Pergamon

Tetrahedron Letters, Vol. 38, No. 40, pp. 7107-7110, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01632-8

Free Radical Phenylthio Group Transfer to Nonactivated δ-Carbon Atom in the Photolysis Reactions of Alkyl Benzenesulfenates

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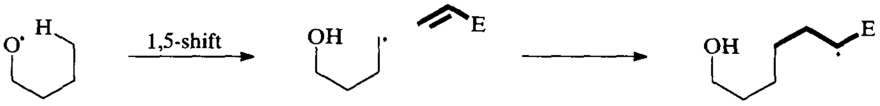
Abstract: A free radical phenylthio group transfer from oxygen to the non-activated δ-carbon atom was achieved by irradiation of alkyl benzenesulfenates **1** in the presence of hexabutylditin, and δ-phenylthio alcohols **2** were obtained in 35-91% yields. However, when reactions were performed in the presence of activated olefins an alkylation of δ-carbon occured and phenylthio ethers of type **3** were obtained in modest yields.

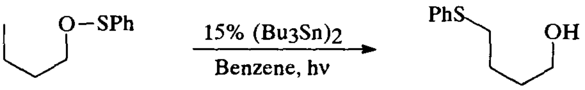
A free radical intramolecular functionalization of remote non-activated carbon atoms is of great synthetic importance. The nature of introduced functional group depends on the alkoxy radical precursors and reagents used.[1] In some of these reactions δ-carbon radicals, generated by 1,5-transposition of radical center, were intercepted by ligand or electron transfer oxidants,[2] intramolecular addition reactions[3] and carbon monoxide.[4]

Recently we found that δ-carbon radicals, arised by 1,5-hydrogen migration to alkoxy radicals, were intercepted by radicophilic olefins and thus Michael type alkylation of the remote non-activated carbon atoms took place (Scheme 1.).[5] δ-Alkylation was accomplished by photolysis of alkyl nitrites or alkyl benzenesulfenates with tributyltin hydride (TBTH), both in the presence of excess of electron deficient olefins. When 10 molar excess of olefinic compounds was used δ-alkyl radicals, generated by TBTH reduction of alkyl benzenesulfenates, rather underwent intermolecular addition ($k_{add} = 3 \times 10^5$ $M^{-1}s^{-1}$) than hydrogen transfer from TBTH ($k_H = 2 \times 10^6$ $M^{-1}s^{-1}$).[6]



Scheme 1.

We now investigated the reaction of δ-carbon radicals, generated by 1,5-hydrogen shift in alkoxy radicals, when alkyl benzenesulfenates **1** were used as precursors of alkoxy radicals[7] and hexabutylditin as a catalytic reagent. Herein we report *a free radical phenylthio group transfer from oxygen to non-activated δ-carbon atom of alkyl benzenesulfenates* (Scheme 2.).

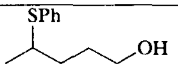
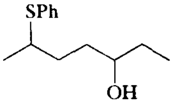
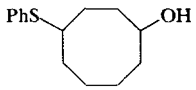
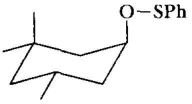
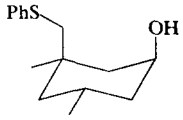
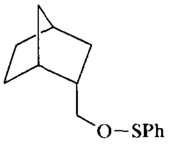
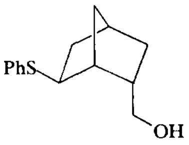
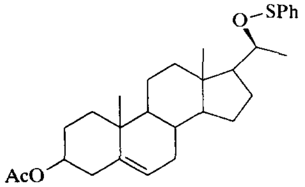
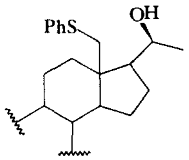
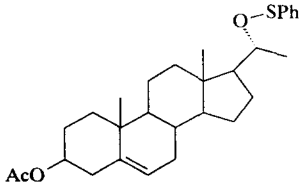
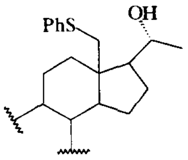


1 **2**

Scheme 2.

The reactions of alkyl benzenesulfenates **1** were carried out in benzene solutions, in the presence of 15 mol% of hexabutylditin under irradiation conditions at r.t., and δ-phenylthio alcohols **2** were obtained in good yields.[8] The results are summarized in Table 1. This free radical mediated transposition of phenylthio group was successfully applied on the primary and secondary alkyl benzenesulfenates possessing a flexible and/or fixed both of the reactive centers.

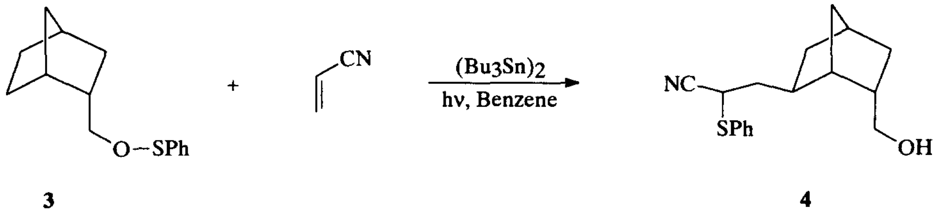
Table 1. Phenylthio group transfer in the reaction of alkyl benzensulfenates catalyzed by hexabutylditin

	Alkyl Benzenesulfenates[a]	δ-Phenylthio alcohols	Yields[b] (%)
a)	1-Pentyl		80
b)	3-Heptyl		91
c)	Cyclooctyl		35[c]
d)			60
e)			65[d]
f)			40
g)			40

a) Prepared according to procedure discribed in refs. 7
b) Isolated yields.
c) Yield by GC analysis was 55%.
d) The isomer with *exo*-phenylthio group was obtained.

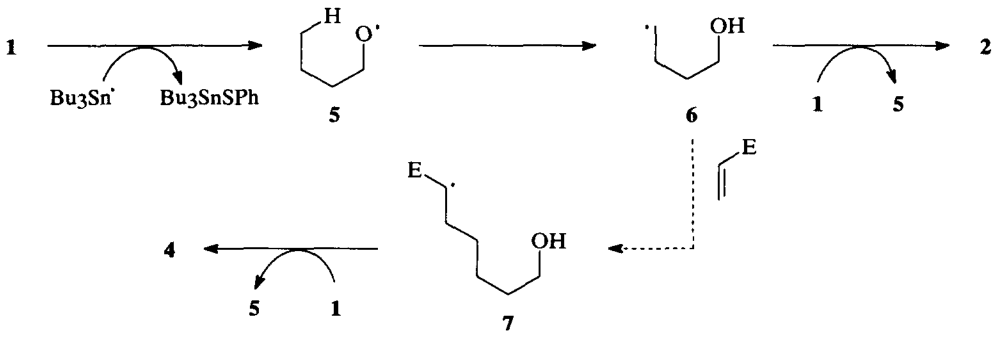
When the reactions of alkyl benzenesulfenates, e.g. **3**, with hexabutylditin were performed in the presence of radicophilic olefins such as acrylonitrile an alkylated product **4**, possessing a phenylthio group adjacent to the electron withdrawing group, was obtained in modest yield (21%)

(Scheme 3.).[5,6] Under the same conditions pentyl benzenesulfenate afforded 2-phenylthio-4-methyl-7-hydroxyheptanenitrile in 24% yield.[9]



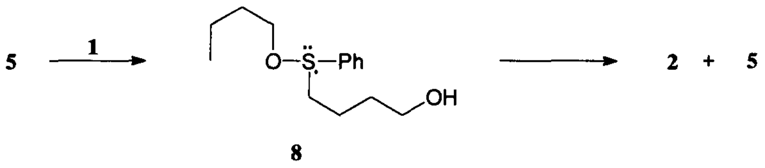
Scheme 3.

This free radical phenylthio group transfer essentially represent a simple interchange of positions of hydrogen and phenylthio group. The sequence of radical reactions is initiated by tributyltin radical and is based on its thiophilic addition to sulfur functional group of **1**. Thus formed alkoxy radical **5**, upon intramolecular 1,5-hydrogen migration, gives δ-carbon radical **6** (Scheme 4.).



Scheme 4.

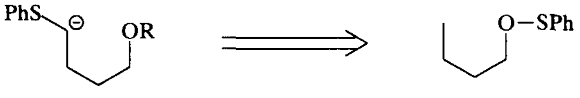
In the absence of any other reactive species the carbon radical **6** undergoes radical substitution at sulfur, in alkyl benzenesulfenate **1**, involving a synchronous C-S bond formation and S-O bond fission, thus generating the alkoxy radical **5**, as a transient radical which continues the chain radical reaction, and affording δ-phenylthio alcohol **2** as a final product.[10] We believe that the intermolecular homolytic phenylthio group transfer involves the intermediary sulfuranyl radical **8** (Scheme 5.).[11]



Scheme 5.

When this reaction was performed in the presence of radicophilic olefins (1.5 molar excess) intermolecular addition of δ-carbon radical **6** took place, thus producing carbon radical **7** (Scheme 4.). Although radical **7** is electrophilic partly it also abstracts a phenylthio group from the starting compound **1** thus affording the δ-alkylated products **4**, possessing a phenylthio group adjacent to the electron withdrawing group. When large excess of radicophilic olefins were used an oligomeric compounds were obtained, because the rates of intermolecular addition and phenylthio group transfer are similar and, with higher concentration of olefins, an oligomerization takes place rather than a phenylthio group transfer.

Introduction of phenylthio group onto the non-activated δ-carbon atom of alcohols could be of synthetic importance, because by deprotonation of phenylthio ethers by strong base the corresponding δ-carbanion could be formed (Scheme 6.)



Scheme 6.

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8. *Representative experimental procedure:* A solution of 3-heptyl benzenesulfenate (0.11 g; 0.5 mmol) in benzene (2 ml) and hexabutylditin (0.04 g; 0.07 mmol) was irradiated at r.t., in an argon atmosphere, by 125 W high-pressure mercury lamp for 15 min. The solvent was evaporated and the reaction products were separated by chromatography on silica gel (petrolether/acetone 9 : 1) and 0.10 g (91% yield) of 2-phenylthio-5-heptanol, as a mixture of diastereoisomers, was obtained. IR (film): 3413, 3075, 2000-1724, 1585, 759, 668 cm^{-1}.
   ^{1}H-NMR (200 MHz, $CDCl_3$), δ: 0.93 (t, 3H, J = 7.40 Hz), 1.30 (d, 3H, J = 6.60 Hz), 1.40=1.60 (m, 6H), 3.24 (m, 1H), 3.50 (m, 1H), 7.20 -7.35 (m, 3H), 7.36-7.46 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$), δ: 135.17, 131.10, 128.78, 126.66, 73.04 (and 72.95), 43.40 (and 43.29), 34.16 (and 33.91), 32.65 (and 32.43), 30.15 (and 30.07), 21.16, 9.77.
9. *Experimental procedure:* Same as in reference 8, in the presence of 2 mol eq of acrylonitrile. 2-Phenylthio-4-methyl-7-hydroxyheptanenitrile (as a mixture of diastereoisoimers) was isolated in 24% yield (by GC analysis 35% yield). IR (film): 3399, 2237, 751, 629 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$), δ: 0.96 (d, 3H, J = 6.20 Hz), 1.16-1.94 (m, 7H), 3.64 (t, 2H, J = 6.20 Hz), 3.68-3.80 (m, 1H) 7.36-7.43 (m, 3H), 7.48-7.63 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$), δ: 134.67, 129.58, 129.47, 62.84, 39.41 (and 39.19), 35.25 (and 35.16), 32.65 (and 31.92), 30.83 (and 30.39) 29.73 (and 29.63), 19.09 (and 18.76).
10. Comparable results were obtained when irradiation of alkyl benzenesulfenates were carried out without hexabutylditin, indicating that its presence is not essential for the reaction; However, the presence of 15 mol% of hexabutylditin in the reaction mixture shortens the reaction times and improves the yields.
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(*Received in UK* 8 *July* 1997; *revised* 4 *August* 1997; *accepted* 8 *August* 1997)