Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 3999–4002

Competing reaction pathways from α-halo-α-protioalkyl aryl sulfoxides initiated by organometallic reagents

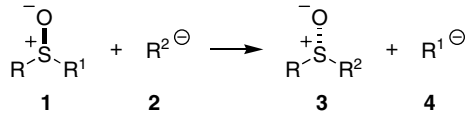
Paul R. Blakemore,* Matthew S. Burge and Mark A. Sephton

Department of Chemistry, Oregon State University, Corvallis, OR 97331-4003, USA

Received 16 October 2006; revised 30 March 2007; accepted 9 April 2007
Available online 14 April 2007

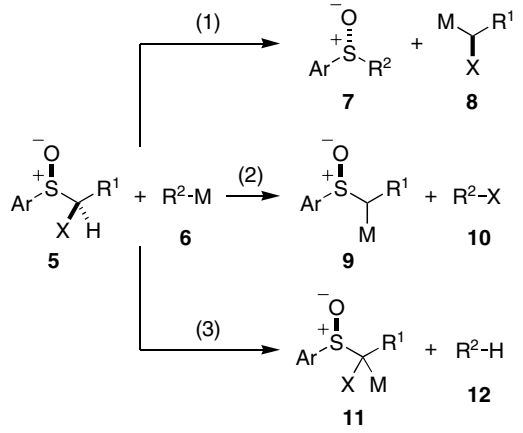
Abstract—The reactions of *syn*-1-haloethyl *p*-chlorophenyl sulfoxides (halogen = Cl, Br) with main-group organometallic reagents (*n*-BuMgCl, MeLi, *n*-BuLi, *s*-BuLi, and *t*-BuLi) in THF and PhMe solvents were examined. Product distributions were analyzed to determine the extent of competing sulfoxide ligand exchange, halogen–metal exchange, and deprotonation reaction pathways. A combination of *t*-BuLi in PhMe was optimal for initiation of sulfoxide ligand exchange from *syn*-1-chloroethyl *p*-chlorophenyl sulfoxide.

The sulfoxide ligand exchange reaction, wherein a carbanionic nucleofuge **4** is substituted for an incoming carbanionic nucleophile **2** with inversion of configuration about a tricoordinate S(IV) center (i.e., **1**→**3**), is a powerful, yet poorly understood process (Scheme 1).[1,2] Traditionally, this transformation has been employed as a means to synthesize sulfoxides (**3**);[1f,g,3] however, attention is now increasingly being directed to the organometallic 'by-product' of the exchange reaction (**4**). A growing body of work by Satoh,[4] and others,[5] demonstrates that sulfoxide ligand exchange may rival better known halogen–metal exchange and transmetalation phenomena as a means to prepare a wide variety of exotic organometallic species. In particular, as first discovered by Durst et al.,[1g] and as later re-investigated by Satoh and Takano,[6] ligand exchange reactions of α-haloalkyl aryl sulfoxides with Grignard or alkyllithium reagents proceed rapidly at low temperature and provide for a superior synthesis of α-haloalkylmetals (i.e., carbenoids). Of great significance, Hoffmann et al. recently reported that a configurationally stable Mg-carbenoid could be accessed in highly enantioenriched form by treatment of a homochiral *syn*-α-chloro-α-protioalkyl aryl sulfoxide with EtMgCl.[7] Work from our laboratory since established that a putative enantioenriched Li-carbenoid is likewise available by an analogous method initiated by *n*-BuLi.[8]



Scheme 1. The sulfoxide ligand exchange reaction.

Three distinct direct pathways may be anticipated upon the reaction of a α-halo-α-protioalkyl aryl sulfoxide (**5**) with a nucleophilic organometallic reagent (**6**), namely: (1) sulfoxide ligand exchange, (2) halogen–metal exchange, and (3) deprotonation (Scheme 2). The



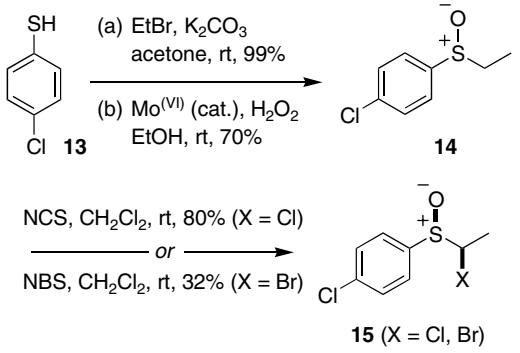
Scheme 2. Competing direct reaction processes from α-halo-α-protioalkyl aryl sulfoxides initiated by organometallic reagents.

Keywords: Sulfoxide ligand exchange; Carbenoids; Halogen–metal exchange.
* Corresponding author. Tel.: +1 541 737 6728; fax: +1 541 737 2062; e-mail: paul.blakemore@science.oregonstate.edu

0040-4039/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2007.04.031

literature reports of Satoh et al. indicate that pathway (1) is almost exclusively preferred from α-protiosulfoxides **5** with **6** (M = MgCl);[4] however, the corresponding reactions of α-protiosulfoxides **5** with **6** (M = Li) have been little studied.[9] Accordingly, wishing to optimize our earlier synthesis of enantioenriched Li-carbenoids from α-halo-α-protiosulfoxides,[8] we elected to study in detail the competing reaction pathways available to sulfoxides **5** in the presence of common organolithium reagents. Herein, we report the results of this investigation.

Suitable α-halo-α-protioalkyl sulfoxide substrates, *syn* α-chloro- and α-bromoethyl *p*-chlorophenyl sulfoxides

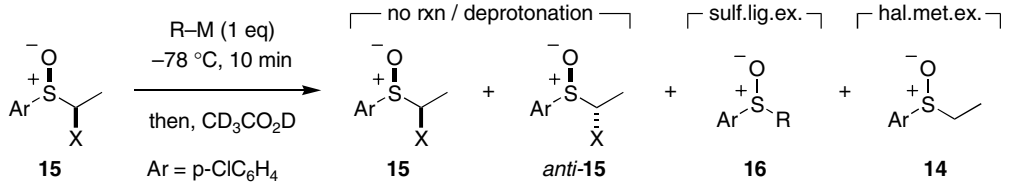


Scheme 3. Synthesis of racemic *syn*-α-haloethyl *p*-chlorophenyl sulfoxides **15**.

(**15**, X = Cl, Br), were prepared as illustrated by the respective treatment of ethyl sulfoxide **14** with either *N*-chloro- or *N*-bromosuccinimide in CH_2Cl_2 (Scheme 3).[10] Sulfoxide **14** was itself derived by a straightforward alkylation/oxidation sequence from thiophenol **13** [$Mo^{(VI)}$ cat. = ammonium molybdate hydrate, $(NH_4)_6Mo_6O_{24}\cdot 4H_2O$].[11]

With sulfoxides **15** in hand, their reactions with a variety of common organometallic reagents were explored (Table 1).[12] In all experiments, the sulfoxide was treated with 1 equiv of the reagent of interest at −78 °C and the reaction mixture quenched after 10 min with a suitable electrophilic deuterium source. To ascertain the extent to which competing pathways (1)–(3) were followed, product distributions were analyzed for recovered or epimerized starting material (**15** + *anti*-**15**) and the expected products from both sulfoxide ligand exchange (**16**) and halogen–metal exchange (**14**).[13] At the outset, to gauge the likely outcome of a simple deprotonation/reprotonation pathway, **15** (X = Cl) was exposed to freshly prepared LDA (1 equiv) in THF and quenched 10 min later with CD_3OD (entry 1). Sulfoxide **15** (X = Cl) and its epimer *anti*-**15** (X = Cl) were isolated in 84% combined yield with dr (*syn*/*anti*) = 1:2. Both compounds exhibited a low level of deuterium incorporation (ca. 30%), the likely consequence of internal proton return (IPR) from an intermediate complex of the lithiated sulfoxide and diisopropylamine, upon quench.[14] Throughout the subsequent phase of the

Table 1. Determination of product distributions from α-halo-α-protioalkyl aryl sulfoxides **15** (X = Cl, Br) following their treatment with organometallic reagents



Entry	X	R–M	Solvent	Product distribution: %yield[a] (%D)[b]			
				15	*anti*-**15**	**16**	**14**
1[c]	Cl	*i*-Pr_2N–Li	THF	28 (32)	56 (34)	0	0
2	Cl	*n*-Bu–MgCl	THF	7	1	67	0
3[c]	Cl	*n*-Bu–Li	THF	23 (22)	32 (48)	37	0
4	Cl	*s*-BuLi	THF	17 (35)	45 (62)	<5	0
5	Cl	*t*-Bu–Li	THF	24 (17)	45 (38)	6	0
6	Cl	Me–Li	THF	18 (90)	40 (92)	29	0
7	Cl	*n*-Bu–MgCl	PhMe	38 (<5)	0	27	0
8[c]	Cl	*n*-Bu–Li	PhMe	0	0	Trace[d]	0
9[c]	Cl	*s*-BuLi	PhMe	31 (18)	23 (50)	<40[e]	0
10	Cl	*t*-Bu–Li	PhMe	13 (15)	12 (67)	50	0
11	Cl	Me–Li	PhMe	0	0	28	0
12	Br	*n*-Bu–MgCl	THF	14 (<5)	<1	61	0
13	Br	*n*-Bu–Li	THF	22 (20)	19 (20)	3	13
14[c]	Br	*n*-Bu–MgCl	PhMe	47 (<5)	<1	35	0
15	Br	*n*-Bu–Li	PhMe	6	3	14	17

[a] Isolated yields; *syn* and *anti* sulfoxides not generally separated, ratio determined by ^1H NMR analysis.
[b] Where given, %D incorporation determined by ^1H NMR analysis; sulfoxides **14** and **16** were undeuterated in all cases.
[c] Quenched with CD_3OD.
[d] Complex mixture obtained, only discernable product was dibutylsulfoxide.
[e] Exchange product obtained as a mixture of diastereoisomers (dr ~ 1:1) associated with minor unidentified components.

study, low levels of deuterium incorporation were routinely encountered in samples of **15** and *anti*-**15** recovered after deuterolysis of reaction mixtures where alkylmetal initiated deprotonation of the sulfoxide had undoubtedly occurred. These low %D figures cannot be explained by IPR and indicate the likely operation of as yet unidentified proton transfer pathways during the reaction (n.b. deuterium incorporation into **14** or **16** was not found).[15]

The reactions of α-chlorosulfoxide **15** (X = Cl) with alkylmetals were examined in both THF and PhMe solvents (entries 2–11).[16] As expected, treatment of **15** (X = Cl) with *n*-BuMgCl in THF gave almost exclusively the product of sulfoxide ligand exchange (entry 2). A comparable reaction conducted in PhMe proceeded less rapidly and afforded only 27% of **16** (R = *n*-Bu), together with recovered starting material in 38% yield (entry 7). In this case, the low level of deuteration of the recovered starting material, taken together with the lack of production of *anti*-**15** (X = Cl), suggested that deprotonation of **15** (X = Cl) with the Grignard reagent was not a significant competing pathway. Reactions of **15** (X = Cl) with alkyllithium reagents were more complex and typically gave a poor mass balance of products from the three competing processes of interest. Deprotonation was the major identifiable pathway for all such reactions when conducted in THF solvent (entries 3–6). In PhMe solvent, significant differences in reactivity were noted between the four alkyllithiums examined (entries 8–11). For example, treatment of **15** (X = Cl) with *n*-BuLi in PhMe gave an intractable mixture, the ^{1}H NMR spectral signature of which clearly indicated the formation of a modest quantity of dibutylsulfoxide (entry 8). By contrast, exposure of **15** (X = Cl) to *s*-BuLi resulted in a significant level of deprotonation (entry 9), while an otherwise identical reaction promoted by *t*-BuLi was observed to prefer a sulfoxide ligand exchange pathway (entry 10). Significantly, in changing from the relatively polar THF solvent to less polar PhMe solvent, the reactivity profile for *t*-BuLi reverses from favoring deprotonation to favoring sulfoxide ligand exchange (cf. entries 5 and 10). As may be expected, halogen–metal exchange was not an observed reaction pathway for any of the experiments performed with α-chlorosulfoxide **15** (X = Cl).

The reactions of α-bromosulfoxide **15** (X = Br) were next investigated in a more limited fashion (entries 12–15). Again, *n*-BuMgCl induced efficient sulfoxide ligand exchange in THF and the same reaction when conducted in PhMe took a similar course but was evidentally slower (cf. entries 12 and 14). Treatment of **15** (X = Br) with *n*-BuLi in either THF or PhMe resulted in identifiable products from all three direct reaction pathways (entries 13 and 15). It is noteworthy that the level of bromine–lithium exchange in these reactions was more pronounced than sulfoxide ligand exchange.

In conclusion, the above results have established that the interactions of alkyllithium reagents with α-halo-α-protioalkyl aryl sulfoxides are indeed complex, but that some degree of control can be obtained by a judicious selection of reaction variables. Pertinent to the motivation behind this survey, it was discovered that a combination of *t*-BuLi with PhMe solvent is optimal for initiation of sulfoxide ligand exchange from sulfoxides **5** (X = Cl). By implication, these reaction conditions may be considered as optimal for the generation of Li-carbenoids from α-chloro-α-protioalkyl aryl sulfoxides.[17] Finally, this work stands to further exemplify the remarkably chemoselective nature of the sulfoxide ligand exchange reaction between α-haloalkyl sulfoxides and alkyl Grignard reagents.

Acknowledgements

Oregon State University is gratefully acknowledged for the financial support of this work. Ms. Selena D. Milicevic is thanked for assistance in compiling the bibliography.

References and notes

1. Reports of sulfoxide ligand exchange reactions have appeared sporadically since 1929. For selected pivotal work, see: (a) Fuchs, K. *Monatsh. Chem.* **1929**, *53–54*, 438–444; (b) Gilman, H.; Eidt, S. H. *J. Am. Chem. Soc.* **1956**, *78*, 3848–3850; (c) Jacobus, J.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 5228–5234; (d) Andersen, K. K.; Yeager, S. A.; Peynircioglu, N. B. *Tetrahedron Lett.* **1970**, 2485–2488; (e) Tsuchihashi, G.-i.; Iriuchijima, S.; Ishibashi, M. *Tetrahedron Lett.* **1972**, 4605–4608; (f) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485–486; (g) Durst, T.; LeBelle, M. J.; Van Den Elzen, R.; Tin, K.-C. *Can. J. Chem.* **1974**, *52*, 761–766; (h) Guetté, E.; Bibang Bi Ekogha, C.; Julia, S. A. *Bull. Chim. Soc. Fr.* **1986**, 325–331; (i) Zhao, S. H.; Samuel, O.; Kagan, H. B. *Tetrahedron* **1987**, *43*, 5135–5144; (j) Furukawa, N.; Ogawa, S.; Matsumura, K.; Fujihara, H. *J. Org. Chem.* **1991**, *56*, 6341–6348.
2. For illuminating discourse on possible pathways for nucleophilic substitution at tricoordinate sulfur, see Ref. 1g and (a) Tillett, J. G. *Chem. Rev.* **1976**, *76*, 747–772; (b) Mislow, K. *Acc. Chem. Res.* **1970**, *3*, 321–331.
3. (a) Cardellicchio, C.; Naso, F.; Capozzi, M. A. M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 1161–1170; (b) Cappozzi, M. A. M.; Cardellicchio, C.; Naso, F. *Eur. J. Org. Chem.* **2004**, 1855–1963.
4. The work of Satoh and co-workers is predominantly directed toward the synthesis of α-haloalkylmagnesium and oxiranyl anion species by sulfoxide ligand exchange reactions. For representative recent work with leading references, see: (a) Satoh, T.; Ogata, S.; Wakasugi, D. *Tetrahedron Lett.* **2006**, *47*, 7249–7253; (b) Satoh, T.; Tanaka, S.; Asakawa, N. *Tetrahedron Lett.* **2006**, *47*, 6769–6773; (c) Satoh, T.; Osawa, A.; Ohbayashi, T.; Kondo, A. *Tetrahedron* **2006**, *62*, 7892–7901; (d) Satoh, T.; Miura, M.; Sakai, K.; Yokoyama, Y. *Tetrahedron* **2006**, *62*, 4253–4261; (e) Satoh, T.; Kobayashi, S.; Nakanishi, S.; Horiguchi, K.; Irisa, S. *Tetrahedron* **1999**, *55*, 2515–2528; (f) Satoh, T.; Kuramochi, Y.; Inoue, Y. *Tetrahedron Lett.* **1999**, *40*, 8815–8818.
5. Recent applications of sulfoxide ligand exchange reactions in the generation of arylmetals: (a) Clayden, J.; Kubinski, P. M.; Sammiceli, F.; Helliwell, M.; Diorazio, L. *Tetrahedron* **2004**, *60*, 4387–4397; (b) Clayden, J.; Stimson, C. C.; Keenan, M. *Synlett* **2005**, 1716–1720; (c) Hitchcock, P.

B.; Rowlands, G. J.; Parmar, R. *Chem. Commun.* **2005**, 4219–4221; Vinylmetals: (d) Sklute, G.; Marek, I. *J. Am. Chem. Soc.* **2006**, *128*, 4642–4649, and references cited therein; Metalated enol ethers: (e) Milne, J. E.; Kocienski, P. J. *Synthesis* **2003**, 584–592; Ferrocenylmetals: (f) Riant, O.; Argouarch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1998**, *63*, 3511–3514; (g) Albrow, V. E.; Blake, A. J.; Fryatt, R.; Wilson, C.; Woodward, S. *Eur. J. Org. Chem.* **2006**, 2549–2557; (h) Kloetzing, R. J.; Knochel, P. *Tetrahedron: Asymmetry* **2006**, *17*, 116–123; Cyclopropylmetals: (i) Kopp, F.; Sklute, G.; Polburn, K.; Marek, I.; Knochel, P. *Org. Lett.* **2005**, *7*, 3789–3791.

6. Satoh, T.; Takano, K. *Tetrahedron* **1996**, *52*, 2349–2358.
7. Hoffmann, R. W.; Nell, P. G.; Leo, R.; Harms, K. *Chem. Eur. J.* **2000**, *6*, 3359–3365.
8. Blakemore, P. R.; Marsden, S. P.; Vater, H. D. *Org. Lett.* **2006**, *8*, 773–776.
9. Satoh and Takano reported the generation of complex product mixtures from the reaction of an α-chloro-α-protioalkyl tolyl sulfoxide and *t*-BuLi in THF (Ref. 6). Durst et al. reported reactions of 1-chloroethyl phenyl sulfoxide with *n*-BuLi, *t*-BuLi, and MeLi (in THF) and obtained sulfoxide exchange products in yields of 22%, 9%, and 36%, respectively (Ref. 1g).
10. For α-halogenation of sulfoxides with *N*-halosuccinimides, see: (a) Jung, F.; Tin, K. C.; Durst, T. *Int. J. Sulfur Chem.* **1973**, *8*, 1–4; (b) Drabowicz, J. *Synthesis* **1986**, 831–833; (c) Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *Tetrahedron Lett.* **1988**, *29*, 313–316.
11. Data for **14**: colorless oil; IR (neat) 2978, 1475, 1391, 1051, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (2H, d, $J = 8.1$ Hz), 7.45 (2H, d, $J = 8.1$ Hz), 2.86 (1H, dq, $J = 13.2$, 7.5 Hz), 2.70 (1H, dq, $J = 13.2$, 7.5 Hz), 1.15 (3H, t, $J = 7.5$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8 (0), 137.0 (0), 129.4 (2C, 1), 125.6 (2C, 1), 50.2 (2), 5.8 (3) ppm. Data for **15** (X = Cl): colorless solid; mp 52–54 °C (EtOAc/hexanes); IR (neat) 2980, 1475, 1082, 1058, 1012, 823, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (2H, d, $J = 8.7$ Hz), 7.52 (2H, d, $J = 8.7$ Hz), 4.71 (1H, q, $J = 6.6$ Hz), 1.61 (3H, d, $J = 6.6$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4 (0), 137.0 (0), 129.2 (2C, 1), 127.3 (2C, 1), 70.3 (1), 17.0 (3) ppm. Data for **15** (X = Br): oily solid; IR (neat) 2953, 1475, 1391, 1082, 1054, 822, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (2H, d, $J = 8.7$ Hz), 7.51 (2H, d, $J = 8.7$ Hz), 4.74 (1H, q, $J = 6.6$ Hz), 1.80 (3H, d, $J = 6.6$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6 (0), 137.7 (0), 129.3 (2C, 1), 127.5 (2C, 1), 61.7 (1), 18.0 (3) ppm. All data in agreement with those previously reported, see: **14** (a) Shukla, V. G.; Salgaonkar, P. D.; Akamanchi, K. G. *J. Org. Chem.* **2003**, *68*, 5422–5425. **15** (X = Cl and Br) (b) Cinquini, M.; Colonna, S.; Landini, D.; Maia, A. M. *J. Chem. Soc., Perkin Trans. 2* **1976**, 996–1000.
12. Solutions (0.20 M) of **15** in the indicated solvent were used throughout. Alkylmetal reagents were dispensed as the following standardized solutions: *n*-BuMgCl (2.4 M in THF), *n*-BuLi (2.1 M in hexanes), *s*-BuLi (1.4 M in cyclohexane), *t*-BuLi (1.5 M in pentane), MeLi (1.6 M in Et_2O).
13. Data for *anti*-**15** (X = Cl): ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (2H, d, $J = 8.7$ Hz), 7.52 (2 H, d, $J = 8.7$ Hz), 4.48 (1H, q, $J = 6.7$ Hz), 1.78 (1H, d, $J = 6.7$ Hz) ppm. Data for *anti*-**15** (X = Br): ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (2H, d, $J = 8.6$ Hz), 7.48 (2H, d, $J = 8.7$ Hz), 4.57 (1H, q, $J = 6.8$ Hz), 1.91 (3H, d, $J = 6.8$ Hz) ppm. Data for **16** (R = *n*-Bu): colorless oil; IR (neat) 2959, 1475, 1081, 1040, 1011, 825, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (2H, d, $J = 8.7$ Hz), 7.46 (2H, d, $J = 8.7$ Hz), 2.74 (2H, t, $J = 7.2$ Hz), 1.75–1.63 (1H, m), 1.60–1.50 (1H, m), 1.48–1.32 (2H, m), 0.88 (3H, t, $J = 7.2$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7 (0), 137.3 (0), 129.7 (2C, 1), 125.6 (2C, 1), 57.3 (2), 24.2 (2), 22.1 (2), 13.8 (3) ppm. Data for **16** (R = *s*-Bu, less polar isomer): colorless oil; IR (neat) 2924, 1459, 1040, 827 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50–7.48 (4H, m), 2.51 (1H, sextet, $J = 7.0$ Hz), 1.94 (1H, d of quintet, $J = 13.6$, 7.2 Hz), 1.47 (1H, d of quintet, $J = 14.0$, 7.0 Hz), 1.09 (3H, t, $J = 7.2$ Hz), 1.04 (3H, d, $J = 6.8$ Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8 (0), 137.1 (0), 129.4 (2C, 1), 126.3 (2C, 1), 61.5 (1), 24.0 (2), 11.8 (3), 10.3 (3) ppm; HRMS (EI+) *m/z* 217.04536 ($C_{10}H_{14}{}^{35}ClOS$ requires 217.04539). Data for **16** (R = *t*-Bu): colorless oil; IR (neat) 2962, 1475, 1169, 1045, 1011, 825, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (2H, d, $J = 8.7$ Hz), 7.46 (2H, d, $J = 8.7$ Hz), 1.16 (9 H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8 (0), 137.6 (0), 128.7 (2C, 1), 127.6 (2C, 1), 56.1 (0), 22.7 (3C, 3) ppm. Data for **16** (R = Me): colorless oil; IR (neat) 2970, 1476, 1090, 1052, 1011, 822, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (2H, d, $J = 8.7$ Hz), 7.51 (2H, d, $J = 8.7$ Hz), 2.71 (3H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5 (0), 137.4 (0), 129.8 (2C, 1), 125.1 (2C, 1), 44.3 (3) ppm. Data in agreement with those previously reported, see: **16** (R = *n*-Bu) (a) Xia, M.; Chen, Z.-C. *Synth. Commun.* **1997**, *27*, 1315–1320. **16** (R = *t*-Bu) (b) Shelton, J. R.; Davis, K. E. *Int. J. Sulfur Chem.* **1973**, *3*, 197–204. **16** (R = Me) (c) Buchanan, G. W.; Reyes-Zamora, C.; Clarke, D. E. *Can. J. Chem.* **1974**, *52*, 3895–3904.
14. (a) Creger, P. L. *J. Am. Chem. Soc.* **1970**, *92*, 1396–1397; (b) Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390–5398; (c) Vedejs, E.; Lee, N. *J. Am. Chem. Soc.* **1995**, *117*, 891–900.
15. The possibility that *anti*-**15** may arise from **15** via a base catalyzed process or via a halide anion mediated substitution ('ping-pong') mechanism was suggested by a reviewer. Additional experiments have established that neither pathway is a significant cause of epimerization for **15** (X = Cl). Thus, exposure of **15** (X = Cl) to excess LiCl or LiBr in THF at temperatures ranging from −78 °C to 65 °C resulted in no observed reaction. Likewise, reaction of **15** (X = Cl) with substoichiometric quantities (0.1–0.25 equiv) of either LDA or *t*-BuLi did not in any experiment result in the production of *anti*-**15** in a quantity greater than the amount of added base.
16. Experiments in pentane and Et_2O were also attempted but gave irreproducible results owing to the poor solubility of sulfoxide **15** (X = Cl) in these solvents at −78 °C.
17. Use of *t*-BuLi with PhMe solvent has now been verified as optimal for the generation of enantioenriched Li-carbenoids for use in stereospecific reagent controlled homologation (StReCH) reactions, see: Blakemore, P. R.; Burge, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3068–3069.