Reaction of Terminal Oxiranes With Arenesulfonic Acid

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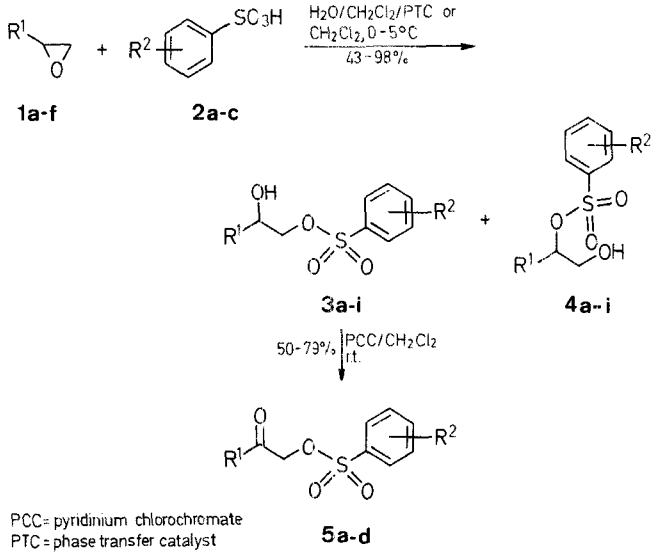
The reaction of oxiranes **1** with arenesulfonic acids under phase transfer catalyst system (water/dichloromethane) or without catalyst (dry dichloromethane) affords regioisomeric arylsulfonyloxy primary and secondary alcohols. The latter is oxidized to 1-arylsulfonyloxy-2-alkanones **5** in good yield.

In previous papers,[1,2] one of the authors reported the synthesis of 1-arylsulfonyloxy-2-alkanones **5** which possess selective es-

terase inhibitory activity as well as hypolipidemic effect. This communication deals with an alternative route for the preparation of compound **5** starting from oxirane **1**.

The reaction of octyloxirane (**1a**) with two equivalents of benzenesulfonic acid (**2a**) in the presence of a catalytic amount of tetra-*n*-butylammonium hydrogensulfate in a stirred two-layer suspension consisting of dichloromethane and water gave a mixture of 1-phenylsulfonyloxy-2-octanol (**3a**) and 2-phenylsulfonyloxy-1-octanol (**4a**) in 90% total yield in a 1:1 ratio (Method A, Table 1). The regioisomers **3a** and **4a** could be separated by column chromatography on silica gel and their structures could be confirmed on the basis of ^{1}N-NMR; the former showed a signal (1 H, doublet) for the hydroxy proton (OH) at $\delta = 2.14$ ppm while the latter (1 H, triplet) at $\delta = 2.10$ ppm (Table 2).



On the other hand, treatment of the oxirane **1a** with anhydrous benzenesulfonic acid[3] (**2a**) in dichloromethane solution (without phase-transfer catalyst) afforded mainly the primary alkanol **4a** accompanied by a small amount of the secondary alkanol **3a** (**4a**:**3a** = 16:1, Method B). It is seen from Table 1 that in method B, the product ratio of **3**/**4** increased to more than seven times as compared to method A. Thus the compounds **3a** and **4a** themselves did not show any mutual interconversion (**3a** to **4a** or **4a** to **3a**) under similar reaction conditions (Method A and Method B). Therefore, the product ratio **3**/**4** in both the methods exactly reflects the kinetics of the respective reactions. A S_N1 type of reaction may be predominant in such high sulfonic acid concentration in method B except for entries 16 and 18 where destabilization of the secondary carbenium ion by the nearby ether function can be presumed. On the other hand, an acid catalyzed S_N2 type of reaction may proceed in method A along with S_N1 type of reaction in such low concentration of sulfonic acid.

The terminal sulfonates **3** were easily oxidized with pyridinium chlorochromate (PPC) in dichloromethane to give the corresponding 1-arylsulfonyloxy-2-alkanones **5**, some of which showed the selective esterase inhibitory and hypolipidemic activities[4] (Table 3).

All melting points were recorded with a Yanagimoto micromelting point apparatus and are uncorrected. MS and ^{1}H-NMR spectral data were recorded on JEOL JMS-01G-2 and JEOL-FX 100 spectrometers, respectively.

1-Arylsulfonyloxy-2-alkanols 3 and 2-Arylsulfonyloxy-1-alkanols 4; General Procedure:

Method A: A solution of arenesulfonic acid **2** (62 mmol) in water (10 ml) is added dropwise with stirring to an ice-cooled mixture of the oxirane **1** (31 mmol) and tetra-*n*-butylammonium hydrogen sulfate (3 mmol) in dichloromethane (100 ml). After stirring for 1 h, the mixture is washed with water (50 ml), and the organic phase is dried with sodium sulfate. The residue obtained after removal of solvent is purified by column chromatography on silica gel (eluent, chloroform/ethanol, 20:1) to give a mixture of **3** and **4**. (Table 1).

Method B: A solution of the oxirane **1** (10 mmol) in dichloromethane (20 ml) is added dropwise with stirring to an ice-cooled solution of the

Table 1. Preparation of 1-Arylsulfonyloxy-2-alkanols **3** and 2-Arylsulfonyloxy-1-alkanols **4**

Entry No.	Starting Material		Method[a]	Product[b]		
	Oxirane **1**, R^1	Sulfonic acid **2**, R^2		Compound No.	Total Yield **3**+**4** (%)	Ratio[c] **3** : **4**
1	$CH_3(CH_2)_5-$	H	A	**3a**, **4a**	90	1 : 1
2			B		90	1 : 16
3	$CH_3(CH_2)_5-$	4-CH_3	A	**3b**, **4b**	93	7 : 6
4			B		94	1 : 10
5	$CH_3(CH_2)_7-$	H	A	**3c**, **4c**	98	3 : 2
6			B		81	1 : 20
7	$CH_3(CH_2)_7-$	4-CH_3	A	**3d**, **4d**	92	9 : 7
8			B		83	1 : 16
9	$CH_3(CH_2)_7-$	2,4,6-$(CH_3)_3$	A	**3e**, **4e**	88	1 : 1
10			B		67	1 : 8
11	$(CH_3)_2CHCH_2-$	4-CH_3	A	**3f**[5], **4f**	61	5 : 4
12			B		96	2 : 15
13	*c*-$C_6H_{11}-$	4-CH_3	A	**3g**, **4g**	92	2 : 1
14			B		80	1 : 7
15	$CH_3(CH_2)_3OCH_2-$	4-CH_3	A	**3h**, **4h**	80	8 : 1
16			B		43	1 : 1
17	$C_6H_5OCH_2-$	4-CH_3	A	**3i**, **4i**	93	15 : 1
18			B		56[d]	2 : 1

[a] See experimental for details.
[b] The product mixture was separated by column chromatography on silica gel.
[c] Determined by ^{1}H-NMR analysis.
[d] 1,2-Dihydroxy-3-phenyloxypropane was also obtained in 18% yield; m.p. 58–59°C (Lit.[6] m.p. 62–64°C).

Table 2. Physical Data of **3** and **4**

Product No.[a]	m.p. (°C)	Molecular Formula[b]	^{1}H-NMR ($CDCl_3$) δ (ppm)
3a	oil	$C_{14}H_{22}O_4S$ (286.4)	0.87 (t, 3H, J = 6.6 Hz); 1.00–1.60 (m, 10H); 2.14 (d, 1H, J = 5.4 Hz); 3.68–4.20 (m, 3H); 7.44–8.10 (m, 5H)
3b	oil	$C_{15}H_{24}O_4S$ (300.4)	0.87 (t, 3H, J = 6.8 Hz); 1.04–1.70 (m, 10H); 2.09 (d, 1H, J = 4.4 Hz); 2.46 (s, 3H); 3.60–4.20 (m, 3H); 7.34 (d, 2H, J = 8.3 Hz); 7.80 (d, 2H, J = 8.3 Hz)
3c	36–38	$C_{16}H_{26}O_4S$ (314.4)	0.88 (t, 3H, J = 6.2 Hz); 1.04–1.70 (m, 14H); 2.17 (d, 1H, J = 4.6 Hz); 3.70–4.20 (m, 3H); 7.40–8.00 (m, 5H)
3d	39–41	$C_{17}H_{28}O_4S$ (328.5)	0.88 (t, 3H, J = 6.4 Hz); 1.00–1.70 (m, 14H); 2.20 (d, 1H, J = 5.4 Hz); 2.46 (s, 3H); 3.80–4.20 (m, 3H); 7.36 (d, 2H, J = 8.6 Hz); 7.80 (d, 2H, J = 8.6 Hz)
3e	oil	$C_{19}H_{32}O_4S$ (356.5)	0.88 (s, 3H); 1.04–1.60 (m, 14H); 2.32 (s, 3H); 2.64 (s, 6H); 2.10 (d, 1H, J = 4.4 Hz); 3.70–4.10 (m, 3H); 6.98 (s, 2H)
3f[5]	oil	$C_{13}H_{20}O_4S$ (272.4)	0.86 (d, 3H, J = 6.6 Hz); 0.92 (d, 3H, J = 6.6 Hz); 1.10–1.94 (m, 3H); 2.10 (br, 1H); 2.45 (s, 3H); 3.80–4.20 (m, 3H); 7.34 (d, 2H, J = 8.5 Hz); 7.80 (d, 2H, J = 8.5 Hz)
3g	oil	$C_{15}H_{22}O_4S$ (298.4)	0.80–1.96 (m, 11H); 2.10 (d, 1H, J = 4.5 Hz); 2.46 (s, 3H); 3.40–3.70 (m, 1H); 3.90–4.20 (m, 2H); 7.35 (d, 2H, J = 8.5 Hz); 7.81 (d, 2H, J = 8.5 Hz)
3h	oil	$C_{14}H_{22}O_5S$ (302.4)	0.89 (t, 3H, J = 6.6 Hz); 1.08–1.70 (m, 4H); 2.45 (s, 3H); 2.47 (d, 1H, J = 6.4 Hz); 3.40 (t, 2H, J = 6.6 Hz); 3.40–3.50 (m, 3H); 4.00–4.18 (m, 2H); 7.34 (d, 2H, J = 8.3 Hz); 7.80 (d, 2H, J = 8.3 Hz)
3i	oil	$C_{15}H_{18}O_5S$ (310.4)	2.40 (s, 3H); 2.66 (d, 1H, J = 5.6 Hz); 2.90–3.08 (m, 2H); 3.08–3.34 (m, 3H); 6.72–7.40 (m, 5H); 7.28 (d, 2H, J = 8.5 Hz); 7.76 (d, 2H, J = 8.5 Hz)
4a	oil	$C_{14}H_{22}O_4S$ (286.4)	0.85 (t, 3H, J = 6.6 Hz); 1.00–1.80 (m, 10H); 2.10 (t, 1H, J = 5.5 Hz); 3.72 (d, 2H, J = 4.5 Hz); 4.50–4.80 (m, 1H); 7.40–8.10 (m, 5H)
4b	oil	$C_{15}H_{24}O_4S$ (300.4)	0.85 (t, 3H, J = 6.4 Hz); 1.00–1.80 (m, 10); 2.16 (t, 1H, J = 6.0 Hz); 2.46 (s, 3H); 3.70 (t, 2H, J = 6.0 Hz); 7.34 (d, 2H, J = 8.3 Hz); 7.80 (d, 2H, J = 8.3 Hz)
4c	oil	$C_{16}H_{26}O_4S$ (314.4)	0.88 (t, 3H, J = 6.2 Hz); 1.00–1.80 (m, 14H); 1.98 (s, 1H); 3.74 (d, 2H, J = 4.6 Hz); 4.50–4.80 (m, 1H); 7.40–8.10 (m, 5H)
4d	oil	$C_{17}H_{28}O_4S$ (328.5)	0.88 (t, 3H, J = 6.4 Hz); 1.00–1.90 (m, 14H); 2.32 (t, 1H, J = 5.4 Hz); 2.45 (s, 3H); 3.70 (t, 2H, J = 5.4 Hz); 4.44–4.70 (m, 1H); 7.34 (d, 2H, J = 8.3 Hz); 7.82 (d, 2H, J = 8.3 Hz)
4e	oil	$C_{19}H_{32}O_4S$ (356.5)	0.87 (t, 3H, J = 7.1 Hz); 1.04–1.80 (m, 14H); 2.18 (t, 1H, J = 6.3 Hz); 2.32 (s, 3H); 2.65 (s, 6H); 3.74 (d, 2H, J = 6.3 Hz); 4.40–4.70 (m, 1H); 6.99 (s, 2H)
4f	oil	$C_{13}H_{20}O_4S$ (272.4)	0.80 (t, 6H, J = 6.4 Hz); 1.20–1.80 (m, 3H); 2.12 (s, 1H); 2.46 (s, 3H); 3.64–3.80 (m, 2H); 4.52–4.80 (m, 1H); 7.34 (d, 2H, J = 8.5 Hz); 7.82 (d, 2H, J = 8.5 Hz)
4g	oil	$C_{15}H_{22}O_4S$ (298.4)	0.70–1.40 (m, 5H); 1.40–2.00 (m, 6H); 2.01 (s, 1H); 2.46 (s, 3H); 3.76 (d, 2H, J = 4.4 Hz); 4.30–4.58 (m, 1H); 7.34 (d, 2H, J = 8.5 Hz); 7.80 (d, 2H, J = 8.5 Hz)
4h	oil	$C_{14}H_{22}O_5S$ (302.4)	0.87 (t, 3H, J = 6.6 Hz); 1.00–1.64 (m, 4H); 2.30 (t, 1H, J = 6.4 Hz); 2.45 (s, 3H); 3.35 (t, 2H, J = 6.6 Hz); 3.57 (d, 2H, J = 6.4 Hz); 3.68–3.90 (m, 2H); 4.50–4.76 (m, 1H); 7.32 (d, 2H, J = 8.3 Hz); 7.82 (d, 2H, J = 8.3 Hz)
4i	105–107	$C_{15}H_{18}O_5S$ (310.4)	2.19 (t, 1H, J = 6.6 Hz); 2.43 (s, 3H); 3.80–4.00 (m, 2H); 4.10 (d, 2H, J = 6.6 Hz); 4.68–4.92 (m, 1H); 6.60–7.30 (m, 5H); 7.28 (d, 2H, J = 8.5 Hz); 7.80 (d, 2H, J = 8.5 Hz)

[a] The compounds **3** and **4** were separated by column chromatography on silica gel.

[b] Satisfactory microanalyses obtained: C ±0.39, H ±0.33.

Table 3. 1-Arylsulfonyloxy-2-alkanones **5** Prepared

Product No.[a]	R^1	R^2	Yield (%)	m.p. (°C)	Molecular Formula or Lit. m.p. (°C)	^{1}H-NMR ($CDCl_3$) δ (ppm)
5a	$CH_3(CH_2)_5-$	4-CH_3	79	oil	oil[2]	0.84 (t, 3H, J = 4.5 Hz); 0.70–1.85 (m, 8H); 2.38 (t, 2H, J = 7.0 Hz); 2.39 (s, 3H); 4.43 (s, 2H); 7.30 (d, 2H, J = 8.0 Hz); 7.76 (d, 2H, J = 8.0 Hz)
5b	$CH_3(CH_2)_7-$	4-CH_3	73	31–33	32–33[2]	0.85 (t, 3H, J = 5.0 Hz); 0.70–1.80 (m, 12H); 2.41 (t, 2H, J = 7.0 Hz); 2.43 (s, 3H); 4.43 (s, 2H); 7.26 (d, 2H, J = 8.0 Hz); 7.73 (d, 2H, J = 8.0 Hz)
5c	$CH_3(CH_2)_7-$	2,4,6-$(CH_3)_3$	76	35–36	36–37[2]	0.85 (t, 3H, J = 5.0 Hz); 0.70–1.79 (m, 12H); 2.29 (s, 3H); 2.45 (t, 2H, J = 7.0 Hz); 2.58 (s, 6H); 4.40 (s, 2H); 6.95 (s, 2H)
5d	c-C_6H_{11}	4-CH_3	50	oil	$C_{15}H_{20}O_4S$[b] (296.4)	0.76–2.10 (m, 10H); 2.26–2.76 (br, 1H); 2.43 (s, 3H); 4.40 (s, 2H); 7.30 (d, 2H, J = 8.0 Hz); 7.79 (d, 2H, J = 8.0 Hz)

[a] Purified by column chromatography on silica gel.

[b] calc. C 60.79 H 6.80
found 61.11 6.80

dry arylsulfonic acid **2**[3] (20 mmol) in dichloromethane (20 ml). After stirring for 0.5 h at the same temperature, the mixture is worked up as given under Method A.

1-Arylsulfonyloxy-2-alkanone (5); General Procedure:
A mixture of 1-arylsulfonyloxy-2-alkanol **3** (3 mmol) and pyridinium chlorochromate (1.4 mmol) in dichloromethane (15 ml) is stirred at room temperature for 24 h. The mixture is extracted with dichloromethane (2 × 20 ml), the organic phase is washed with water (10 ml) and dried with sodium sulfate. The residue obtained after removal of the solvent is chromatographed on a silica gel column (eluent, chloroform) (Table 3).

Received: 5 March 1986
(Revised form: 14 July 1986)

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(3) Commercially available arenesulfonic acids were azeotropically dehydrated using benzene followed by drying in a vacuum oven.
(4) Unpublished work.
(5) Optically active form (*S*-form) is known: Mori, K. *Tetrahedron* **1976**, *32*, 1101.
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