JOC*Article*

Stereoselective Synthesis of *Z* Alkenyl Halides via Julia Olefination

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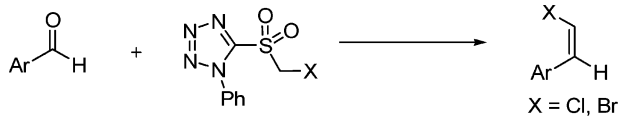
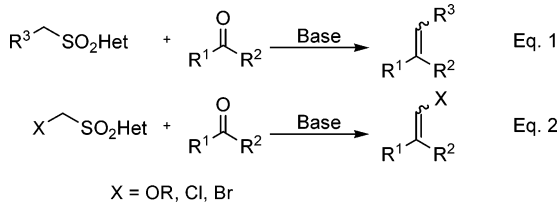


Julia olefination between α-halomethyl sulfones and a variety of aldehydes afforded alkenyl halides in good to excellent yields with high *E*/*Z* stereoselectivities. Sulfones were readily prepared in two or three steps from commercially available reagents in good yields. Optimization revealed that the nature of the solvent, the base, and the additive were crucial to obtain the desired alkenyl halides.

Introduction

Alkenyl halides are important precursors in many useful organic transformations including the well-known Stille,[1] Suzuki,[2] and Sonogashira[3] couplings, as well as the Buchwald[4] methodology, to introduce heteroatoms such as nitrogen yielding enamides. Two major reactions are used to prepare alkenyl halides starting from aldehydes and ketones. The first one is the Wittig-type olefination involving an α-halomethyltriphenylphosphorane and the $CrCl_2$ reduction of trichloroalkanes, which both give high *Z* stereoselectivity.[5,6] In contrast, the Takai methodology provides selectively the *E* isomer.[7] While both of these methods are useful, the development of an alternative approach could be useful when an incompatibility with previous reaction conditions appears. Recently, during our medicinal chemistry efforts, we reported an extension of the modified Julia olefination using an α-alkoxysubstituent on the sulfone moiety to afford vinyl ethers in good yields (Scheme 1, eq 2 with X = OR).[8] We envisioned that the use of α-halomethyl sulfones would generate the corresponding alkenyl halides (Scheme 1, eq 2 with X = Cl or Br). To date, only one example of this approach has been reported by Julia, in 1993, though with moderate *E*/*Z* stereoselectivity (83:17).[9] In this regard, we wish to report our findings on alkenyl halide syntheses using the modified Julia olefination.[10] Herein, we will describe the scope and limitations of this methodology using aldehydes and two different α-halomethyl sulfones.

SCHEME 1. Extension of the Modified Julia Olefination



Results and Discussion

Synthesis of α-Halomethyl Sulfones. Syntheses of the starting sulfone substrates were accomplished employing a two or a three-step process from commercially available reagents

* To whom correspondence should be addressed. Phone: (514) 428-3359. Fax: (514) 428-4900.

(1) (a) Stille, J. K. *Angew. Chem.* **1986**, *98*, 504. (b) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (c) Recent review: Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704 and references therein.

(2) For a review on Suzuki cross-coupling reactions, see: Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(3) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627. (c) Negishi, E.-i.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979.

(4) Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 3667.

(5) (a) Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173. (b) Seyferth, D.; Heeren, J. K.; Singh, G.; Grim, S. O.; Hughes, W. B. *J. Organomet. Chem.* **1966**, *5*, 267. (c) Taber, D. F.; Meagley, R. P.; Doren, D. J. *J. Org. Chem.* **1996**, *61*, 5723 (alkenyl chloride and bromide, 1:1 *E*/*Z* ratio). (d) Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1980**, *21*, 4021.

(6) Baati, R.; Barma, D. K.; Krishna, U. M.; Mioskowski, C.; Falck, J. R. *Tetrahedron Lett.* **2002**, *43*, 959.

(7) (a) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408. (b) Takai, K.; Ichiguchi, T.; Hikasa, S. *Synlett* **1999**, *8*, 1268.

(8) Surprenant, S.; Chan, W. Y.; Berthelette, C. *Org. Lett.* **2003**, *5*, 4851.

(9) (a) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Tetrahedron Lett.* **1991**, *32*, 1175. (b) Baudin, J. B.; Hareau, G.; Julia, S. A.; Lorne, R.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 856. (c) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 336.

(10) For an excellent review on the modified Julia olefination, see: Blakemore, P. R. *J. Chem. Soc., Perkin Trans. 1* **2002**, *23*, 2563.

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SCHEME 2. Synthesis of α-Halomethyl Sulfones 2a,b

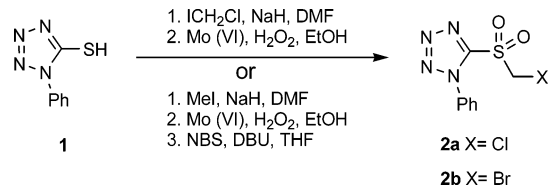
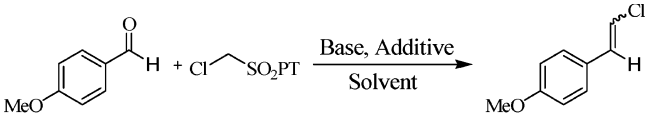


TABLE 1. Exploration of the Reaction Conditions



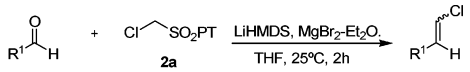
entry	base[a]	solvent	additive[b]	(*E*/*Z*)[c]
1	LiHMDS	DCM		74:26
2	LiHMDS	tol		67:33
3	LiHMDS	THF		32:68
4	NaHMDS	THF		33:67
5	KHMDS	THF		60:40
6	LDA	THF		36:64
7	P(4)-*t*-Bu	THF		38:62
8	LiHMDS[d]	THF		30:70
9	LiHMDS[d]	THF	$BF_3{\cdot}Et_2O$	40:60
10	LiHMDS[d]	THF	HMPA	8:92
11	LiHMDS[d]	THF	$MgBr_2{\cdot}Et_2O$	93:7
12	LDA[e]	THF	DMPU	67:33
13	LDA[e]	THF	$MgBr_2{\cdot}Et_2O$	60:40
14	LDA[e]	THF	12-C-4	76:24
15	LDA[e]	THF	LiBr	83:17

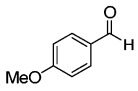
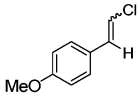
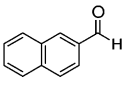
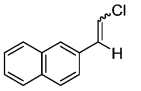
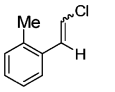
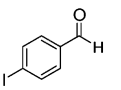
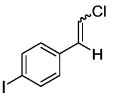
[a] Base (2 equiv) was added to a solution of aldehyde (1 equiv) and sulfone **2a** (1 equiv) at 0 °C (Barbier conditions). All reactions gave >95% yields. [b] Additive (2 equiv) was added in the reaction mixture prior to the base. [c] *E*/*Z* ratio was determined by ^{1}H NMR spectroscopy. [d] The reaction was run at 25 °C. [e] The reaction was run at −78 °C.

(Scheme 2). We decided to use phenyltetrazole as the desired heterocyclic partner, because this group usually gives better *E*/*Z* stereoselectivity compared to that of benzothiazole.[11] Simple alkylation with chloroiodomethane or iodomethane, followed by an oxidation of these thioethers with a catalytic amount of ammonium molybdate[12] in the presence of hydrogen peroxide afforded the desired α-chloromethyl sulfone **2a** in 60% yield and the methyl sulfone, which was directly brominated to access the desired α-bromomethyl sulfone **2b** in 32% overall yield.[13]

Having in hand our desired α-halomethyl sulfones, we first began our investigations by exploring the coupling between sulfone **2a** and *p*-anisaldehyde to parallel the only example found in the original paper by Julia (Table 1). In all cases, the desired alkenyl chloride **3** was obtained in greater than 95% yield. LiHMDS (2 equiv, 1 M hexanes) was first used in three different solvents, and the first result compared favorably with the *E*/*Z* ratio obtained by Julia using a benzothiazole sulfone moiety (Table 1, entries 1−3). Higher *Z* stereoselectivity was obtained by using THF as a solvent. Different bases were tried

TABLE 2. Limitations of *E* Alkenyl Chloride Formation



entry	aldehyde	product[a]		yield (%)[b]	(*E*:*Z*)[c]
1			**3**	69	94:6
2			**4**	47	71:29
3			**5**	43	12:88
4			**6**	38	27:73

[a] Conditions: To a mixture of aldehyde (1 equiv), sulfone (1 equiv), and $MgBr_2/Et_2O$ (2 equiv) in THF at room temperature was added slowly LiHMDS (2 equiv, 1 M hexanes) via a syringe pump over 2 h. [b] Isolated yields after purification. [c] *E*/*Z* ratio determined by ^{1}H NMR spectroscopy.

to increase the stereoselectivity. LiHMDS provided the highest *Z* selectivity, whereas the KHMDS reversed the stereoselectivity in favor of the *E* isomer (Table 1, entries 3−7). We then explored a range of temperatures and found that 0 or 25 °C provided similar stereoselectivities (Table 1, entries 3 and 8). Decreasing the temperature to −40 or −78 °C did not further improve the *E*/*Z* ratio. Inspired by literature precedent for the incorporation of additives,[14] we were very pleased to note that HMPA and $MgBr_2/Et_2O$ gave excellent and complementary stereoselectivities (Table 1, entries 10 and 11).[15] In fact, HMPA afforded an 8:92 ratio favoring the *Z* alkenyl chloride isomer.[16] In contrast, $MgBr_2/Et_2O$ completely reversed the isomer ratio to 93:7 favoring the *E* alkenyl chloride isomer. Therefore, we tried a large number of additives (2 equiv) but found that the former two were the best (Table 1, entries 12−15). We also investigated the order of addition (barbier or premetalate) as well as the concentration of the reaction without further improvement.

Synthesis of *E* Alkenyl Halides. Next we sought to evaluate the scope and limitations of the modified Julia olefination reaction through the use of *p*-anisaldehyde and the conditions for selective *E* isomer formation involving $MgBr_2/Et_2O$ as an additive. An initial examination revealed that the reaction with *p*-anisaldehyde proceeded smoothly to afford the desired *E* alkenyl chloride **3** in 69% isolated yield (Table 2, entry 1).

(11) Other heterocycles have been used. For BT and PT, see: (a) Blakemore, P. R.; Cole, W. J.; Kocienski, P. J.; Morley, A. *Synlett* **1998**, 26. (b) Bellingham, R.; Jarowicki, K.; Kocienski, P.; Martin, V. *Synthesis* **1996**, 285. For PYR, see: (c) Charette, A. B.; Berthelette, C.; St-Martin, D. *Tetrahedron Lett.* **2001**, *42*, 5149 and 6619. For TBT, see: (d) Kocienski, P. J.; Bell, A.; Blakemore, P. R. *Synlett* **2000**, 365.

(12) Schultz, H. S.; Freyermuth, H. B.; Buc, S. R. *J. Org. Chem.* **1963**, *28*, 1140.

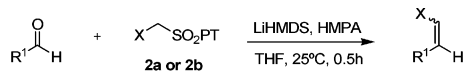
(13) The reaction was not pushed to completion to avoid dibromo compound formation, which was previously observed. The starting methyl sulfone was recovered.

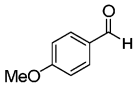
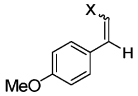
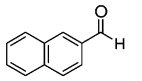
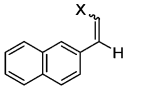
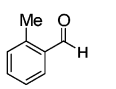
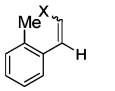
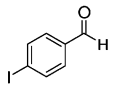
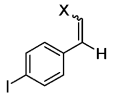
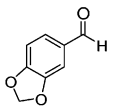
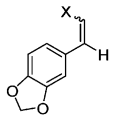
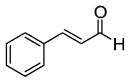
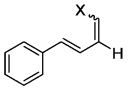
(14) (a) Liu, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 10772 (DMPU). (b) Smith, A. B., III; Brandt, B. M. *Org. Lett.* **2001**, *3*, 1685 (DME-HMPA).

(15) Precomplexation between the sulfone and the aldehyde by using $MgBr_2/Et_2O$ as an additive should occur and lead to a closed transition state (chairlike), as described earlier in the literature. In contrast, HMPA is known to break the complexation of the two partners, and an open transition state should operate. Nevertheless, this hypothesis cannot lead us to predict which isomer, *E* or *Z*, will predominate. Further studies should be completed to validate these hypotheses.

(16) In Kocienski−Julia olefination, as the polarity and the coordinating ability of the solvent increase, the *E* selectivity of the reaction increases, which is opposite in our case with α-halomethyl sulfones, because we obtained predominantly the *Z* isomer. We do not have a rationale at the moment to explain this reversal.

TABLE 3. Stereoselective Synthesis of *Z* Alkenyl Halides Using Sulfones 2a and 2b



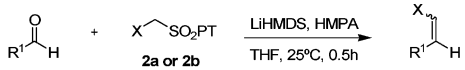
entry	aldehyde	product		yield (%)[a]	(*E*:*Z*)[b]
1			**3a** X=Cl	95	10:90
2			**3b** X=Br	70	5:95
3			**4a** X=Cl	86	9:91
4			**4b** X=Br	79	5:95
5			**5a** X=Cl	99	10:90
6			**5b** X=Br	69	5:95
7			**6a** X=Cl	79	18:82
8			**6b** X=Br	63	7:93
9			**7a** X=Cl	80	9:91
10			**7b** X=Br	75	6:94
11			**8a** X=Cl	75	14:86
12			**8b** X=Br	69	8:92

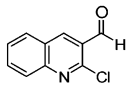
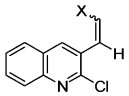
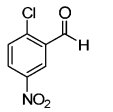
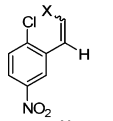
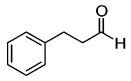
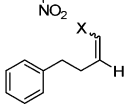
[a] Isolated yields after purification. [b] *E*/*Z* ratio determined by ^{1}H NMR spectroscopy.

We were pleased to obtain a 94:6 ratio favoring the *E* isomer, which represents an improvement over the 83:17 ratio previously reported in the literature.[17] Encouraged by this result, we expanded the scope of the reaction to access stereoselective *E* alkenyl halides. Applying the same conditions to a variety of aldehydes immediately revealed several limitations. For instance, 2-naphthaldehyde afforded only a 71:29 ratio of the desired *E* isomer **4** with a 47% isolated yield (Table 2, entry 2). In the cases of *o*-tolualdehyde and *p*-iodobenzaldehyde, the isomer ratio shifted completely to favor the *Z* isomer, and the yields were only 43 and 38%, respectively (Table 2, entries 3 and 4). Electronic and steric effects seemed to play an important role in this transformation, and all attempts to improve conversion, stereoselectivities, or yields were met with limited success.[18]

Synthesis of *Z* Alkenyl Halides. Because we had also found excellent conditions for the *Z* isomer formation using HMPA as an additive, we decided to explore the scope and limitations of this stereoselective transformation (Table 3). We were delighted to see that we obtained good to excellent *Z* stereoselectivities as well as good yields with a variety of electron-donating and electron-withdrawing aldehydes. Conversions were no longer a problem, and all reactions were completed within 30 min using the standard protocol. Thus, the best reaction conditions to obtain *Z* stereoselectivity were the addition of LiHMDS (2 equiv, 1 M hexanes) to a mixture of the aldehyde (1 equiv), the sulfone (1 equiv), and HMPA (2 equiv) in THF at room temperature.

TABLE 4. Limitations of *Z* Alkenyl Halide Formation



entry	aldehyde	product		yield (%)[a]	(*E*:*Z*)[b]
1			**9a** X=Cl	62	52:48
2			**9b** X=Br	50	50:50
3			**10a** X=Cl	48	62:38
4			**10b** X=Br	73	55:45
5			**11a** X=Cl	64	35:65
6			**11b** X=Br	73	23:77

[a] NMR yields using an internal standard. [b] *E*/*Z* ratio determined by ^{1}H NMR spectroscopy.

First, the chloromethyl sulfone **2a** was reacted with *p*-anisaldehyde to afford the corresponding alkenyl chloride **3a** in 95% yield with a 10:90 (*E*/*Z*) ratio (Table 3, entry 1). Sulfone **2b** gave the desired alkenyl bromide **3b** in 70% yield with an excellent 5:95 (*E*/*Z*) ratio (Table 3, entry 2). Furthermore, 2-naphthaldehyde reacted well to give a high level of *Z* stereoselectivity for both halogens (Table 3, entries 3 and 4). Surprisingly, steric hindrance in *o*-tolualdehyde did not affect the outcome of this reaction as the corresponding alkenyl halides **5a** and **5b** were obtained in good yields and excellent *Z* stereoselectivities (Table 3, entries 5 and 6). Electron-withdrawing substituents on the aromatic aldehyde gave slightly lower yields and *Z* stereoselectivities as seen with alkenyl halides **6a** and **6b** (Table 3, entries 7 and 8). Conjugated alkenyl chloride **8a** was obtained in 75% yield with a 14:86 (*E*/*Z*) ratio, whereas the corresponding bromide **8b** gave a similar yield with an increased stereoselectivity of 8:92 (Table 3, entries 11 and 12). In general, the bromomethyl sulfone **2b** gave higher *Z* stereoselectivity than that of the corresponding chloromethyl sulfone **2a**, even though sulfone **2b** is bulkier and gives rise to greater steric hindrance.

We also found some limitations to this methodology. By further increasing the ortho substituent bulk on the aromatic aldehyde and by changing the electronic nature of the starting aldehydes, we have started to see a decrease in the *Z* stereoselectivity, as illustrated by the entries of Table 4.

Starting from 2-chloroquinoline-3-carbaldehyde, we obtained the corresponding alkenyl halides **9a** and **9b** in moderate yields without any stereoselectivities (Table 4, entries 1 and 2). The 2-chloro-5-nitrobenzaldehyde afforded the desired compounds, **10a** and **10b**, with a slight preference for the *E* isomer (Table 4, entries 3 and 4). Finally, we observed the expected stereoselectivity under the selected reaction conditions with the aliphatic aldehyde to afford compounds **11a** and **11b** with moderate isomer ratios of 35:65 and 23:77, respectively, favoring the *Z* isomer (Table 4, entries 5 and 6).

Conclusion

In conclusion, we have demonstrated that α-halomethyl sulfones can be efficiently coupled to aldehydes to afford the

(17) Julia used LDA in a mixture of THF/hexanes at −78 °C for 3 h, and then warmed the mixture to room temperature for 1 h to afford a 17:83 ratio, favoring the *E* alkenyl chloride.

(18) Many parameters were investigated to push *E* isomer formation, including temperature (−78 °C to reflux), time (5 min to 2 days), solvents (DCM, toluene, THF, and DMF), bases (LiHMDS, NaHMDS, KHMDS, $Mg(HMDS)_2$, LDA, and phosphazanes), slow addition (syringe pump over 3 h), barbier or premetalate, and different additives (monodentate, bidentate, and tridentate), without any success.

corresponding alkenyl halides in good yields with excellent *Z* stereoselectivities using the modified Julia olefination. The α-halomethyl sulfones can be easily prepared in two or three steps from commercially available reagents. Further investigations on substituent effects and mechanistic studies of these reactions are currently underway.

Experimental Section

Synthesis of Sulfone 2a. 5-[(Chloromethyl)sulfonyl]-1-phenyl-1*H*-tetrazole (2a). Step 1: To a solution of 2-mercaptophenyltetrazole (10 g, 56.1 mmol) in DMF (300 mL, 0.187 M) at −5 °C was slowly added 60% sodium hydride (2.24 g, 56.1 mmol, 1 equiv). The reaction was stirred at −5 °C for 10 min. Chloroiodomethane (4.27 mL, 58.9 mmol, 1.05 equiv) diluted in ∼5 mL of DMF was then slowly added, and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was quenched with a saturated NH_4Cl solution at room temperature and diluted with EtOAc. The aqueous layer was washed with EtOAc (3×). The organic layers were washed with water (3×) and brine, dried over $MgSO_4$, and concentrated. Purification was done by using a silica gel plug filtration with 40% EtOAc/hexanes as the eluent, which afforded the desired sulfide (11.27 g, 89% yield). The product was directly oxidized to the sulfone. **Step 2:** To a solution of the previous sulfide (3.8 g, 15.66 mmol) in ethanol (100 mL, 0.157 M) at 0 °C was added ammonium molybdate tetrahydrate (3.87 g, 3.13 mmol, 0.2 equiv), followed by 30% hydrogen peroxide (4.8 mL, 47 mmol, 3 equiv). The reaction was stirred at room temperature overnight. The reaction mixture was quenched with a sodium sulfite solution at room temperature and diluted with EtOAc. The aqueous layer was washed with EtOAc (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. Purification was done by flash chromatography using 10−20% EtOAc/hexanes as the eluent to afford the corresponding chloromethyl sulfone **2a** (3.26 g, 81% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57−7.66 (m, 5H), 5.12 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.4, 132.6, 131.8, 129.8, 125.2, 58.6. HRMS calcd for $C_8H_8ClN_4O_2S$: 259.0056. Found: 259.0057.

Synthesis of Sulfone 2b. 5-[(Bromomethyl)sulfonyl]-1-phenyl-1*H*-tetrazole (2b). Step 1: To a solution of 2-mercaptophenyltetrazole (5.0 g, 28.1 mmol) in DMF (120 mL, 0.234 M) at 0 °C was slowly added 60% sodium hydride (1.124 g, 28.1 mmol, 1 equiv). The reaction was stirred at 0 °C for 20 min, then methyl iodide (1.757 mL, 28.1 mmol) was introduced, and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with a saturated NH_4Cl solution and diluted with EtOAc. The aqueous layer was washed with EtOAc (3×). The combined organic layers were washed with water (4×) and brine, dried over $MgSO_4$, and concentrated. Purification was done by flash chromatography using a gradient of 10−40% EtOAc/hexanes to afford the corresponding methyl sulfide (5.3 g, 99% yield). This compound was used directly for the next step. **Step 2:** To a solution of the previous methyl sulfide (3 g, 15.6 mmol) in ethanol (70 mL, 0.223 M) at 0 °C was added ammonium molybdate tetrahydrate (9.64 g, 7.8 mmol, 0.5 equiv), followed by 30% hydrogen peroxide (7.17 mL, 70.2 mmol, 4.5 equiv). The reaction was stirred at room temperature overnight. The reaction mixture was quenched with a sodium sulfite solution at room temperature and diluted with EtOAc. The aqueous layer was washed with EtOAc (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. Purification was done by flash chromatography using 0−40% EtOAc/hexanes as the eluent to afford the corresponding methyl sulfone (2.84 g, 81% yield) as a white solid that was used directly for the next step. **Step 3:** To a solution of the previous methyl sulfone (2.84 g, 12.67 mmol) in THF (250 mL, 0.051 M) at −40 °C was added DBU (1.91 mL, 12.67 mmol, 1 equiv). The reaction was cooled to −40 °C. NBS (2.255 g, 12.67 mmol, 1 equiv) diluted in THF was then added, and the reaction was stirred at −40 °C for 30 min and then at room temperature for 5 h. The reaction mixture was quenched with water at room temperature and diluted with EtOAc. The aqueous layer was washed with EtOAc (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. Purification was done by flash chromatography using 15% EtOAc/hexanes as the eluent to afford the desired sulfone **2b** (1.53 g, 40% yield), while some starting material (0.402 g) was recovered. The reaction was not pushed to completion to avoid dibromo compound formation, which was previously observed. Compound **2b** was obtained as a white crystal after crystallization in ether/hexanes. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57−7.64 (m, 5H), 5.02 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.3, 132.6, 131.8, 129.8, 125.2, 43.9. HRMS calcd for $C_8H_8BrN_4O_2S$: 302.9551. Found: 302.9550.

Representative Procedure for the Synthesis of *Z* Alkenyl Halide (3a). To a solution of sulfone **2a** (100 mg, 0.387 mmol) and *p*-anisaldehyde (47 μL, 0.387 mmol, 1 equiv) in THF (1.5 mL, 0.258M) at room temperature was added HMPA (135 μL, 0.774 mmol, 2 equiv), followed by LiHMDS (774 μL, 0.774 mmol, 2 equiv) as a 1.0 M hexanes solution. The reaction was stirred at room temperature for 30 min, after which it was filtered through a silica gel cartridge (1.5 g), washed with 5% ether/pentane, and evaporated. The crude NMR indicated a ratio of 10:90 favoring the *Z* isomer. Purification was done by flash chromatography using 0−20% ether/pentanes to give alkenyl chloride **3a** (62 mg, 95% yield) as a colorless oil.

1-[(*Z*)-2-Chlorovinyl]-4-methoxybenzene (3a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 8.1 Hz, 1H), 6.19 (d, *J* = 8.1 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.3, 130.7, 128.6, 126.8, 115.4, 113.6, 55.2. GC-MS calcd for C_9H_9ClO: 168.04. Found: 168. See ref 19 for compound 7.

1-[(*Z*)-2-Bromovinyl]-4-methoxybenzene (3b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.34 (d, *J* = 8.1 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.4, 131.6, 130.4, 127.5, 113.6, 104.1, 55.2. GC-MS calcd for C_9H_9BrO: 211.98. Found: 212. See ref 20 for compound 3c.

2-[(*Z*)-2-Chlorovinyl]naphthalene (4a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.81−7.87 (m, 4H), 7.46−7.52 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.35 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 133.1, 132.9, 131.6, 129.3, 128.8, 128.3, 127.8, 127.6, 126.7, 126.4, 126.2, 117.8. GC-MS calcd for $C_{12}H_9ClO$: 188.04. Found: 188.

2-[(*Z*)-2-Bromovinyl]naphthalene (4b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.75−7.87 (m, 4H), 7.44−7.53 (m, 2H), 7.18−7.27 (m, 1H), 6.50 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 133.1, 133.0, 132.4, 128.6, 128.3, 127.69, 127.66, 126.6, 126.39, 126.41, 126.3, 106.7. GC-MS calcd for $C_{12}H_9BrO$: 231.99. Found: 232. See ref 20 for compound 3q.

1-[(*Z*)-2-Chlorovinyl]-2-methylbenzene (5a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62−7.65 (m, 1H), 7.19−7.24 (m, 3H), 6.77 (d, *J* = 7.9 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 136.3, 133.0, 129.9, 129.0, 128.4, 128.0, 125.4, 118.8, 19.8. GC-MS calcd for C_9H_9Cl: 152.04. Found: 152. See ref 19 for compound 11.

1-[(*Z*)-2-Bromovinyl]-2-methylbenzene (5b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58−7.62 (m, 1H), 7.22−7.29 (m, 3H), 7.19 (d, *J* = 7.9 Hz, 1H), 6.57 (d, *J* = 7.9 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 136.2, 134.3, 132.0, 130.0, 128.6, 128.1, 125.4, 108.4, 19.8. GC-MS calcd for C_9H_9Br: 195.99. Found: 196. See ref 21 for compound 2c.

(19) Schlosser, M.; Ladenberger, V. *Chem. Ber.* **1967**, *100*, 3901.
(20) Kuang, C.; Yang, Q.; Senbokuc, H.; Tokudac, M. *Tetrahedron* **2005**, *61*, 4043.
(21) Uenishi, J.; Kawahama, R.; Yonemitsu, O. *J. Org.* Chem. **1998**, *63*, 8965.

1-[(*Z*)-2-Chlorovinyl]-4-iodobenzene (6a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, J = 8.5 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 6.54 (d, J = 8.2 Hz, 1H), 6.28 (d, J = 8.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 137.4, 133.4, 130.8, 128.3, 118.6, 93.9. GC-MS calcd for C_8H_6ClI: 263.92. Found: 264.

1-[(*Z*)-2-Bromovinyl]-4-iodobenzene (6b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.2 Hz, 1H), 6.45 (d, J = 8.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 137.4, 133.6, 131.4, 130.6, 107.4, 94.0. GC-MS calcd for C_8H_6BrI: 307.87. Found: 308.

5-[(*Z*)-2-Chlorovinyl]-1,3-benzodioxole (7a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, J = 1.7 Hz, 1H), 7.10 (dd, J = 8.1, 1.7 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 6.56 (d, J = 8.1 Hz, 1H), 6.18 (d, J = 8.1 Hz, 1H), 6.01 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 147.5, 147.3, 128.7, 128.2, 124.0, 115.8, 109.0, 108.1, 101.2. GC-MS calcd for $C_9H_7ClO_2$: 182.01. Found: 182.

5-[(*Z*)-2-Bromovinyl]-1,3-benzodioxole (7b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, J = 1.7 Hz, 1H), 7.07 (dd, J = 8.1, 1.7 Hz, 1H), 6.94 (d, J = 8.1 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.29 (d, J = 8.1 Hz, 1H), 5.97 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 147.5, 147.4, 131.7, 128.9, 123.8, 108.7, 108.1, 104.6, 101.2. GC-MS calcd for $C_9H_7BrO_2$: 225.96. Found: 226. See ref 20 for compound 3e.

[(1*E*,3*Z*)-4-Chlorobuta-1,3-dien-1-yl]benzene (8a). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (d, J = 7.6 Hz, 2H), 7.28−7.36 (m, 2H), 7.22−7.29 (m, 1H), 7.17 (dd, J = 15.8, 10.5 Hz, 1H), 6.68 (d, J = 15.7 Hz, 1H), 6.46 (dd, J = 10.5, 7.1 Hz, 1H), 6.06 (d, J = 7.1 Hz, 1H). GC-MS calcd for $C_{10}H_9Cl$: 164.04. Found: 164. See ref 19 for compound 15.

[(1*E*,3*Z*)-4-Bromobuta-1,3-dien-1-yl]benzene (8b). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44−7.49 (m, 2H), 7.30−7.36 (m, 2H), 7.23−7.30 (m, 1H), 7.10 (ddd, J = 15.8, 10.2, 1.1 Hz, 1H), 6.78 (ddd, J = 10.2, 7.1, 0.8 Hz, 1H), 6.74 (d, J = 15.8 Hz, 1H), 6.23 (d, J = 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 136.6, 136.1, 132.7, 128.7, 128.3, 126.8, 124.3, 108.5. GC-MS calcd for $C_{10}H_9Br$: 207.99. Found: 208. See ref 22 for compound 6b.

2-Chloro-3-[(*Z*)-2-chlorovinyl]quinoline (9a). A mixture of two isomers (*E*/*Z* ratio of 52:48). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.65 (s, 1H), 8.13 (s, 1H), 7.96 (m, 2H), 7.82 (d, J = 8.3 Hz, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.70 (q, J = 8.4 Hz, 2H), 7.53 (q, J = 7.5 Hz, 2H), 7.20 (d, J = 13.6 Hz, 1H), 6.97 (d, J = 8.2 Hz, 1H), 6.75 (d, J = 13.6 Hz, 1H), 6.54 (d, J = 8.1 Hz, 1H). GC-MS calcd for $C_{11}H_7Cl_2N$: 223.00. Found: 223.

2-Chloro-3-[(*Z*)-2-bromovinyl]quinoline (9b). A mixture of two isomers (*E*/*Z* ratio of 50:50). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62 (s, 1H), 8.13 (s, 1H), 7.93−8.02 (m, 2H), 7.81−7.87 (m, 1H), 7.76−7.82 (m, 1H), 7.67−7.77 (m, 2H), 7.51−7.61 (m, 2H), 7.50 (d, J = 14.0 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 6.88−6.97 (d, J = 14.0 Hz, 1H), 6.71−6.78 (d, J = 8.1 Hz, 1H). GC-MS calcd for $C_{11}H_7BrClN$: 266.95. Found: 267.

2-[(*Z*)-2-Chlorovinyl]-1-chloro-4-nitrobenzene (10a). A mixture of two isomers (*E*/*Z* ratio of 62:38). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.72 (dd, J = 6.3, 2.7 Hz, 1H), 8.25 (d, J = 2.7 Hz, 1H), 8.08 (dd, J = 8.9, 2.9 Hz, 1H), 8.02−8.06 (m, 1H), 7.53 (m, 2H), 7.12−7.16 (d, J = 13.7 Hz, 1H), 6.86 (d, J = 8.8 Hz, 1H), 6.84 (d, J = 13.7 Hz, 1H), 6.55 (d, J = 8.2 Hz, 1H). GC-MS calcd for $C_8H_5Cl_2NO_2$: 216.97. Found: 217.

2-[(*Z*)-2-Bromovinyl]-1-chloro-4-nitrobenzene (10b). A mixture of two isomers (*E*/*Z* ratio of 55:45). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J = 2.7 Hz, 1H), 8.27 (d, J = 2.7 Hz, 1H), 8.09−8.13 (m, 1H), 8.04−8.09 (m, 1H), 7.50−7.59 (m, 2H), 7.45 (d, J = 14.1 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.02 (d, J = 14.0 Hz, 1H), 6.77 (d, J = 8.2 Hz, 1H). GC-MS calcd for $C_8H_5BrClNO_2$: 260.92. Found: 261.

[(3*Z*)-4-Chlorobut-3-en-1-yl]benzene (11a). A mixture of two isomers (*E*/*Z* ratio of 35:65). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11−7.29 (m, 10H), 6.01 (d, J = 7.1 Hz, 1H), 5.89−5.94 (m, 2H), 5.76 (q, J = 7.0 Hz, 1H), 2.65−2.74 (m, 4H), 2.53 (q, J = 7.5 Hz, 3H), 2.35 (q, J = 7.1 Hz, 1H). GC-MS calcd for $C_{10}H_{11}Cl$: 166.05. Found: 166. See ref 23.

[(3*Z*)-4-Bromobut-3-en-1-yl]benzene (11b). A mixture of two isomers (*E*/*Z* ratio of 23:77). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13−7.31 (m, 10H), 6.17−6.21 (m, 2H), 6.01−6.17 (m, 2H), 2.68−2.74 (m, 4H), 2.48−2.54 (m, 3H), 2.35 (q, J = 7.6 Hz, 1H). GC-MS calcd for $C_{10}H_{11}Br$: 210.00. Found: 210. See ref 21 for compound 2m.

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Supporting Information Available: Additional experimental procedures, copies of ^{1}H NMR and ^{13}C NMR spectra for compounds (**2a**,**b**−**8a**,**b**) and ^{1}H NMR spectra for compounds (**9a**,**b**−**11a**,**b**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Babudri, F.; Cicciomessere, A. R.; Farinola, G. M.; Fiandanese, V.; Marchese, G.; Musio, R.; Naso, F.; Sciacovelli, O. *J. Org. Chem.* **1997**, *62*, 3291.

(23) Baati, R.; Barma, D. K.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **2002**, *43*, 959 and 2183.