

Hydrohalogenation Reactions of 1,2-Allenic Sulfones. A Novel Synthesis of 2-Haloallylic Sulfones

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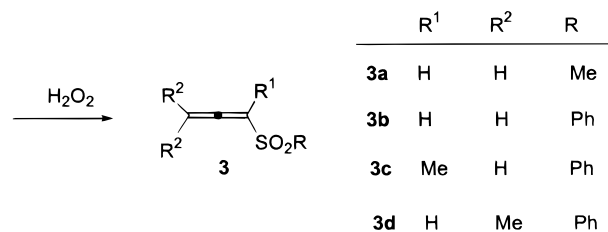
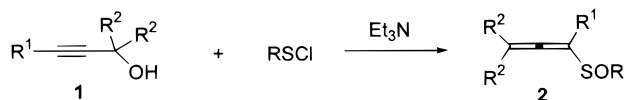
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Introduction

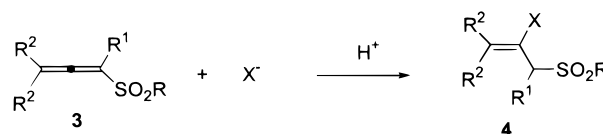
Hydrohalogenation reactions of electron-deficient C–C triple bonds, i.e., 2-alkynoic acids,¹ 2-alkynonates,¹ 2-alkynamides,¹ 2-propyne nitriles,¹ 2-alkynones,¹ 1-alkynyl phosphonates,² 1-alkynyl sulfoxides,³ 1-alkynyl triflate,⁴ 1-alkynyl iodonium salts,⁵ etc., have become a very powerful tool for the highly stereoselective synthesis of 3-halo-(2*Z*)-alkenoic acids and the corresponding equivalents. Another class of compounds attracting our interest is electron-deficient 1,2-dienes. Due to the unique arrangement of the two sets of π -orbitals, the reactivity of electron-deficient 1,2-dienes should be higher than that of the corresponding alkynes.⁶ Recently, we developed a methodology for the efficient syntheses of 3-halo-3-butenic acids/methyl esters and 4-halo-4-penten-2-ones via the hydrohalogenation reactions of 2,3-butadienoic acid/methyl ester and 3,4-pentadien-2-one, respectively.⁷ In this paper, we wish to disclose our recent results on the corresponding hydrohalogenation reactions of 1,2-allenic sulfones.

The known methods for the synthesis of these compounds are (1) the oxidation of 2-chloroallyl sulfide, which could be prepared via the reaction of thiophenols with the corresponding 2,3-dihalopropenes;⁸ (2) the reaction of 1-(phenylsulfonyl)propyne with hydrazonyl chlorides to afford a mixture of the allylic sulfone, the vinylic sulfone, and many other products;⁹ (3) the radical addition of alkylsulfonyl iodide with allenes to produce a mixture of several adducts;¹⁰ (4) the reaction of 2-haloallyl iodides with PhSO₂Na.¹¹ It should be noted that 2-haloallyl iodides, especially the bromo and iodo analogues, are not stable and usually are not readily available. Thus,

Scheme 1



Scheme 2^a



X = Cl, Br, I

^a Conditions A: MX (M = Na or Li), HOAc (solvent). Conditions B: MX (M = Na or Li), HOAc (1 equiv), CH₃CN (solvent). Conditions C: HX (as the solvent and the reagent).

a general, clean, and high-yielding method for the efficient synthesis of the title compounds is highly desirable.

Results and Discussion

1,2-Allenic sulfones are readily available from the oxidation of their corresponding sulfoxides, which can be easily prepared from the reaction of propargylic alcohols with RSCl (Scheme 1).¹² Four such compounds were synthesized via the chemistry shown in Scheme 1.

Three sets of reaction conditions were established to carry out the hydrohalogenation reactions of 1,2-allenic sulfones with metallic halides (Scheme 2). Some typical results are summarized in Table 1 and Table 2.

From the results of the hydrohalogenation reactions shown in Tables 1 and 2, as well as the results with allenic ketones, carboxylic acids, and esters, the following conclusions are obvious. (1) The electron-withdrawing ability of SO₂R is somewhat similar to that of the carbonyl group in esters and is much weaker than that of keto groups (compare the results with that in ref 7).¹³ A very slow reaction of 3a with LiI in HOAc at room temperature was observed. (2) The migration of the C=C bond in product 4ac was not observed even when 4ac was heated in HOAc at 118 °C for 11 h.^{7,9} (3) For the synthesis of the iodides, both NaI and LiI worked well, although the yield with LiI was higher under the same reaction conditions (compare entries 1 with 2 in Table 1), while for bromides and chlorides, lithium salts afforded the products in much higher yields than those

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Table 1. Hydrohalogenation Reactions of 1,2-Allenic Sulfone (3a)

entry	MX (equiv)	condns	temp (°C)	time (h)	product	yield (%) ^a
1	NaI (1.1–2)	A	80	0.5	4aa	80
2	LiI (1.7)	A	reflux	0.5	4aa	87
3	NaBr (2)	A	reflux	4	4ab	61 ^b
4	LiBr·H ₂ O (2)	A	reflux	1.5	4ab	79
5	NaCl (4.4)	A	reflux	11	4ac	28 ^c
6	LiCl·H ₂ O (5)	A	reflux	11	4ac	83
7	LiI (2)	B	80	12	4aa	76
8	LiBr·H ₂ O (2)	B	80	12	4ab	76
9	LiCl·H ₂ O (2)	B	80	12	4ac	85
10	HI ^d	C	80	8	4aa	65
11	HCl ^e	C	80	8	4ac	83

^a Isolated yield, unless otherwise stated. ^b 30% of **3a** was recovered. ^c 70% of **3a** was recovered. ^d Aqueous acid (45%) was used. ^e Aqueous acid (37%) was used.

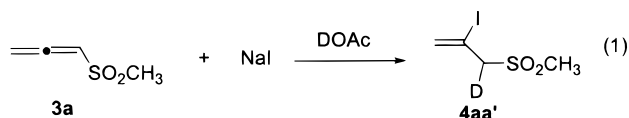
Table 2. Hydrohalogenation Reactions of 3b–d

entry	3	MX (equiv)	condns	temp (°C)	time (h)	product	yield (%) ^a
1	3b	NaI (2)	A	80	0.5	4ba	82
2	3b	LiBr·H ₂ O (2)	A	90	0.5	4bb	78
3	3b	NaBr (5)	A	90	8	4bb	67
4	3b	LiCl·H ₂ O (2)	A	90	2	4bc	69
5	3b	NaCl (5)	A	90	13	4bc	14 ^b
6	3b	LiI (2.5)	B	80	12	4ba	76
7	3b	LiBr·H ₂ O (2.5)	B	80	12	4bb	67
8	3b	LiCl·H ₂ O (2.5)	B	80	12	4bc	76
9	3b	HI ^c	C	80	0.5	4ba	44
10	3b	HBr ^d	C	80	22	4bb	53
11	3b	HCl ^e	C	80	22	4bc	81
12	3c	NaI (3.5)	A	80	4	4ca	88
13	3c	NaI (1.2)	A	reflux	4	4ca	83
14	3c	LiBr·H ₂ O (5)	A	110	20	4cb	77
15	3c	LiBr·H ₂ O (2)	A	reflux	10	4cb	74
16	3c	NaBr (5)	A	110	20	4cb	41 ^f
17	3d	NaI (3)	A	reflux	2	4da	74
18	3d	NaI (1.2)	A	reflux	2.5	4da	69

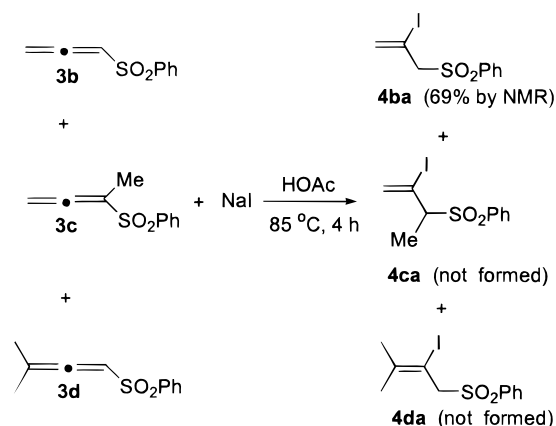
^a Isolated yield, unless otherwise stated. ^b 36% of **3b** was recovered. ^c Aqueous acid (45%) was used. ^d Aqueous acid (40%) was used. ^e Aqueous acid (37%) was used. ^f NMR yield.

of the sodium salts (compare entries 3 with 4 and 5 with 6 in Table 1, compare entries 2 with 3, 4 with 5, and 14 with 16 in Table 2). (4) The reaction can proceed in CH₃CN using only 1 equiv of HOAc (conditions B). (5) The reaction of HX with 1,2-allenic sulfones also afforded the hydrohalogenation products in reasonable yields (entries 10 and 11 in Table 1, entries 9–11 in Table 2).

This reaction proceeded via a nucleophilic addition of X[−] to the α,β C=C bond of the two C=C bonds in 1,2-allenic sulfones.⁷ The proton came from HOAc or HX; thus, methyl 1-deuterio-2-iodo-2-propenyl sulfone (**4aa'**) could be conveniently prepared via the reaction of **3a** with NaI in DOAc in 77% yield. The extent of D-incorporation is >97% as determined by 300 MHz ¹H NMR and 75.48 MHz ¹³C NMR spectra (eq 1).



The methyl group at the α-position greatly slowed the hydrohalogenation reaction, probably due to the increase of steric hindrance at the α-position to pick up a proton from either HOAc or HX (compare Tables 1 and 2). Even the two methyl groups in **3d** affected the rate of this reaction. A reaction of a mixture of **3b** (0.1 mmol), **3c**

Scheme 3

(0.1 mmol), and **3d** (0.1 mmol) with NaI (0.1 mmol) in HOAc at 85 °C for 4 h afforded the hydroiodination product **4ba** in 69% NMR yield, while the formations of **4ca** and **4da** were not observed during the specified reaction time (Scheme 3).

In summary, the hydrohalogenation reaction of 1,2-allenic sulfones afforded 2-haloallyl sulfones in high yields using conditions A, B, and C. Allylic sulfones are a class of compounds with significant synthetic potential: (1) the α-positions can be regioselectively alkylated;¹⁴ (2) the sulfone groups can be easily removed by reduction;¹⁵ (3) the nucleophilic (S_N2') and radical (S_H2') allylic substitution reactions can take place.¹⁶ Vinyl halides, especially iodides and bromides, are novel starting materials for radical reactions and transition metal catalyzed C–C bond formation reactions. All these make 2-haloallylic sulfones prepared by the method described in this paper valuable synthetic intermediates. The investigation regarding the synthetic utility of these compounds is currently being carried out in our laboratory.

Experimental Section

General. NaI, LiI, NaBr, LiBr·H₂O, NaCl, LiCl·H₂O, hydrochloric acid, hydrobromic acid, hydroiodic acid, and acetic acid are commercially available and used as is. ¹H NMR spectra were measured using CDCl₃ as the solvent and Me₄Si as the internal standard. The NMR yields were measured using CH₂Br₂ as the internal standard. 1-(Methylsulfonyl)-1,2-propadiene (**3a**), (1,2-propadienylsulfonyl)benzene (**3b**), (1-methyl-1,2-propadienylsulfonyl)benzene (**3c**), and (3-methyl-1,2-butadienylsulfonyl)benzene (**3d**) were prepared according to the published procedure.^{12,17}

Hydrohalogenation Reactions of 1,2-Allenic Sulfones. (a) Synthesis of 2-Iodo-3-(methylsulfonyl)-1-propene (4aa'). Typical Procedure. Conditions A. A solution of 1-(methylsulfonyl)-1,2-propadiene (**3a**) (118 mg, 1 mmol) and NaI (165 mg, 1.1 mmol) in HOAc (0.5 mL) was stirred at 80 °C for 1.5 h. After complete conversion of the starting material as monitored by TLC (eluent: petroleum ether/ethyl acetate = 1:1), the mixture was quenched with water (3 mL), neutralized with NaHCO₃, and then extracted with ether (4 × 10 mL). The combined ether layer was dried over MgSO₄. Evaporation of the

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solvent and flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2:1) afforded 197 mg (80%) of **4aa**: solid, mp 56–57 °C (dichloromethane/petroleum ether) (reported:¹⁰ mp 57–58 °C); ¹H NMR 6.57 (d, *J* = 1.5 Hz, 1H), 6.25 (d, *J* = 1.5 Hz, 1H), 4.12 (s, 2H), 3.00 (s, 3H); MS *m/e* 247 (M⁺ + 1, 12.12), 246 (M⁺, 4.15), 167 (100); IR (KBr) 1600, 1294, 1118 cm⁻¹.

Typical Procedure. Conditions B. A solution of 1-(methylsulfonyl)-1,2-propadiene (**3a**) (59 mg, 0.5 mmol), HOAc (0.03 mL, 0.52 mmol), and LiI (134 mg, 1 mmol) in acetonitrile (1 mL) was stirred at 80 °C for 12 h. After complete conversion of the starting material, the mixture was quenched with water (1 mL), neutralized with NaHCO₃, and then extracted with ether (4 × 5 mL). The combined ether layer was dried over MgSO₄. Evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2:1) afforded 93 mg (76%) of **4aa**.

Typical Procedure. Conditions C. A solution of 1-(methylsulfonyl)-1,2-propadiene (**3a**) (59 mg, 0.5 mmol) and hydriodic acid (45%, 1 mL) was stirred at 80 °C for 8 h. After complete conversion of the starting material, the mixture was quenched with water (1 mL), neutralized with NaHCO₃, and then extracted with ether (4 × 5 mL). The combined ether layer was dried over MgSO₄. Evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2:1) afforded 80 mg (65%) of **4aa**.

The following compounds were prepared similarly. The details of reactions under conditions A are listed below.

(b) 2-Bromo-3-(methylsulfonyl)-1-propene (4ab). Using **3a** (60 mg, 0.51 mmol) and LiBr·H₂O (104 mg, 1 mmol) afforded 80 mg (79%) of **4ab**:¹⁸ liquid; ¹H NMR δ 6.12 (d, *J* = 2 Hz, 1H), 5.94 (d, *J* = 2 Hz, 1H), 4.09 (s, 2H), 3.04 (s, 3H); MS *m/e* 201 (M⁺ + 1 (⁸¹Br), 31.42), 199 (M⁺ + 1 (⁷⁹Br), 31.55), 119 (100); IR (neat) 1622, 1304, 1128 cm⁻¹.

(c) 2-Chloro-3-(methylsulfonyl)-1-propene (4ac). Using **3a** (25 mg, 0.21 mmol) and LiCl·H₂O (60 mg, 1 mmol) afforded 27.2 mg (83%) of **4ac**: liquid; ¹H NMR δ 5.66 (d, *J* = 2 Hz, 1H), 5.65 (d, *J* = 2 Hz, 1H), 3.96 (s, 2H), 3.02 (s, 3H); MS *m/e* 157 (M⁺ + 1 (³⁷Cl), 2.42), 156 (M⁺ (³⁷Cl), 1.61), 155 (M⁺ + 1 (³⁵Cl), 6.71), 154 (M⁺ (³⁵Cl), 3.50), 75 (100); IR (neat) 1630, 1306, 1134 cm⁻¹; HRMS calcd for C₄H₇O₂³⁷ClS 155.9826, found 155.9871; calcd for C₄H₇O₂³⁵ClS 153.9855, found 153.9827.

(d) ((2-Iodo-2-propenyl)sulfonyl)benzene (4ba). Using **3b** (36 mg, 0.2 mmol) and NaI (60 mg, 0.4 mmol) afforded 51 mg (82%) of **4ba**: solid, mp 90.5–91.5 °C (dichloromethane/petroleum ether) (reported:¹⁰ mp 89.5–92 °C); ¹H NMR δ 7.93 (d, *J* = 7 Hz, 2H), 7.68 (t, *J* = 7 Hz, 1H), 7.58 (t, *J* = 7 Hz, 2H), 6.27 (q, *J* = 2 Hz, 1H), 6.08 (d, *J* = 2 Hz, 1H), 4.16 (d, *J* = 0.9 Hz, 2H); MS *m/e* 308 (M⁺, 7.40), 77 (100); IR (KBr) 1612, 1306, 1134 cm⁻¹.

(e) ((2-Bromo-2-propenyl)sulfonyl)benzene (4bb). Using **3b** (36 mg, 0.2 mmol) and LiBr·H₂O (42 mg, 0.4 mmol) afforded 41 mg (78%) of **4bb**: solid, mp 75.5–76.5 °C (dichloromethane/petroleum ether); ¹H NMR δ 7.93 (d, *J* = 6 Hz, 2H), 7.68 (t, *J* = 6 Hz, 1H), 7.57 (t, *J* = 6 Hz, 2H), 5.82 (d, *J* = 2 Hz, 1H), 5.77 (d, *J* = 2 Hz, 1H), 4.13 (s, 2H); MS *m/e* 263 (M⁺ + 1 (⁸¹Br), 1.69), 261 (M⁺ + 1 (⁷⁹Br), 1.68), 77 (100); IR (KBr) 1624, 1306, 1134 cm⁻¹; HRMS calcd for C₉H₉O₂⁷⁹BrS 259.9507, found 259.9542.

(f) ((2-Chloro-2-propenyl)sulfonyl)benzene (4bc). Using **3b** (36 mg, 0.2 mmol) and LiCl·H₂O (24 mg, 0.4 mmol) afforded 30 mg (69%) of **4bc**: solid, mp 54–55.5 °C (dichloromethane/petroleum ether) (reported:⁸ mp 57–58 °C); ¹H NMR δ 7.88 (d, *J* = 7 Hz, 2H), 7.63 (t, *J* = 7 Hz, 1H), 7.52 (t, *J* = 7 Hz, 2H), 5.45 (s, 1H), 5.32 (s, 1H), 4.03 (s, 2H); MS *m/e* 219 (M⁺ + 1 (³⁷-Cl), 1.07), 217 (M⁺ + 1 (³⁵Cl), 2.80), 77 (100); IR (KBr) 1628, 1320, 1150 cm⁻¹.

(g) ((2-Iodo-1-methyl-2-propenyl)sulfonyl)benzene (4ca). Using **3c** (29 mg, 0.15 mmol) and NaI (80 mg, 0.53 mmol) afforded 42 mg (88%) of **4ca**: liquid; ¹H NMR δ 7.89 (d, *J* = 7 Hz, 2H), 7.67 (t, *J* = 7 Hz, 1H), 7.55 (t, *J* = 7 Hz, 2H), 6.31 (t, *J* = 2 Hz, 1H), 6.07 (d, *J* = 2 Hz, 1H), 3.70 (q, *J* = 7 Hz, 1H), 1.55 (d, *J* = 7 Hz, 3H); MS *m/e* 322 (M⁺, 8.00) 53 (100); IR (neat) 1600, 1300, 1140 cm⁻¹; HRMS calcd for C₁₀H₁₁O₂IS 321.9523, found 321.9532.

(h) ((2-Bromo-1-methyl-2-propenyl)sulfonyl)benzene (4cb). Using **3c** (21 mg, 0.11 mmol) and LiBr·H₂O (52 mg, 0.5 mmol) afforded 23 mg (77%) of **4cb**: liquid; ¹H NMR δ 7.4–7.9 (m, 5H), 5.71 (d, *J* = 2 Hz, 1H), 5.63 (d, *J* = 2 Hz, 1H), 3.85 (q, *J* = 7 Hz, 1H), 1.50 (d, *J* = 7 Hz, 3H); MS *m/e* 276 (M⁺ (⁸¹Br), 63.02), 274 (M⁺ (⁷⁹Br), 60.38), 125 (100); IR (neat) 1608, 1300, 1140 cm⁻¹; HRMS calcd for C₁₀H₁₁O₂⁸¹BrS 275.9643, found 275.9595; calcd for C₁₀H₁₁O₂⁷⁹BrS 273.9663, found 273.9662.

(i) ((2-Iodo-3-methyl-2-butenyl)sulfonyl)benzene (4da). Using **3d** (36 mg, 0.17 mmol) and NaI (80 mg, 0.53 mmol) afforded 43 mg (74%) of **4da**: solid; mp 85–86 °C (dichloromethane/petroleum ether); ¹H NMR δ 7.87 (d, *J* = 7 Hz, 2H), 7.65 (t, *J* = 7 Hz, 1H), 7.54 (t, *J* = 7 Hz, 2H), 4.37 (s, 2H), 1.91 (s, 3H), 1.65 (s, 3H); MS *m/s* 336 (M⁺, 12.74), 209 (100); IR (neat) 1616, 1308, 1136 cm⁻¹; HRMS calcd for C₁₁H₁₃O₂IS 335.9680, found 335.9687.

Reaction of 3a with NaI in DOAc. Synthesis of 3-Deuterio-2-iodo-3-(methylsulfonyl)-1-propene (4aa'). Using **3a** (118 mg, 1 mmol), NaI (300 mg, 2 mmol), and DOAc (1 mL) afforded 191 mg (77%) of **4aa'**: liquid; ¹H NMR δ 6.56 (d, *J* = 1 Hz, 1H), 6.24 (d, *J* = 1 Hz, 1H), 4.10 (s, 1H), 2.99 (s, 3H); ¹³C NMR δ 136.381, 88.412, 68.009 (t, *J*_{D-C} = 21.44 Hz), 41.071.

Comparison of Reactivities of 3b, 3c, and 3d. A solution of **3b** (11.8 mg, 0.1 mmol), **3c** (19.4 mg, 0.1 mmol), **3d** (20.8 mg, 0.1 mmol), and NaI (15 mg, 0.1 mmol) in HOAc (1.5 mL) was stirred at 85 °C for 4 h. After usual workup, the ¹H NMR spectrum of the crude product showed **4ba** was formed in 69% yield by NMR. The formations of **4ca** and **4da** were not observed.

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Supporting Information Available: ¹H NMR spectra of the compounds **4ac**, **4bb**, **4ca**, **4cb**, **4da**, and **4aa'** as well as ¹³C NMR spectrum of the compound **4aa'** (8 pages). See any current masthead page for ordering and Internet access information.

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