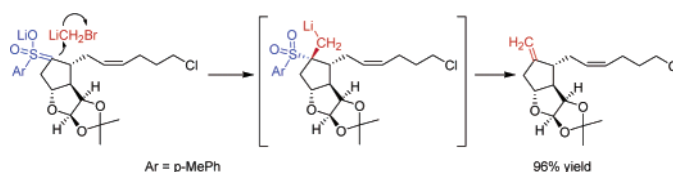# Lithium Carbenoids−Ultra-Reactive Yet Selective Reagents for Methylenation and Halomethylenation of Sulfones[1]

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Ar = p-MePh   96% yield

The first efficient, one-pot method for methylenation of *p*-toluyl sulfones (i.e., the transformation of *p*-MePhSO$_2$CHR$_2$ into R$_2$CCH$_2$) is described. Methods for effecting that transformation involving alkylation of sulfones with reagents of the general formula MCH$_2$X, where M = SiMe$_3$, SnR$_3$, and MgCl (the Julia method) have been previously described. However, the silicon reagent is completely unreactive toward many sulfones, the tin reagent typically affords only moderate yields, and the magnesium reagent typically gives incomplete reaction (9−40% starting material). This article reports that excellent yields are obtained by alkylating the sulfone with the more ionic lithium methylene carbenoids (LiCH$_2$X, where X = Cl, Br, and I). For example, treatment of sulfone **1** with 3 equiv of *n*-BuLi (THF, −100 °C) followed by 2 equiv of CH$_2$Br$_2$ affords olefin **2** in 96% yield. Although the carbenoid is generated in the presence of a 1:2 mixture of α-lithio-sulfone and *n*-BuLi, it reacts selectively with the α-lithio-sulfone (K_{rel} = 9.6 ± 0.8 with LiCH$_2$Br). The chlorocarbenoid LiCH$_2$Cl reacts somewhat less selectively (K_{rel} = 3.5). The alkyl-substituted carbenoid *n*-BuCHBrLi reacts ≥ 40 times more slowly than LiCH$_2$Br, suggesting that olefination occurs by the S$_N$2 mechanism rather than by metal-assisted ionization (MAI), the mechanism by which cyclopropyl and vinylidene carbenoids react with nucleophiles. Finally, sulfones can be transformed into vinyl halides by treatment with 3 equiv of *n*-BuLi (THF, −78 °C), followed by >2 equiv of diisopropylamine, followed by 3 equiv of dihalomethane (CH$_2$X$_2$, where X$_2$ = Cl$_2$, BrCl, Br$_2$, or I$_2$). All products are formed in high yield and purity.

Introduction

A family of methods for olefin synthesis conceptually involve the alkylation of a metalated sulfone with a reagent with "latent carbene" character (Scheme 1).

Vedejs et al. reported the first example of this class of olefination reaction, where the "latent carbene" was a tosylhydrazone.[2] Reich et al. then reported the reaction of α-lithio-sulfones with acyl silanes to give silyl enol ethers.[3] Kocienski then reported a two-step procedure for the methylenation of

SCHEME 1.   Olefin Synthesis from Sulfones and "Latent Carbenes"
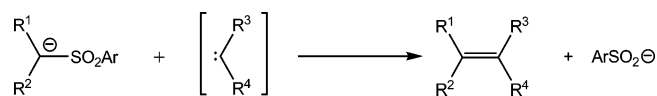
sulfones, consisting of alkylation with Me$_3$SiCH$_2$I, followed by *n*-Bu$_4$NF·3H$_2$O-induced fragmentation.[4] Although effective for many sulfones, a number of complex sulfones were reported to undergo alkylation in low yield or not at all.[5,6]

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(1) Part 3 of series entitled "Olefin Synthesis by Reaction of Stabilized Carbanions with Carbene Equivalents." (a) Part 1: Pearlman, B. A.; Putt, S. R.; Fleming, J. A. *J. Org. Chem.* **1985**, *50*, 3622. (b) Part 2: Pearlman, B. A.; Putt, S. R.; Fleming, J. A. *J. Org. Chem.* **1985**, *50*, 3625.

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SCHEME 2. Methylenation Step in the Meteneprost Potassium Process

1   2   Meteneprost Potassium
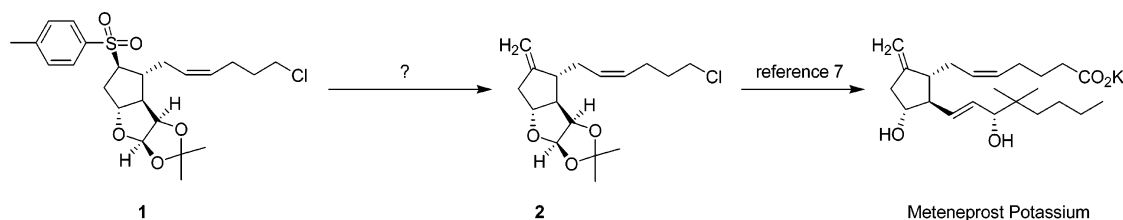
SCHEME 3. Julia Process for the Methylenation of Sulfones

60-82%   9-40%
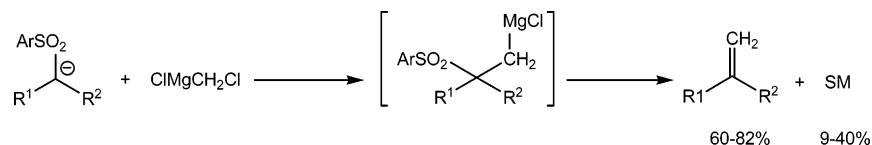
Methylenation of sulfone **1** is a key step in a process to produce meteneprost potassium (Scheme 2),[7] a drug candidate in development by The Upjohn Company in the early 1980s for cervical dilatation.

Initial attempts to effect this transformation using Me_3SiCH_2I resulted in no reaction.[1a] Aware of precedent that the reactivity of MCH_2X increases with increasing polarization of the C−M bond,[8] we explored the analogous tin reagent $n\text{-}Bu_3SnCH_2I$ and found that it alkylated sulfone **1** to afford (after fluoride-induced fragmentation of the adduct) olefin **2** in moderate (77.7%) yield.[1a] Fujita et al. independently developed a method for sulfone methylenation using $n\text{-}Bu_3SnCH_2I$.[9] Subsequently, Julia and De Lima reported that sulfonyl-stabilized carbanions undergo alkylation by $ClMgCH_2Cl$ (2 equiv; THF, −78 °C → rt) to afford olefins in one step (Scheme 3).[10] However, reactions were incomplete with all sulfones studied (9−40% unreacted sulfone). Others have encountered the same problem of incomplete reaction.[11] Metz et al. have recently overcome this problem by using >5 molar equivalents of $IMgCH_2I$ in the presence of HMPA.[12] Satoh et al. have extended the reaction to substituted alkylmagnesium carbenoids.[13]

Speculating that the problem of incomplete reaction might be solved by switching to a more reactive reagent, we decided to investigate lithium carbenoids ($LiCH_2X$, where X is Cl, Br, or I) because lithium is much more ionic than any of the metals previously studied.

Lithium methylene carbenoids have been extensively studied and are known to be highly unstable. Koebrich et al. showed that $LiCH_2Cl$ can be generated by the reaction of n-BuLi with CH_2ClBr in THF/Et_2O/pentane at −110 °C but is "very unstable."[14,15] Cainelli et al. found that $LiCH_2Br$ is "very unstable and practically impossible to prepare even at −110 °C."[16] Villieras et al. found that $LiCH_2Br$ and $LiCH_2Cl$ decomposed immediately even at −130 °C, but that mixtures with LiBr are stable for up to 30 min in THF/Et_2O/pentane at −115 °C.[17] Yet previous researchers have shown that $LiCH_2\text{-}Br$ and $LiCH_2Cl$, when generated in the presence of ketones, aldehydes,[16−18] alkoxyboranes,[15,19] and chlorosilanes,[20] form adducts in high yield. These reactions are conducted by adding n-BuLi or MeLi to a mixture of CH_2Br_2 or CH_2ICl and the electrophile ("Barbier" procedure). Thus, it was decided to investigate the Barbier addition mode for methylenation of α-lithio-sulfones.

Results

Addition Mode with *n*-BuLi Added Last. A solution of sulfone **1** and 3.0 equiv of CH_2Br_2 in THF was treated with 4.0 equiv of n-BuLi/hexane (THF, ≤−50 °C) in the hope that the carbenoid and α-lithio sulfone would be generated at equal rates and then react with each other efficiently (Scheme 4). In practice, olefin **2** was formed in 64.6% yield, however, 9β-methyl sulfone **3a** was also formed in 28.4% yield. Presumably, this byproduct was formed by the reaction of α-lithio-**1** with MeBr, the byproduct of deprotonation of sulfone **1** by $LiCH_2\text{-}Br$ (unproven).

Addition Mode with CH_2Br_2 Added Last. The inverse addition mode (CH_2Br_2 added last) was next investigated. With this addition mode, the carbenoid is generated in the presence of both α-lithio-**1** and n-BuLi, thus raising the issue of whether the carbenoid would react faster with α-lithio-**1** or with n-BuLi.

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TABLE 1.   Effect of Stoichiometry, Rate of Addition of CH$_2$Br$_2$, and Temperature on Yields of Methylenation and Homologation[a]

entry	n-BuLi (equiv)	CH$_2$Br$_2$ (equiv)	add rate[b]	exotherm[c]	2 (%)	7b (%)	1 (%)	4 (%)	5 (%)	6 (%)	K[d]
1	2.00	1.00	slow	$-97 \rightarrow -82$ °C	81.3	0.0	17.6	1.6	7.1	0.6	8.8
2	2.00	1.00	fast	$-98 \rightarrow -74$ °C	90.6	0.0	7.9	2.5	1.3	0.0	
3	3.00	2.00	slow	$-98 \rightarrow -70$ °C	94.4	1.5	2.0	9.2	27.2	5.6	10.4
4	3.00	2.00	fast	$-99 \rightarrow -63$ °C	96.4	0.0	2.1	8.8	4.9	0.4	
5	3.00	1.00	slow	$-100 \rightarrow -83$ °C	62.7	1.0	35.5	2.7	8.0[e]	0.8[e]	
6	3.00	1.00	fast	$-99 \rightarrow -77$ °C	81.9	0.0	17.2	2.2	3.5[e]	0.3[e]	
7	2.00	1.00	fast	$-28 \rightarrow -7$ °C	69.3	9.2	18.4	1.6	8.3	0.9	
8	3.00	2.00	fast	$-29 \rightarrow +5$ °C	86.4	4.3	5.5	5.1	26.2	4.8	
9	3.00	1.70	fast	$-27 \rightarrow -7$ °C	69.4	0.1					

[a] General procedure: a solution of sulfone **1** in THF at -100 °C or -30 °C was treated with n-BuLi/hexanes followed by CH$_2$Br$_2$. [b] Addition rate of CH$_2$Br$_2$ (fast means "all at once," slow means over 2 min). [c] Exotherm on addition of CH$_2$Br$_2$. [d] $K \equiv k^S/k^B$. [e] In these experiments, the yields of **5** and **6** do not reflect the true extent of homologation, because not all of the alkyllithium is converted to alkyl bromide.

SCHEME 4.   Addition Mode with n-BuLi Added Last
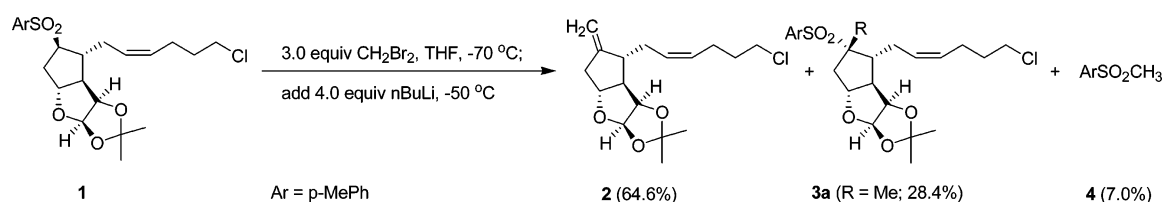
Kirmse and von Wedel,[21] Huisgen and Burger,[22] and Friedman et al.[23] have shown that LiCH$_2$X reacts with n-BuLi to afford a homologous series of alkyllithium derivatives, n-Bu(CH$_2$)$_n$-Li, $n = 0, 1, 2$, and so on ("homologation"). A set of experiments was carried out in which sulfone **1** was treated in THF at -100 °C with either 2.00 or 3.00 equiv of n-BuLi/hexanes, followed by a solution of either 1.00 or 2.00 equiv of CH$_2$Br$_2$ in THF. The stoichiometry was varied to generate kinetic data. The experiments were done at cryogenic temperature, where the carbenoid intermediate is maximally stable with gradual addition of the CH$_2$Br$_2$ over 2 min to minimize the temperature rise. The crude reaction mixtures were analyzed by quantitative GC to determine the yields of n-C$_5$H$_{11}$Br (**5**) and n-C$_6$H$_{13}$Br (**6**), then flash chromatographed to determine yields of olefin **2**, sulfone **1**, and p-MePhSO$_2$Me (**4**). Results are compiled in Table 1.

The relative reactivity of α-lithio-**1** versus n-BuLi ($K \equiv k^S/k^B$) was calculated from the yields of olefin **2**,[24] n-C$_5$H$_{11}$Br **5**, and n-C$_6$H$_{13}$Br **6**, using eq 1[25] (where S is the amount of sulfone, D is the total amount of CH$_2$Br$_2$ added, and B^i is the initial amount of n-BuLi) to correct for the different kinetics with which the two species react. Because S, D, and B^i are each known with reasonable accuracy, and mass recoveries are close to the theoretical, the calculated values for K should be reasonably accurate. By averaging the results of entries 1 and 3 of Table 1, it was determined that LiCH$_2$Br reacts 9.6 ± 0.8

times faster with α-lithio-**1** than with n-BuLi.

$$(KB^i - B^i - K)S^{(1/K)} + KS + (K - 1)(D - B^i) = 0 \quad (1)$$

In the course of experimentation, it was discovered that adding the CH$_2$Br$_2$ "all at once" rather than over a period of 2 min increased the yield of olefin **2** and effectively suppressed formation of the homologated alkyl bromides **5** and **6** (see Table 1, entries 1 vs 2, 3 vs 4, and 5 vs 6). Because the period of time during the CH$_2$Br$_2$ add when both n-BuLi and LiCH$_2$Br are present is passed without the two reacting with each other, homologation must be slower than lithium−bromide exchange. At the end of the add, the mixture contains an approximately equimolar mixture of α-lithio-**1** and LiCH$_2$Br, which react together efficiently to give olefin **2** cleanly and in high yield.

Simultaneous addition of n-BuLi and CH$_2$Br$_2$ was also investigated and found to be a viable addition mode. By adding 2.5 equiv of n-BuLi and 1.1 equiv of CH$_2$Br$_2$ simultaneously at -68 °C, a 91.3% yield was obtained.

Two experiments (Table 1, entries 7 and 8) were run at -30 °C (initial temperature) to assess the need for cryogenic conditions. That temperature was chosen because it can be relatively easily reached in noncryogenic general purpose pilot/production equipment. The experiments gave lower yields of **2**

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(24) The digit after the decimal in the yields of olefin **2** is not significant. However, the digit after the decimal in the yields of the byproducts (**7b**, **4**, **5**, **6**, and recovered **1**) is significant. Thus, to maintain consistency of presentation, the digit after the decimal is reported for **all** yields. Note that 100% minus the yield of recovered sulfone **1** is used rather than the yield of olefin **2** in all selectivity calculations. Thus, the legitimacy of including the digit after the decimal is a moot point.

(25) See Supporting Information (Appendix) for derivation.

SCHEME 5.   Reaction of Lithiated Model Sulfone with CH$_2$Br$_2$
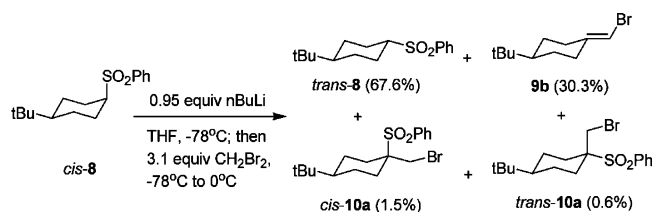
and higher yields of **5**, along with high levels of vinyl bromide **7b** (9.2 and 4.3%).

7a (X = Cl)
7b (X = Br)
7c (X = I)
7d (X = nBu)
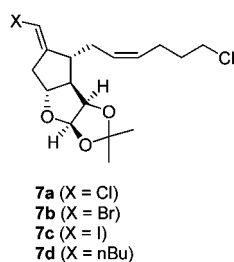
The mechanism of vinyl bromide formation was investigated using a model sulfone (*cis*-**8**; Scheme 5). It was found that α-lithio-**8** reacts with CH$_2$Br$_2$ in the absence of *n*-BuLi to form vinyl bromide **9b**. Thus, the elevated level of vinyl bromide **7b** formed in the noncryogenic temperature experiments is attributed to the consumption of *n*-BuLi prior to the end of the CH$_2$Br$_2$ add by deprotonation pathways, so that there is not enough *n*-BuLi left at the end of the CH$_2$Br$_2$ add to react with all of the CH$_2$Br$_2$. Formation of vinyl bromide **7b** can be effectively suppressed by decreasing the CH$_2$Br$_2$ charge to 1.7 equiv (with 3.0 equiv of *n*-BuLi), which ensures that some *n*-BuLi remains at the end of the CH$_2$Br$_2$ add (Table 1, entry 9). Alternatively, the vinyl bromide can be effectively suppressed by running at cryogenic temperature (Table 1, entries 2, 4, and 6).

Compounds *cis*-**10a** and *trans*-**10a** were identified by spectroscopic comparison with authentic samples prepared by the route outlined in Scheme 6.

LiCH$_2$I. A set of experiments was done to compare LiCH$_2$I with LiCH$_2$Br with both sulfone **1** and *cis*-**8** as test substrates (Table 2). The yields were equal within experimental error.

LiCH$_2$Cl. With the chlorocarbenoid LiCH$_2$Cl (generated from either *n*-BuLi/CH$_2$BrCl or *t*-BuLi/CH$_2$BrCl), lower yields of olefin **2** and higher yields of the homologated alkyl bromides were obtained than with the bromocarbenoid (Table 3). It was calculated that LiCH$_2$Cl reacts with α-lithio-**1** 3.5 times faster than with *n*-BuLi and 0.7 times as fast as with *t*-BuLi.

CH$_2$Br$_2$ was chosen for a preparative scale experiment (starting with 50 g of sulfone **1**) because it reacted with higher

selectivity than CH$_2$BrCl and is cheaper than CH$_2$I$_2$. The yield (88%) was comparable with that obtained on a 0.9 g scale (96%; Table 1, entry 4), and the quality was equal.

Alternative Alkyllithium Reagents. Repeating the Table 1, entry 1 experiment but with *t*-BuLi instead of *n*-BuLi gave olefin **2** in 68% yield along with *t*-BuCH$_2$Br (**12**) in 25.0% yield (Table 4). Analysis of the data reveals that LiCH$_2$Br reacts with α-lithio-**1** 2.8 ± 0.9 times faster than with *t*-BuLi, and with *t*-BuLi approximately $^{9.6}/_{2.8} = 3.4$ times faster than with *n*-BuLi. Previous studies have also found that *t*-BuLi is more nucleophilic than *n*-BuLi (in THF).[26]

Adding the CH$_2$Br$_2$ "all at once" reduced the amount of byproduct *t*-BuCH$_2$Br **12** from 25.0 to 12.1% and increased the yield of olefin **2** from 67.7 to 80.5% (Table 4, entries 1 vs 2). The incomplete suppression of the byproduct is due to the fact that *t*-BuLi undergoes homologation faster than *n*-BuLi.

Repeating the Table 1, entry 1 experiment but with MeLi instead of *n*-BuLi resulted in formation of approximately equal yields of olefin **2** and 9β-methyl sulfone **3a** (Table 5), indicating that both LiCH$_2$Br and MeBr alkylate α-lithio-**1** faster than they are formed by halogen−metal exchange between MeLi and CH$_2$Br$_2$ (i.e., halogen−metal exchange is the rate-determining step). To quantify the rate of halogen−metal exchange, an experiment (Table 5, entry 2) was run at low temperature (−96 °C) and quenched with methanol as soon as possible after the end of the CH$_2$Br$_2$ add (8 s).[27] From the results, it is estimated that the half-life of sulfone **1** at −96 °C is ∼30 s.[28] Halogen−metal exchange must be slower because it is the rate-determining step.

Trisubstituted and Tetrasubstituted Olefin Synthesis. Attempts were made to extend the new olefin synthesis to the preparation of trisubstituted olefins (Table 6).

Olefination did occur to give trisubstituted olefin **7d**, but very slowly. The rate of alkylation of α-lithio-**1** by *n*-BuCHBrLi could be roughly estimated as follows. From the results of entry 2, Table 6, it is estimated that the half-life of α-lithio-**1** in the presence of *n*-BuCHBrLi is 170 s at −74 °C. Ample carbenoid *n*-BuCHBrLi (85.6−113.3%) as well as α-lithio-**1** (70.6−94.4%) were present throughout that time frame to justify the assumption of first-order kinetics.[29] By comparison, from the results of entry 2, Table 1, it is estimated that the half-life of α-lithio-**1** in the presence of LiCH$_2$Br at −74 °C is <4.3 s. Thus, it can be estimated that LiCH$_2$Br reacts ≥40 times more rapidly than *n*-BuCHBrLi with α-lithio-**1**.

As a consequence of the slow rate of olefination, carbenoid dimerization to 5-decene (stereochemistry unassigned) was competitive. No other significant byproducts could be detected by TLC or GC. In particular, nC$_5$H$_{11}$SO$_2$Ar could not be detected, suggesting that the dimerization is not mediated by ArSO$_2^-$ but rather occurs by Wurtz−Fittig coupling of the carbenoid, which is the mechanism proposed by Koebrich for dimerization of LiCHCl$_2$ to *trans*-ClCHCHCl.[30]
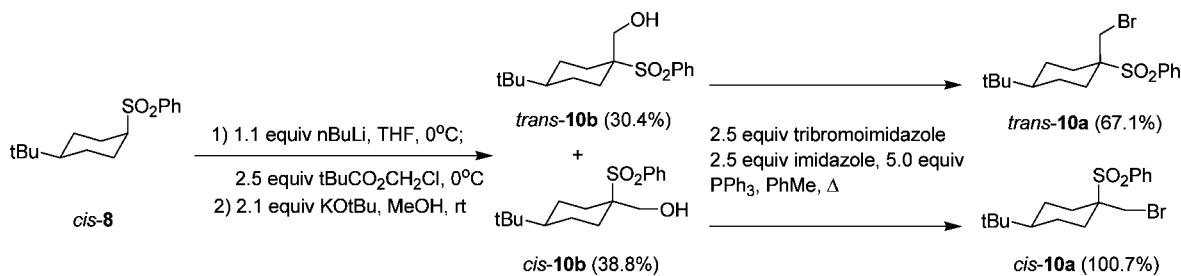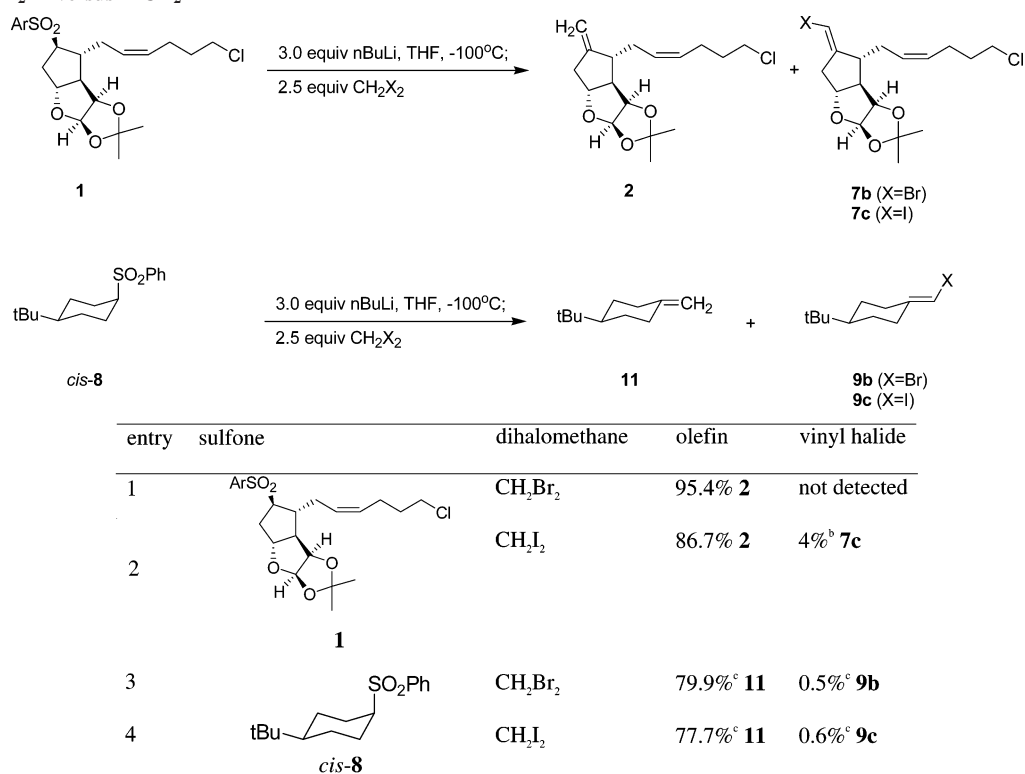
SCHEME 6.   Synthesis of Bromomethyl Sulfones

TABLE 2. LiCH$_2$Br versus LiCH$_2$I[a]

entry	sulfone	dihalomethane	olefin	vinyl halide
1		CH$_2$Br$_2$	95.4% **2**	not detected
2		CH$_2$I$_2$	86.7% **2**	4%[b] **7c**
3		CH$_2$Br$_2$	79.9%[c] **11**	0.5%[c] **9b**
4		CH$_2$I$_2$	77.7%[c] **11**	0.6%[c] **9c**

[a] General procedure: a solution of sulfone in THF (0.12 M) was cooled to −100 °C, treated with 3.0 equiv of n-BuLi, recooled to −100 °C, treated with 2.5 equiv of CH$_2$X$_2$ in one portion, and quenched 30 s later with methanol. [b] By ^{13}C NMR peak height ratio. [c] By integration of ^{1}H NMR vs internal standard (DMSO).

TABLE 3. Methylenation Experiments with LiCH$_2$Cl[a]
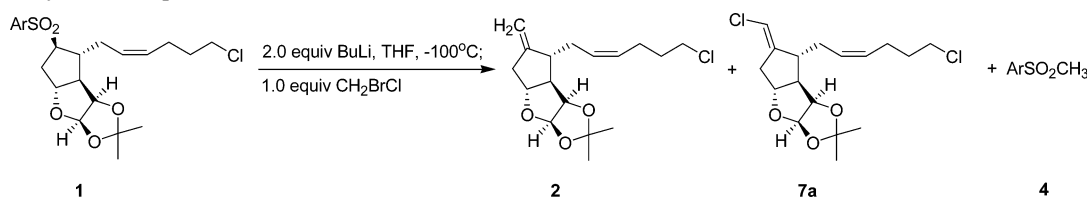
entry	BuLi	add rate[b]	exotherm	2 (%)	7a (%)	1 (%)	4 (%)	RCH$_2$Br	RCH$_2$CH$_2$Br	K[c]
1	n-BuLi	slow	−99 → −80 °C	65.4	1.2	32.5	0.3	11.7	2.1	3.5
2	n-BuLi	fast	−101 → −85 °C[d]	83.7	0.0	15.0	0.5	0.5	0.0	
3	t-BuLi	slow	−100 → −78 °C	49.7	0.0	50.2	0.0	39.2	2.0	0.7
4	t-BuLi	fast	−101 → −83 °C[d]	83.1	0.0	15.6	0.4	7.4	0.0	

[a] General procedure: a solution of sulfone **1** in THF (0.12 M) was cooled to −100 °C, treated with 2.0 equiv of [n]BuLi/hexanes or tBuLi/pentane, re-cooled to −100 °C, then treated with 1.0 equiv of CH$_2$BrCl. [b] Add rate of CH$_2$BrCl (fast means "all at once," slow means over 2 min). [c] $K \equiv k^S/k^B$. [d] Anomalously small exotherm may be attributable to low initial temperature.

Interestingly, the trans/cis isomer ratio of the product **7d** decreased continuously over the course of the reaction: 89/11

(26) Waack, R.; Doran, M. A. *J. Org. Chem.* **1967**, *32*, 3395.

(27) Methanol is expected to be an effective quenching agent based on the fact that water quenches t-BuCHILi to give t-BuCH$_2$I at below −90 °C, see: Goldstein, M. J.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 2293.

(28) Half-lives were calculated using the formula $t^{1/2} = (t \ln(1/2))/(\ln(1 − M)$, where t is the time (in seconds) and M is the yield of olefin **2** (expressed in decimal format).

(29) Halogen−metal exchange to form n-BuCHBrLi was 64% complete in 20 s at −95 °C, by comparison of the sum of the yields of all the carbenoid-derived products (5.9% yield of **2**, 2.3% yield of 5-decene, and 113.3% yield of n-C$_5$H$_{11}$Br **5** [the product of protonation of the carbenoid]) with the yield of unreacted n-BuCHBr$_2$ (34.3%).

at −95 °C, 78/22 at −74 °C, and 73/27 at −62 °C. This suggests that the two enantiomers of n-BuCHLiBr[31] react at different rates with sulfone **1** (which is enantiomerically pure because it is synthesized from glucose) to afford different ratios of the two geometric isomers of the product. The enantiomeric excess of the unreacted carbenoid was not measured to test this hypothesis.[32]

(30) (a) Koebrich, G.; Merkle, H. R. *Chem. Ber.* **1966**, *99*, 1782. (b) Koebrich, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 41. (c) Koebrich, G. *Bull. Soc. Chim. Fr.* **1969**, 2712.

(31) Hoffmann has shown that the two enantiomers of n-BuCHBrLi do not interconvert at −120 °C: Hoffmann, R. W.; Julius, M.; Chemla, F.; Ruhland, T.; Frenzen, G. *Terahedron* **1994**, *50*, 6049.

TABLE 4. Methylenation Experiments with *t*-BuLi[a]

entry	*t*-BuLi (equiv)	CH$_2$Br$_2$ (equiv)	add rate[b]	exotherm[c]	2 (%)	7b (%)	1 (%)	4 (%)	12 (%)	K[d]
1	2.00	1.00	slow	−99 → −84 °C	67.7	0.0	32.1	0.3	25.0	1.9
2	2.00	1.00	fast	−99 → −77 °C	80.5	0.0	18.8	1.6	12.1	
3	3.00	2.00	slow	−96 → −68 °C	77.2	2.4	19.3	1.7	54.0	3.6
4	3.00	2.00	fast	−98 → −58 °C	88.7	0.0	10.5	3.8	57.2	
5	3.00	1.00	slow	−100 → −80 °C	43.6	0.0	57.3	1.2	27.1	
6	3.00	1.00	fast	−98 → −75 °C	42.7	0.0	56.7	1.5	27.0	

[a] General procedure: a solution of sulfone in THF (0.13 M) was cooled to −100 °C, treated with *t*-BuLi/pentane, recooled to −100 °C, and treated with CH$_2$Br$_2$. [b] Add rate of CH$_2$Br$_2$ (fast means "all at once," slow means over 2 min). [c] Exotherm on addition of CH$_2$Br$_2$. [d] $K \equiv k^S/k^B$.

TABLE 5. Experiments with MeLi[a]

entry	MeLi (equiv)	CH$_2$Br$_2$ (equiv)	exotherm	2 (%)	3a (%)	1 (%)	4 (%)	13 (%)
1	2.00	1.00	−96 → −78 °C	51.0	48.8	0.0	2.9	1.5
2	2.00	1.00	−96 °C[b]	17.1	11.9	71.1	0.0	0.0
3	3.00	2.00	−100 → −50 °C	53.3	46.2	0.0	0.0	4.1
4	3.00	1.99	−72 → −42 °C	64.4	36.2	0.0	0.0	4.9
5	3.00	2.00	−20 → +9 °C	44.1	55.7	0.0	0.0	2.5

[a] General procedure: a solution of sulfone **1** in THF (0.12 M) was cooled to −70 °C, treated with MeLi/Et$_2$O, re-cooled to the indicated temperature, and treated all at once with neat CH$_2$Br$_2$. [b] Quenched with methanol 8 s after the CH$_2$Br$_2$ add.

TABLE 6. Experiments with *n*-BuCHBr$_2$/*n*-BuLi[a]

entry	exotherm	time[b]	7d (%)	trans/cis	1 (%)	*n*-C$_5$H$_{11}$Br (%)	*n*-BuCHBr$_2$ (%)	5-decene (%)
1	−102 → −95 °C	20 s	5.9	89/11	94.4	113.3	69.3	2.3
2	−102 → −74 °C	85 s	28.8	78/22	70.6	85.6	34.3	23.1
3	−97 → −62 °C	3.0 m	54.0	73/27	46.5	12.0	17.9	51.7

[a] General procedure: a solution of sulfone **1** in THF (19 mL/g) was cooled to −100 °C and treated with 3.0 equiv of *n*-BuLi, followed by 2.0 equiv of *n*-BuCHBr$_2$. [b] Time between the end of the *n*-BuCHBr$_2$ add and the methanol quench.

The disubstituted carbenoid Me$_2$CBrLi proved to be even less reactive toward sulfone **1**, affording tetrasubstituted olefin **15** in only 16.3% yield along with unreacted sulfone (Scheme 7).
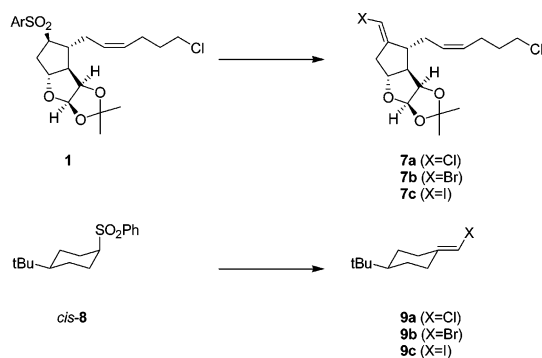
Vinyl Halide Synthesis. Sulfones **1** and *cis*-**8** can be converted into vinyl halides in high yield and purity by the application of the standard procedure, but with LDA rather than *n*-BuLi (Table 7). The reaction of metalated sulfones with dihalomethylene carbenoids to afford vinyl halides has been previously reported by Julia et al.,[33] but the procedure involved transferring a cold (−78 °C) solution of metalated sulfone to a cold (−78 °C) solution of carbenoid. The in situ procedure described herein is operationally simpler. Isolated yields of chromatographically homogeneous products are uniformly excellent (Table 7).

(32) The stereochemistry of the sulfinate elimination step (*syn*-coplanar or *anti*-periplanar) could also be deduced from the absolute configuration of the unreacted, kinetically resolved carbenoid.

(33) (a) Charreau, P.; Julia, M.; Verpeaux, J. N. *J. Organomet. Chem.* **1989**, *379*, 201. (b) Charreau, P.; Julia, M.; Verpeaux, J. N. *Bull. Soc. Chim. Fr.* **1990**, 275.

SCHEME 7. Attempted Synthesis of a Tetrasubstituted Olefin

1   3.0 equiv nBuLi, THF, -100°C;   4.0 equiv Me₂CBr₂, -100°C to 0°C   **15** (16.3% yield)
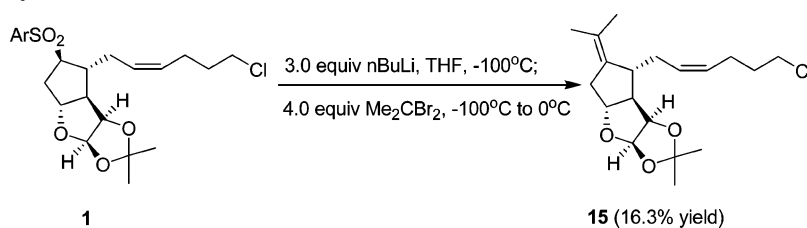
TABLE 7. Synthesis of Vinyl Halides[a]

7a (X=Cl)
7b (X=Br)
7c (X=I)

9a (X=Cl)
9b (X=Br)
9c (X=I)

entry	sulfone	dihalomethane	vinyl halide	*trans/cis*
1		CH₂Cl₂	92.7% **7a**	94/6
2		CH₂Cl₂[b]	95.7% **7a**	95/5
3	**1**	CH₂BrCl	89.7% **7a**	82/18
4		CH₂Br₂	93.0% **7b**	93/7
5		CH₂I₂	86.4% **7c**	93/7
6		CH₂Cl₂	82.8% **9a**	
7	*cis*-**8**	CH₂BrCl	86.6% **9a**	
8		CH₂Br₂	88.3% **9b**	
9		CH₂I₂	75.0% **9c**	

[a] General procedure: a solution of the sulfone in THF (10 mL/g) at −78 °C is treated with 3.0 equiv of *n*-BuLi, followed by >2.0 equiv of *i*-Pr₂NH. After 7 min, 3.0 equiv of CH₂X₂ is added all at once. [b] *i*-Pr₂NH add omitted.

The only caveat is that the CH₂X₂ must be added "all at once" as, otherwise, the vinyl halide product will be in contact with the LDA for a sufficient length of time to be deprotonated to a vinylidene carbenoid species, which decompose by various pathways depending on structure. In the case of **7b**, the corresponding vinylidene carbenoid decomposes cleanly to cyclobutane dimer **16** by the cascade of cycloadditions depicted in Scheme 8. Thus, an experiment in which the CH₂Br₂ was added over 6 min at −78 °C (Scheme 8) afforded cyclobutane dimer **16** in 59.2% isolated yield. Koebrich previously encountered a remarkably similar case of cyclobutane dimer formation on treatment of a simple γ,δ-unsaturated vinyl chloride with *n*-BuLi. He established that the stereochemistry was trans, head-to-head, by X-ray crystallography.[34] Accordingly, the head-to-head stereochemistry is assigned for cyclobutane dimer **16**. The stereochemistry around the cyclopropane ring is unassigned. The control experiment in which the CH₂Br₂ was added all at once (Table 7, entry 4) gave a negligible amount of **16**, showing that

(34) Koebrich, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 464.

LDA deprotonates CH₂Br₂ much faster than it deprotonates the vinyl bromide.

The major isomer of vinyl bromide **7b** was determined to be trans by NOE (irradiation of H⁸ of **7b** resulted in ∼10% enhancement in the integral of H⁹′). Julia et al. previously assigned the trans stereochemistry to a vinyl bromide formed by similar chemistry.[33a]

The vinyl halides **7** are formed with high trans/cis stereoselectivity (Table 7). Interestingly, the stereoselectivity was lower with the unsymmetrical dihalide CH₂BrCl than with the symmetrical dihalides (CH₂Cl₂, CH₂Br₂, and CH₂I₂), and the ratio decreased as the reaction progressed (Tables 7 and 8). These observations suggest that LiCHBrCl, like *n*-BuCHBrLi (see above), exists as a racemic mixture of enantiomers that do not interconvert under the conditions of the reaction and which react at different rates with sulfone **1** (single enantiomer).

Chlorovinylation of a Nitrile. Application of the chlorovinylation process to 2-methyl-tetradecanitrile afforded vinyl chloride **17** (as a 3:2 mixture of geometric isomers) in 55.0% yield (Scheme 9).

Selectivity (k^S/k^R) of a Noncarbenoid Electrophile. A competition experiment was carried out between α-lithio-**1** and *n*-BuLi for *n*-BuBr, a noncarbenoid electrophile (Scheme 10). From the relative yields (17.8% α-*n*-butyl sulfone **3b** and 35.6% *n*-octane), it is estimated that *n*-BuBr reacts about twice as fast with *n*-BuLi as with α-lithio-**1**.

Discussion

Reactivity. Lithium methylene carbenoids are considerably more reactive toward lithiated sulfones than the more covalent carbene equivalents that have been previously investigated (MCH₂I, where M = SiMe₃, SnR₃, or MgCl). From the results of Table 1, entry 2, it is estimated that the half-life of α-lithio-**1** in the presence of LiCH₂Br at −74 °C is <4.3 s, and from the results of Table 5, entry 2, the half-life at −96 °C is estimated to be ∼30 s. Thus, while the methylenation reaction is quite fast, it is slow enough to be measurable (Table 9). Also relevant to the discussion of rates is the observation that "all at once" addition of CH₂Br₂ suppresses homologation. This indicates that homologation is slower than bromine−lithium exchange by a sufficient amount that very little occurs in the time period of an "all at once" CH₂Br₂ addition. Thus the carbenoid, while highly reactive, is "tame" enough to react with *t*-BuLi at less than the diffusion-controlled rate.

Selectivity. To gather information about the factors that affect partitioning between the methylenation and homologation pathways, sets of competition experiments between α-lithio-**1** and either *n*-BuLi or *t*-BuLi for LiCH₂Br, LiCH₂Cl, and *n*-BuBr were carried out. Results are summarized in Table 10. The following empirical trends are evident: (1) both LiCH₂Br and LiCH₂Cl react faster with α-lithio-**1** than with *n*-BuLi; (2) LiCH₂Br reacts 2.5−2.7 times more selectively than LiCH₂Cl

SCHEME 8. Mechanism of Cyclobutane Dimer Formation
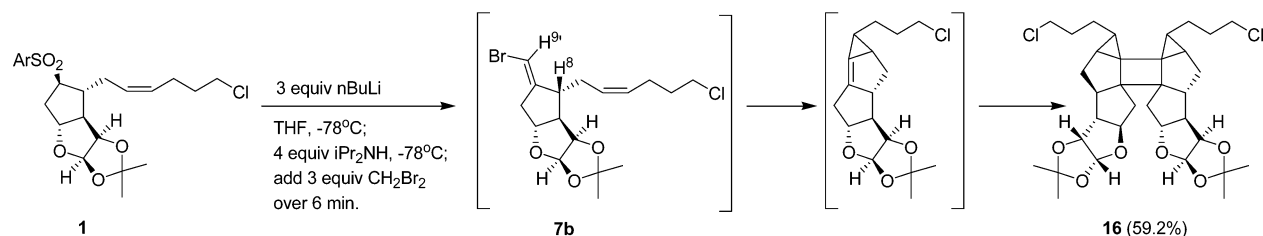
TABLE 8. Chlorovinylation of 1 with LiCHBrCl[a]

| | | | | | 7a | | 1 |
entry	*n*-BuLi	*i*-Pr$_2$NH	CH$_2$BrCl	exotherm, time	(%)	trans/cis	(%)
1	3.99	3.49	3.01	$-99 \rightarrow -55$ °C over 7 m	95.8	92.2/7.8	not detected
2	2.00	1.50	1.00	$-101 \rightarrow -75$ °C over 4 m	87.7	81.7/18.3	8.4%
3	3.00	2.50	2.00	$-101 \rightarrow -75$ °C over 5 m	96.2	91.3/8.7	0.9%
4	2.00	1.50	1.00	$-101 \rightarrow -75°$ over 6 m	74.4	82.5/17.5	20.1%

[a] General procedure: a solution of sulfone **1** in THF (0.06 M) at -100 °C was treated with *n*-BuLi, treated with *i*-Pr$_2$NH, re-cooled to -100 °C, and treated all at once with a solution of CH$_2$X$_2$ in THF.

SCHEME 9. Chlorovinylation of a Nitrile
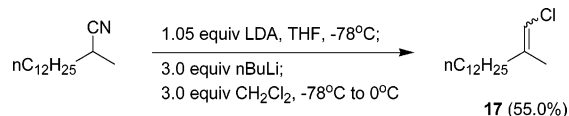
(with *n*-BuLi and *t*-BuLi, respectively); and (3) the selectivity of LiCH$_2$Br was higher in the experiments with 2 equiv of LiCH$_2$Br than in the experiments with 1 equiv of LiCH$_2$Br.

Huisgen and Burger[35] and Friedman et al.[23] have previously reported that LiCH$_2$Br is more selective than LiCH$_2$Cl for cyclopropanation of olefins, by factors of 1.5 and 1.9, respectively, in line with the findings of this study.

The possibility that the selectivity of both LiCH$_2$Br and LiCH$_2$Cl for α-lithio-**1** over *n*-BuLi and *t*-BuLi could be due to formation of a heterodimer between α-lithio-**1** and BuLi was considered (Scheme 11). Because each molecule of carbenoid LiCH$_2$X would be generated in close proximity to a molecule of α-lithio-**1**, the system would be biased in favor of methylenation over homologation.

However, a 1:1 mixture of *n*-BuLi and α-lithio-**1** should contain a higher percentage of heterodimer (*n*-BuLi)(α-lithio-**1**) and less homodimer (*n*-BuLi)$_n$ than a 2:1 mixture, for statistical reasons. Thus, the selectivity of carbenoid for the reaction with α-lithio-**1** versus *n*-BuLi should be higher with the 1:1 mixture than with the 2:1 mixture. In fact, the selectivity with the 2:1 mixture was higher, with both *n*-BuLi ($k^S/k^B =$ 8.8 for 1:1 and 10.4 for 2:1) and *t*-BuLi ($k^S/k^B = 1.9$ for 1:1 and 3.6 for 2:1). Thus, the heterodimer (BuLi)(LiCH$_2$Br) either is not formed or, if formed, dissociates into the solvent separated component molecules faster than they react with each other. Matteson has reported that addition of 0.94 equiv of *n*-BuLi/ hexane to a solution of triisopropylborate and 1.0 equiv of CH$_2$-ClI in THF at -78 °C afforded diisopropyl (chloromethyl)-boronate in 84% yield,[19a] which also shows that any initially formed heterodimer or heterotetramer (*n*-BuLi)$_n$(LiCH$_2$Cl), if formed, must dissociate into the component molecules faster than they react with each other.

Moreover, the carbenoid is selective for α-lithio-**1** over both *n*-BuLi, which exists as a mixture of dimers and tetramers under the conditions of the methylenation reaction (THF, -100 °C),

and *t*-BuLi, which is monomeric under those conditions.[36] This is compelling evidence against the involvement of aggregation phenomena in determining the selectivity of carbenoid for α-lithio-**1** over alkyllithium.

Because the remarkable selectivity of carbenoids for the reaction with α-lithio-sulfones is not explicable by invoking aggregation phenomena, it presumably derives from the intrinsic nature of the carbenoid species itself.

Mechanism. It is well-established that vinylidene carbenoids[37–39] and cyclopropyl carbenoids[40,41] react with carbanion nucleophiles by a metal-assisted ionization (MAI)[14b,38,42] mechanism. This is a solvolytic S$_N$1-type mechanism in which the halogen associates with lithium to form a bridged zwitterionic intermediate prior to the encounter with the nucleophile. The bridged intermediate has been studied computationally and verified to be the low-energy structure.[43,44] However, these special types of carbenoids are biased for displacement by solvolytic (S$_N$1-type) mechanisms over S$_N$2-type mechanisms because S$_N$2 displacement at vinyl and cyclopropyl carbon atoms is inherently slow.

The fact that LiCH$_2$Br reacts ≥ 40 times faster than *n*-BuCHLiBr is inconsistent with the MAI mechanism because

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(42) (a) Rachon, J.; Goedken, V.; Walborsky, H. M. *J. Am. Chem. Soc.* **1986**, *108*, 7435. (b) Topolski, M.; Duraisamy, M.; Rachon, J.; Gawronski, J.; Gawronska, K.; Goedken, V.; Walborsky, H. M. *J. Org. Chem.* **1993**, *58*, 546.

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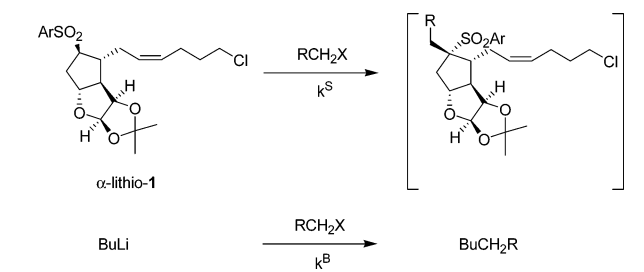
(44) For two excellent recent reviews, see: (a) Braun, M. In *The Chemistry of Alkyllithium Compounds*; Rappoport, Z., Marek, I., Eds.; John Wiley and Sons: New York, 2004; Chapter 13, pp 829–900. (b) Boche, G.; Lohrenz, J. C. W. *Chem. Rev.* **2001**, *101*, 697.

SCHEME 10. Competition Experiment between α-Lithio-1 and *n*-BuLi for *n*-BuBr
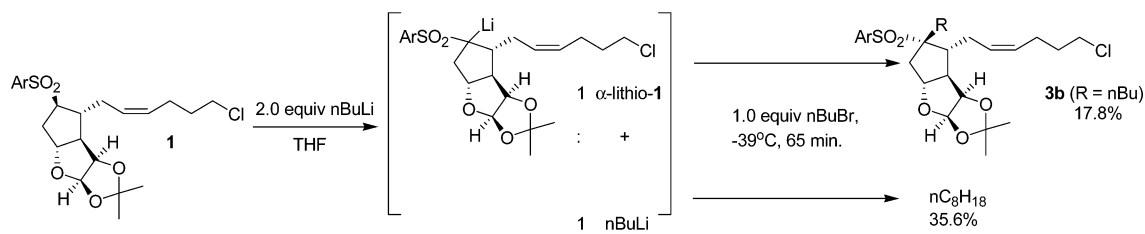
TABLE 9. Effect of Metal M on Rate and Yield of Methylenation by MCH₂Iᵃ
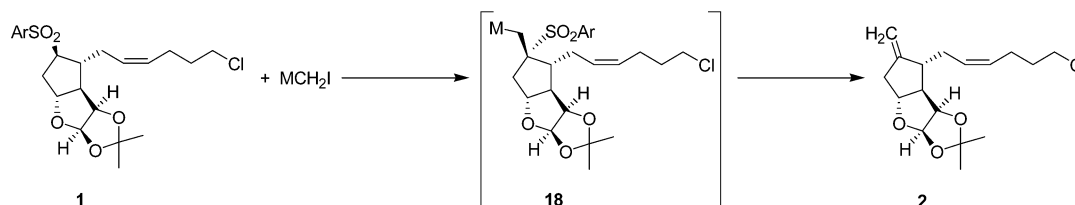
entry	M (in MCH₂I)	K^{rel} ($1 \rightarrow 18$)	yield ($1 \rightarrow 2$; %)
1[b]	Me₃Si	≤1	0.0
2[b]	n-Bu₃Sn	6×10^2	77.7
3	n-Pr	10^4	
4	Me₃Sn	10^4	85.8
5	Li	$>2 \times 10^{5\ c}$	86.7
6	Li[d]	$>3 \times 10^{5\ e}$	95.4

*ᵃ Relative rates measured in THF at −78 °C by competition experiments. Data in entries 1−4 taken from ref 1a. ᵇ Data obtained using cis-**8**: see footnote 11 of ref 1a for explanation of calculation procedure. ᶜ Lower limit, based on the fact that methylenation is at least 86.7% complete (>3 half-lives, assuming bimolecular kinetics) in 30 s at −65 °C. ᵈ Experiment with LiCH₂Br. ᵉ Lower limit, based on fact that reaction is at least 95.4% complete (>4 half-lives) in 30 s at −73 °C. The half-life at −96 °C is <30 s (Table 5, entry 2).*

SCHEME 11. Heterodimer Hypothesis to Rationalize Selectivity of LiCH₂X for α-Lithio-1 over BuLi
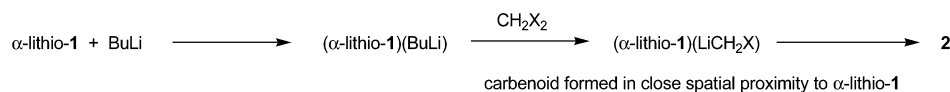
TABLE 10. Selectivities of Electrophiles for α-Lithio-1 vs *n*-BuLi and *t*-BuLi

	k^S/k^B (n-BuLi)		k^S/k^B (t-BuLi)	
electrophile	1:1ᵃ	2:1	1:1	2:1
LiCH₂Br	8.8	10.4	1.9	3.6
LiCH₂Cl	3.5		0.7	
CH₃CH₂CH₂CH₂Br	~0.5			

*ᵃ Ratio of alkyllithium to α-lithio-**1** prior to addition of alkyl halide.*

secondary alkyl halides are expected to solvolyze faster than primary alkyl halides. Thus, it is proposed that lithium methylene carbenoids alkylate α-lithio-sulfones by the S_N2 mechanism. Both Me₃SiCH₂I and R₃SnCH₂I also alkylate sulfones by the S_N2 mechanism.[1a] Koebrich has proposed that *n*-BuLi reacts with LiCHCl₂ by an S_N2 mechanism.[30] The fact that LiCH₂Br is more reactive than *n*-BuBr can be rationalized either by invoking chelation between the lithium of the carbenoid and one of the oxygens of the sulfone in the transition state or by

invoking a lithium-induced lengthening and, thus, weakening of the carbon−bromine bond, as proposed by Bent[45] and Seebach et al.[46]

The observation that LiCH₂Br is ~2.6 times more selective than LiCH₂Cl toward methylenation versus homologation is hard to understand in light of computational studies showing that the two carbenoids have similar lithium−halogen-bridged structures and that their electrophilicities are "essentially the same."[47] One possible explanation is that the LiBr evolved in the methylenation stabilizes the LiCH₂Br, rendering it more selective in accord with the "reactivity/selectivity principle."[48] Villieras et al. have reported that LiCH₂Br is stabilized by LiBr.[17] The hypothesis that LiBr enhances selectivity also would explain the observation that selectivity is higher with 2 equiv of LiCH₂Br than with 1 equiv of LiCH₂Br because the concentration of LiBr increases over the course of the reaction.[49] An alternative explanation is that the LiBr may act as a Lewis

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(48) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; John Wiley and Sons: New York, 1963; pp 156−168. (b) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755. (c) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 125. (d) McLennan, D. J. *Tetrahedron* **1978**, *34*, 2331. (e) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1980**, *45*, 3320.

acid catalyst for the methylenation, as zinc salts catalyze the Simmons−Smith cyclopropanation reaction.[50]

Conclusions

Lithium carbenoids are highly unstable, decomposing above −110 °C, but this study has shown that lithium methylene and dihalomethylene carbenoids, when generated at −100 °C in the presence of α-lithio-sulfones (and one α-lithio-nitrile), react to form olefins and vinyl halides in high yield and purity. The carbenoids exhibit practical selectivity for methylenation over homologation and other pathways. $LiCH_2Br$ was found to be 2.6 times more selective than $LiCH_2Cl$, an effect attributed to the LiBr byproduct. The demonstration that lithium methylene carbenoids, though highly reactive, are capable of reacting with high selectivity among potential partners encourages further investigation of practical applications of these reagents in synthesis.

Experimental Section

Sulfone 1. Sulfone **1** was synthesized by the process described in ref 7. ^{13}C NMR (20 MHz, CD_2Cl_2): δ 145.6 (s), 135.3 (s), 130.7 (d), 130.5 (d), 129.4 (d), 127.6 (d), 113.7 (d), 112.66 (s), 80.4 (d), 76.5 (d), 71.8 (d), 59.5 (d), 45.0 (t), 33.9 (d), 32.7 (t), 31.9 (t), 28.3 (t), 26.3 (q), 26.1 (q), 24.9 (t), 21.7 (q). ^1H NMR (200 MHz, CD_2Cl_2): δ 1.22 (3H, s), 1.32 (3H, s), 1.4−2.4 (10H, m's), 2.40 (3H, s), 3.50 (2H, t, J = 6.5 Hz), 3.54 (1H, ddd, J = 12, 7, 2 Hz), 3.77 (1H, td, J = 11.5, 6 Hz), 4.35 (1H, t, J = 3 Hz), 5.40 (2H, m), 5.90 (1H, d, J = 3 Hz), 7.37 (2H, d, J = 8 Hz), 7.75 (2H, d, J = 8 Hz). Mp 123−124.5 °C (white plates). Anal. Calcd for $C_{23}H_{31}ClO_5S$: C, 60.71; H, 6.87; Cl, 7.79; S, 7.05 (%). Found: C, 60.83; H, 6.83; Cl, 7.85%; S, 6.92 (%).

Olefin 2 (Fast Addition, 2 equiv of CH_2Br_2/n-BuLi; Table 1, Entry 4). A solution of sulfone **1** (mw 455.02; 0.9102 g, 2.0004 mmol) in 17.0 mL THF under argon was cooled to −100 °C using a liquid nitrogen/ethanol slush bath and treated over ∼1 min with n-BuLi/hexanes (3.64 mL of 1.65 M solution,[51] 6.01 mmol, 3.00 equiv), resulting in an exotherm to −73 °C. The mixture was recooled to −99 °C over 3 min and then treated all at once with neat CH_2Br_2 (mw 173.85; d 2.477; 0.281 mL, 0.696 g, 4.00 mmol, 2.00 equiv), resulting in an exotherm to −63 °C. After 15 s, the mixture was quenched with 1.00 mL methanol and analyzed by GC.[52] The mixture contained n-$C_5H_{11}Br$ **5** (mw 151.05; 14.708 mg, 0.0974 mmol, 4.9% yield) and n-$C_6H_{13}Br$ **6** (mw 165.08; 1.337 mg, 0.0081 mmol, 0.4% yield). The mixture was poured into 40 mL 3% aq NaOH, extracted with CH_2Cl_2 (2 × 25 mL), dried (MgSO₄), and concentrated to give a yellow oil (weight: 0.6655 g) consisting of one major (R_f = 0.62) and one minor (R_f = 0.23) component by TLC (eluent: 25% ethyl acetate/cyclohexane). The

oil was flash chromatographed on 60 g silica gel (3 cm × 6″ column; fraction size: 50 mL); gradient elution, 10 → 20% ethyl acetate/cyclohexane). The fractions containing the R_f = 0.62 component were combined and concentrated to a pale yellow oil identified as olefin **2** in pure form by ^{13}C and ^1H NMR comparison with an authentic standard.[1b] Weight: 0.6034 g (mw 312.84; 1.9288 mmol, 96.4% yield). ^{13}C NMR (75 MHz, CDCl₃): δ 154.5 (s), 129.2 (d), 128.7 (d), 112.6 (d), 111.9 (s), 110.2 (t), 80.3 (d), 76.3 (d), 59.4 (d), 44.4 (t), 37.4 (d), 35.1 (t), 32.3 (t), 30.3 (t), 26.1 (q), 24.5 (t). ^1H NMR (300 MHz, CDCl₃): δ 1.34 (3H, s), 1.52 (3H, s), 1.5−2.7 (10H, m's), 3.55 (2H, t, J = 6.5 Hz), 4.06 (1H, m), 4.50 (1H, t, J = 3.4 Hz), 5.01 (1H, s), 5.08 (1H, s), 5.49 (2H, m's), 6.04 (1H, d, J = 3.3 Hz). MS (EI): m/e 312, 314 (P⁺, 2.2%); 297, 299 (P⁺ − CH₃, 100%). Anal. Calcd for $C_{17}H_{25}{}^{35}ClO_3$: m/e 312.1492. Found: m/e 312.1495. The fractions containing the R_f = 0.23 component were combined and concentrated to a white crystalline solid (weight: 0.0494 g), consisting of a 39.3:60.7 (w/w) mixture of sulfone **1** (mw 455.02; 19.4 mg, 0.043 mmol, 2.1% yield) and methyl p-toluyl sulfone **4** (mw 170.23; 30.0 mg, 0.176 mmol, 8.8% yield) by ^{13}C and ^1H NMR comparison with an authentic standard. Spectra for methyl p-toluyl sulfone **4**: ^{13}C NMR (75 MHz, CD_2Cl_2): δ 145.1 (s), 138.4 (s), 130.3 (d), 127.7 (d), 44.9 (q), 21.7 (q). ^1H NMR (90 MHz, CDCl₃): δ 2.47 (3H, s), 3.06 (3H, s), 7.37 (2H, d, J = 8 Hz), 7.87 (2H, d, J = 8 Hz). Mp 86.5−88.5 °C (cf. lit. 88 °C[53]). MS (EI): m/e 170 (P⁺, 60.5%), 91 (P⁺ − SO₂CH₃, 100%). Anal. Calcd for $C_8H_{10}SO_2$: m/e 170.0401. Found: m/e 170.0404.

Trisubstituted Olefin 7d (Table 6, Entry 3). A solution of sulfone **1** (mw 455.02; 0.9102 g, 2.0004 mmol) in 17.0 mL THF under argon was cooled to −95 °C using a liquid nitrogen/ethanol slush bath and treated over 30 s with a solution of n-BuLi/hexane (3.64 mL of 1.65 M solution, 6.01 mmol, 3.00 equiv), resulting in an exotherm to −72 °C. The resulting orange reaction mixture was cooled to −97 °C over 10 min, then treated all at once with neat n-BuCHBr₂ (mw 229.95; d 1.624; 0.567 mL, 0.921 g, 4.00 mmol, 2.00 equiv). Over the next 3 min, the temperature rose gradually to −62 °C, at which time the reaction mixture was quenched with 1.0 mL of methanol, which discharged the orange color to yellow. To the mixture was added 156.3 mg of n-Bu₂O as GC internal standard. The mixture was assayed twice by quantitative GC,[54] and the results were averaged. The following products were detected: n-$C_5H_{11}Br$ (mw 151.05; 36.14 mg, 0.239 mmol, 12.0% yield), n-BuCHBr₂ (mw 229.95; 82.11 mg, 0.357 mmol, 17.9% yield), and cis- and/or $trans$-decene (mw 140.27; 144.96 mg, 1.033 mmol, 51.7% yield). The product mixture was poured into 40 mL of 3% aq NaOH, extracted with CH_2Cl_2 (3 × 15 mL), dried (MgSO₄), and concentrated to a pale yellow oil (weight: 0.8881 g), consisting of a mixture of two components (R_f = 0.27 and 0.72) by TLC (eluent: 25% ethyl acetate/cyclohexane). The oil was flash chromatographed on 60 g of silica gel (3 cm × 6″ column; fraction size: 50 mL; gradient elution: 5 → 20% ethyl acetate/cyclohexane). The fractions containing the R_f = 0.72 component were combined and concentrated to a yellow oil identified as olefin **7d** (trans/cis = 73/27) by NMR spectroscopy. Weight: 0.3984 g (mw 368.95; 1.0798 mmol, 54.0% yield). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 145.0 (s), 129.4 (d), 129.3 (d), 125.8 (d), 113.1 (d), 112.0 (s), 81.2 (d), 77.0 (d), 59.8 (d), 45.0 (t), 37.6 (d), 32.9 (t), 32.0 (t), 31.5 (t), 31.1 (t), 29.3 (t), 26.3 (q), 26.2 (q), 25.0 (t), 22.7 (t), 14.2 (q). ^1H NMR (300 MHz, CD_2Cl_2): δ 0.88 (3H, distorted t, J = 7.0 Hz), 1.29

(49) Since the half-life of $LiCH_2Br$ is much shorter than the CH_2Br_2 add time (2 min), the steady-state concentration of $LiCH_2Br$ is low throughout the course of the reaction, while the concentration of LiBr increases linearly with the amount of CH_2Br_2 that has been added.

(50) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2003**, *125*, 2341.

(51) Titrated by the procedure described in: Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(52) GC assay: column, 8′ 20% SE30; temperature program, 60 → 140 °C at 4 °C/min; attenuation, 8 × 10⁻¹¹; sample prep, inject 5 μL of neat reaction mixture; retention times: ethylene, 0.57 min; CH_2Br_2, 4.75 min; n-BuBr, 5.97 min; n-octane (ISTD), 9.80 min; n-$C_5H_{11}Br$, 10.90 min; n-$C_6H_{13}Br$, 16.19 min. Yields were determined relative to n-octane (present in commercial n-BuLi/hexane) as internal standard. No n-nonane (product of the Wurtz−Fittig coupling of n-BuLi and n-$C_5H_{11}Br$) could be detected in the crude reaction mixtures by GC. Therefore, no n-octane (product of the Wurtz−Fittig coupling between n-BuLi and n-BuBr) was formed under the conditions of the experiments, thus validating the use of n-octane as internal standard.

(53) Truce, W. E.; Vriesen, C. W. *J. Am. Chem. Soc.* **1953**, *75*, 5032.

(54) GC assay: column, 8′ 20% SE30; temperature program, 60 → 180 °C at 4 °C/min.; attenuation setting, 8 × 10⁻¹¹; injector temp, 275 °C; detector temp, 290 °C; sample prep, inject 5 μL of neat reaction mixture; retention times: n-BuBr, 4.59 min; n-octane, 7.78 min; n-$C_5H_{11}Br$, 8.95 min; n-Bu₂O (ISTD), 12.11 min; cis-5-decene, 18.27 min; $trans$-5-decene, 18.45 min; n-BuCHBr₂, 20.13 min. cis- and $trans$-5-Decene were not sufficiently resolved to permit individual quantitation. Response factors were determined for each component by injection of pure samples purchased from commercial supply houses.

(3H, s), 1.46 (3H, s), 1.3−2.5 (11H, m's), 1.83 (2H, quint, $J = 6.9$ Hz), 2.22 (2H, q, $J = 7.2$ Hz), 2.61 (1H, dd, $J = 14.3, 6.2$ Hz), 3.55 (2H, t, $J = 6.6$ Hz), 3.99 (1H, td, $J = 11.2, 6.6$ Hz), 4.46 (1H, t, $J = 3.5$ Hz), 5.3−5.6 (3H, m's), 5.97 (1H, d, $J = 3.4$ Hz). MS (EI): $m/e = 368/370$ (P$^+$, 3.0%), 353/355 (27.3%), 251/253 (83.3%), 193 (100%). Anal. Calcd for $C_{21}H_{33}{}^{35}ClO_3$: m/e 368.2118. Found: 368.2123. The fractions containing the $R_f = 0.27$ component were combined and concentrated to a white solid identified as sulfone **1** by ^{13}C and ^1H NMR comparison with an authentic sample. Weight: 0.4230 g (mw 455.02; 0.9296 mmol, 46.5% recovery).

Vinyl Chloride 7a (Table 7, Entry 3). A solution of sulfone **1** (mw 455.02; 0.3001 g, 0.6595 mmol) in 3.0 mL of THF was cooled to −78 °C and treated with *n*-BuLi/hexane (1.65 mL of 1.6 M solution, 2.64 mmol, 4.00 equiv), followed by neat diisopropylamine (mw 101.19; d 0.722; 0.37 mL, 0.267 g, 2.64 mmol, 4.00 equiv). After stirring at −78 °C for 7 min, the yellow solution was treated with neat CH$_2$BrCl (mw 129.38; d 1.991; 0.13 mL, 0.259 g, 2.00 mmol, 3.03 equiv), which caused the mixture to turn dark brown. The mixture was allowed to warm to 0 °C, quenched with 0.4 mL water, poured into 25 mL 3% aq NaOH, extracted with CH$_2$Cl$_2$ (3 × 25 mL), dried (MgSO$_4$), and concentrated to a dark brown oil (weight: 0.2588 g) consisting of one major ($R_f = 0.46$) and one minor ($R_f = 0.40$) component, along with lesser amounts of more polar components by TLC (eluent: 25% ethyl acetate/cyclohexane). No starting sulfone **1** ($R_f = 0.08$) could be detected. The dark brown oil was flash chromatographed on 20 g of silica gel (gradient elution, 5 → 15% ethyl acetate/cyclohexane). The fractions containing the $R_f = 0.46$ and 0.40 components were combined and concentrated to a pale yellow oil identified as vinyl chloride **7a** as an 82:18 trans/cis isomer mixture by ^1H and ^{13}C NMR. None of the corresponding vinyl bromide **7b** was detected (estimated threshold of detection: 1%). Weight: 0.2055 g (mw 347.29; 0.5917 mmol, 89.7% yield). ^{13}C NMR (75 MHz, CD$_2$Cl$_2$): δ 149.2 (s), 130.1 (d), 128.4 (d), 113.8 (d), 113.2 (s), 80.1 (d), 76.6 (d), 59.9 (d), 44.9 (t), 38.0 (d), 32.8 (t), 32.6 (t), 30.6 (t), 26.20 (q), 26.18 (q), 24.9 (t). ^1H NMR (300 MHz, CDCl$_3$): δ 1.30 (3H, s), 1.48 (3H, s), 1.56 (1H, td, $J = 11.4, 3.5$ Hz), 1.84 (2H, quint, $J = 6.9$ Hz), 2.21 (4H, narrow m), 2.52 (2H, m's), 2.79 (1H, dd, $J = 15.2, 6.6$ Hz), 3.55 (2H, t, $J = 6.5$ Hz), 4.04 (1H, td, $J = 11.2, 6.7$ Hz), 4.48 (1H, t, $J = 3.4$ Hz), 5.48 (2H, sym m), 6.00 (1H, d, $J = 3.4$ Hz), 6.00 (1H, m). MS (EI): m/e 331/333/335 (P$^+$ − CH$_3$, 100%), 43 (83.6%). Anal. Calcd for $C_{16}H_{21}{}^{35}ClO_3$ (P$^+$ − CH$_3$): m/e 331.0868. Found: 331.0852.

Vinyl Bromide 7b (Table 7, Entry 4). A solution of sulfone **1** (mw 455.02; 0.2389 g, 0.5250 mmol) in 2.0 mL of THF was cooled to −78 °C and treated with *n*-BuLi/hexane (1.00 mL of 1.6 M solution, 1.60 mmol, 3.05 equiv), which produced a bright yellow color. The mixture was treated with neat diisopropylamine (mw 101.19; d 0.722; 0.32 mL, 0.231 g, 2.28 mmol, 4.35 equiv), stirred at −78 °C for 7.5 min, and then treated with neat CH$_2$Br$_2$ (mw 173.85; d 2.477; 0.11 mL, 0.272 g, 1.57 mmol, 2.99 equiv), causing the mixture to turn brown immediately. The mixture was warmed to 0 °C, quenched with 0.5 mL methanol, added to 20 mL 3% aq NaOH, extracted with CH$_2$Cl$_2$ (2 × 20 mL), dried (MgSO$_4$), and concentrated to a dark brown oil (weight: 0.2108 g) consisting of a mixture of one major ($R_f = 0.52$) and one minor ($R_f = 0.33$) component by TLC (eluent: 20% ethyl acetate/cyclohexane); sulfone **1** ($R_f = 0.16$) was not detectable. The oil was flash chromatographed on 20 g of silica gel (2 cm × 6″ column; gradient elution, 10 → 20% ethyl acetate/cyclohexane). The fractions containing the $R_f = 0.52$ component were combined and concentrated to a brownish yellow oil identified as vinyl bromide **7b** in pure form (as 93:7 trans/cis mixture, by ratio of heights of peak pairs in ^{13}C NMR spectrum) by spectroscopic analysis. Weight: 0.1913 g (mw 391.74; 0.488 mmol, 93.0% yield). ^{13}C NMR (75 MHz, CDCl$_3$): δ 151.4 (s), 129.8 (d; coupled to proton at 5.48), 128.0 (d; coupled to proton at 6.04), 112.6 (d; coupled to proton at 6.11), 112.1 (s), 102.2 (d; coupled to proton at 4.08), 79.6 (d; coupled to proton at 4.48), 76.3 (d; coupled to proton at 4.48), 59.6

(d; coupled to proton at 1.58), 44.4 (t; coupled to protons at 3.54), 38.9 (d; coupled to proton at 2.50), 34.9 (t; coupled to protons at 2.21 and 2.79), 32.1 (t; coupled to protons at 1.84), 30.1 (t; coupled to protons at 2.21 and 2.50), 26.1 (q; coupled to protons at 1.51), 26.0 (q; coupled to protons at 1.32). ^1H NMR (300 MHz, CDCl$_3$): δ 1.32 (3H, s), 1.51 (3H, s), 1.58 (1H, td, $J = 11.3, 3.4$ Hz), 1.84 (2H, quint, $J = 6.8$ Hz), 2.21 (4H, overlapping m's; NOE on irr at 2.79), 2.50 (2H [H8 and one H7 proton], overlapping m's; NOE on irr at 6.11), 2.79 (1H [H10β], dd, $J = 15.5, 5.8$ Hz), 3.54 (2H, t, $J = 6.4$ Hz), 4.08 (1H [H11], td, $J = 11.2, 6.7$ Hz; NOE on irr at 2.50, 2.79), 4.48 (1H, t, $J = 3.4$ Hz), 5.48 (2H [H5 and H6], sym m; NOE on irr at 2.50), 6.04 (1H, d, $J = 3.3$ Hz), 6.11 (1H [H9'], br s; NOE on irr at 2.50, no NOE on irr at 2.79). MS (EI): m/e 375/377/379 (P$^+$ − CH$_3$, 100%), 332/334/336 (30.4%), 253, 255 (22.7%). Anal. Calcd for $C_{16}H_{21}{}^{79}Br^{35}ClO_3$ (P$^+$ − CH$_3$): m/e 375.0362. Found: 375.0376.

Vinyl Iodide 7c (Table 7, Entry 5). A solution of sulfone **1** (mw 455.02; 0.4581 g, 1.0068 mmol) in 5 mL of THF was cooled to −78 °C under argon and treated with *n*-BuLi/hexane (2.00 mL of 1.6 M solution, 3.20 mmol, 3.18 equiv), producing an orange color. The mixture was treated with neat diisopropylamine (mw 101.19; d 0.722; 0.56 mL, 0.404 g, 4.00 mmol, 3.97 equiv), stirred at −78 °C for 9 min, then treated with neat CH$_2$I$_2$ (mw 267.84; d 3.325; 0.24 mL, 0.798 g, 2.98 mmol, 2.96), producing a dark purple solution. The mixture was allowed to warm to 0 °C, stirred at 0 °C for 10 min, quenched with 3% aq NaOH, and extracted with CH$_2$Cl$_2$ (3×). The purple solution was shaken with aq Na$_2$S$_2$O$_3$, which discharged the color, dried (MgSO$_4$), and concentrated to a purple oil (weight: 0.5037 g) consisting of one component ($R_f = 0.59$) by TLC (eluent: 30% ethyl acetate/cyclohexane); sulfone **1** ($R_f = 0.21$) was not detectable. The oil was flash chromatographed on silica gel (2 cm × 6″ column; gradient elution, 10 → 20% ethyl acetate/cyclohexane). The fractions containing the $R_f = 0.59$ component were combined and concentrated to a residue identified as vinyl iodide **7c** in pure form (as 93:7 trans/cis mixture, by ratio of heights of peak pairs in ^{13}C NMR spectrum) by spectroscopic analysis. Weight: 0.3818 g (mw 438.74; 0.8702 mmol, 86.4% yield). ^{13}C NMR (75 MHz, CD$_2$Cl$_2$): δ 158.4 (s), 130.2 (d), 128.3 (d), 113.0 (d), 112.3 (s), 79.6 (d), 77.0 (d), 74.4 (d), 60.5 (d), 45.0 (t), 41.0 (d), 39.8 (t), 32.7 (t), 30.4 (t), 26.2 (q), 26.2 (q), 25.0 (t). ^1H NMR (90 MHz, CDCl$_3$): δ 1.38 (3H, s), 1.55 (3H, s), 1.5−2.9 (10H, m's), 3.55 (2H, t, $J = 6$ Hz), 4.10 (1H, td, $J = 11, 7$ Hz), 4.50 (1H, t, $J = 4$ Hz), 5.49 (2H, sym m), 6.04 (1H, d, $J = 3$ Hz), 6.19 (1H, narrow m). MS (EI): m/e 438/440 (P$^+$, 0.7%), 423/425 (P$^+$ − CH$_3$, 69.5%), 311/313 (57.7%), 81 (100%). Anal. Calcd for $C_{16}H_{21}{}^{35}ClIO_3$ (P − CH$_3$): m/e 423.0223. Found: 423.0243.

Cyclobutane Dimer 16 (Scheme 8). A solution of sulfone **1** (mw 455.02; 1.5155 g, 3.331 mmol) in 12 mL THF was cooled to −78 °C and treated with *n*-BuLi/hexane (6.25 mL of 1.6 M solution, 10.00 mmol, 3.00 equiv), followed by a solution of diisopropylamine (mw 101.19; 1.3461 g, 13.30 mmol, 3.99 equiv) in 2.0 mL of THF. After stirring at −78 °C for 10 min, the yellow solution was treated dropwise over 6 min with a solution of CH$_2$Br$_2$ (mw 173.83; 1.7597 g, 10.123 mmol, 3.04 equiv) in 8 mL of THF. After the addition was complete, the reaction mixture was allowed to warm to 0 °C over 15 min, stirred at 0 °C for 10 min, poured into 40 mL of 3% aq NaOH, extracted with CH$_2$Cl$_2$ (2 × 25 mL), dried (MgSO$_4$), and concentrated to a light brown glass (weight: 1.1701 g) consisting of one major component ($R_f = 0.39$) contaminated with trace amounts of vinyl bromide **7b** ($R_f = 0.58$ with shoulder at 0.56) and sulfone **1** ($R_f = 0.20$) by TLC (eluent: 20% ethyl acetate/cyclohexane). This glass was flash chromatographed on 69 g of silica gel (eluent: 15% ethyl acetate/cyclohexane). The fractions containing the $R_f = 0.39$ component were pooled and concentrated to a white glass, identified as cyclobutane dimer **16** as a single isomer (stereochemistry about the cyclopropane ring is undetermined) by 500 MHz ^1H NMR, ^{13}C NMR, MS, and TLC. Weight: 0.6130 g (mw 621.65; 0.9861 mmol, 59.2% yield). ^{13}C NMR (spectrum taken on Varian XL-200 in CD$_2$Cl$_2$): δ 113.0 (1C,

d), 112.0 (1C, s), 82.7 (1C, d), 76.3 (1C, d), 74.6 (1C, s), 58.6 (1C, d), 48.2 (1C, s), 45.4 (1C, t), 43.7 (1C, d), 33.5 (1C, t), 31.5 (2C, t), 31.5 (1C, d), 26.5 (1C, q), 25.9 (1C, q), 25.6 (1C, d), 22.4 (1C, t). ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): δ 0.78 (1H, td, J = 8.74, 5.89 Hz), 1.24 (3H, s), 1.40 (3H, s), 1.40 (1H, ddd, J = 8.74, 7.84, 2.40 Hz), 1.49 (1H, m), 1.50 (1H, ddd, J = 14.95, 4.91, 2.40 Hz), 1.67 (1H, m), 1.70 (1H, t, J = 11.56 Hz), 1.72 (1H, td, J = 11.1, 3.46 Hz), 1.80 (2H, m), 2.17 (1H, dd, J = 11.56, 5.6 Hz), 2.31 (1H, ddd, J = 14.95, 10.70, 7.84), 2.66 (1H, td, J = 10.70, 4.91 Hz), 3.56 (2H, t, J = 6.51 Hz), 3.63 (1H, ddd, J = 11.56, 11.15, 5.6 Hz), 4.93 (1H, t, J = 3.46 Hz), 5.91 (1H, d, J = 3.46 Hz). MS (CI): m/e 621/623/625 (P$^+$ + H, 60.9%), 563/565/567 (100%). Anal. Calcd for C$_{34}$H$_{46}$^{35}Cl$_2$O$_6$: m/e 620.2671. Found: 620.2668.

Vinyl Chloride 17 from 2-Methyl-tetradecanitrile (Scheme 9). A solution of diisopropylamine (mw 101.19; d 0.722; 0.27 mL, 0.1949 g, 1.93 mmol, 1.08 equiv) in 5.0 mL of THF was cooled to 0 °C, treated with *n*-BuLi/hexane (1.18 mL of 1.6 M solution, 1.89 mmol, 1.06 equiv), stirred for 10 min, cooled to −78 °C, and treated with a solution of 2-methyl-tetradecanitrile (mw 223.41; 399.7 mg, 1.789 mmol) in 3.0 mL THF. After 6 min at −78 °C, *n*-BuLi/hexane (3.4 mL, 5.44 mmol, 3.04 equiv) was added, followed by CH$_2$Cl$_2$ (mw 84.93; d 1.325; 0.34 mL, 0.450 g, 5.30 mmol, 2.96 equiv). The mixture was stirred at −78 °C for 2 min, then warmed to 0°, poured into 75 mL of 3% aq NaOH, extracted with CH$_2$Cl$_2$ (2 × 75 mL), dried (MgSO$_4$), and concentrated to a dark brown solid (weight: 0.5807 mg) consisting of two major components (R_f = 0.81 and 0.75) and polar material by TLC (eluent: 3% ethyl acetate/cyclohexane) together with a small amount of starting nitrile (R_f = 0.27). The dark brown solid was flash chromatographed on 42 g of silica gel (eluant: cyclohexane). The fractions containing the R_f = 0.81 and 0.75 components were pooled and concentrated to a colorless oil, identified as 1-chloro-2-methyl-1-tetradecene **17** (as a 3:2 mixture of geometric isomers) by ^{1}H and ^{13}C NMR. Weight: 0.2408 g (mw 244.85; 0.9835 mmol, 55.0% yield). ^{13}C NMR (20 MHz, CD$_2$Cl$_2$): δ 139.4 (s), 112.0 ($\sim$0.4C, d), 111.5 ($\sim$0.6 C, d), 37.4 (t), 32.4 (t), 32.2 (t), 29.5−30.1 (5 overlapping t's), 28.0 (t), 27.2 (t), 23.1 (t), 20.9 (q), 14.2 (q). ^{1}H NMR (90 MHz, CD$_2$Cl$_2$): δ 0.89 (3H, t, J = 6 Hz), 1.30 (20H, br s), 1.72 ($\sim$1.8H, d, J = 1.5 Hz), 1.75 ($\sim$1.2H, d, J = 1.5 Hz), 2.1 (2H, m), 5.76 (1H, narrow m). MS (EI): m/e 244/246 (P$^+$, 100%). Anal. Calcd for C$_{15}$H$_{29}$^{35}Cl: m/e 244.1958. Found: 244.1954.

Supporting Information Available: Experimental procedures, compound characterization data, ^{13}C and ^{1}H NMR spectra for all new compounds, and derivation of eq 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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