Stereoselective Synthesis of 2-Aryl-5-halo-2-pentenyl Methyl Sulfoxides and Sulfones

Michel Madesclaire,*[a] Danielle Roche,[a] André Boucherle,[b] Alain Carpy[c]

[a] Laboratoire de Chimie Pharmaceutique, Faculté de Pharmacie, B. P. 38, F-63001 Clermont-Ferrand Cédex, France

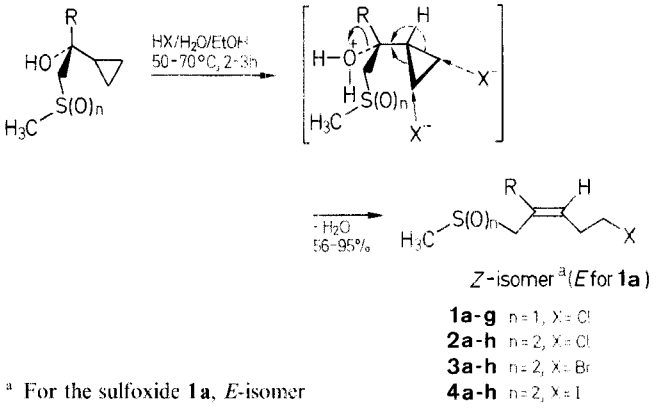
[b] Laboratoire de Chimie et Toxicologie, U.E.R. des Sciences Pharmaceutiques, Avenue de Verdun, F-38240 Meylan, France

[c] Laboratoire de Chimie Analytique, Faculté de Pharmacie, 91, rue Leyteire, F-33000 Bordeaux, France

Stereoselective formation of 2-aryl-5-halo-2-pentenyl methyl sulfoxides and sulfones is achieved by treatment of 2-aryl-2-cyclopropyl-2-hydroxyethyl methyl sulfoxides or sulfones, respectively, with hydrogen halides. In all cases, only the *Z*-isomer is isolated except for the 2-thiophenyl derivative which is designated as the *E*-isomer in accord with the Cahn sequence rule. Structures were determined by ^{1}H-NMR spectrometry and for one product by X-ray crystallography.

The three most widely used methods for obtaining 2-alkenyl sulfoxide and sulfone synthons are gentle or complete oxidation of 2-alkenyl sulfides,[1-4] dehydration of 3-hydroxyalkyl sulfoxides and sulfones,[2,5,6] and the Julia-Johnson olefin synthesis from cyclopropyl carbinols.[7,8]

We used the third method to prepare the title compounds by hydrohalic acid-catalyzed dehydration of 2-aryl-2-cyclopropyl-2-hydroxyethyl sulfoxides[9] and sulfones, respectively, the latter being obtained by oxidation of the sulfoxides with peracetic acid.[10] Dehydration occurs with stereoselective opening of the cyclopropane ring and homoallylic rearrangement.



[a] For the sulfoxide **1a**, *E*-isomer

Whatever R and X, a single stereoisomer was isolated in each case in an average yield of ~ 70%.

The configuration of triclinic bromosulfone **3b** was found by X-ray crystallography to be *Z* (Table 1). The configuration of the other derivatives was determined by analogy using ^{1}H-NMR spectrometry and theoretical calculation of the chemical shift of the olefinic proton. In this way, the *Z*-configuration could be assigned to sulfoxides **1b–g** and to sulfones **2a–h, 3a–h, 4a–h**. Sulfoxide **1a** has the *E*-configuration, however, since replacing the benzene ring by a thiophene ring reverses the order of priorities according to the Cahn sequence rule.

Thus, the stereoselective opening of the cyclopropane ring is confirmed since in all compounds **1–4** the two aliphatic chains are *cis*.

Table 1. X-Ray Data of Methyl (*Z*)-5-Bromo-2-(4-fluorophenyl)-2-pentenyl Sulfone (**3b**) [$C_{12}H_{14}BrFO_2S$ (321.2); m.p. 363°K]

V: 664.93 Å^3; density calc. 1.61, found 1.65 ± 0.05;
Triclinic; space group P1; Z = 2 (two independent molecules); a: 4.663 (2) Å; b: 9.484 (1) Å; c: 15.070 (1) Å; α: 90.01 (1)°; β: 93.88 (2)°; γ: 89.98 (2) Å

Table 2. 5-Chloro-2-aryl-2-pentenyl Methyl Sulfoxides **1** Prepared

Product	R	Yield[a] (%)	Isomer	m.p. (°C)	Molecular Formula[b]
1a		69	*E*	81	$C_{10}H_{13}ClOS_2$ (248.8)
1b	C_6H_5	68	*Z*	70	$C_{12}H_{15}ClOS$ (242.8)
1c	4-FC_6H_4	62	*Z*	68	$C_{12}H_{14}ClFOS$ (260.8)
1d	4-ClC_6H_4	86	*Z*	91	$C_{12}H_{14}Cl_2OS$ (277.2)
1e	4-BrC_6H_4	61	*Z*	135	$C_{12}H_{14}BrClOS$ (321.7)
1f	4$CH_3OC_6H_4$	74	*Z*	76	$C_{13}H_{17}ClO_2S$ (272.8)
2g	4-*i*-$C_3H_7C_6H_4$	63	*Z*	55	$C_{15}H_{21}ClOS$ (284.85)

[a] Yield of isolated pure product.
[b] Satisfactory microanalyses obtained: C ±0.23, H ±0.15, Br ±0.24, Cl ±0.20, F ±0.16, S ±0.20.

Table 3. (*Z*)-5-Halo-2-aryl-2-pentenyl Methyl Sulfones **2**, **3** and **4** Prepared

Product	R	Yield[a] (%)	m.p. (°C)	Molecular Formula[b]
2a	C_6H_5	74	73	$C_{12}H_{15}ClO_2S$ (258.8)
3a		71	88	$C_{12}H_{15}BrO_2S$ (303.2)
4a		62	89	$C_{12}H_{15}IO_2S$ (350.2)
2b	4-FC_6H_4	74	69–70	$C_{12}H_{14}ClFO_2S$ (276.8)
3b		70	90	$C_{12}H_{14}BrFO_2S$ (321.2)
4b		56	97	$C_{12}H_{14}FIO_2S$ (368.2)
2c	4-ClC_6H_4	66	84	$C_{12}H_{14}Cl_2O_2S$ (293.2)
3c		59	83	$C_{12}H_{14}BrClO_2S$ (337.7)
4c		71	86	$C_{12}H_{14}ClIO_2S$ (384.7)
2d	4-BrC_6H_4	85	98	$C_{12}H_{14}BrClO_2S$ (337.7)
3d		95	99	$C_{12}H_{14}Br_2O_2S$ (382.1)
4d		67	109	$C_{12}H_{14}BrIO_2S$ (429.1)
2e	4-$CH_3OC_6H_4$	84	90	$C_{13}H_{17}ClO_3S$ (288.8)
3e		80	98–99	$C_{13}H_{17}BrO_3S$ (333.25)
4e		86	97–98	$C_{13}H_{17}IO_3S$ (380.2)
2f	3,4-$(CH_3)_2C_6H_3$	93	88	$C_{14}H_{19}ClO_2S$ (286.8)
3f		65	85	$C_{14}H_{19}BrO_2S$ (331.3)
4f		66	86.5	$C_{14}H_{19}IO_2S$ (378.3)
2g	4-*i*-$C_3H_7C_6H_4$	65	90	$C_{15}H_{21}ClO_2S$ (300.85)
3g		62	83	$C_{15}H_{21}BrO_2S$ (345.3)
4g		65	70	$C_{15}H_{21}IO_2S$ (392.3)
2h	4-*t*-$C_4H_9C_6H_4$	94	101	$C_{16}H_{23}ClO_2S$ (314.9)
3h		74	108	$C_{16}H_{23}BrO_2S$ (359.3)
4h		88	86.5	$C_{16}H_{23}IO_2S$ (406.3)

[a] Yield of isolated pure product.
[b] Satisfactory microanalyses obtained: C ±0.23, H ±0.15, Br ±0.24, Cl ±0.20, F ±0.16, S ±0.20.

Table 4. ^{1}H-NMR[a] ($CDCl_3$/TMS) Spectral Data of Compounds **1–4**

Compound	δ, *J*(Hz)
1a	2.65 (s, 3H); 2.83 (q, 2H, *J* = 7.5); 3.70 (t, 2H, *J* = 7.5); 3.88 (d, 1H, *J* = 13.8); 4.10 (d, 1H, *J* = 13.8); 6.33 (t, H, *J* = 7.5); 6.95–7.45 (m, 3H)

Table 4. (Continued)

Compound	δ, J(Hz)
1b	2.47 (s, 3H); 2.80 (q, 2H, J = 7.5); 3.65 (t, 2H, J = 7.5); 3.81 (d, 1H, J = 13.2); 4.09 (d, 1H, J = 13.2); 6.10 (t, H, J = 7.5); 7.34 (s, 5H)
1c	2.55 (s, 3H); 2.77 (q, 2H, J = 7.5); 3.62 (t, 2H, J = 7.5); 3.77 (d, 1H, J = 13.5); 4.06 (d, 1H, J = 13.5); 6.18 (t, H, J = 7.5); 6.97–7.70 (m, 4H)
1d	2.45 (s, 3H); 2.75 (q, 2H, J = 7.5); 3.58 (t, 2H, J = 7.5); 3.79 (d, 1H, J = 12.4); 4.01 (d, 1H, J = 12.4); 6.10 (t, H, J = 7.5); 7.10 (s, 4H)
1e	2.40 (s, 3H); 2.82 (q, 2H, J = 7.5); 3.64 (t, 2H, J = 7.5); 3.75 (d, 1H, J = 12.75); 4.05 (d, 1H, J = 12.75); 6.05 (t, 1H, J = 7.5); 7.02–7.50 (m, 4H)
1f	2.49 (s, 3H); 2.81 (q, 2H, J = 7.5); 3.66 (t, 2H, J = 7.5); 3.84 (d, 1H, J = 13.1); 4.17 (d, 2H, J = 13.1); 6.07 (t, H, J = 7.5); 6.91 (d, 2H, J = 9); 7.37 (d, 2H, J = 9)
1g	2.47 (s, 3H); 2.60–3.10 (m, 2H + 1H); 3.61 (t, 2H, J = 7.5); 3.86 (d, 1H, J = 13.25); 4.14 (d, 2H, J = 13.25); 6.08 (t, H, J = 7.5); 7.25 (s, 4H)
2a	2.57 (s, 3H); 2.85 (q, 2H, J = 7.5); 3.72 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.22 (t, H, J = 7.5); 7.37 (s, 5H)
3a	2.58 (s, 3H); 2.99 (q, 2H, J = 7.5); 3.58 (t, 2H, J = 7.5); 4.31 (s, 2H); 6.21 (t, H, J = 7.5); 7.4 (s, 5H)
4a	2.60 (s, 3H); 2.8–3.55 (m, 2H + 2H); 4.3 (s, 2H); 6.15 (t, H, J = 7.5); 7.4 (s, 5H)
2b	2.65 (s, 3H); 2.9 (q, 2H, J = 7.5); 3.72 (t, 2H, J = 7.5); 4.25 (s, 2H); 6.18 (t, H, J = 7.5); 7.05–7.6 (m, 4H)
3b	2.67 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.58 (t, 2H, J = 7.5); 4.29 (s, 2H); 6.19 (t, H, J = 7.5); 6.9–7.63 (m, 4H)
4b	2.65 (s, 3H); 2.8–3.5 (m, 2H + 2H); 4.25 (s, 2H); 6.07 (t, H, J = 7.5); 6.90–7.65 (m, 4H)
2c	2.67 (s, 3H); 2.9 (q, 2H, J = 7.5); 3.75 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.26 (t, H, J = 7.5); 7.4 (s, 4H)
3c	2.67 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.57 (t, 2H, J = 7.5); 4.25 (s, 2H); 6.17 (t, H, J = 7.5); 7.32 (s, 4H)
4c	2.67 (s, 3H); 2.78–3.48 (m, 2H + 2H); 4.27 (s, 2H); 6.12 (t, H, J = 7.5); 7.35 (s, 4H)
2d	2.65 (s, 3H); 2.87 (q, 2H, J = 7.5); 3.72 (t, 2H, J = 7.5); 4.5 (s, 2H); 6.25 (t, H, J = 7.5); 7.2–7.7 (m, 4H)
3d	2.69 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.6 (t, 2H, J = 7.5); 4.27 (s, 2H); 6.22 (t, H, J = 7.5); 7.1–7.7 (m, 4H)
4d	2.65 (s, 3H); 2.75–3.45 (m, 2H + 2H); 4.25 (s, 2H); 6.12 (t, H, J = 7.5); 7.2–7.7 (m, 4H)
2e	2.60 (s, 3H); 2.85 (q, 2H, J = 7.5); 3.7 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.17 (t, H, J = 7.5); 6.95 (d, 2H, J = 9); 7.42 (d, 2H, J = 9)
3e	2.57 (s, 3H); 2.95 (q, 2H, J = 7.5); 3.57 (t, 2H, J = 7.5); 4.31 (s, 2H); 6.17 (t, H, J = 7.5); 6.95 (d, 2H, J = 9); 7.37 (d, 2H, J = 9)
4e	2.57 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.27 (t, 2H, J = 7.5); 4.23 (s, 2H); 6.02 (t, H, J = 7.5); 6.92 (d, 2H, J = 9); 7.35 (d, 2H, J = 9)
2f	2.57 (s, 3H); 2.86 (q, 2H, J = 7.5); 3.72 (t, 2H, J = 7.5); 4.28 (s, 2H); 6.17 (t, H, J = 7.5); 7.15 (br. s, 3H)
3f	2.57 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.57 (t, 2H, J = 7.5); 4.28 (s, 2H); 6.15 (t, H, J = 7.5); 7.15 (br. s, 3H)
4f	2.56 (s, 3H); 2.97 (q, 2H, J = 7.5); 3.27 (t, 2H, J = 7.5); 4.27 (s, 2H); 6.07 (t, H, J = 7.5); 7.12 (s, 3H)
2g	2.57 (s, 3H); 2.65–3.15 (m, 2H + 1H); 3.7 (t, 2H, J = 7.5); 4.27 (s, 2H); 6.15 (t, H, J = 7.5); 7.25 (s, 4H)
3g	2.60 (s, 3H); 2.82–3.25 (m, 2H + 1H); 3.6 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.2 (t, H, J = 7.5); 7.3 (s, 4H)
4g	2.57 (s, 3H); 2.7–3.5 (m, 2H + 2H + 1H); 4.27 (s, 2H); 6.1 (t, H, J = 7.5); 7.28 (s, 4H)
2h	2.60 (s, 3H); 2.85 (q, 2H, J = 7.5); 3.7 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.2 (t, H, J = 7.5); 7.37 (s, 4H)
3h	2.60 (s, 3H); 2.99 (q, 2H, J = 7.5); 3.57 (t, 2H, J = 7.5); 4.3 (s, 2H); 6.20 (t, H, J = 7.5); 7.37 (s, 4H)
4h	2.60 (s, 3H); 2.75–3.45 (m, 2H + 2H); 4.31 (s, 2H); 6.13 (t, H, J = 7.5); 7.41 (s, 4H)

[a] Recorded with a Jeol C60 HL spectrometer.

The concentrated hydrohalic acids used are:

37% hydrochloric acid (d = 1.19);
47% hydrobromic acid (d = 1.49);
57% hydroiodic acid (d = 1.70).

2-Aryl-5-halo-2-pentenyl Methyl Sulfoxides 1 and Sulfones 2, 3, 4; General Procedure:

The methyl 2-aryl-2-cyclopropyl-2-hydroxyethyl sulfoxide or sulfone (10 mmol) is dissolved in a mixture of the conc. hydrohalic acid (15 mL) and pure EtOH (35 mL). The mixture is heated at 50–70 °C for 2–3 h on a water bath. After cooling, the solution is poured into ice water (200 mL). The unsaturated product precipitates out slowly. It is isolated by suction, thoroughly washed with water (3 × 20 mL), and recrystallized (from cyclohexane for **1a**, from petroleum ether for **1b** and **1g**, from benzene/hexane 1:2 for **1c–f**, and from 50% aqueous EtOH for sulfones **2**, **3**, and **4**).

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