^{1}H NMR spectrum of the crude reaction residue.

Triene sulfoxides **2a** and **3a** (entries 4 and 5) and monoene sulfoxides **11a** and **11b** (entries 7 and 8) afforded much lower yields of reduced products **30** and **32a**, respectively. The attenuated yields appear to be due to competing pathways including deprotonation of the vinylic α-proton.

Desulfurization of allene sulfoxide **10** gave good yields of the allene **31a** (87% yield) with excellent retention of configuration (entry 6). The ratio of **31a** (*R* configuration, retention product) to **31b** (*S* configuration, inversion product) was >97/3 as determined by ^{1}H NMR integration.[16]

The methyl-substituted monoene sulfoxides **11c** and **11d** were reduced stereospecifically with retention to **32b** and **32c** (entries 9 and 10), albeit in relatively low yields. Significant amounts of a side product, allene **33**, were also isolated. A similar base-promoted allene-forming process from a 2-alkenyl sulfoxide has been reported by Posner.[17] Posner's proposed pathway involves abstraction of a proton from the allylic methyl group to give an intermediate lithiated species, which upon vicinal elimination of the phenylsulfinyl group affords an allene.

It is evident from the results summarized in Table I that the in situ quench method with *t*-BuLi and MeOH is uniquely practical for the reductive desulfurization of complex polyene sulfoxides.[18] This method of reduction gave somewhat lower yields for simple monoene sulfoxides. Fortunately alternative methods for desulfurization of these simpler vinyl sulfoxides have been developed.[19]

Deuterium-Labeling Studies. The in situ proton quench procedure could be nicely extended to the preparation of deuterium-labeled materials. In a procedure identical with the reductive protonation just described, an ethereal solution of **2b** at −78 °C was treated with 2.5 equiv of methanol-d_1 (MeOD) as the in situ quench followed by 4 equiv of *t*-BuLi in pentane (and unlabeled methanol workup) to afford the labeled material **6b** in 79% yield.

(16) The presence of the (*R*)-allene **31a** was indicated by a signal at δ 0.63 assigned to the C-18 methyl group and one at δ 1.57 assigned to the allenic methyl. The corresponding resonances for its diastereomer, (*S*)-allene **31b**, appear at δ 0.68 and 1.63, respectively. The diastereomeric ratios were determined by integration of the peak areas of the δ 0.63 signal for the (*R*)-allene **31a** (retention) and the δ 0.68 signal for the (*S*)-allene **31b** (inversion) by the cut and weigh method.

(17) Posner, G. H.; Tang, P.-W.; Mallamo, J. P. *Tetrahedron Lett.* **1978**, 3995.

(18) For additional examples from this laboratory, see: Elnagar, H. Y.; Okamura, W. H. *J. Org. Chem.* **1988**, *53*, 3060.

(19) Examples for effecting this type of reduction include the following: (a) Pettit, G. R.; van Tamelen, E. E. *Org. React.* **1962**, *12*, 356. (b) Trost, B. M.; Ornstein, P. L. *Tetrahedron Lett.* **1981**, *22*, 3463. (c) Wenkert, E.; Ferreira, T. W. *J. Chem. Soc., Chem. Commun.* **1982**, 840. (d) Truce, W. E.; Tate, D. P.; Burdge, D. N. *J. Am. Chem. Soc.* **1960**, *82*, 2872. (e) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477. (f) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1964**, *86*, 1639. (g) Wenkert, E.; Hanna, J. M., Jr.; Leftin, M. H.; Michelotti, E. L.; Potts, K. T.; Usifer, D. *J. Org. Chem.* **1985**, *50*, 1125. (h) Eisch, J. J.; Behrooz, M.; Galle, J. E. *Tetrahedron Lett.* **1984**, *25*, 4851.

Table II. Labeling Experiments for 2b, 3b, and 10

entry	sulfoxide[a]	product[b]	in situ quench[c]	post quench[d]	% d[e]	yield, %
1	**2b**	**6b**	MeOD	MeOH	83	78
2	**2b**	**6b**	MeOD	MeOD	90	72
3	**2b**	**6b**	MeOH	MeOD	2	76
4	**3b**	**8b**	MeOD	MeOD	94[f]	65
5	**10**	**31c/d**	MeOD	MeOH	90	93 (96:4)
6	**10**	**31c/d**	MeOD	MeOD	90	86 (96:4)

[a] The structures of the substrates are shown in Chart I. [b] The product structures are shown in Chart II. [c] MeOH (MeOD) present before addition of *t*-BuLi. [d] MeOH (MeOD) added 10 min after addition of *t*-BuLi to the solution of substrate/MeOH (MeOD). [e] % *d* by NMR analysis. [f] 91% d_1 by MS analysis.

That a deuterium replaced the sulfoxide moiety was evidenced by comparison of the ^1H and ^{13}C NMR spectra of the labeled and unlabeled compounds. The results of the labeling experiments for triene sulfoxides **2b** and **3b** and allene sulfoxide **10** are summarized in Table II. Various combinations of in situ and post-quench experiments with MeOH and MeOD were carried out. It should be emphasized with respect to Table II that in situ quench refers to the presence of the proton source (MeOH or MeOD) in the solution with substrate prior to addition of *t*-BuLi. Post quench refers to the proton source (MeOH and MeOD) added to the reaction mixture 10 min after addition of *t*-BuLi to the solution of substrate–MeOH (or substrate–MeOD) mixture.

The yields of the reduced, deuterium-labeled products are comparable to the results obtained for preparing unlabeled materials. However, the % deuterium (% d_1) incorporation varied depending on the method of quenching.[20] For the case of **2b**, all possible combinations of in situ and post-quench labeling experiments were examined (entries 1–3). From these experiments, it can be seen that 83–90% of the deuterium label comes from the in situ proton source and thus up to ~7% of the label was due to the post quench proton source (entries 1 and 2). However, the maximum % d_1 obtainable with in situ and post MeOD quench was about 90%, which leads to the conclusion that approximately 10% of the product is protonated by a source other than the in situ or post-quenching proton source (cf. entries 2 and 4).

The allene sulfoxide **10** was also stereospecifically labeled with deuterium by employing MeOD rather than MeOH as the in situ proton source (entries 5 and 6). The yields in these cases were excellent, and **31c** was obtained with very high retention of configuration in both experiments.[16] Regardless of the quenching procedure, **31c** was obtained with 90% d_1 incorporation, demonstrating that 90% of the deuterium label was delivered prior to addition of the external quench, a result analogous to the labeling results obtained with the triene sulfoxides **2b** and **3b**.

A limited number of labeling experiments were carried out with monoene sulfoxides since it was demonstrated (Table I) that these compounds were poor substrates for the desulfurization. Only the in situ MeOD/post MeOH quenching procedures were carried out with the monoene sulfoxides **11a** and **11b** to afford labeled 1-tridecene **32d** in yields (29 and 54%, respectively) similar to those using unlabeled MeOH (see entries 9 and 10 in Table I). However, MS analysis revealed that a mixture of d_0, d_1, and d_2 labeled tridecene resulted. The sites of labeling were not determined, but the presence of d_2 species could be reflective of competing α-deprotonation as discussed above.

Other Quenching Experiments. If a vinyllithium intermediate is expelled in the reaction of a vinyl sulfoxide and *t*-BuLi as previously suggested for other substrates,[3,4] electrophiles such as methyl iodide or trimethylsilyl chloride should react to give alkylated or silylated products. Thus in order to develop an effective method for replacing the sulfoxide moiety with alkyl, silyl, or halogen groups, triene sulfoxide **2b** was used as the substrate for exploring other quenching agent processes.

Table III. Reduction of 2b to 6a with RLi

entry	RLi	in situ quench	post quench	yield, %
1	CH_3Li	–	MeOH	–
2	*n*-BuLi	–	MeOH	26
3	*n*-BuLi	*s*-BuOH	MeOH	32
4	*s*-BuLi	MeOH	MeOH	~73
5	*t*-BuLi	–	MeOH[a]	47%

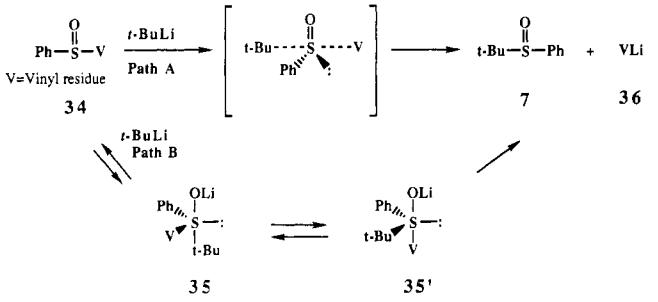
[a] Similarly, treatment of **9** with excess *t*-BuLi followed by post quenching with MeOH afforded a 42% yield of **29**, whereas the in situ quench procedure increased the yield to 70% (see Table I, entry 3).

When methyl iodide (CH_3I) was used as a post quench (1.5 equiv of *t*-BuLi at −100 °C in ether then excess CH_3I) or as an in situ quench (similar to the method using methanol as the in situ proton source), hydrocarbon **6a** and *tert*-butyl phenyl sulfoxide **7** or starting material **2b** were the products identified from the complex product mixtures. As indicated earlier for the bromo substrate **9**, attempts to enhance the rate of alkylation by tethering the alkylating agent to the triene sulfoxide led to simple sulfoxide reduction (footnote *a*, Table III). Dimethyl sulfate as quenching agent was also examined, but the ^1H NMR spectrum of the crude reaction mixture although complex also revealed that starting sulfoxide **2b** remained along with **6a** and *tert*-butyl phenyl sulfoxide (**7**). When trimethylsilyl chloride (TMSCl) was used as an in situ quench, only **6a** and *tert*-butyl phenyl sulfoxide (**7**) could be detected in the complex product mixture (^1H NMR analysis). Similarly poor results were obtained when TMSCl was used as a post quench (2.5 equiv TMSCl added after addition of 4 equiv of *t*-BuLi to **2b** at −78 °C).

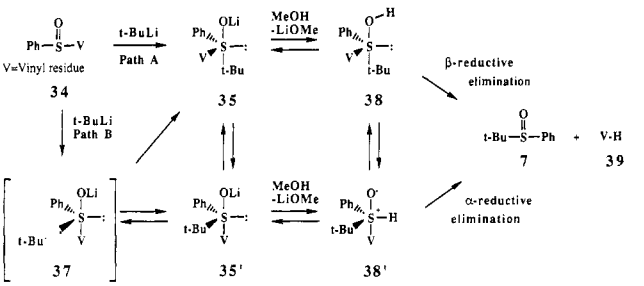
Desulfurization of Triene Sulfoxides with Other Alkyllithium Reagents. It was also of interest from a mechanistic point of view to determine whether other alkyllithium reagents such as CH_3Li, *n*-BuLi, or *s*-BuLi could reduce the sulfoxide moiety of **2b** in the same manner as *t*-BuLi. Thus as tabulated in Table III, when vinyl sulfoxide **2b** was treated with 2 equiv of CH_3Li in ether at −78 °C, the hydrocarbon **6a** was not a product (entry 1). Instead, 32% starting material was recovered, along with unidentified polar compounds. The desulfurization of **2b** with *n*-BuLi using either the in situ quench (entry 3) or the Johnson type conditions[3] (*n*-BuLi only, entry 2) gave low yields of **6a** while *s*-BuLi/MeOH gave good yields of the reduced product (entry 4). However, the product in the latter case was contaminated with a small amount of an unidentified impurity, which could not be separated from **6a** upon chromatography. Thus, al-

(20) The % d_1 incorporation was determined by ^1H NMR integration of the residual proton signals at the site of labeling relative to the intensity of another signal assigned to one proton at an unlabeled position.

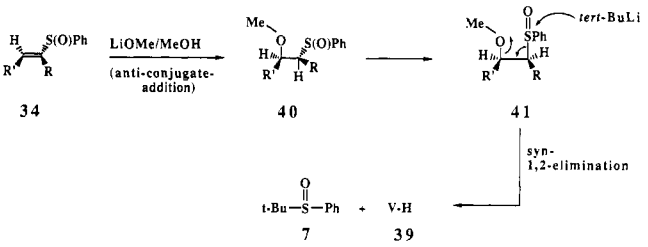
Scheme III



Scheme IV



Scheme V



though the yield of **6a** (entries 2 and 3) using *s*-BuLi were similar to the results with *t*-BuLi, the formation of cleaner products attests to the latter as a superior reagent for the reduction (at least for the substrate studied). As is also evident from Table III, CH_3Li and *n*-BuLi are not effective in the desulfurization reaction. It is conjectured that since *t*-BuLi and *s*-BuLi are more effective than MeLi and *n*-BuLi, an electron-transfer process involving radical intermediates may be involved.

Mechanistic Pathways. The mechanistic pathway involved in the reductive desulfurization with *t*-BuLi and an in situ proton source is intriguing and the facts which must be accommodated include: (1) for polyene sulfoxides, the in situ quench method is required for obtaining better yields; (2) *tert*-butyl phenyl sulfoxide (**7**) is formed in an amount essentially equal to that of the reduced polyene product; (3) the added in situ proton source replaces the sulfoxide moiety with retention of configuration; and (4) ~90% of the proton (as determined by deuterium labeling experiments) is delivered by the in situ MeOH present during the addition of *t*-BuLi.

In the simplest case, we can envisage as suggested by previous workers[3,4] that a vinyl anion (i.e., vinyllithium) is generated directly from vinyl sulfoxide as depicted in Scheme III. The *t*-BuLi is envisaged to attack the sulfoxide **34** in an S_N2-like fashion (path A) to give *tert*-butyl phenyl sulfoxide (**7**) and a vinyllithium **36** directly. Alternatively, in a pathway involving sulfuranes,[21] axial attack of *t*-BuLi (path B) would afford a pentacoordinate intermediate such as **35**. Pseudorotation could give sulfurane **35′** in which the vinyl ligand is axial as might be assumed for elimination to give the vinyllithium **36** and *tert*-butyl phenyl sulfoxide (**7**).[22]

We propose that either pathway A or B or *any other pathway involving a vinyllithium intermediate* is unlikely based on several lines of reasoning. (1) There is a necessity for in situ quench to afford good yields of reduced products. If a vinyllithium were involved it would seemingly not be necessary to use an in situ quench for obtaining satisfactory yields; only post quenching should have been necessary. (2) Reaction of vinyl sulfoxide with *t*-BuLi in combination with an alkylating or silylating agent should have also proceeded more efficiently. (3) In a more subtle experiment, our laboratories have previously shown that metalation of allene **31a** (*n*-BuLi, KOt-Bu) followed by quenching with D_2O affords **31d**, the inversion product. On the other hand, the metalation–deuteration sequence of **31b** also affords **31d**, *the retention product*. A similar experiment with related substrates using *t*-BuLi alone afforded the same result. Thus, allenyllithium species are configurationally unstable.[23] The fact that the allene sulfoxide **10** afforded mainly **31a** with excellent retention supports the hypothesis that a free allenyllithium species is not involved. By implication, the pathway for reduction of vinyl sulfoxides may not involve a vinyllithium such as **36**.

Protonation of a vinyllithium species generated via path A or B (Scheme III) within a solvent cage containing MeOH cannot be rigorously ruled out at this point. If this were the case however, there should have been no advantage to the in situ quenching procedure since vinyllithium compounds should be stable.[24] It may be noted at the outset that because we are dealing with a stereospecific (retention) reduction process, we felt it unreasonable to invoke vinyl radicals as intermediates since it is known that vinyl radicals are configurationally unstable.[25]

It is proposed (Scheme IV) as an extention of path B of Scheme III that reductive elimination of a protonated sulfurane intermediate is involved. The first step can be envisaged (Scheme IV) as axial attack of *t*-BuLi on vinyl sulfoxide **34** to afford the sulfurane **35** (path A). Sulfurane intermediates such as **35** or **35′** have been hypothesized as reactive intermediates along reaction pathways for a variety of reactions involving sulfoxide and sulfonium salts with organometallic reagents.[26]

(21) (a) Sulfuranes are hypervalent molecules in which the valence shell of the central sulfur atom has expanded to exceed the octet state [Musher, J. I. *Angew. Chem. Internat. Ed. Engl.* **1969**, *8*, 54]. Pentacoordinate sulfuranes are considered to possess approximately trigonal-bipyramid geometry in which the lone pair is considered to occupy one of the equatorial sites and electronegative elements prefer axial sites. For a review of sulfuranes, see: (b) Martin, J. C.; Perozzi, E. F. *Science* **1976**, *191*, 154. For a review on the structure of pentacoordinated molecules, see: (c) Holmes, R. R. *Acc. Chem. Res.* **1979**, *12*, 257. (d) Mislow, K. *Record Chem. Progr.* **1967**, *28*, 217. Also see: (e) Cram, D. J.; Day, J.; Rayner, D. C.; von Schriltz, D. M.; Duchamp, D. J.; Garwood, D. C. *J. Am. Chem. Soc.* **1970**, *92*, 7369.

(22) When considering the formation of sulfuranes, it is assumed that in analogy to pentacoordinate phosphorus chemistry, axial attack is favored. Similarly, departure of a ligand is considered to occur from an axial site. See ref 21, and for reviews of pentacoordinate phosphorus chemistry, see: (a) Mislow, K. *Acc. Chem. Res.* **1970**, *3*, 321. (b) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.

(23) van Kruchten, E. M. G. A.; Haces, A.; Okamura, W. H. *Tetrahedron Lett.* **1983**, *24*, 3939 and references cited therein.

(24) Although vinyllithium reagents should be stable (Seyferth, D.; Vaughan, L. G. *J. Am. Chem. Soc.* **1964**, *86*, 883), there exist cases where organolithium compounds react more slowly than lithium alkoxides with water. For example, see: Levine, R.; Karten, M. J.; Kadunce, W. M. *J. Org. Chem.* **1975**, *40*, 1770. Levine, R.; Karten, M. J. *J. Org. Chem.* **1976**, *41*, 1176. We are grateful to Dr. A. G. Anderson (DuPont) for helpful discussions.

(25) Kampmeier, J. A.; Fantazier, R. M. *J. Am. Chem. Soc.* **1966**, *88*, 1959.

Alternatively, since *t*-BuLi (or *s*-BuLi) was superior to *n*-BuLi and MeLi, single-electron transfer from *t*-BuLi to **34** to afford the radical pair **37** (path B) as the initial step can be envisaged.[27] The geometry of a species such as **37** is not clear but it is represented as a trigonal-bipyramid with an equatorial orbital containing the single electron. Thus rapid coupling of **37** with *t*-Bu radical[28] could afford sulfurane **35** or **35'** directly without pseudorotation.

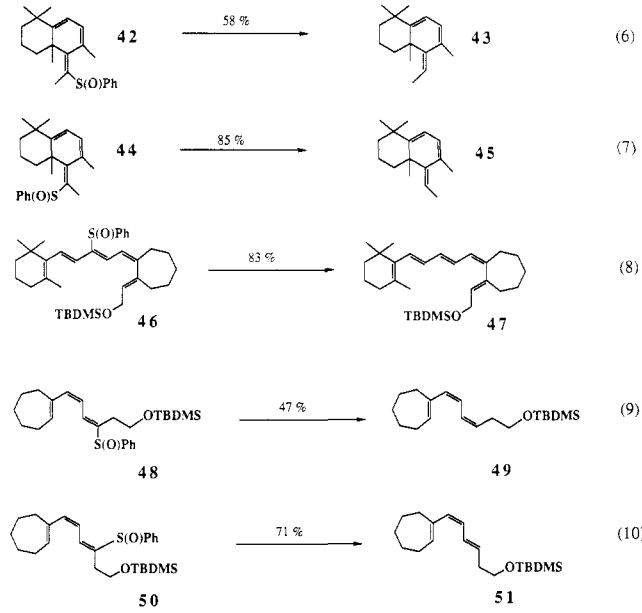
Direct protonation[29] of the putative sulfurane **35** or **35'** can be anticipated to afford species such as **38** or **38'**. Stereospecific coupling of the hydrogen and vinyl moiety thus can be envisaged to provide the reduced hydrocarbon **39** and *tert*-butyl phenyl sulfoxide (**7**) directly. The α-reductive elimination mechanism including the formation of **35** or **35'** formally resembles the well-known stereospecific oxidative addition–reductive elimination process characteristic of transition metal derivatives.[30,31]

Both the vinyllithium pathway and the sulfurane pathway require that *t*-BuLi react with the sulfoxide competitively with its reaction in an acid–base manner with the MeOH. Of course, the fact remains that a proton is delivered by the in situ MeOH as evidenced by the labeling experiments. A third mechanistic pathway (Scheme V) which may be considered involves initial formation of LiOMe, which then adds to the vinyl sulfoxide in a conjugate Michael fashion[32] with subsequent protonation to result in overall anti addition of MeOH to the double bond affording putative intermediate **40**. Attack of *t*-BuLi on the sulfoxide (either via an S_N2-like pathway or a sulfurane pathway) with concommittant syn β-elimination of methoxide via syn conformer **41** would lead to **39** with net retention and **7**. Alternatively, MeOH can add in a syn fashion, and the corresponding elimination can occur in an anti fashion to afford the same stereochemical result.

The results that we have obtained cannot distinguish between this conjugate addition pathway (Scheme V) and the protonated sulfurane pathway (Scheme IV). Both mechanisms satisfactorily account for the observations outlined above. However, unless sulfoxide has a unique ability to induce strictly conjugate addition of LiOMe only to its α,β-double bond, it is somewhat difficult to understand why methanol does not add across the other conjugated positions of the polyene sulfoxide. A case in point are the reductions of **42** and **44** reported recently by this laboratory.[18] Both substrates were readily reduced to **43** and **45**, respectively, with retention of configuration despite their crowded β-carbon. Moreover, in the stereospecific reduction of allenyl sulfoxide **10**, if conjugate addition of methoxide and proton had occurred in the mechanistic sense of Scheme V, it might be anticipated that a product other than allene **31a** would have been obtained (e.g., an allyl-substituted derivative).

Conclusions

The unique reagent combination of *t*-BuLi in the presence of a proton source (in situ proton source) stereospecifically reduces polyene and allene sulfoxides in good yields. The method is procedurally very simple. Moreover, the sulfoxide moiety can be stereospecifically replaced by a deuterium by simply employing MeOD as the internal proton source. Simple monoene sulfoxides afford attenuated yields of the reduced product, but fortunately alternative methods exist for these simpler systems.[19] The generality of the method described herein is further attested to by the two examples shown in eq 6 and 7 (substrates **42** and **44**) and also the additional example equations 8–10 (substrates **46**, **48**, and **50**) recently uncovered by our laboratories.[33]



We find the sulfurane protonation–reductive elimination pathway shown in Scheme IV, attractive, although we would certainly agree with the reviewers of this article as

(26) (a) Wittig, G.; Fritz, H. *Justus Liebigs Ann. Chem.* **1952**, *577*, 39. (b) Franzen, V.; Mertz, C. *Justus Liebigs Ann. Chem.* **1961**, *643*, 24. (c) Sheppard, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 3058. (d) Sheppard, W. A. *J. Am. Chem. Soc.* **1971**, *93*, 5597. (e) Franzen, V.; Joschek, H.-I.; Mertz, C. *Justus Liebigs Ann. Chem.* **1962**, *654*, 82. (f) Andersen, K. K.; Yeager, S. A. *J. Org. Chem.* **1963**, *28*, 865. (g) Khim, Y. H.; Oae, S. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 1968. (h) Trost, B. M.; LaRochelle, R.; Atkins, R. C. *J. Am. Chem. Soc.* **1969**, *91*, 2175. (i) LaRochelle, R. W.; Trost, B. M. *J. Am. Chem. Soc.* **1971**, *93*, 6077. (j) Trost, B. M.; Arndt, H. C. *J. Am. Chem. Soc.* **1973**, *95*, 5288. (k) Andersen, K. K.; Yeager, S. A.; Peynircioglu, N. B. *Tetrahedron Lett.* **1970**, *28*, 2485. (l) Ackerman, B. K.; Andersen, K. K.; Karup-Nielsen, I.; Peynircioglu, N. B.; Yeager, S. A. *J. Org. Chem.* **1974**, *39*, 964. (m) Knapczyk, J. W.; McEwen, W. E. *J. Am. Chem. Soc.* **1969**, *91*, 145. (n) Oae, S.; Kawai, T.; Furukawa, N. *Tetrahedron Lett.* **1984**, *25*, 69. (o) Wildi, B. S.; Taylor, S. W.; Potratz, H. A. *J. Am. Chem. Soc.* **1951**, *73*, 1965. (p) Gilman, H.; Eidt, S. H. *J. Am. Chem. Soc.* **1956**, *78*, 3848. (q) Meutterties, E. L.; Phillips, W. D. *J. Am. Chem. Soc.* **1959**, *81*, 1084.

(27) Durst proposed the intermediacy of a similar type radical to account for racemization of optically active *tert*-butyl tolyl sulfoxide with *t*-BuLi. See ref 3b.

(28) It is assumed that if a *t*-Bu radical is involved in the initial step its combination with radical anion **37** must be rather rapid, perhaps occurring in a solvent cage, because of the propensity of *t*-Bu radicals to undergo disproportionation. Blackham, A. V.; Eatough, N. L. *J. Am. Chem. Soc.* **1962**, *84*, 2922.

(29) The isolation of S-alkylated dimethyl sulfoxide derivatives has been reported: Smith, S. G.; Winstein, S. *Tetrahedron* **1958**, *3*, 317.

(30) For a review of organocuprate reactions, see: House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.

(31) Similarly, pentacoordinate intermediates have been postulated as intermediates in the metal–halogen exchange reaction of organolithium or organostannanes with aryl halides. For examples, see: (a) Wittig, G.; Schöllkopf, U. *Tetrahedron* **1958**, *3*, 91. (b) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101. (c) Reich, H. J.; Phillips, N. H. *J. Am. Chem. Soc.* **1986**, *108*, 2102. (d) Ashby, E. C.; Pham, T. N. *J. Org. Chem.* **1987**, *52*, 1291.

(32) (a) We have previously conjectured that a Michael type addition of $LiAlH_4$ to a vinyl sulfoxide may occur via coordination of reagent to the sulfoxide moiety. See: Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, *107*, 1034. (b) Tsuchihashi, G.; Mitamura, S.; Inoue, S.; Ogura, K. *Tetrahedron Lett.* **1973**, *323*. (c) Abbott, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1971**, 471. (d) Buese, M. A.; Hogen-Esch, T. E. *Macromolecules* **1984**, *17*, 118. (e) Buese, M. A.; Hogen-Esch, T. E. *J. Am. Chem. Soc.* **1985**, *107*, 4509.

(33) (a) de Lera, A. R.; Silveira, M. H.; Okamura, W. H. *Abstracts of Papers*, 194th National Meeting of the American Chemical Society; New Orleans, August 1987; American Chemical Society: Washington, DC; ORGN 112. (b) Wu, K.-M.; Okamura, W. H. *Abstracts of Papers*, 196th National Meeting of the American Chemical Society; Los Angeles, September 1988; American Chemical Society: Washington, DC; ORGN 3.

well as others that the mechanistic discussion presented here rests primarily on two observations: retention of stereochemistry and the higher yields obtained when the internal proton source is present. These observations certainly do not exclude any of the mechanistic pathways suggested above, assuming that post quenching alone simply permits more extensive side reactions to occur resulting in lower yields. The actual pathway involved still needs to be established, but on the basis of the quenching experiments, the intermediacy of a vinyllithium species seems less likely.[34a] We well recognize that the mode of quenching as well as mixing rates may well lead to variable results.[34b] However, there is no question in this study that the internal proton source is primarily responsible for quenching whatever species may be involved as a reactive intermediate.[34b] The possibility of trapping the putative intermediate with other electrophiles besides a proton or deuteron has not yet been fully explored, and it remains for future experiments to more fully delineate the mechanistic pathway involved.

Experimental Section[35]

(2(1′)*Z*,2*Z*)- and (2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-(3′-(phenylsulfinyl)-2′-propenylidene)cyclohexane (2a and 3a, Respectively). The triene sulfoxides **2a** and **3a** were prepared as previously described.[1]

(2(1′)*Z*,2′*Z*)- and (2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-(3′-(phenylsulfinyl)-2′-butenylidene)cyclohexane (2b and 3b, Respectively). The triene sulfoxides **2b** and **3b** were prepared as previously described.[1]

(2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-butenylidenecyclohexane (6a). Desulfurization in Et_2O. A solution of *tert*-butyllithium (1.1 mL, 1.80 M in pentane, 2.0 mmol) was added rapidly to a solution of vinyl sulfoxide **2b** (150.6 mg, 0.50 mmol) and anhydrous methanol (0.05 μL, 1.25 mmol) in ether (10 mL) at −78 °C. The solution was stirred for 10 min at −78 °C, after which time methanol (1.0 mL) was added to quench the reaction. After warming the mixture to room temperature, a saturated solution of $NaHCO_3$ (20 mL) and ether (20 mL) were added, and the layers were separated. The aqueous layer was extracted with ether (2 × 20 mL), and the organic layers were combined and dried over $MgSO_4$. After filtration and concentration, the residue was subjected to flash column chromatography (hexanes) followed by 50% ethyl acetate/hexanes. The nonpolar fractions from the flash column were combined and concentrated. The resulting residue was further purified by HPLC (Whatman Partisil M10 20/50 column, hexanes, 7.9 mL/min flow rate) to afford 57.4 mg of **6a** (65% yield). The polar fractions of the flash column were subjected to HPLC (Rainin Microsorb M8 10/25, 40% ethyl acetate/hexanes, 4.0 mL/min) to afford 54.8 mg of *tert*-butyl phenyl sulfoxide (**7**, 60%). Although the yield of **6a** in this particular experiment directed toward isolating both **6a** and **7** was on the slightly low side, the typical yield was >70% (Table I and entries 1–3 in Table II).

Desulfurization in THF. To a solution of **2b** (42 mg, 0.14 mmol) and MeOH (14 μL, 0.35 mmol) in THF (3.0 mmol) at −78 °C was added *t*-BuLi (0.32 mL, 1.74 M in pentane, 0.56 mmol). After stirring for 10 min at −78 °C the reaction was quenched with additional MeOH (0.5 mL), and the reaction was worked up in the usual manner as given above. After flash column purification (silica gel, 100% hexanes) of the residue, a mixture of hydrocarbon **6a** and *tert*-butylbenzene (**7**) was obtained which was purified by HPLC (Whatman Partisil M10 20/50 column, hexanes, 5 mL/min flow rate) to afford 20 mg of **6a** (81% yield). The *tert*-butylbenzene (**7**) (produced in approximately 70% yield relative to **6a** by examination of the ^1H NMR spectrum of the crude mixture prior to chromatography) was identified by GC/MS and by ^1H NMR spectroscopy.

Desulfurization in Et_2O Using Other Alkyllithium Reagents and Conditions. The results are summarized in Table III. The procedure was essentially identical with that described above using ether as solvent including both internal (in situ) and post quench. In several cases given in Table III, the internal quench was omitted.

(2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-(3′-deuteriobutenylidene)cyclohexane (6b). Internal Methanol-*O*-d_1 Quench Followed by Methanol Workup. Using the general procedure for the reduction of **2b**, *t*-BuLi (0.53 mL, 1.80 M in pentane, 0.95 mmol) was added to a solution of **2b** (71.3 mg, 0.24 mmol) and methanol-*O*-d_1 (24.4 μL, 0.60 mmol) in Et_2O (4.8 mL) at −78 °C. The reaction was quenched with unlabeled methanol (0.5 mL) after 10 min at −78 °C. Flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **6b** (83% d_1 by ^1H NMR integration, 32.9 mg, 78%).

Internal Methanol-*O*-d_1 Quench Followed by Methanol-*O*-d_1 Workup. Via the procedure just described, *t*-BuLi (0.46 mL, 1.88 M in pentane, 0.86 mmol) was added to a solution of **2b** (64.5 mg, 0.22 mmol) and methanol-*O*-d_1 (22 μL, 0.54 mmol) in Et_2O (4.3 mL) at −78 °C. The reaction was quenched with methanol-*O*-d_1 (0.5 mL) after 10 min at −78 °C. Flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **6b** (90% d_1 by ^1H NMR integration, 27.4 mg, 72%).

Internal Unlabeled Methanol Quench Followed by Methanol-*O*-d_1 Workup. Via the same procedure just described, *t*-BuLi (0.39 mL, 1.80 M in pentane, 0.70 mmol) was added to a solution of **2b** (52.3 mg, 0.17 mmol) and methanol (17.5 μL, 0.44 mmol) in Et_2O (3.5 mL) at −78 °C. After stirring 10 min at −78 °C, the reaction was quenched with 0.5 mL of methanol-*O*-d_1. Flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) purification afforded **6b** (2% d_1 by ^1H NMR integration, 23.3 mg, 76%).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(butenylidene)cyclohexane (8a). Via the standard procedure for the reduction of the corresponding 2′*Z* isomer **2b**, *t*-BuLi (0.30 mL, 1.88 M in pentane, 0.57 mmol) was added to a solution of **3b** (42.7 mg, 0.14 mmol) in Et_2O (2.8 mL) at −78 °C. Purification by flash chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **8a** (17.6 mg, 70%).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(3′-deuteriobutenylidene)cyclohexane (8b). As described for the reduction of **2b**, *t*-BuLi (0.28 mL, 1.88 M in pentane, 0.52 mmol) was added to a solution of **3b** (39.3 mg, 0.13 mmol) and methanol-*O*-d_1 (13.5 μL, 0.33 mmol) in Et_2O (2.6 mL) at −78 °C. The reaction was quenched with 0.5 mL of methanol-*O*-d_1 after 10 min at −78 °C. Purification by flash column chromatography (hexanes) and HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **8b** (94% d_1 by ^1H NMR integration and 91% d_1 by mass spectral analysis; 15.0 mg, 65%).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(3′-((*p*-chlorophenyl)sulfinyl)-8′-bromo-2′-octenylidene)cyclohexane (9). Triphenylphosphine (128 mg, 0.48 mmol) in 6 mL of THF was added via cannula to a stirred mixture of the alcohol **20** (97 mg, 0.24 mmol) and CBr_4 (159 mg, 0.48 mmol) in 0.5 mL of Et_2O. The course of reaction was monitored by TLC, and then the reaction was quenched with saturated brine when the starting material had disappeared (~45 min). The mixture was diluted with 5 mL of Et_2O, and then 5 mL of saturated $NaHCO_3$ was added. The organic layer was separated, and the aqueous layer was washed with Et_2O (2 × 15 mL). The ether extracts were combined and dried over $MgSO_4$. The excess triphenylphosphine and phosphine oxide byproducts were removed by crystallization from hexanes. The crude product was purified by flash column chromatography (15% ethyl acetate/hexanes) to yield after vacuum drying **9** (95 mg, 85%).

(34) (a) Yet additional possibilities as to mechanistic pathways (including suggestions involving new experiments) have been suggested to the authors while this manuscript was in preparation. Of course, the mechanistic discourse presented here should simply be treated as a starting point for discussion. (b) Beak, P.; Musick, T. J.; Chen, C. *J. Am. Chem. Soc.* **1988**, *110*, 3538.

(35) General experimental details are presented in the supplementary material section. Samples after purification and vacuum drying were shown to be homogeneous by analytical HPLC analysis and ^1H and ^{13}C NMR analyses before MS determination. Unless otherwise indicated, silica gel (Sigma, 230–400 mesh) was used for flash column chromatography; see: Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

De-*A*,*B*-8-(2′α-methyl-2′β-(phenylsulfinyl)-ethenylidene)cholestane (10). A solution of propargylic alcohol **22** (304 mg, 1.00 mmol) and triethylamine (0.28 μL, 2.0 mmol) in 10 mL of CH_2Cl_2 was cooled to −78 °C with stirring for 15 min. Phenylsulfenyl chloride (0.75 mL, 2 M in CH_2Cl_2, 1.5 mmol) was added dropwise, and then the resulting mixture was stirred for 3 h at −78 °C, warmed to room temperature, and stirred for an additional 20 min. After addition of saturated $NaHCO_3$ solution (10 mL), the mixture was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under vacuum to afford a residue, which was purified by flash column chromatography (25% ethyl acetate/hexanes) to afford **10**[6] (289 mg, 70%) as a mixture of sulfoxide diastereomers.

(*E*)- and (*Z*)-1-(Phenylsulfinyl)tridec-1-ene (11a and 11b). A solution of *n*-butyllithium (4.2 mL, 1.70 M in hexanes, 7.1 mmol) was added to a solution of (dimethylphosphoryl)methyl phenyl sulfoxide (**24**) (1.548 g, 6.24 mmol) in 15 mL of THF at −78 °C. Stirring was continued for 1 h and then dodecyl aldehyde (96% purity grade, 1.4 mL, 6.5 mmol) in 9 mL of THF was added via cannula at −78 °C. The reaction mixture was stirred an additional 30 min at −78 °C and then warmed to room temperature and stirred for 2 h. The solvent was removed at aspirator pressure, and then the residue was treated with water (25 mL) and extracted with chloroform (3 × 15 mL). The chloroform extracts were washed with water (10 mL) and dried over $MgSO_4$. After solvent evaporation, the crude product was subjected to flash column chromatography (25% ethyl acetate/hexanes) to yield in order of elution: 459 mg of *E* sulfoxide **11a**, 667 mg of an isomeric mixture of sulfoxides, and 984 mg of *Z* sulfoxide **11b** for a total yield of 93% (~2:1 ratio of *Z* to *E* isomers).

(*E*)-2-(Phenylsulfinyl)tetradec-2-ene (11c). To a solution (*E*)-vinyl sulfide **28a** (380 mg, 1.24 mmol) in 6 mL of CH_2Cl_2 at −10 °C was added via cannula MCPBA (267 mg, 80% titer, 1.25 mmol) in 6 mL of CH_2Cl_2. The course of the reaction was monitored by TLC, and when starting material had disappeared (~5 min), the reaction was quenched with a saturated $NaHCO_3$ solution (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over $MgSO_4$, and after concentration under vacuum, the residue was subjected to flash column chromatography (15% ethyl acetate/hexanes) to afford after vacuum drying **11c** (426 mg, 98%).

(*Z*)-2-(Phenylsulfinyl)tetradec-2-ene (11d). A solution of MCPBA (180 mg, 82.5% titer, 0.86 mmol) in 4 mL of CH_2Cl_2 was added to the (*Z*)-vinyl sulfide **28b** (261 mg, 0.86 mmol), in 4 mL of CH_2Cl_2 at −10 °C. When the reaction was judged to be complete by TLC (~5 min), 1 mL of saturated $NaHCO_3$ solution was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under vacuum. The residue was subjected to flash column chromatography (15% ethyl acetate/hexanes) to yield **11d** (222 mg, 81%).

6-Heptyn-1-ol (13). Some difficulty was encountered in the preparation of potassium aminopropylamide (KAPA), but the latter could be routinely prepared in the following manner. A vessel containing a mixture of potassium (5.56 g, 142 mmol), aminopropylamine (APA, 125.5 mL, dried by titration with *n*-butyllithium to a phenanthroline endpoint and then distilled), and a catalytic amount of ferric nitrate hydrate (~10 mg) was heated to ~80–90 °C while immersed in an ultrasonic cleaning bath for approximately 1.5 h. The mixture was sonicated an additional 12 h at room temperature to insure complete formation of the reagent. The internal acetylene **12** (3.022 g, 26.9 mmol) was then added via cannula to the flask containing the greenish-brown solution of KAPA (1.25 M in APA) immersed in the sonicator. A colloidal, tan precipitate was immediately evident upon addition of the alkynol. The resulting mixture was sonicated for 1.5 at room temperature and then poured over 200 g of crushed ice. The solution was acidified with 6 M HCl and then extracted with ether (4 × 250 mL). The ether extracts were combined and dried over $MgSO_4$. Solvent evaporation under reduced pressure followed by Kugelrohr distillation afforded **13** (2.357 g, 78%) as a colorless liquid.

1-(*tert*-Butyldimethylsiloxy)-6-heptyne (14). Imidazole (851 mg, 12.5 mmol) and *tert*-butyldimethylsilyl chloride (904 mg, 6 mmol) were added to 6-heptyn-1-ol (**13**; 561 mg, 5 mmol) in dimethylformamide (1.1 mL), and then the mixture was stirred 12 h at room temperature under nitrogen. The solution was diluted with ether and washed with two portions of water. The ether layer was dried over Na_2SO_4 and concentrated under reduced pressure to yield 1.053 g of crude product. Purification by flash chromatography (5% ethyl acetate/hexanes) afforded 0.963 g (85%) of **14** as a colorless liquid.

1-(2′,6′,6′-Trimethyl-1′-cyclohexen-1′-yl)-1-hydroxy-8-(*tert*-butyldimethylsiloxy)-2-octyne (16). A solution of *n*-butyllithium (1.3 mL, 1.54 M in hexanes, 2.0 mmol) was added dropwise to the protected alkynol **14** (463 mg, 2.0 mmol) in 4 mL of dry THF at −78 °C. The mixture was stirred for 15 min at −78 °C, and then a solution of β-cyclocitral (320 mg, 2.1 mmol) in THF (1 mL) was added via cannula. The mixture was stirred for an additional 0.5 h at −78 °C and allowed to warm to room temperature. The reaction was then quenched with 1 mL of water, and sufficient solid K_2CO_3 added until a paste had formed. The organic layer was decanted, and the paste was washed with ether (3 × 20 mL). The combined ether portions were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (5% ethyl acetate/hexanes) afforded **16** (603 mg, 78%) as a pale yellow liquid.

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(3′-(*p*-chlorophenylsulfinyl)-8′-(*tert*-butyldimethylsiloxy)-2′-octenylidene)cyclohexane (19a). *p*-Chlorophenylsulfenyl Chloride. A solution of Cl_2 in CCl_4 (7.7 mL, 1.3 M, 10 mmol) was added dropwise to bis(*p*-chlorophenyl) disulfide (2.872 g, 10 mmol) at 0 °C. The resulting bright red solution was then warmed to room temperature, and the CCl_4 was removed under aspirator pressure. The *p*-chlorophenylsulfenyl chloride was then distilled under reduced pressure (0.1 mmHg, 39 °C) and then stored in sealed ampoules at −60 °C.

Triethylamine (0.70 μL, 5 mmol) was added to a solution of **16** (946 mg, 2.5 mmol) in 50 mL of CH_2Cl_2 at −78 °C and stirred for 15 min. *p*-Chlorophenylsulfenyl chloride (0.32 μL, 2.7 mmol) was added dropwise to the cooled solution, and the resulting mixture was stirred for 2.5 h at −78 °C. The dry ice–acetone bath was then removed, and the mixture stirred for an additional 21 h at room temperature. Saturated $NaHCO_3$ (20 mL) was added to the reaction mixture, and the resulting layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic extracts were washed once with saturated NH_4Cl (30 mL) and then dried over $MgSO_4$. After concentration, purification of the residue by flash chromatography (5% ethyl acetate/hexanes) afforded after vacuum drying **19a** (0.767 g, 59%). Minor amounts of the $\Delta^{2',3'}$-*E* isomer **19b** was not investigated further (the ratio of $\Delta^{2',3'}$ *Z*/*E* geometric isomers was ~10:1).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(3′-((*p*-chlorophenyl)sulfinyl)-8′-hydroxy-2′-octenylidene)cyclohexane (20). A 1.0 M solution of tetrabutylammonium fluoride in THF (2.3 μL, 2.3 mmol) was added to **19a** (406 mg, 0.78 mmol) and stirred for 2.5 h at room temperature. The solution was then quenched with 1 mL of saturated brine. Ether (5 mL) was added, the mixture was washed with saturated $NaHCO_3$ (10 mL), and the layers were separated. The aqueous layer was extracted with ether (3 × 10 mL), and then the organic layers were combined and dried over $MgSO_4$. After evaporation of the solvent the crude alcohol was purified by flash column chromatography (30% ethyl acetate/hexanes) to yield after vacuum drying **20** (258 mg, 81%).

De-*A*,*B*-8α-(1′-propynyl)-8β-cholestanol (22). The propargyl alcohol **22** was prepared from Grundmann's ketone **21** as previously described.[6]

(Dimethylphosphoryl)methyl Phenyl Sulfoxide (24). A solution of *n*-BuLi (32 mL, 1.72 M in hexanes, 55 mmol) was added under nitrogen to a stirred solution of dimethyl methylphosphonate (**23**, 6.2 g, 50 mmol) in 75 mL of THF at −78 °C. After stirring for 30 min at −78 °C, a solution of methyl phenylsulfinate (4.1 g, 26 mmol) in 50 mL of THF was added via cannula. The resulting mixture was stirred an additional 15 min at −78 °C and then warmed to −20 °C and quenched with a saturated NH_4Cl solution. After evaporation of the solvent under vacuum, the residue was extracted with chloroform (3 × 100 mL), and the combined organic layers were dired over $MgSO_4$ and concentrated under vacuum. Chromatotron separation (4-mm silica gel plate, 25% acetone/chloroform) afforded after vacuum

drying 3.6 g of **24** (56%) as a colorless oil.

Chloromethyl Phenyl Sulfide (25b). To a stirred solution of thioanisole **25a** (6.21 g, 50 mmol) in 50 mL of CCl_4 was added *N*-chlorosuccinimide (7.34 g, 55 mmol). The mixture was stirred for 11 h at room temperature and then filtered. After removal of the solvent under vacuum, fractional distillation of the residue afforded **25b** (7.86 g, 99%) as a colorless oil: bp 70 °C, 0.04 mmHg.

Diethyl ((Phenylthio)methyl)phosphonate (26). To neat chloromethyl phenyl sulfide **25b** (1.83 g, 11.5 mmol) was added triethylphosphite (2.5 mL, 13.8 mmol), and then the mixture was heated for 48 h at 120 °C. Fractional distillation under reduced pressure afforded **26** (2.19 g, 73%) as a colorless oil: bp 117–121 °C (0.3 mmHg).

Diethyl (1-(Phenylthio)ethyl)phosphonate (27). To a solution of diethyl ((phenylthio)methyl)phosphonate (**26**) (316 mg, 1.2 mmol) in 4 mL of THF cooled to −78 °C was added dropwise *n*-BuLi (0.8 mL, 1.6 M in hexanes, 1.3 mmol). The resulting solution was stirred 5 h at −78 °C, and then CH_3I (0.1 mL, 1.4 mmol) was added to the reaction mixture, which was subsequently warmed to room temperature, and the solvent was removed under vacuum. Ether (20 mL) and saturated NaCl (50 mL) were added to the residue, and then the organic layer was separated. The aqueous layer was extracted with ether (2 × 50 mL), and then the combined organic fractions were dried over $MgSO_4$ and concentrated. Kugelrohr distillation of the residue under reduced pressure afforded **27** (250 mg, 75% yield; external air bath temperature of 130 °C (0.3 mmHg)).

(*E*)- and (*Z*)-2-(Phenylthio)tetradec-2-ene (28a and 28b, Respectively). A solution of *n*-BuLi (5.0 mL, 1.63 M in hexanes, 8.2 mmol) was added to diethyl (1-(phenylthio)ethyl)phosphonate (**27**, 2.141 g, 7.8 mmol) in THF (45 mL) at −78 °C. After the mixture was stirred at −78 °C for 5 h, freshly distilled dodecylaldehyde (2.1 mL, 9.4 mmol) was added, and stirring at −78 °C was continued for 1 h. The solution was then heated at 50 °C for 16 h. After the mixture had cooled to room temperature, 20 mL of H_2O and 20 mL of saturated NH_4Cl were added to quench. The resulting mixture was extracted with 75 mL of ether, and the organic layer was washed with successive portions (50 mL) of saturated $NaHCO_3$ and brine. The aqueous layers were then backwashed with ether (50 mL), and then the combined organic extracts were dried over $MgSO_4$. After concentration under vacuum, the crude product was purified by flash column chromatography (hexanes) to yield in order of elution, 380 mg of cis sulfide **28b**, 844 mg of a cis and trans mixture, and 453 mg of trans sulfide **28a** (70% total yield; ~1:1 ratio of **28a** and **28b**).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(8′-bromo-2′-octenylidene)cyclohexane (29). Via the general procedure for the reduction of **2b**, *t*-BuLi (0.18 mL, 2.02 M in pentane, 0.36 mmol) was added to a solution of **9** (42.5 mg, 0.09 mmol) and methanol (9 μL, 0.23 mmol) in Et_2O (1.8 mL) at −78 °C. After purification by flash column chromatography (hexanes), **29** (19.6 mg, 70%) was obtained as a colorless oil.

(*Z*)-1,1-Dimethyl-3-methylene-2-(2′-propenylidene)cyclohexane (30). From (2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-(3′-(phenylsulfinyl)-2′-propenylidene)cyclohexane (2a). Via the procedure for the reduction of **2b**, *t*-BuLi (0.32 mL, 1.74 M in pentane, 0.56 mmol) was added to a solution of **2a** (41.0 mg, 0.14 mmol) and methanol (14.2 μL, 0.35 mmol) in Et_2O (2.8 mL) at −78 °C. Flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **30** (6.4 mg, 28%) as a colorless oil.

From (2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-(3′-(phenylsulfinyl)-2′-propenylidene)cyclohexane (3a). Via the same procedure for the reduction above, *t*-BuLi (0.17 mL, 1.74 M in pentane, 0.30 mmol) was added to a solution of **3a** (21.8 mg, 0.08 mmol) and methanol (7.7 μL, 0.19 mmol) in Et_2O (1.5 mL) at −78 °C. After flash column chromatography (hexanes) and HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) purification, **30** (2.3 mg, 19%) was obtained as a colorless oil.

De-*A*,*B*-8-(2′α-methylethenylidene)cholestane (31a). Via the standard procedure for the reduction of **2b**, *t*-BuLi (0.16 mL, 1.84 M in pentane, 0.29 mmol) was added to a solution of **10** (30 mg, 0.07 mmol) and methanol (7.1 μL, 0.18 mmol) in Et_2O (1.4 mL). Purification by flash chromatography (100% hexanes) afforded **31a** (18.3 mg, 87%) contaminated with 2.7% (by ^{1}H-NMR integration) of the *S* isomer **31b**.

De-*A*,*B*-8-(2′β-deuterio-2′α-methylethenylidene)cholestane (31c). Internal Methanol-*O*-d_1 Quench Followed by Methanol Workup. Via the standard procedure outlined for the reduction of **2b**, *t*-BuLi (0.10 mL, 1.95 M in pentane, 0.20 mmol) was added to a solution of **10** (21.0 mg, 0.05 mmol) and methanol-*O*-d_1 (5.2 μL, 0.13 mmol) in Et_2O (1.0 mL) at −78 °C. After 10 min at −78 °C, the reaction was quenched with 0.5 mL of methanol and then worked up. Flash chromatography (hexanes) followed by HPLC purification (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded *R* isomer **31c** (90% d_1 by ^{1}H-NMR analysis, 13.7 mg, 93%) contaminated by 3.7% (by ^{1}H NMR integration) of the *S* isomer **31d**.

Internal Methanol-*O*-d_1 Quench Followed by Methanol-*O*-d_1 Workup. As described for the reduction of **2b**, *t*-BuLi (0.28 mL, 1.70 M in pentane, 0.47 mmol) was added to a solution of **10** (48.0 mg, 0.12 mmol) and methanol-*O*-d_1 (12.2 μL, 0.30 mmol) in Et_2O (2.4 mL) at −78 °C. The reaction was quenched at −78 °C after 10 min with methanol-*O*-d_1 (0.5 mL) and then worked up as usual. Purification by flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded *R* isomer **31c** (90% d_1 by ^{1}H NMR integration, 29 mg, 86%), which was contaminated with 4.3% of the *S* isomer **31d**.

1-Tridecene (32a). From (*Z*)-1-(Phenylsulfinyl)-1-tridecene (11b). As described for the standard reduction of **2b**, *t*-BuLi (0.52 mL, 1.79 M in pentane, 0.93 mmol) was added to a solution of **11b** (71.2 mg, 0.23 mmol) and methanol (23 μL, 0.58 mmol) in Et_2O (4.6 mL) at −78 °C. Flash column chromatography (hexanes) afforded **32a** (24.3 mg, 57%). More polar components were eluted (ethyl acetate) as a single fraction, and the polar residue was then purified further by HPLC. Purification of the combined polar residue by HPLC (Rainin Microsorb M8 10/25, 50% ethyl acetate/hexanes, flow rate 6 mL/min) afforded in order of elution: impure (*E*)-1-(phenylsulfinyl)-1-tridecene (**11a**); impure (*Z*)-1-(phenylsulfinyl)-1-tridecene (**11b**); 6.1 mg (9%) of what appears to be (*E*)-1-(*tert*-butylsulfinyl)-1-tridecene (by ^{1}H NMR analysis only); and 11.9 (28%) mg of *tert*-butyl phenyl sulfoxide (**7**).

From (*E*)-1-(Phenylsulfinyl)-1-tridecene (11a). Via the standard procedure outlined for the reduction of **2b**, *t*-BuLi (0.56 mL, 1.89 M in pentane, 1.1 mmol) was added to a solution of **11a** (80.7 mg, 0.26 mmol) and methanol (26.4 μL, 0.65 mmol) in Et_2O (5.2 mL) at −78 °C. After flash column chromatography (hexanes), **32a** (13.3 mg, 28%) was obtained as a colorless oil.

(*Z*)-Tetradec-2-ene (32b). Via the standard procedure outlined for the reduction of **2b**, *t*-BuLi (0.24 mL, 1.98 M in pentane, 0.47 mmol) was added to a solution of **11c** (38.0 mg, 0.12 mmol) and methanol (12 μL, 0.30 mmol) in Et_2O (2.4 mL) at −78 °C. Purification by flash column chromatography (hexanes) followed by HPLC (Whatman Partisil M10 20/50, hexanes, 8 mL/min flow rate) afforded **32b** (6.5 mg, 28%) and allene **33** (6.7 mg, 29%) as colorless oils.

(*E*)-Tetradec-2-ene (32c). As described for the reduction of **2b**, *t*-BuLi (0.53 mL, 1.72 M in pentane, 0.91 mmol) was added to a solution of **11d** (73.0 mg, 0.23 mmol) and methanol (23 μL, 0.57 mmol) in Et_2O (4.6 mL) at −78 °C. After workup and purification by flash column chromatography (100% hexanes) and HPLC (Whatman Partisil M10 20/50, hexanes, 7.9 mL/min flow rate), **32c** (23.1 mg, 52%) and allene **33** (6.2 mg, 14%) were obtained as colorless oils.

1-Deuterio-1-tridecene (32d). From (*E*)-1-(Phenylsulfinyl)-1-tridecene (11b). As described for the standard reduction of **2b**, *t*-BuLi (0.51 mL, 1.79 M in pentane, 0.91 mmol) was added to a solution of **11b** (70.0 mg, 0.23 mmol) and MeOD (24 μL, 0.58 mmol) in Et_2O (4.6 mL) at −78 °C. Workup followed by flash column chromatography (hexanes) afforded **32d** (12 mg, 29% yield).

From (*Z*)-1-(Phenylsulfinyl)-1-tridecene (11a). Via the standard procedure for the standard reduction described for **2b**, to a solution of **11a** (74 mg, 0.24 mmol) and MeOD (25 μL, 0.60 mmol) in Et_2O (4.8 mL) at −78 °C was added *t*-BuLi (0.54 mL, 1.79 M in pentane, 0.97 mmol). Workup followed by flash column chromatography (hexanes) afforded **32d** (24 mg, 54%).

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Registry No. **2a**, 103149-79-7; **2b**, 103149-81-1; **3a**, 103149-80-0; **3b**, 103149-81-1; **6a**, 116205-38-0; **6b**, 116205-43-7; **7**, 4170-71-2; **8a**, 116205-42-6; **8b**, 116205-44-8; **9**, 124267-06-7; **10**, 83239-24-1; **11a**, 116205-47-1; **11b**, 116205-46-0; **11c**, 116205-45-9; **11d**, 116205-39-1; **12**, 14916-79-1; **13**, 63478-76-2; **14**, 119837-81-9; **15**, 432-25-7; **16**, 124267-07-8; **19a**, 124267-10-3; **19b**, 124267-11-4; **20**, 124267-08-9; **21**, 756-79-6; **22**, 83239-22-9; **24**, 58496-74-5; **25a**, 100-68-5; **25b**, 7205-91-6; **26**, 38066-16-9; **27**, 55264-89-6; **28a**, 124267-12-5; **28b**, 124267-13-6; **29**, 124267-09-0; **30**, 99647-15-1; **31a**, 83239-21-8; **31b**, 83290-11-3; **31c**, 124375-83-3; **31d**, 88165-98-4; **32a**, 2437-56-1; **32b**, 35953-53-8; **32c**, 35953-54-9; **32d**, 124267-14-7; **33**, 116205-40-4; DAPA, 54856-92-7; APA, 4726-85-6; *tert*-butyllithium, 594-19-4; methanol, 67-56-1; *n*-butyllithium, 109-72-8; *sec*-butyllithium, 598-30-1; *sec*-butyl alcohol, 78-92-2; methanol-*O*-d_1, 1455-13-6; phenylsulfenyl chloride, 931-59-9; dodecyl aldehyde, 112-54-9; *p*-chlorophenylsulfenyl chloride, 933-01-7; bis(*p*-chlorophenyl) disulfide, 1142-19-4; methyl phenyl sulfinate, 670-98-4; triethyl phosphite, 122-52-1; (*E*)-1-(*tert*-butylsulfinyl)-1-tridecene, 124267-15-8.

Supplementary Material Available: Spectral data and general experimental details (23 pages). Ordering information is given on any current masthead page.

Notes

New Synthesis of 1-Alkyl(aryl)-2,3-dihydro-2-thioxo-1*H*-imidazole-4-carboxaldehydes

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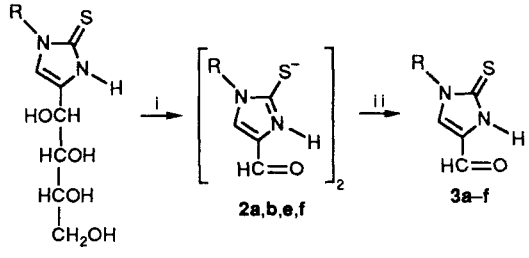
A general method for the synthesis of heterocyclic carboxaldehydes is the degradative oxidation of polyhydroxyalkylheterocycles with lead tetraacetate or sodium periodate.[1] We have reported[2,3] the utilization of this procedure for the preparation of 1,3-alkyl(aryl)-2,3-dihydro-2-thioxo-1*H*-imidazole-4-carboxaldehydes from 1,3-alkyl(aryl)-1,3-dihydro-4-(polyhydroxyalkyl)-2*H*-imidazole-2-thiones. We have also described[3-5] the synthesis of 1-aryl(H)-2-(benzylthio)-1*H*-imidazole-4-carboxaldehydes by oxidation of the corresponding 4-polyhydroxyalkyl derivatives. After acetalization of these aldehydes and reduction with Na/NH_3, 1-aryl(H)-2,3-dihydro-2-thioxo-1*H*-imidazole-4-carboxaldehydes were obtained.[3] However, this procedure requires several steps and the overall yields are low. We now report an improved method for the synthesis of carboxaldehydes **3** that avoids the use of protecting groups. This method employs the oxidation of 1-alkyl(aryl)-1,3-dihydro-4-(D-*arabino*-tetritol-1-yl)-2*H*-imidazole-2-thiones (**1**) to the corresponding 2,2′-dithiobis[1-alkyl(aryl)-1*H*-imidazole-4-carboxaldehydes] (**2**) followed by the reduction of the S–S bond. (Scheme I).

Scheme I[a]



a, R = C_4H_9; **b**, R = C_8H_{17}; **c**, R = $C_{12}H_{25}$; **d**, R = Ph; **e**, R = *p*-MeC_6H_4; **f**, R = *p*-$EtOC_6H_4$

[a] (i) $(AcO)_4Pb$; (ii) SO_2.

Compounds **3** are of interest because they are intermediates in the synthesis of imidazole derivatives with potential biological importance, such as thiolhistidines and thiolhistamines.

The oxidation of 1-alkyl(aryl)-1,3-dihydro-4-(D-*arabino*-tetritol-1-yl)-2*H*-imidazole-2-thiones (**1**) with 2.5 molar excess of lead tetraacetate in acetic acid benzene (1:2) gave a mixture of **2** and **3**, in which the disulfide was the major product.

Crystallization of the crude product of the reaction from ethyl acetate afforded the disulfides **2a,b,e,f** in 20–50% yield. In parallel experiments, the crude mixtures were reduced with SO_2, giving 1-alkyl(aryl)-2,3-dihydro-2-thioxo-1*H*-imidazole-4-carboxaldehydes (**3a–f**) in 50–70% yield from **1**.

The structures of compounds **2** and **3** were assigned on the basis of analytical, UV, IR, ^1H and ^{13}C NMR (Table I), and mass spectroscopic data, and in the case of **2e** X-ray data.

The IR,[3-5] ^1H NMR,[3] and ^{13}C NMR[6-8] spectroscopic data

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