

Effect of EtOH on the *E*-Iodohydroxylation of 1,2-Allenyl Sulfoxides with I₂[†]

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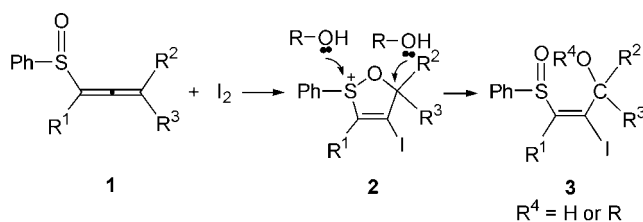
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The *E*-iodohydroxylation of 1,2-allenyl sulfoxides with I₂ in the presence of EtOH afforded 3-phenylsulfinyl-2-iodo-2(*E*)-alkenols in good yields and regio/stereo-selectivities under very mild conditions.

Keywords electrophilic addition, iodohydroxylation, allene, sulfoxide

Allenes are a class of versatile compounds for organic synthesis.^{1,2} Recently we have observed the highly selective *E*-iodohydroxylation of 1,2-allenyl sulfoxides^{3,4} affording *E*-3-phenylsulfinyl-2-iodo-2-alkenols in high yields.⁵ The reaction of substituted 1,2-allenyl phenyl sulfoxides was usually carried out at r.t. while that of 1,2-propadienyl phenyl sulfoxide should be conducted at 55 °C. In addition, it should be noted that the stereoselectivity of this reaction was determined by the formation of the cyclic intermediate **2**. Thus, we were interested to see the effect of EtOH on the structure of the final products (Scheme 1).

Scheme 1



When we ran this reaction with EtOH, it was quite interesting to observe that the reaction of 1,2-propadienyl phenyl sulfoxide (**1a**) with I₂ could proceed at 0 °C. The *E*-iodohydroxylation product **4a** was formed in 58% yield with 27% of **1a** being recovered. Through careful analysis of the reaction mixture, it was observed that sulfide **5a** was also formed in 6%—10% yield (entries 1 and 2, Table 1). With 2 equiv. of I₂ and 20 equiv. of EtOH the reaction of **1a** with I₂ at 0 °C afforded **4a** in 87% yield (entry 7, Table 1). When the reaction was carried out at a higher temperature the

yield of **5a** increased dramatically (entries 8—10, Table 1). Control experiment showed that the reaction in the absence of EtOH afforded *E*-**4a**⁵ in 58% yield with 17% of **1a** being recovered (entry 12, Table 1). It should be noted that under the reaction conditions used in Ref. 5, *E*-**4a** was formed in 80% yield with 20% of **1a** being recovered (entry 13, Table 1). Under the current reaction conditions, the addition of LiOAc is not necessary.

This effect of EtOH on the rate of the *E*-iodohydroxylation reaction is quite general for different mono-, di-, and tri-substituted 1,2-allenyl sulfoxides⁶ with the results summarized in Table 2. The reaction is very fast at 0 °C and the yields of **4** are from moderate to excellent while those of **5** are in the range of 6%—14%.

In order to study the effect of different alcohol on the iodohydroxylation of **1a**, benzyl alcohol, *i*-PrOH, or *n*-pentanol was used instead of EtOH. Although the yield of **4a** was comparable with **5a** being formed in 3%—9% yield, the reaction was not as clean as what we observed with EtOH (Table 3).

In conclusion, we have observed an interesting effect of alcohol on the rate of *E*-iodohydroxylation of 1,2-allenyl sulfoxides and I₂. Further studies in this area are being pursued in our laboratory.

Experimental

Synthesis of *E*-2-iodo-3-phenylsulfinyl-2-propen-1-ol (**4a**)^{5a}

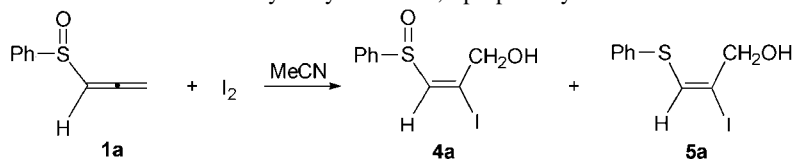
To a solution of **1a** (82 mg, 0.5 mmol) in MeCN (2 mL) was added I₂ (254 mg, 1 mmol). After 5 min, a solution of EtOH (0.3 mL) in MeCN (4 mL) was added

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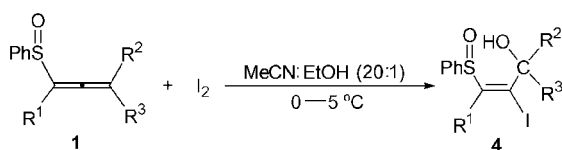
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[†]Dedicated to Professor Chengye Yuan on the occasion of his 80th birthday.

Table 1 Iodohydroxylation of 1,2-propadienyl sulfoxide^a

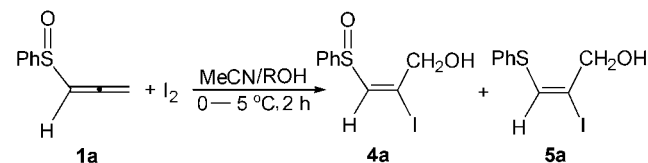
Entry	I ₂ (equiv.)	C ₂ H ₅ OH/mL	Temp./°C	Time/h	Yield ^b /%		Recovered/%
					4a	5a	1a
1	1.5	0.1	0—5	1.3	58	6	27
2	1.5	0.2	0—5	2.5	52	10	16
3	2	0.1	0—5	1.3	71	5	23
4	2	0.2	0—5	1.3	71	4	6
5	1.5	3	0—5	2	43	17	25
6	2	0.25	0—5	1.6	82	11	0
7	2	0.3	0—5	1.3	88	13	0
8	2	0.25	16	1.6	64	31	0
9	1.5	0.6	15	2	62	25	0
10 ^c	2	0.25	16	1.6	45	46	0
11	2.4	0.3	55	1	11	0	0
12	1.5	0	0—5	2	58	14	17
13 ^d	2	0	0—5	2	80	0	20

^a The reaction was conducted using **1a** (0.5 mmol) in 6 mL of MeCN. ^b Isolated yield. ^c The reaction was carried out under an atmosphere of N₂. ^d The reaction was carried out with the addition of LiOAc•2H₂O (1 mmol) in CH₃CN/H₂O=7 : 1.

Table 2 Iodohydroxylation of 1,2-allenyl sulfoxides in MeCN-EtOH^a

Entry	1			Time/h	Yield ^b /%
	R ¹	R ²	R ³		
1 ^c	H	H	H (1a)	1.3	88 (4a)
2	H	H	<i>n</i> -C ₄ H ₉ (1b)	0.7	84 (4b)
3	H	H	<i>n</i> -C ₇ H ₁₅ (1c)	0.5	82 (4c)
4	H	C ₂ H ₅	C ₂ H ₅ (1d)	0.3	91 (4d)
5	H	CH ₃	<i>i</i> -C ₄ H ₉ (1e)	0.3	80 (4e)
6	H	(CH ₂) ₅ (1f)		0.3	94 (4f)
7	H	CH ₃	CH ₂ CH ₃ (1g)	0.6	91 (4g)
8	H	CH ₃	CH ₃ (1h)	0.3	87 (4h)
9 ^d	<i>n</i> -C ₄ H ₉	CH ₃	CH ₃ (1i)	1	74 (4i)
10	<i>n</i> -C ₄ H ₉	H	H (1j)	1	58 (4j)
11	H	CH ₃	<i>n</i> -C ₃ H ₇ (1k)	0.5	84 (4k)

^a Condition A: To a solution of **1** (0.4 mmol) and EtOH (0.3 mL) in MeCN (2 mL) was added a solution of I₂ (0.8 mmol) in MeCN (4 mL). Before chromatography on silica gel, the reaction mixture was treated with Na₂S₂O₃ to remove the excess I₂. ^b Isolated yield. ^c To a solution of **1a** (0.5 mmol) in anhydrous MeCN (2 mL) was added I₂ (1 mmol). After 5 min, a solution of EtOH (0.3 mL) in MeCN (4 mL) was added with stirring. ^d The reaction mixture was submitted directly to chromatography on silica gel (eluent: petroleum ether/ethyl acetate=3 : 1, V : V) without the prior treatment of Na₂S₂O₃. With the treatment of Na₂S₂O₃, only the starting material **1i** was obtained.

Table 3 Effect of ROH on the iodohydroxylation of **1a**^a

Entry	R	Yield ^b /% of 4a
1	Bn	88
2	<i>i</i> -C ₃ H ₇	85
3	<i>n</i> -C ₅ H ₁₁	86

^a The reaction was conducted using **1a** (0.5 mmol) and I₂ (1.2 mmol) in MeCN (6 mL)-ROH (0.3 mL). ^b Isolated yield.

with stirring. After being stirred at 0—5 °C for 1.3 h, the mixture was quenched with 4 mL of water followed by the addition of a saturated aqueous solution of Na₂-S₂O₃. The mixture was extracted with dichloromethane (25 mL×3), washed with NaCl, and dried over MgSO₄. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate=2 : 1, V : V) afforded **4a** (136.0 mg, 88%) as a white solid. m.p. 115—117 °C (dichloromethane-petroleum ether) (lit.^{5a} 115.5—116.5 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.69—7.71 (m, 2H), 7.54—7.57 (m, 3H), 6.91 (s, 1H), 4.82 (t, *J*=6.4 Hz, 1H), 4.70 (dd, *J*=15.2, 6.4 Hz, 1H), 4.55 (dd, *J*=15.2, 6.4 Hz, 1H).

Synthesis of *E*-1-[1'-iodo-2'-(phenylsulfinyl)vinyl]-1-cyclohexanol (**4f**)^{5a}

Typical procedure A To a solution of **1f** (69.6 mg, 0.3 mmol) and EtOH (0.3 mL) in MeCN (3 mL) was added a solution of I₂ (152.4 mg, 0.6 mmol) in

MeCN (3 mL) with stirring at 0 °C. After being stirred at 0 °C for 0.3 h, the mixture was quenched with 6 mL of water at this temperature. While the temperature rose to 0 °C, a saturated aqueous solution of Na₂S₂O₃ was added. The mixture was extracted with dichloromethane (25 mL × 3), washed with NaCl, and dried over MgSO₄. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3 : 1, V : V) afforded **4f** (106.4 mg, 94%) as a white solid. m.p. 173—174 °C (dichloromethane-petroleum ether) (lit.^{5a} 173—174 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.81—7.83 (m, 2H), 7.49—7.54 (m, 3H), 6.78 (s, 1H), 4.50 (s, 1H), 2.14—1.84 (m, 2H), 1.77—1.42 (m, 6H), 1.19—1.15 (m, 2H).

Following compounds were prepared according to typical procedure A.

E-2-Iodo-1-phenylsulfinyl-1-hepten-3-ol (E-4b)^{5b}: The reaction of 66 mg (0.3 mmol) of **1b** and 152.4 mg (0.6 mmol) of I₂ afforded 91.4 mg (84%) of **4b**. White solid, m.p. 107—108 °C (dichloromethane-petroleum ether) (lit.^{5b} 107—108 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.62—7.69 (m, 2H), 7.50—7.55 (m, 3H), [7.00 (s, 0.72H), 6.93 (s, 0.28H)], 4.82 (bs, 1H), [4.47 (t, *J* = 6.8 Hz, 0.28H), 4.41 (t, *J* = 6.8 Hz, 0.72H), 1.66—1.74 (m, 1H), 1.33—1.50 (m, 5H), 0.90 (t, *J* = 7 Hz, 3H).

E-2-Iodo-1-phenylsulfinyl-1-decen-3-ol (E-4c): The reaction of 131 mg (0.5 mmol) of **1c** and 254 mg (1 mmol) of I₂ afforded 167.1 mg (82%) of **4c**. White solid, m.p. 64—66 °C (dichloromethane-petroleum ether); ¹H NMR (CDCl₃, 400 MHz) δ: 7.60—7.68 (m, 2H), 7.49—7.53 (m, 3H), [6.98 (s, 0.58H), 6.91 (s, 0.42H)], 4.98 (bs, 1H), [4.45 (t, *J* = 6.4 Hz, 0.42H), 4.39 (t, *J* = 6 Hz, 0.58H)], 1.62—1.71 (m, 1H), 1.27—1.49 (m, 11H), 0.87 (t, *J* = 6 Hz, 3H); IR (KBr) *v*: 3406, 1632, 1585, 1443, 1021 cm⁻¹; MS (70 eV, EI) *m/z* (%): 407 (M⁺ + 1, 4.95), 127 (100). Anal. calcd for C₁₆H₂₃SO₂I: C 47.30, H 5.71; found C 47.40, H 5.86.

E-3-Ethyl-2-iodo-1-phenylsulfinyl-1-penten-3-ol (E-4d): The reaction of 88 mg (0.4 mmol) of **1d** and 203.2 mg (0.8 mmol) of I₂ afforded 132.4 mg (91%) of **4d**. White solid, m.p. 137—138 °C (dichloromethane-petroleum ether); ¹H NMR (CDCl₃, 400 MHz) δ: 7.75—7.78 (m, 2H), 7.49—7.52 (m, 3H), 6.96 (s, 1H), 2.98 (s, 1H), 1.93—2.08 (m, 2H), 1.61—1.73 (m, 2H), 1.01 (t, *J* = 10 Hz, 3H), 0.76 (t, *J* = 10 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 147.8, 145.5, 130.9, 129.2, 125.2, 118.2, 82.9, 34.33, 33.1; IR (KBr) *v*: 3421, 3198, 1581, 1461, 1442, 1015 cm⁻¹; MS (70 eV, EI) *m/z* (%): 365 (M⁺ + 1, 8.30), 335 (100). Anal. calcd for C₁₃H₁₇O₂SI: C 42.87, H 4.70; found C 42.87, H 4.85.

E-2-Iodo-3,5-dimethyl-1-phenylsulfinyl-1-hexen-3-ol (E-4e): The reaction of 93.6 mg (0.4 mmol) of **1e** and 203.2 mg (0.8 mmol) of I₂ afforded 121.5 mg (80%) of **4e**. White solid, m.p. 112—113 °C (dichloromethane-petroleum ether); ¹H NMR (CDCl₃, 400 MHz) δ: 7.77—7.80 (m, 2H), 7.48—7.50 (m, 3H), 6.80 (s, 1H), 4.50 (bs, 1H), 1.57—1.69 (m, 6H), 0.90 (d, *J* = 6 Hz, 3H), 0.84 (d, *J* = 6 Hz, 3H); IR (KBr) *v*: 3363, 2975, 1653, 1382, 1090, 1050 cm⁻¹; MS (70 eV, EI) *m/z* (%):

379 (M⁺ + 1, 13.62), 43 (100); HRMS (EI) calcd for C₁₄H₁₉O₂SI: 378.01505. found 378.01740.

E-2-Iodo-3-methyl-1-phenylsulfinyl-1-penten-3-ol (E-4g): The reaction of 81.7 mg (0.4 mmol) of **1g** and 203.2 mg (0.8 mmol) of I₂ afforded 132.3 mg (91%) of **4g**. White solid, m.p. 120—121 °C (dichloromethane-petroleum ether); ¹H NMR (CDCl₃, 400 MHz) δ: 7.78—7.82 (m, 2H), 7.54—7.52 (m, 3H), 6.84 (s, 0.47 H), 6.83 (s, 0.53 H), 4.28 (s, 0.47H), 3.82 (s, 0.53H), 1.81—2.06 (m, 2H), 1.70 (s, 1.41H), 1.62 (s, 1.59H), 1.02 (t, *J* = 7.6 Hz, 1.59H), 0.78 (t, *J* = 7.6 Hz, 1.41H); IR (KBr) *v*: 3252, 1632, 1578, 1443, 1007 cm⁻¹; MS (70 eV, EI) *m/z* (%): 351 (M⁺ + 1, 8.20), 321 (100). Anal. calcd. for C₁₂-H₁₅O₂SI: C 41.14, H 4.28; found: C 41.20, H 4.21.

E-3-Iodo-2-methyl-4-phenylsulfinyl-3-buten-2-ol (E-4h)^{5a}: The reaction of 76.8 mg (0.4 mmol) of **1h** and 203.2 mg (0.8 mmol) of I₂ afforded 117.2 mg (87%) of **4h**. White solid, m.p. 147—149 °C (dichloromethane-petroleum ether) (lit.^{5a} 147.5—148.5 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.82—7.84 (m, 2H), 7.52—7.56 (m, 3H), 6.76 (s, 1H), 4.53 (bs, 1H), 1.69 (s, 3H), 1.47 (s, 3H).

E-3-Iodo-2-methyl-4-phenylsulfinyl-3-octen-2-ol (E-4i)^{5a}: The reaction of 74.4 mg (0.3 mmol) of **1i** and 114.3 mg (0.45 mmol) of I₂ afforded 85.7 mg (74%) of **4i**. White solid, m.p. 150—152 °C (dichloromethane-petroleum ether). (lit.^{5a} 150—152 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.83—7.84 (m, 2H), 7.44—7.48 (m, 3H), 4.18 (s, 1H), 2.54—2.58 (m, 1H), 2.41—2.45 (m, 1H), 1.79 (s, 3H), 1.67 (s, 3H), 1.43—1.48 (m, 1H), 1.22—1.28 (m, 2H), 0.94—1.03 (m, 1H), 0.80 (t, *J* = 6 Hz, 3H); MS *m/z* (%): 364 (M⁺ + 1, 47.48), 41 (100).

E-2-Iodo-3-phenylsulfinyl-2-hepten-1-ol (E-4j)^{5a}: The reaction of 66 mg (0.3 mmol) of **1j** and 152.4 mg (0.6 mmol) of I₂ afforded 65.2 mg (58%) of **4j**. White solid, m.p. 83—84 °C (dichloromethane-petroleum ether) (lit.^{5a} 83—84 °C); ¹H NMR (CDCl₃, 400 MHz) δ: 7.62 (d, *J* = 4.8 Hz, 2H), 7.48—7.51 (m, 3H), 4.96 (d, *J* = 10.8 Hz, 1H), 4.84 (d, *J* = 10.8 Hz, 1H), 3.50 (bs, 1H), 2.41—2.48 (m, 1H), 2.13—2.19 (m, 1H), 1.40—1.44 (m, 1H), 1.16—1.26 (m, 2H), 0.65—0.85 (m, 4H).

E-2-Iodo-3-methyl-1-phenylsulfinyl-1-hexen-3-ol (E-4k): The reaction of 88.2 mg (0.4 mmol) of **1k** and 203.2 mg (0.8 mmol) of I₂ afforded 127.1 mg (84%) of **4k**. White solid, m.p. 123—124 °C (dichloromethane-petroleum ether); ¹H NMR (CDCl₃, 400 MHz) δ: 7.69—7.72 (m, 2H), 7.43—7.44 (m, 3H), 6.74 (s, 1H), 4.19 (s, 1H) 1.68—1.75 (m, 2H), 1.57 (s, 3H), 1.21—1.24 (m, 1H), 1.07—1.09 (m, 1H), 0.78 (t, *J* = 6 Hz, 3H); IR (KBr) *v*: 3421, 1632, 1579, 1446, 1019 cm⁻¹; MS (70 eV, EI) *m/z* (%): 364 (M⁺, 1.00), 321 (100). Anal. calcd. for C₁₃H₁₇O₂SI: C 42.87, H 4.70; found C 42.95, H 4.92.

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