Fritsch–Wiechell Rearrangement of 1-Chlorovinyl Sulfoxides: A New Method for Synthesizing Acetylenes from Aldehydes with One-Carbon Homologation

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(Received February 17, 1993)

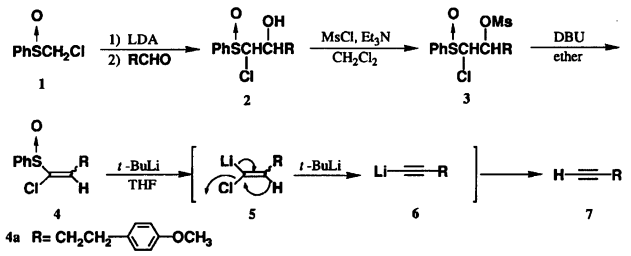
Synopsis. 1-Chlorovinyl sulfoxides, easily prepared from aldehydes and chloromethyl phenyl sulfoxides, were treated with *t*-butyllithium to afford one-carbon homologated acetylenes via alkylidene carbenoids in high yields.

Acetylenes are important compounds in synthetic organic chemistry.[1] They are useful in various synthetic reactions, such as the Diels–Alder reaction, and as building blocks in natural product synthesis. In the method for obtaining acetylenes the Fritsch–Wiechell rearrangement of vinyl halides upon treatment with strong bases has long been known.[2] This classical reaction has recently been reinvigorated and several new Fritsch–Wiechell-type reactions have been reported.[3]

In previous papers, we and others reported the desulfinylation of sulfoxides with alkylmetals[4] via the ligand exchange of sulfoxide.[5] Specifically, we found that the ligand exchange reaction of α-halo α-sulfinyl ketones and their derivatives gave enolates,[6] haloalkenes,[7] and carbenoid.[8] In continuation of our studies[9] on the ligand exchange reaction of sulfoxides in organic synthesis we report here a new method for a synthesis of acetylenes **7** from aldehydes via the Fritsch–Wiechell rearrangement of 1-chlorovinyl sulfoxides **4** (Scheme 1).[10]

Results and Discussion

1-Chlorovinyl sulfoxides **4** were easily prepared from aldehydes and chloromethyl phenyl sufoxide **1** as follows. Synthesis of **4a** is described as an example. Addition of the carbanion of **1** in THF at −60 °C to 3-(4-methoxyphenyl)propanal gave the adduct **2a** in quantitative yield as a mixture of two diastereomers. The adduct **2a** was mesylated with methanesulfonyl chloride and triethylamine in CH_2Cl_2 at 0 °C to afford the mesylate **3a** in 89% yield. Dehydromesylation of **3a** with DBU in ether at 0 °C gave the desired 1-chlorovinyl sulfoxide **4a** in high yield. Other results for the synthesis of **4** are listed in Table 2. In the case of aromatic aldehydes and α,β-unsaturated aldehydes, the mesylation of **2c—f** directly gave **4c—f** in good overall yields.



Scheme 1.

Next, the desulfinylation of **4a** with several alkylmetals was investigated. Treatment of **4a** with EtMgBr in THF at −78 °C gave an inseparable mixture of acetylene **7a** and vinyl chloride **8** (see Table 1). The reaction with *n*-BuLi gave a similar result (Run 2). This reaction was thought to take place via ligand exchange of sulfoxide **4** with alkylmetals and the intermediate should be **5**. Then, **5** gave lithium acetylide **6** via alkylidene carbenoid (Fritsch–Wiechell rearrangement).

In the case of the reaction with EtMgBr and *n*-BuLi some of the intermediate **5** picks up the acidic hydrogen from the produced ethyl phenyl sulfoxide or butyl phenyl sulfoxide (and/or acidic hydrogen in the produced acetylene) to afford the by-product **8**. To overcome this problem, we finally found the best conditions; a solution of **4a** was added to three equivalents of *t*-BuLi at −78 °C (Run 5).

Representative examples of the synthesis of acetylenes **7** from aldehydes are summarized in Table 2. Both aliphatic and aromatic aldehydes gave acetylenes (**7** and **10**) in good to excellent overall yields. Interestingly, the desulfinylation of **4f**, which was prepared from cinnamaldehyde, gave the diene **9** bearing a *t*-butyl group as a major product (Run 6). This result indicated that the reaction proceeded via the alkylidene carbenoid

Table 1. Conditions for the Desulfinylation Reaction of Vinyl Sulfoxide **4a**

Run	Alkylmetal	Equiv	Method[a)]	**7a**, **8** Yield[b)]/%
1	EtMgBr	2.2	A	**7a** (74), **8** (15)
2	*n*-BuLi	2.2	A	**7a** (71), **8** (7)
3	*t*-BuLi	2.2	A	**7a** (74), **8** (5)
4	*t*-BuLi	2.2	B	**7a** (76), **8** (0)
5	*t*-BuLi	3.0	B	**7a** (93), **8** (0)
6	*t*-BuMgCl	3.0	B	No Reaction

a) All reactions were carried out in THF at −78 °C for 10 min. Method A: A solution of alkylmetal was added dropwise to a solution of vinyl sulfoxide **4a**; Method B: A solution of vinyl sulfoxide **4a** was added dropwise to a solution of alkylmetal. b) Inseparable mixture of **7a** and **8**. The yields of **7a** and **8** were calculated by ^{1}H NMR spectra.

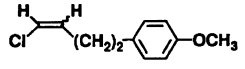


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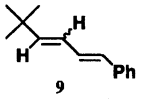
Table 2. A Synthesis of Acetylenes from Aldehydes and Chloromethyl Phenyl Sulfoxide **1**

Run	RCHO	**2**	**3**	**4**	Acetylene
		Yield[a]/%	Yield[a]/%	Yield[b]/%	Yield[c]/%
1	CH_3O-C$_6$H$_4$-$(CH_2)_2CHO$	**2a**(99)	**3a**(89)	**4a**(91)	**7a**(93)
2	CH_3O-C$_6$H$_4$-CH_2CHCHO (CH_3)	**2b**(88)	**3b**(91)	**4b**(77)	**7b**(91)
3	C$_6$H$_5$-CHO	**2c**(92)	—	**4c**(86)[d]	**10c**(67)[e]
4	CH_3O-C$_6$H$_4$-CHO	**2d**(97)	—	**4d**(89)[d]	**10d**(71)[e]
5	C$_{10}$H$_7$-CHO	**2e**(86)	—	**4e**(73)[d]	**7e**(84)
6	Ph-CH=CH-CHO	**2f**(85)	—	**4f**(71)[d]	**7f**(18) **9**(76)[b]

a) A mixture of two diastereomers. b) A mixture of *E* and *Z* isomers. c) Isolated yield. d) Treatment of chloro alcohol **2** with MsCl and Et_3N in CH_2Cl_2 directly afforded vinyl sulfoxide **4**. e) Isolated as an adduct with propanal; see text and Table 3.

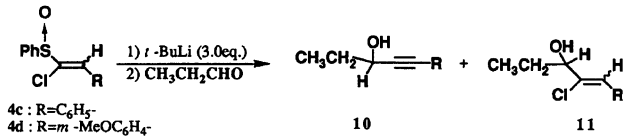


9

intermediate.[11]

In Runs 3 and 4, the product in the desulfinylation was trapped with propanal to avoid the volatile acetylenes. The product was a mixture of the desired propargylic alcohol **10** and vinyl chloride **11** (Scheme 2; Table 3). Little difference was observed when this reaction was carried out at −100 °C. However, warming the reaction from −78 to −30 °C for 30 min, then quenching with propanal, we obtained the desired **10** without **11** (Runs 3 and 6). From these results, generation of the carbenoid from **4c** and **4d** was found to be much slower than that of other 1-chlorovinyl sulfoxides.

In conclusion, we developed a versatile method for a synthesis of acetylenes from aldehydes with one-carbon homologation. Because the procedure is simple and the overall yields are good, the present method will prove to be valuable in the synthesis of acetylenic compounds.



4c : R=C$_6$H$_5$-
4d : R=*m* -MeOC$_6$H$_4$-

10 **11**

Scheme 2.

Experimental

IR spectra were measured directly on a NaCl plate. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with a JEOL FX-100 spectrometer using Me_4Si as an internal standard. Electron-impact mass spectra (MS) were obtained on a Hitachi M-80 double-focusing spectrometer at 70 eV by direct insertion. In experiments requiring a dry solvent, THF was distilled from diphenylketyl; diisopropylamine and CH_2Cl_2 were dried over CaH_2 and distilled.

1-Chloro-4-(4-methoxyphenyl)-1-phenylsulfinyl-1-butene (4a). A solution of chloromethyl phenyl sulfoxide (611 mg; 3.5 mmol) in dry THF (2 ml) was added dropwise to a stirring solution of LDA (4.2 mmol) in 4 ml of THF at −60 °C under Ar atmosphere. The reaction mixture was stirred at −60 °C for 10 min, then a solution of 2-(4-methoxyphenyl)propanal (690 mg; 4.2 mmol) in 1 ml of THF was added to the mixture. The reaction mixture was stirred for 10 min, then the reaction was quenched with sat. NH_4Cl. The whole was extracted with ether-benzene. The usual workup followed by silica-gel column chromatography gave the alcohol **2a** (1.17 g; 99%) as a colorless oil (a diastereomeric mixture). IR (neat) 3400 (OH), 1090, 1040 (SO) cm^{-1}. Found: *m/z* 338.0734. Calcd for $C_{17}H_{19}ClO_3S$: M, 338.0741.

To an ice-cooling solution of **2a** (1.15 g; 3.4 mmol) in dry CH_2Cl_2 (10 ml) was added triethylamine (0.72 ml; 5.18 mmol) and then methanesulfonyl chloride (0.3 ml; 3.8 mmol) with stirring. The reaction mixture was stirred at 0 °C for 30 min, then the reaction was quenched with water. The whole was extracted with CH_2Cl_2 then the organic layer was washed successively with 10% HCl, sat. $NaHCO_3$, and sat. brine. The product was purified by silica-gel column chromatography (hexane : AcOEt=2 : 1) to afford **3a** (1.28 g; 89%) as a colorless oil (a diastereomeric mixture). IR (neat) 1360, 1180 (SO_2) cm^{-1}; ^{1}H NMR δ=3.76 (3H, s, OCH_3), 4.6—4.7 (1H, m), 4.9—5.2 (1H, m). Found: *m/z* 416.0528. Calcd for $C_{18}H_{21}ClO_5S_2$: M, 416.0518.

DBU (0.5 ml; 3.36 mmol) was added dropwise to a solution of **3a** (1.17 g; 2.8 mmol) in 15 ml of dry THF at 0 °C. The reaction mixture was stirred at 0 °C for 20 min, then water was added. The whole was extracted with ether–ben-

Table 3. Trapping of the Carbanions from **4c** and **4d** with Propanal

Run	Vinyl sulfoxide **4**	Temp/°C	Time/min	**10**, **11** Yield/%
1	**4c**	−78	10	**10c**(47), **11c**(34)
2	**4c**	−100	10	**10c**(47), **11c**(29)
3	**4c**	−78 to −30	30	**10c**(67)
4	**4d**	−78	10	**10d**(61), **11d**(36)
5	**4d**	−100	10	**10d**(35), **11d**(46)
6	**4d**	−78 to −30	30	**10d**(71)

zene and the organic layer was washed successively with 10% HCl, sat. $NaHCO_3$, and sat. brine. The product was purified by silica-gel column chromatography to give **4a** (817 mg; 91%) as a colorless oil (a mixture of geometrical isomers; *E*/*Z* about 1/1). IR (neat) 1615 (C=C), 1090, 1055 (SO) cm^{-1}; ^1H NMR δ=2.4—3.1 (4H, m), 3.76, 3.78 (each 1.5H, s), 6.30 (0.5H, t, J=7 Hz), 6.6—7.6 (9.5H, m); MS *m*/*z* (%) 320 (M^+, 2), 303 (4), 195 (2), 158 (4), 121 (100). Found: *m*/*z* 320.0640. Calcd for $C_{17}H_{17}ClO_2S$: M, 320.0636.

1-Chloro-4-(4-methoxyphenyl)-3-methyl-1-phenylsulfinyl-1-butene (4b). Colorless oil (a mixture of four distereomers); IR (neat) 1620 (C=C), 1100, 1060 (SO) cm^{-1}; ^1H NMR δ=1.0—1.3 (3H), 2.4—3.2 (3H, m), 3.75, 3.77, 3.79 (total 3H, each s), 6.15 (0.5H, dd, J=11, 3 Hz), 6.4—7.6 (9.5H, m); MS *m*/*z* (%) 334 (M^+, 2), 317 (3), 209 (5), 121 (100). Found: *m*/*z* 334.0796. Calcd for $C_{18}H_{19}ClO_2S$: M, 334.0793.

1-Chloro-2-phenyl-1-(phenylsulfinyl)ethene (4c). To a solution of **2c** (744 mg; 2.65 mmol) in dry CH_2Cl_2 was added triethylamine (2.2 ml) followed by methanesulfonyl chloride (0.25 ml; 3.2 mmol) with stirring at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, then at room temperature for 4 h. The reaction was quenched with water, and the whole was extracted with CH_2Cl_2. The organic layer was washed successively with 10% HCl, sat. $NaHCO_3$, then sat. brine. The usual workup followed by silica-gel column chromatography gave **4c** (597 mg; 86%) as a colorless oil. IR (neat) 1090, 1060 (SO) cm^{-1}; ^1H NMR δ=7.2—7.9 (m); MS *m*/*z* (%) 262 (M^+, 12), 214 (45), 199 (24), 126 (100). Found: *m*/*z* 262.0205. Calcd for $C_{14}H_{11}ClOS$: M, 262.0217.

1-Chloro-2-(3-methoxyphenyl)-1-(phenylsulfinyl)-ethene (4d). Colorless oil; IR (neat) 1095, 1060 (SO) cm^{-1}; ^1H NMR δ=3.79, 3.83 (total 3H, each s), 6.7—7.8 (10H, m); MS *m*/*z* (%) 292 (M^+, 20), 274 (3), 244 (14), 167 (70), 126 (100). Found: *m*/*z* 292.0332. Calcd for $C_{15}H_{13}ClO_2S$: M, 292.0324.

1-Chloro-2-(1-naphthyl)-1-(phenylsulfinyl)ethene (4e). Colorless oil; IR (neat) 1090, 1060 (SO) cm^{-1}; ^1H NMR δ=7.1—8.1 (12.5H, m), 8.29 (0.5H, s); MS *m*/*z* (%) 312 (M^+, 10), 186 (100). Found: *m*/*z* 312.0374. Calcd for $C_{18}H_{13}ClOS$: M, 312.0374.

1-Chloro-4-phenyl-1-phenylsulfinyl-1,3-butadiene (4f). Light yellow oil; IR (neat) 1620 (C=C), 1090, 1060 (SO) cm^{-1}; ^1H NMR δ=6.9—7.8 (m); MS *m*/*z* (%) 288 (M^+, 17), 240 (40), 205 (57), 115 (100). Found: *m*/*z* 288.0380. Calcd for $C_{16}H_{13}ClOS$: M, 288.0375.

4-(4-Methoxyphenyl)-1-butyne (7a). A solution of **4a** (160 mg; 0.5 mmol) in dry THF (2 ml) was added a solution of *t*-BuLi (1.5 mmol) in 3 ml of THF at −78 °C under Ar atmosphere with stirring. The reaction mixture was stirred at −78 °C for 10 min, and then quenched with sat. NH_4Cl. The whole was extracted with ether-benzene and the product was purified by silica-gel column chromatography to give **7a** (75 mg; 93%) as a colorless oil. IR (neat) 3320 (acetylenic H), 2130 (C≡C) cm^{-1}; ^1H NMR δ=1.95 (1H, t, J=2 Hz), 2.3—2.5 (2H, m), 2.7—2.9 (2H, m), 3.75 (3H, s), 6.7—7.2 (4H, m); MS *m*/*z* (%) 160 (M^+, 13), 121 (100). Found: *m*/*z* 160.0891. Calcd for $C_{11}H_{12}O$: M, 160.0888.

4-(4-Methoxyphenyl)-3-methyl-1-butyne (7b). Colorless oil; IR (neat) 3320 (acetylenic H), 2120 (C≡C) cm^{-1}; ^1H NMR δ=1.16 (3H, d, J=7 Hz), 2.05 (1H, d, J=2 Hz), 2.5—2.8 (3H, m), 3.75 (3H, s), 6.7—7.2 (4H, m); MS *m*/*z* (%) 174 (M^+, 11), 121 (100). Found: *m*/*z* 174.1060. Calcd for $C_{12}H_{14}O$: M, 174.1044.

1-Naphthylethyne (7e). See Ref. 13.

1-Phenyl-1-buten-3-yne (7f). Colorless oil; IR (neat) 3320 (acetylenic H), 2110 (C≡C) cm^{-1}; ^1H NMR δ=3.02 (1H, m), 6.09 (1H, dd, J=16, 2 Hz), 7.02 (1H, d, J=16 Hz), 7.1—7.6 (5H, m); MS *m*/*z* (%) 128 (M^+, 100). Found: *m*/*z* 128.0615. Calcd for $C_{10}H_{18}$: M, 128.0625.

5,5-Dimethyl-1-phenyl-1,3-hexadiene (9). Colorless oil (*E*/*Z*-mixture; ratio about 11:7); IR (neat) 1610 (C=C) cm^{-1}; ^1H NMR δ=1.07 (5.5H, s), 1.31 (3.5H, s), 5.7—6.8 (4H, m), 7.0—7.4 (5H, m); MS *m*/*z* (%) 186 (M^+, 89), 171 (100). Found: *m*/*z* 186.1418. Calcd for $C_{14}H_{18}$: M, 186.1408.

1-Phenyl-1-pentyn-3-ol (10c) and 2-Chloro-1-phenyl-1-penten-3-ol (11c). A solution of **4c** (131 mg; 0.5 mmol) in THF (2.5 ml) was added to a solution of *t*-BuLi (1.5 mmol) in THF (2.5 ml) at −78 °C with stirring. The reaction mixture was stirred at −78 °C for 10 min, then propanal (1 mmol) was added. After 10 min, the reaction was quenched with sat. NH_4Cl. The products were purified by silica-gel column chromatography to give **10c**[12] (38 mg; 47%) and **11c** (33 mg; 34%). **11c**: Colorless oil (single isomer); IR (neat) 3360 (OH), 1630 (C=C) cm^{-1}; ^1H NMR δ=0.89 (3H, t, J=7 Hz), 1.73 (2H, quintet, J=7 Hz), 4.59 (1H, t, J=7 Hz), 6.84 (1H, s), 7.0—7.4 (5H, m); MS *m*/*z* (%) 196 (M^+, 36), 167 (100). Found: *m*/*z* 196.0645. Calcd for $C_{11}H_{13}ClO$: M, 196.0653.

1-(3-Methoxyphenyl)-1-pentyn-3-ol (10d). Colorless oil ; IR (neat) 3380 (OH), 2240 (C≡C) cm^{-1}; ^1H NMR δ=1.07 (3H, t, J=7 Hz), 1.81 (2H, quintet, J=7 Hz), 3.77 (3H, s), 4.53 (1H, t, J=7 Hz), 6.7—7.3 (4H, m); MS *m*/*z* (%) 190 (M^+, 30), 161 (100). Found: *m*/*z* 190.0988. Calcd for $C_{12}H_{14}O$: M, 190.0992.

2-Chloro-1-(3-methoxyphenyl)-1-penten-3-ol (11d). Colorless oil (single isomer); IR (neat) 3420 (OH) cm^{-1}; ^1H NMR δ=0.89 (3H, t, J=7 Hz), 1.73 (2H, quintet, J=7 Hz), 3.77 (3H, s), 4.61 (1H, t, J=7 Hz), 6.7—7.3 (4H,

m); MS m/z (%) 226 (M^+, 86), 197 (38), 161 (100). Found: m/z 226.0768. Calcd for $C_{12}H_{15}ClO_2$: M, 226.0759.

This work was supported by Takeda Science Foundation, which is gratefully acknowledged.

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