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RESEARCH ARTICLE

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Efficient one-pot synthesis of 1-chlorovinyl *p*-tolyl sulfoxides from aldehydes and ketones by the Horner-Wadsworth-Emmons reaction

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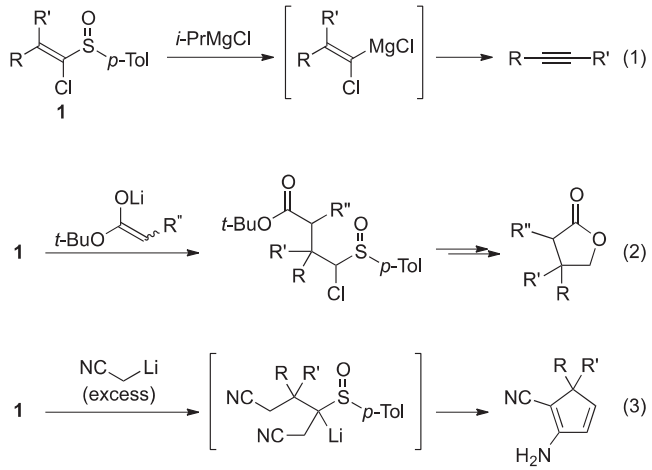
Abstract

A variety of 2-monosubstituted and 2,2-disubstituted 1-chlorovinyl *p*-tolyl sulfoxides was synthesized through a one-pot procedure by the Horner-Wadsworth-Emmons reaction of carbonyl compounds with [chloro(diethoxyphosphoryl)(*p*-tolylsulfinyl)methyl]lithium, which was generated from diethyl chlorophosphate, chloromethyl *p*-tolyl sulfoxide, and lithium diisopropylamide in advance. The in situ-prepared sulfoxides were directly converted into alkynes via the sulfoxide/magnesium exchange reaction with *i*-PrMgCl and the subsequent Fritsch-Buttenberg-Wiechell rearrangement of the resulting magnesium alkylidene carbenoids.

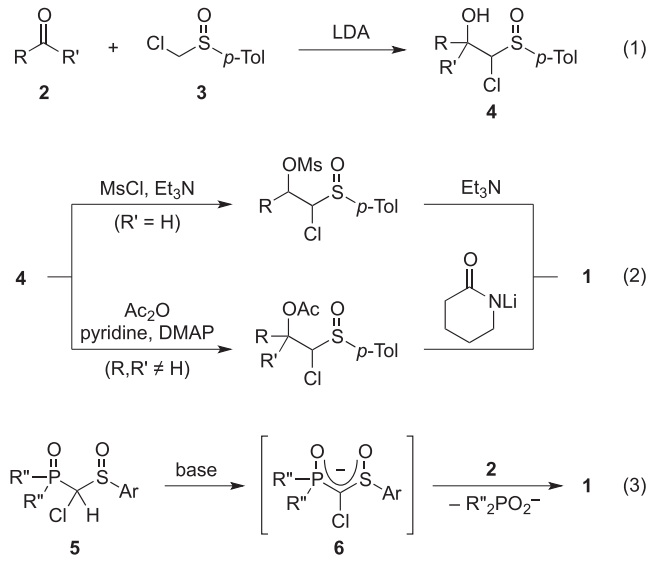
1 | INTRODUCTION

1-Chlorovinyl *p*-tolyl sulfoxides **1** are versatile synthetic intermediates in organic synthesis.[1] The sulfoxide/magnesium exchange reaction of sulfoxides **1** with *i*-PrMgCl generates magnesium alkylidene carbenoids as reactive intermediates, and the resulting magnesium alkylidene carbenoids are converted into various compounds utilizing their diverse reactivity.[2] For instance, the 1,2-rearrangement of magnesium alkylidene carbenoids, referred to as Fritsch-Buttenberg-Wiechell (FBW) rearrangement, leads to the formation of alkynes (Scheme 1, Equation 1).[3,4] Sulfoxides **1** also act as Michael acceptors toward nucleophiles. The conjugate addition of lithium ester enolates to sulfoxides **1** occurs in a highly diastereoselective manner to give adducts, and the Pummerer-type cyclization of the adducts gives γ-lactones (Scheme 1, Equation 2).[5] In several cases, 2 equivalents of a nucleophile consecutively react with sulfoxides **1**.[6] For instance, the reaction of sulfoxides **1** with excess (cyanomethyl) lithium affords 2-aminocyclopenta-1,3-dienecarbonitriles (Scheme 1, Equation 3).

A conventional synthetic method for sulfoxides **1** consists of 3 steps (Scheme 2, eqs 1 and 2): (1) nucleophilic addition of [chloro(*p*-tolylsulfinyl)methyl]lithium to carbonyl compounds **2**, (2) conversion of the hydroxy group of adducts **4** to a leaving group, such as a mesyloxy or acetoxy group, and (3) β-elimination in the presence of an appropriate base.[3,7] While this synthetic route is faithful and highly reproducible, the number of steps is a considerable drawback. Alternatively, 3 independent groups have reported the synthesis of 2-monosubstituted 1-chlorovinyl sulfoxides **1** by the Horner-Wadsworth-Emmons (HWE) reaction of aldehydes with *P*-[(arylsulfinyl)chloromethyl]-substituted phosphonates or phosphine oxides **5** (Scheme 2, Equation 3).[8-10] This synthetic approach is potentially attractive because sulfoxides **1** can be prepared from carbonyl compounds **2** in a single step; however, the key phosphorus reagents **5** have to be elaborated over several steps from commercially available materials. In addition, only the synthesis of 2-monosubstituted sulfoxides **1** from aldehydes has been attempted, and the synthesis of more challenging 2,2-disubstituted sulfoxides from ketones has not been examined. The development of an efficient synthetic method that permits convenient access to a wide range of sulfoxides **1** is expected to facilitate further advancement of the chemistry using sulfoxides **1**.[1-6] Herein, we report a one-pot synthesis of 1-chlorovinyl *p*-tolyl sulfoxides from chloromethyl *p*-tolyl sulfoxide, diethyl chlorophosphate, and carbonyl compounds. The one-pot synthesis of one-carbon elongated terminal alkynes from aldehydes



SCHEME 1 Synthetic applications of 1-chlorovinyl *p*-tolyl sulfoxides **1**



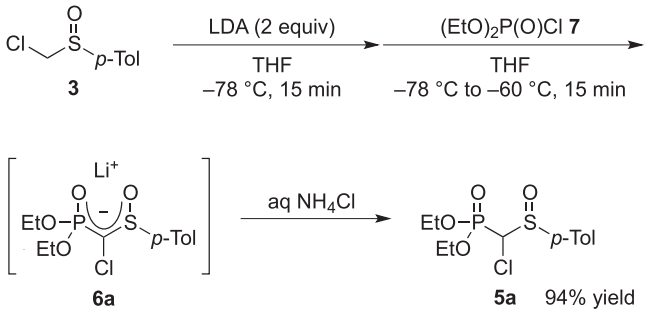
SCHEME 2 Synthetic routes to 1-chlorovinyl *p*-tolyl sulfoxides **1**

via the FBW rearrangement of magnesium alkylidene carbenoids generated from sulfoxides **1** and *i*-PrMgCl is also described.

2 | RESULTS AND DISCUSSION

2.1 | One-pot synthesis of 2-monosubstituted 1-chlorovinyl *p*-tolyl sulfoxides from aldehydes

Initially, we tested the generation of [chloro(diethoxyphosphoryl)(*p*-tolylsulfinyl)methyl]lithium (**6a**) from chloromethyl *p*-tolyl sulfoxide (**3**) and diethyl chlorophosphate (**7**) as readily available materials (Scheme 3). Sulfoxide **3** was treated with 2 equivalents of lithium diisopropylamide (LDA), and the resulting [chloro(*p*-tolylsulfinyl)methyl]lithium was reacted with chlorophosphate **7** at low



SCHEME 3 Generation of [chloro(diethoxyphosphoryl)(*p*-tolylsulfinyl)methyl]lithium (**6a**) from chloromethyl *p*-tolyl sulfoxide (**3**) and diethyl chlorophosphate (**7**)

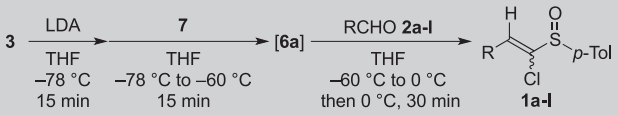
temperature for 15 minutes. As a result, diethyl [chloro(*p*-tolylsulfinyl)methyl]phosphonate (**5a**) was obtained in 94% yield.

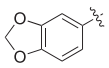
As phosphonate **5a** could be prepared from sulfoxide **3** and chlorophosphate **7** with high efficiency, we then examined the one-pot synthesis of 2-monosubstituted 1-chlorovinyl *p*-tolyl sulfoxides **1a-l** from aldehydes **2a-l** (Table 1). To a solution of deprotonated phosphonate **6a** (one equiv) in THF, which was prepared from sulfoxide **3**, chlorophosphate **7**, and LDA in advances, was added benzaldehyde (**2a**) at −60°C, and the reaction mixture was stirred at 0°C for 30 minutes (entry 1). The desired 2-phenyl-substituted sulfoxide **1a** was formed in 72% yield as a 1:1 mixture of geometric isomers. The reaction of aldehyde **2a** with 1.25 equivalents of deprotonated phosphonate **6a** gave the product **1a** in an improved yield (entry 2). A variety of 2-monoaryl-substituted sulfoxides **1b-g** was synthesized from aryl and heteroaryl aldehydes **2b-g** through the one-pot procedure in 86%-96% yields (entries 3-8). When paraformaldehyde was subjected to the reaction with deprotonated phosphonate **6a**, 2-unsubstituted sulfoxide **1h** was obtained in 76% yield (entry 9). Enolizable aliphatic aldehydes, such as acetaldehyde (**2i**), hydrocinnamaldehyde (**2j**), and cyclohexanecarboxaldehyde (**2k**), could also be converted into the corresponding 2-monoalkyl-substituted sulfoxides **1i-k** in 72%-96% yields, whereas pivalaldehyde (**2l**) was less reactive at 0°C (entries 10-13). The reaction of aldehyde **2l** with 3 equivalents of deprotonated phosphonate **6a** at room temperature for 3 hours gave sulfoxide **1l** in an improved yield (entry 14).

2.2 | One-pot synthesis of 2,2-disubstituted 1-chlorovinyl *p*-tolyl sulfoxides from ketones

Encouraged by the successful one-pot synthesis of 2-monosubstituted sulfoxides **1a-l**, the synthesis of 2,2-disubstituted sulfoxides **1m-p** from ketones **2m-p** was carried out (Table 2). When acetone (**2m**) was subjected to the HWE reaction under the reaction conditions described above, the desired 2,2-dimethyl-substituted sulfoxide **1m**

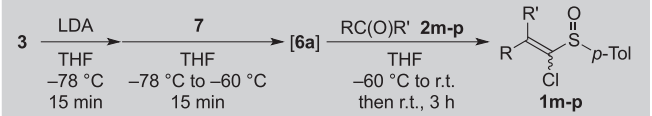
TABLE 1 One-pot synthesis of 2-monosubstituted 1-chlorovinyl *p*-tolyl sulfoxides **1a-l** from aldehydes **2a-l**[a]



Entry	2	R	1	Yield (%)	*E*/*Z* ratio
1[b]	**2a**	Ph	**1a**	72	1:1
2	**2a**	Ph	**1a**	96	1:1
3	**2b**	4-$MeOC_6H_4$	**1b**	96	1:1.2
4	**2c**	4-$CF_3C_6H_4$	**1c**	93	1:2.3
5	**2d**	4-ClC_6H_4	**1d**	90	1:1.7
6	**2e**	4-NCC_6H_4	**1e**	90	1.7:1
7	**2f**		**1f**	92	1:1
8	**2g**	2-thienyl	**1g**	86	1.1:1
9[c]	**2h**	H	**1h**	76[d]	–
10	**2i**	Me	**1i**	96	1:2
11	**2j**	$PhCH_2CH_2$	**1j**	92	1:1.7
12	**2k**	*cyclo*-C_6H_{11}	**1k**	72	1.2:1
13	**2l**	*t*-Bu	**1l**	4	3.6:1
14[e]	**2l**	*t*-Bu	**1l**	73	3.3:1

[a]The molar ratio of LDA/**3**/**7**/**2** = 2.5/1.25/1.25/1 (except entries 1, 9, and 14).
[b]The molar ratio of LDA/**3**/**7**/**2** = 2/1/1/1.
[c]Paraformaldehyde (5 equiv) was used.
[d]Yield based on sulfoxide **3**.
[e]The reaction was carried out with 3 equivalents of deprotonated phosphonate **6a** at room temperature for 3 hours.

TABLE 2 One-pot synthesis of 2,2-disubstituted 1-chlorovinyl *p*-tolyl sulfoxides **1m-p** from ketones **2m-p**[a]



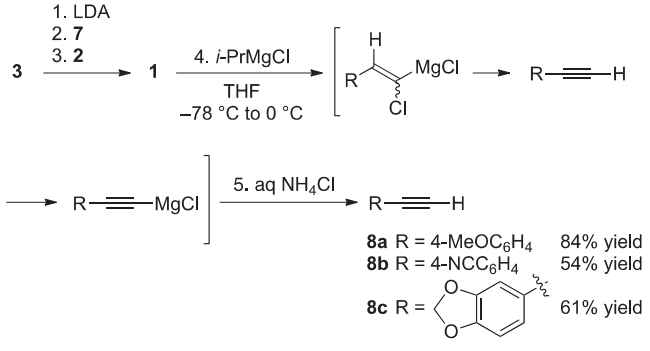
Entry	2	R	R′	1	Yield (%)
1[b,c]	**2m**	Me	Me	**1m**	49
2	**2m**	Me	Me	**1m**	82
3	**2n**	Ph	Me	**1n**	67[d]
4	**2o**	$–(CH_2)_4–$		**1o**	89
5	**2p**	$–(CH_2)_5–$		**1p**	96
6[e]	**2p**	$–(CH_2)_5–$		**1p**	93

[a]The molar ratio of LDA/**3**/**7**/**2** = 6/3/3/1 (except entries 1 and 6).
[b]The molar ratio of LDA/**3**/**7**/**2** = 2.5/1.25/1.25/1.
[c]The reaction was carried out at 0°C for 30 minutes.
[d]*E*/*Z* ratio = 3.3:1.
[e]Recovered HWE reagent **5a** (3 equiv) and LDA (3.3 equiv) were used.

was formed in only 49% yield (entry 1). To improve the reaction efficiency, 3 equivalents of deprotonated phosphonate **6a** were used, and the reaction was performed at room temperature for 3 hours. Consequently, sulfoxide **1m** was obtained in 82% yield (entry 2). The reaction of aryl and cyclic aliphatic ketones **2n-p** with deprotonated phosphonate **6a** gave the corresponding 2,2-disubstituted sulfoxides **1n-p** in 67%-96% yields (entries 3-5). Excess HWE reagent **5a** in the reaction of entry 5 was recovered by column chromatography on silica gel and used for the reaction with cyclohexanone (**2p**) in the presence of LDA (entry 6). Sulfoxide **1p** was obtained in 93% yield. Benzophenone was unreactive toward deprotonated phosphonate **6a**.

2.3 | Conversion of aldehydes into alkynes with one-carbon elongation

The conversion of aldehydes into alkynes with one-carbon elongation is a useful method for the synthesis of terminal alkynes.[11] Much effort has been devoted to developing a synthetic method of alkynes from aldehydes, and Corey-Fuchs reaction, Seyferth-Gilbert homologation, and Ohira-Bestmann modification have been developed. If magnesium alkylidene carbenoids can be directly generated from in situ-prepared 1-chlorovinyl *p*-tolyl sulfoxides **1** and a Grignard reagent via the sulfoxide/magnesium exchange reaction, the following FBW rearrangement of the resulting magnesium alkylidene carbenoids is expected to give alkynes (Scheme 1, Equation 1).[3,4] We examined the one-pot conversion of aldehydes into alkynes through the sequential HWE reaction-sulfoxide/magnesium exchange reaction-FBW rearrangement (Scheme 4). A solution of *i*-PrMgCl in THF was added to a solution of 1-chlorovinyl *p*-tolyl sulfoxide **1b** in THF, which was prepared from *p*-anisaldehyde (**2b**) and deprotonated phosphonate **6a** according to the procedure described above, at −78°C, and the reaction mixture was allowed to warm to 0°C. Gratifyingly, the reaction gave the desired alkyne **8a** in



SCHEME 4 One-pot synthesis of terminal alkynes **8** from aldehydes **2**

84% yield. Terminal alkynes **8b** and **8c** were also obtained from aldehydes **2e** and **2f** in 54% and 61% yields, respectively.

3 | CONCLUSION

We developed an efficient one-pot synthetic method of 1-chlorovinyl *p*-tolyl sulfoxides from readily available materials by the HWE reaction. The synthetic method was applied to the one-pot conversion of aldehydes into alkynes with one-carbon elongation. This efficient synthetic method will help advance the chemistry using 1-chlorovinyl *p*-tolyl sulfoxides.

4 | EXPERIMENTAL

4.1 | General methods

All reactions involving air- or water-sensitive compounds were conducted under an argon atmosphere. Argon gas was dried by passage through P_2O_5. Anhydrous THF was purchased and used as supplied. Acetaldehyde and acetone were distilled before use. Silica gel (60N) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography, and the products that absorbed UV light were detected by UV irradiation. Gel permeation chromatography (GPC) was performed on JAIGEL-1HH and JAIGEL-2HH using a recycling preparative HPLC LC-9210 II NEXT system (Japan Analytical Industry, Tokyo, Japan). The melting points were measured using a Yanaco MP-S3 apparatus (Yanaco, Kyoto, Japan) and are uncorrected. IR spectra were recorded on a Perkin-Elmer Frontier FT IR in ATR mode. NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 300, JEOL JNM-LA 500 (JEOL, Tokyo, Japan), Bruker AVANCE DPX 300, and Bruker AVANCE DPX 400 spectrometers (Bruker Biospin, Billerica, MA, USA). Mass spectra (MS) were obtained at 70 eV by direct injection with a HITACHI M-80B mass spectrometer. Fast atom bombardment (FAB) mass spectra were obtained with a mixture of *m*-nitrobenzyl alcohol and glycerol as the matrix. Sulfoxides **1a**, **1b**, and **1e-p** and alkynes **8** are known compounds.[3b,6a,7,8c,12,13]

4.2 | Synthesis of diethyl [chloro(*p*-tolylsulfinyl)methyl]phosphonate (5a)

A 1.60 mol/L solution of BuLi in hexane (12.5 mL, 20.0 mmol) was added to a solution of *i*-Pr_2NH (2.02 g, 20.0 mmol) in THF (15.0 mL) at 0°C, and the mixture was stirred at 0°C for 15 minutes. A solution of chloromethyl *p*-tolyl sulfoxide (**3**, 1.89 g, 10.0 mmol) in THF (5.0 mL) was added to the solution of LDA in THF at −78°C, and the mixture was stirred at −78°C for 15 minutes. Diethyl chlorophosphate (**7**, 1.73 g, 10.0 mmol) was added to the solution of [chloro(*p*-tolylsulfinyl)methyl]lithium in THF at −78°C, and the mixture was allowed to warm to −60°C over a period of 15 minutes. The reaction was quenched with sat. aq NH_4Cl (1.0 mL), and the mixture was extracted with $CHCl_3$ (3 × 20 mL). The combined organic layer was washed with water (60 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane–EtOAc, 1:1) to give **5a** (3.04 g, 9.36 mmol, 94%, $R_f = 0.18$ [hexane–EtOAc, 1:1]) as a 7:3 mixture of diastereomers. One of the diastereomers isomerized to the other diastereomer spontaneously at room temperature within several hours, and the diastereomeric mixture became a single diastereomer; colorless crystals (hexane/EtOAc); mp 91.2-93.6°C; IR (ATR) 2985, 2904, 1592, 1496, 1441, 1399, 1240, 1158, 1090, 1059, 1013, 847, 815, 770, 717 cm^{-1}; ^1H NMR (399 MHz, $CDCl_3$) δ 1.35-1.43 (m, 3H), 2.43 (s, 3H), 4.24-4.37 (m, 4H), 4.50 (d, $J = 11.4$ Hz, 1H), 7.36 (d, $J = 8.1$ Hz, 2H), 7.57 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.28 (d, $J = 6.0$ Hz), 16.29 (d, $J = 6.3$ Hz), 21.5, 64.7 (d, $J = 7.0$ Hz), 64.8 (d, $J = 6.5$ Hz), 70.8 (d, $J = 150.5$ Hz), 124.9, 129.9, 137.6 (d, $J = 7.7$ Hz), 142.7; MS (FAB^+): *m/z* (%) 325 ($[M+H]^+$, 100), 186 (21), 123 (19); HRMS (FAB^+) calcd for $C_{12}H_{19}ClO_4PS$: 325.0430, found: 325.0431.

4.3 | Typical procedure for the synthesis of 2-monosubstituted 1-chlorovinyl *p*-tolyl sulfoxides 1 from aldehydes

A 1.60 mol/L solution of BuLi in hexane (1.68 mL, 2.69 mmol) was added to a solution of *i*-Pr_2NH (274 mg, 2.71 mmol) in THF (3.0 mL) at 0°C, and the mixture was stirred at 0°C for 15 minutes. A solution of chloromethyl *p*-tolyl sulfoxide (**3**, 253 mg, 1.34 mmol) in THF (2.0 mL) was added to the solution of LDA in THF at −78°C, and the mixture was stirred at −78°C for 15 minutes. Diethyl chlorophosphate (**7**, 234 mg, 1.36 mmol) was added to the solution of [chloro(*p*-tolylsulfinyl)methyl]lithium in THF at −78°C, and the mixture was allowed to warm to −60°C over a period of 15 minutes. 4-Methoxybenzaldehyde (**2b**, 146 mg, 1.07 mmol) was added to the solution of **6a** in THF at −60°C. The reaction mixture was immediately warmed to 0°C and stirred at 0°C for 30 minutes. The reaction was quenched with sat. aq NH_4Cl (3.0 mL), and the mixture was extracted with $CHCl_3$ (3 × 3.0 mL). The combined organic layer was washed with water (3.0 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane-EtOAc, 3:1) to give **1b** (317 mg, 1.03 mmol, 96%, $R_f = 0.28$ [hexane–EtOAc, 3:1]) as a colorless solid.

4.3.1 | (*E*)-1-({1-Chloro-2-[4-(trifluoromethyl)phenyl]vinyl}sulfinyl)-4-methylbenzene [(*E*)-2c]

Colorless crystals (hexane/EtOAc); mp 111.8-112.4°C; IR (ATR) 3009, 1616, 1493, 1415, 1323, 1164, 1108, 1086, 1068, 1058, 1015, 920, 908, 834, 820, 802, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.34 (s, 1H), 7.47 (d, $J = 8.1$ Hz, 2H), 7.64 (d, $J = 8.5$ Hz, 2H), 7.72 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.8, 124.0 (q, $J = 272.4$ Hz), 125.0, 126.1 (q, $J = 3.6$ Hz), 130.0, 130.3, 131.6 (q, $J = 33.1$ Hz), 136.3, 136.8, 137.9, 142.7, 143.3; MS (FAB^+): *m/z* (%) 345 ($[M+H]^+$, 100); HRMS (FAB^+) calcd for $C_{16}H_{13}ClF_3OS$: 345.0328, found: 345.0329.

4.3.2 | (*Z*)-1-({1-Chloro-2-[4-(trifluoromethyl)phenyl]vinyl}sulfinyl)-4-methylbenzene [(*Z*)-2c]

Colorless crystals (hexane/EtOAc); mp 90.8-93.1°C; IR (ATR) 3001, 1617, 1412, 1323, 1194, 1171, 1114, 1086, 1067, 1017, 899, 885, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.656 (d, $J = 8.0$ Hz, 2H), 7.660 (d, $J = 8.5$ Hz, 2H), 7.68 (s, 1H), 7.84 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.6, 123.8 (q, $J = 272.1$ Hz), 125.6 (q, $J = 3.8$ Hz), 126.0, 126.5, 129.9, 130.2, 131.2 (q, $J = 32.7$ Hz), 135.6 (q, $J = 1.5$ Hz), 138.2, 138.3, 143.2; MS (FAB^+): *m/z* (%) 345 ($[M+H]^+$, 100); HRMS (FAB^+) calcd for $C_{16}H_{13}ClF_3OS$: 345.0328, found: 345.0328.

4.3.3 | (*E*)-1-Chloro-4-[2-chloro-2-(*p*-tolylsulfinyl)vinyl]benzene [(*E*)-2d]

Colorless crystals (hexane/EtOAc); mp 148.4-150.8°C; IR (ATR) 3031, 1591, 1488, 1403, 1084, 1050, 1013, 918, 887, 825, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.27 (s, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.41-7.49 (m, 6H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 21.1, 124.3, 128.8, 129.6, 130.4, 130.6, 135.3, 136.7, 137.3, 140.7, 141.8; MS (FAB^+): *m/z* (%) 311 ($[M+H]^+$, 100), 154 (17), 136 (16), 93 (24); HRMS (FAB^+) calcd for $C_{15}H_{13}Cl_2OS$: 311.0064, found: 311.0062.

4.3.4 | (*Z*)-1-Chloro-4-[2-chloro-2-(*p*-tolylsulfinyl)vinyl]benzene [(*Z*)-2d]

Colorless crystals (hexane/EtOAc); mp 131.0-134.1°C; IR (ATR) 3031, 1592, 1490, 1403, 1084, 1051, 1013, 919, 886, 817, 671, 622 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.38 (d, $J = 8.6$ Hz, 2H), 7.58 (s, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.70 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.8, 126.2, 127.5, 129.2, 130.3, 130.9, 131.2, 136.0, 136.3, 138.7, 143.2; MS (FAB^+): *m/z* (%) 311 ($[M+H]^+$, 100), 185 (18), 154 (20), 137 (16), 93 (24); HRMS (FAB^+) calcd for $C_{15}H_{13}Cl_2OS$: 311.0064, found: 311.0063.

4.4 | Typical procedure for the synthesis of 2,2-disubstituted 1-chlorovinyl *p*-tolyl sulfoxides 1 from ketones

A 1.60 mol/L solution of BuLi in hexane (3.63 mL, 5.81 mmol) was added to a solution of *i*-Pr_2NH (587 mg, 5.80 mmol) in THF (3.0 mL) at 0°C, and the mixture was stirred at 0°C for 15 minutes. A solution of chloromethyl *p*-tolyl sulfoxide (**3**, 547 mg, 2.90 mmol) in THF (2.0 mL) was added to the solution of LDA in THF at −78°C, and the mixture was stirred at −78°C for 15 minutes. Diethyl chlorophosphate (**7**, 499 mg, 2.89 mmol) was added to the solution of [chloro(*p*-tolylsulfinyl)methyl] lithium in THF at −78°C, and the mixture was allowed to warm to −60°C over a period of 15 minutes. Cyclohexanone (**2p**, 94.8 mg, 0.966 mmol) was added to the solution of **6a** in THF at −60°C. The reaction mixture was immediately warmed to room temperature and stirred at room temperature for 3 hours. The reaction was quenched with sat. aq NH_4Cl (1 mL), and the mixture was extracted with $CHCl_3$ (3 × 5 mL). The combined organic layer was washed with water (15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane–EtOAc, 3:1) to give **1p** (250 mg, 0.930 mmol, 96%, $R_f = 0.30$ [hexane–EtOAc, 3:1]) as a colorless solid.

4.5 | Typical procedure for the synthesis of alkynes from aldehydes

A 1.60 mol/L solution of BuLi in hexane (1.68 mL, 2.69 mmol) was added to a solution of *i*-Pr_2NH (274 mg, 2.71 mmol) in THF (3.0 mL) at 0°C, and the mixture was stirred at 0°C for 15 minutes. A solution of chloromethyl *p*-tolyl sulfoxide (**3**, 253 mg, 1.34 mmol) in THF (2.0 mL) was added to the solution of LDA in THF at −78°C, and the mixture was stirred at −78°C for 15 minutes. Diethyl chlorophosphate (**7**, 234 mg, 1.36 mmol) was added to the solution of [chloro(*p*-tolylsulfinyl)methyl]lithium in THF at −78°C, and the mixture was allowed to warm to −60°C over a period of 15 minutes. 4-Methoxybenzaldehyde (**2b**, 146 mg, 1.07 mmol) was added to the solution of **6a** in THF at −60°C. The reaction mixture was immediately warmed to 0°C and stirred at 0°C for 30 minutes. A 2.0 mol/L solution of *i*-PrMgCl in THF (1.88 mL, 3.76 mmol) was added to the reaction mixture at −78°C, and the reaction mixture was allowed to warm to 0°C over a period of 2 hours. The reaction was quenched with sat. aq NH_4Cl (1 mL), and the mixture was extracted with $CHCl_3$ (3 × 5 mL). The combined organic layer was washed with water (15 mL),

dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane–EtOAc, 50:1) and gel permeation chromatography ($CHCl_3$) to give **8a** (119 mg, 0.900 mmol, 84%, $R_f = 0.28$ [hexane–EtOAc, 50:1]) as colorless oil.

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