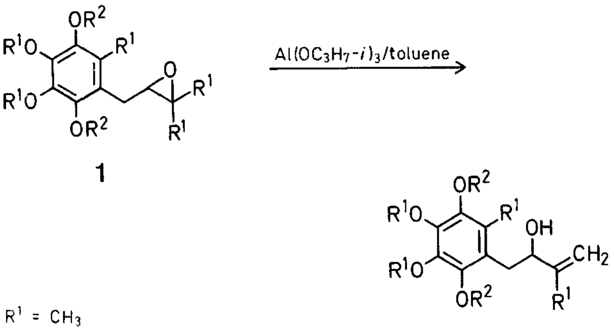
A Facile Synthesis of Allylic Alcohols

S. Terao*, M. Shiraishi, K. Kato

Chemical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd., 17-85, Jusohonmachi 2-Chome, Yodogawa-ku, Osaka 532, Japan

In connection with our interest in the synthetic chemistry of (poly)-prenylated compounds[1,2] we had occasion to prepare a series of allylic alcohols. A survey of the literature indicated that several methods[3-7] are available for the synthesis of allylic alcohols. However, it appears that these methods can be hardly adapted to large-scale production. We report a convenient synthetic route to allylic alcohols from epoxy compounds, applying a method made possible by the recent discovery of Eschinasi[8]. We have recently described that the epoxy compound **1** can be readily converted by reaction with aluminum isopropoxide in refluxing toluene into the allylic alcohol **2** in an excellent yield[2].



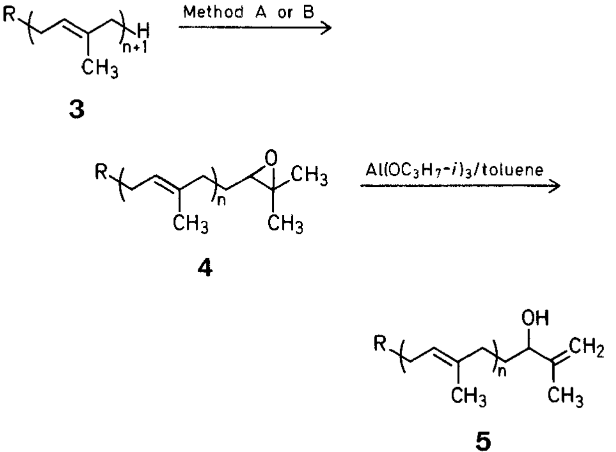
1

2

$R^1 = CH_3$

$R^2 = C_6H_5CH_2$

We have now extended the scope of this one-step reaction to the preparation of various types of allylic alcohols **5** according to Scheme **A**.



3

4

5

Scheme A

As shown in the Table, the isomerization of the epoxy compounds **4** proceeds readily in refluxing toluene in the presence of aluminum isopropoxide and affords the desired allylic alcohols **5** in good yields. The catalyst can be removed by acidification with hydrochloric acid. The products can be readily obtained by chromatography on silica gel. The allylic alcohols **5** obtained above are important intermediates for synthesis of polyprenyl alcohols, polyprenylated quinones, and other numerous naturally occurring (poly)-prenylated compounds. This method has been found to be superior to the known procedures[3-7] in terms of both convenience and efficiency. It has been proved by us that this method can be applied in the process of large-scale production of ubiquinone-10[2].

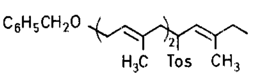
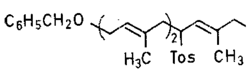
Epoxy Compounds 4; General Procedures:

Epoxy compounds **4** can be prepared either by Method A or B described below. Epoxy compound **4d** is preferably prepared by Method A. The yields and properties of the epoxy compounds **4a–e** are shown in the Table.

Method A: To a stirred solution of a (poly)-prenylated compound **3** (0.1 mol) in aqueous 1,2-dimethoxyethane (200 ml + 40 ml of water) is added *N*-bromosuccinimide (0.1–0.12 mol) portionwise at −4 to −7° over a period of 30 min. After the addition of the reagent, the reaction mixture is stirred for 1 h under the same conditions. Subsequently, the mixture is poured into water (300 ml), and the product extracted with ethyl acetate (500 ml). The organic layer is washed with water, dried (Na_2SO_4), and concentrated in vacuo. The residue is dissolved in methanol (100 ml) and the solution treated with potassium carbonate (14 g) for 2 h. The reaction mixture is concentrated in vacuo and the residue dissolved in diisopropyl ether (300 ml). The solution is

0039-7881/79/0632-0467 $ 03.00

Table. Epoxy Compounds **4** and Allylic Alcohols **5**

Product	R	n	Method	Yield[a] [%]	Molecular formula[b]	^{1}H-N.M.R. (90 MHz, $CDCl_3$/TMS) δ [ppm]
4a	$C_6H_5CH_2O$	0	A B	92 96	$C_{12}H_{16}O_2$ (192.3)	1.23 and 1.29 (s, 6H); 2.94 (t, 1H); 3.56 (oct, 2H); 4.53 (q, 2H); 7.27 (s, 5H)
4b	$C_6H_5CH_2O$	1	A B	93 87	$C_{17}H_{24}O_2$ (260.4)	1.24 and 1.26 (s, 6H); 1.65 (m, 2H); 1.66 (s, 3H); ~2.2 (t, 2H); 2.67 (t, 1H); 3.98 (d, 2H); 4.46 (s, 2H); 5.42 (t, 1H); 7.30 (s, 5H)
4c	4-H_3C—C_6H_4—SO_2	1	A B	86 94	$C_{17}H_{24}O_3S$ (308.5)	1.23 and 1.27 (s, 6H); 1.56 (t, 2H); 2.14 (t, 2H); 2.43 (s, 3H); 2.63 (t, 1H); 3.76 (d, 2H); 5.20 (t, 1H); 7.28 and 7.71 (q, 4H)
4d	$C_6H_5CH_2O$	8	A	38	$C_{52}H_{80}O_2$ (737.2)	1.23 and 1.27 (s, 6H); 1.58 (s, 21H); 1.64 (s, 3H); ~2.0 (m, 32H); 2.66 (t, 1H); 3.98 (d, 2H); 4.47 (s, 2H); 5.0–5.2 (m, 7H); 5.37 (t, 1H); 7.28 (s, 5H)
4e		0	A B	83 86	$C_{34}H_{46}O_4S$ (550.8)	1.23 and 1.27 (s, 6H); 1.50 and 1.59 (s, 6H); 2.40 (s, 3H); 2.60 (t, 1H); 2.21 and 2.82 (m, 2H); 3.83 (sextet, 1H); 3.72 (d, 2H); 4.46 (s, 2H); 4.90 (m, 1H); 5.10 and 5.33 (t, 2H); 7.29 (s, 5H); 7.25 and 7.67 (q, 4H)
5a	$C_6H_5CH_2O$	0	—	99	$C_{12}H_{16}O_2$ (192.3)	1.71 (s, 3H); 3.36 and 3.55 (oct, 2H); 4.24 (q, 1H); 4.54 (s, 2H); 4.88 and 5.01 (m, 2H); 7.29 (s, 5H)
5b	$C_6H_5CH_2O$	1	—	93	$C_{17}H_{24}O_2$ (260.4)	1.64 (s, 3H); 1.72 (s, 3H); ~1.70 (m, 2H); ~2.1 (m, 2H); 3.98 (m+d, 3H); 4.46 (s, 2H); 4.80 and 4.90 (m, 2H); 5.40 (t, 1H); 7.30 (s, 5H)
5c	4-H_3C—C_6H_4—SO_2	1	—	94	$C_{17}H_{24}O_3S$ (308.5)	1.35 (s, 3H); 1.69 (s, 3H); 1.5–2.2 (m, 4H); 2.42 (s, 3H); 3.75 (d, 2H); 3.95 (t, 1H); 4.80 and 4.90 (m. 2H); 5.18 (t, 1H); 7.28 and 7.71 (q, 4H)
5d	$C_6H_5CH_2O$	8	—	74	$C_{52}H_{80}O_2$ (737.2)	1.58 (s, 21H); 1.64 (s, 3H); 1.71 (s, 3H); ~2.0 (m. 32H); ~4.0 (m+d, 3H); 4.47 (s, 2H); 4.80 and 4.90 (m, 2H); 5.0–5.2 (m, 7H); 5.37 (t, 1H); 7.28 (s, 5H)
5e		0	—	97	$C_{34}H_{46}O_4S$ (550.8)	1.23, 1.50, 1.58, and 1.67 (s, 12H); ~2.0 (m, 5H); 2.40 (s, 3H); 2.22 and 2.82 (q, 2H); 3.7–4.1 (m+d+t, 3H); 4.46 (s, 2H); 4.80 and 4.90 (m, 2H); 4.89 (d, 1H); 5.10 and 5.33 (t, 2H); 7.29 (s, 5H); 7.25 and 7.68 (q, 4H)

[a] Yields determined after chromatography on silica gel.

[b] All products gave satisfactory microanalyses (C ±0.2%; H ±0.2%).

washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue is chromatographed on silica gel using an eluent system of hexane and diisopropyl ether to give the desired epoxy compound **4**.

Method B: To a solution of a (poly)-prenylated compound **3** (0.1 mol) and sodium acetate (8 g) in dichloromethane (200 ml) is added 40% peracetic acid (20 g) at −10°. The reaction temperature is maintained below 0° during the reaction. After the reaction is completed, the reaction mixture is treated with aqueous sodium hydrogen carbonate, washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue is purified by distillation and/or by chromatography on silica gel to yield the desired epoxy compound **4**.

Allylic Alcohols 5; General Procedure:

A mixture of the epoxy compound **4** (30 mmol) and aluminum isopropoxide (30 mmol) in toluene (50 ml) is heated under reflux for 6 to 20 h. After cooling to room temperature, the reaction mixture is treated with 2 normal hydrochloric acid (50 ml) to decompose the aluminum complex. The organic layer is separated, washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue is chromatographed on silica gel using an eluent system of hexane and diisopropyl ether to give the desired allylic alcohol **5**. The yields and properties of the allylic alcohols **5a–e** are shown in the Table.

Received: January 17, 1979

---

[1] S. Terao, K. Kato, M. Shiraishi, H. Morimoto, *J. Chem. Soc. Perkin Trans. 1* **1978**, 1101.

[2] S. Terao, K. Kato, M. Shiraishi, H. Morimoto, *J. Org. Chem.*, **44**, 868 (1979).

[3] R. W. Denny, A. Nickon, *Org. React.* **20**, 133 (1973).

[4] J. F. Crandall, L.-Ho Chang, *J. Org. Chem.* **32**, 435 (1967).

[5] A. Yasuda, S. Tanaka, K. Oshima, H. Yamamoto, H. Nozaki, *J. Am. Chem. Soc* **96**, 6513 (1974).

[6] T. Inoue, T. Uchimaru, T. Mukaiyama, *Chem. Lett.* **1977**, 1215.

[7] K. Hayakawa, H. Schmid, *Helv. Chim. Acta* **60**, 1942 (1977).

[8] E. H. Eschinasi, *J. Org. Chem.* **35**, 1598 (1970).