Regiospecific Ene Reaction of Benzenesulfinyl Chloride with Linear Isoprenoids

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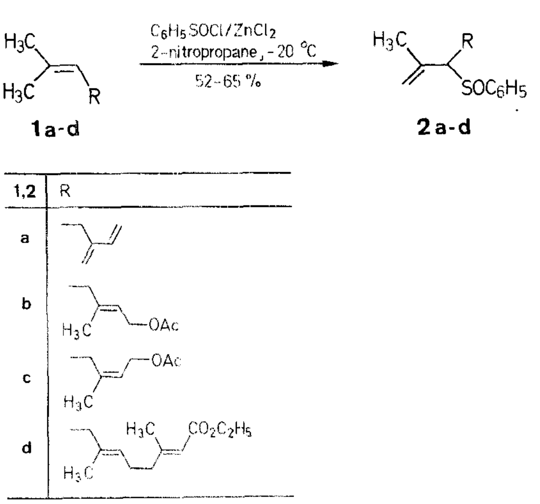
The Lewis acid (e.g., ZnCl$_2$) catalyzed ene reaction of benzenesulfinyl chloride with myrcene, geranyl and neryl acetates, as well as ethyl (*E,E*)-farnesoate proceeds smoothly and chemoselectively by exclusive attack at the terminal trisubstituted C=C bond to give allylic sulfoxides.

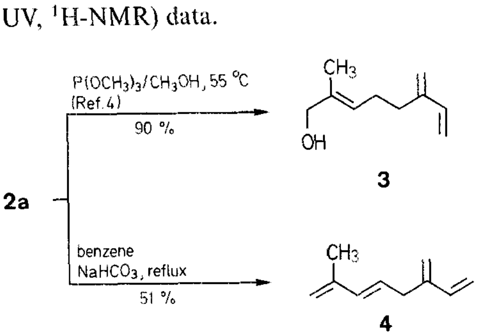
Among the few methods known for the terminal functionalization of linear isoprenoid polyolefins, the most selective are the interaction of these compounds with *N*-bromosuccinimide[1] or selenium dioxide.[2] Here we propose a novel approach based on our recent findings on the Lewis acid-catalyzed ene reaction of isoprene with benzenesulfinyl chloride.[3] Extension of this reaction to the mono- and sesquiterpene oligoolefins **1** revealed that under similar conditions these compounds are converted with excellent selectivity into the respective terminal allylic sulfoxides **2**.

Thus, the treatment of compounds **1a–d** with a slight excess of benzenesulfinyl chloride and zinc chloride in 2-nitropropane at −20 °C leads to sulfoxides **2a–d** in 52–65 % yield. Fairly stable compounds **2** were isolated by flash-column chromatography on silica gel as an oily mixture of diastereoisomers; their structure was established by microanalysis and spectral data (Table). ^{1}H-NMR analysis of the crude reaction mixtures indicated the complete absence of other sulfinylation products in all cases.

Among the compounds prepared, the sulfoxides **2a–c** have been obtained earlier,[4] without full characterization, in three steps starting from addition products of benzensulfenyl chloride with olefins **1a, b, c**; the reaction proved to be of good regioselectivity with monoterpene substrates but it was found to be rather unselective with higher terpenoids.[5] In this connection, it is noteworthy that the described terminal ene sulfinylation of the sesquiterpene ester **1d** is as effective as that of geranyl (**1b**) and neryl (**1c**) acetates.



The most obvious application of the sulfoxides **2** involve their conversion into terminal allylic alcohols or into 1,3-dienes *via* sulfoxide-sulfenate rearrangement or thermolysis, respectively, as illustrated here for the myrcene derivative **2a**. Thus, treatment of the latter with trimethyl phosphite in methanol affords almost quantitatively the alcohol **3** which was has earlier been prepared from myrcene (**1a**) in the same overall yield (~ 47 %) but *via* a four-step sequence.[4] For comparison, the direct oxidation of **1a** with selenium dioxide produces the alcohol **3** with less than 20 % yield.[6] Heating of **2a** in boiling benzene in the presence of sodium hydrogen carbonate leads smoothly to the known[7] (*E*)-tetraene **4** the structure of which was confirmed by spectral (IR, UV, ^{1}H-NMR) data.



3-Phenylsulfinyl-2-methyl-6-methylene-1,7-octadiene (2a); Typical Procedure:

To a vigorously stirred solution of myrcene (**1a**; 0.84 g, 6.16 mmol) and benzenesulfinyl chloride[8] (1.17 g, 7.28 mmol) in 2-nitropropane (5 mL) under argon, zinc chloride (1.00 g, 7.34 mmol) is added at −20 °C. The resulting suspension is stirred at −20 °C for 1.5 h, then quenched at −50 °C with a solution of pyridine (1.19 g, 15 mmol) in Et$_2$O (7 mL) and diluted at 0 °C with Et$_2$O (60 mL) followed by H$_2$O (20 mL). The aqueous phase is separated and extracted with Et$_2$O (2 × 30 mL) and the combined organic layers are washed with H$_2$O (20 mL) and dried (MgSO$_4$). The solvent is removed *in vacuo*, and the residue (1.63 g) is chromatographed on silica gel (60 g) using gradient elution from hexane to hexane/Et$_2$O (1 : 1) to give **2a** as a colorless oil (Table); yield: 0.83 g (52 %).

2-Methyl-6-methylene-2(*E*),7-octadieneol (3):

A solution of sulfoxide **2a** (0.23 g, 0.88 mmol) and trimethyl phosphite (0.2 g, 1.61 mmol) in MeOH (2 mL) is heated at 55 °C for 1.5 h. After removal of the solvent *in vacuo*, the residue (0.25 g) is chromatographed on silica gel (10 g) using gradient elution from hexane to hexane/Et$_2$O (7 : 3) to give **3** as a colorless liquid; yield: 0.12 g (90 %); b. p. 59–60 °C/1 Torr (Lit.[6], b. p. 53 °C/0.02 Torr); n_D^{20}: 1.4958; ^{1}H-NMR values in agreement with Lit.[4]).

2-Methyl-6-methylene-1,3(*E*),7-octatriene (4):

A suspension of **2a** (0.73 g, 2.8 mmol) and NaHCO$_3$ (0.5 g) in benzene (5 mL) is refluxed with stirring under argon for 5 h. The mixture is transferred to a chromatography column with silica gel (30 g), and the

Table. Unsaturated Sulfoxides **2** Prepared

Product	Yield (%)	R_f Value[a]	Molecular Formula[b]	IR ($CHCl_3$) ν (cm^{-1})	^1H-NMR ($CDCl_3$/TMS) δ, J (Hz)
2a	52	0.60	$C_{16}H_{20}OS$ (260.4)	3090, 3070, 3010, 2950, 2880, 1640, 1600, 1480, 1445, 1380, 1330, 1310, 1240, 1150, 1090, 1070, 1040, 1000, 910	1.56, 1.64 (br. s, 3H, CH_3); 1.7–2.4 (m, 4H, CH_2); 3.1 (m, 1H, H-3); 4.6–5.2 (m, 6H, $H_2C{=}C$); 6.29 (dd, J = 11.0, 18.0, 1H, H-7); 7.5 (m, 5H, C_6H_5)
2b	61	0.34	$C_{18}H_{24}O_3S$ (320.5)	3080, 2990, 2940, 2860, 1735, 1670, 1645, 1485, 1480, 1445, 1380, 1365, 1330, 1270, 1085, 1040, 1000, 955, 910	1.50, 1.56, 1.59 (br. s, 6H, CH_3); 1.8–2.2 (m, 4H, CH_2); 1.95 (s, 3H, CH_3CO); 2.9–3.0 (m, 1H, H-3); 4.49 (br. d, J = 8, 2H, H-8); 4.61, 4.70, 4.97 (br. s, 2H, H-1); 5.25 (br. t, J = 8, 1H, H-7); 7.5 (m, 5H, C_6H_5)
2c	62	0.36	$C_{18}H_{24}O_3S$ (320.5)	3080, 3000, 2940, 2870, 1730, 1670, 1640, 1585, 1445, 1380, 1370, 1305, 1265, 1180, 1090, 1070, 1030, 1000, 960, 910	1.55, 1.67 (br. s, 6H, CH_3); 2.0 (s, 3H, CH_3CO); 2.1 (m, 4H, CH_2); 3.0–3.2 (m, 1H, H-3); 4.45 (br. d, J = 7, 2H, H-8); 4.65, 4.75, 5.04 (br. s, 2H, H-1); 5.35 (m, 1H, H-7); 7.5 (m, 5H, C_6H_5)
2d	65	0.57	$C_{23}H_{32}O_3S$ (388.6)	3080, 2990, 2940, 2845, 1705, 1645, 1585, 1480, 1445, 1380, 1350, 1325, 1285, 1260, 1140, 1090, 1040, 1000, 910, 870	1.25 (t, J = 7, 3H, $C\underline{H}_3CH_2$); 1.49, 1.54, 1.63 (br. s, 6H, CH_3); 1.8–2.2 (m, 8H, CH_2); 2.13 (br. s, 3H, $CH_3{-}C^3$); 3.0–3.2 (m, 1H, H-10); 4.13 (q, J = 7, 2H, CH_2O); 4.65, 4.73, 5.01 (br. s, 2H, H-12); 5.0 (m, 1H, H-6); 5.63 (s, 1H, H-2); 7.5 (m, 5H, C_6H_5)

[a] Determined using "Silufol UV-254" plates with a bound layer of silica gel (Kavalier, Czechoslovakia); ether/hexane (4:1).

[b] Satisfactory microanalyses obtained: C ±0.47, H ±0.20, S ±0.39.

product eluted with pentane. The elutant is concentrated under reduced pressure and the residue (0.3 g) is distilled in the presence of hydroquinone (5 mg) to give **4** as a colorless liquid of 98% purity (GLC, ^1H-NMR); yield: 0.19 g (51%); b.p. 62–63°C/15 Torr (Lit.[7], b.p. 54°C/9 Torr); n_D^{20}: 1.5043.

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