Samarium(II) iodide-mediated deoxygenative debromination of α-bromo-β-hydroxy (acetoxy) phenyl sulfones: synthesis of α,β-unsaturated sulfones

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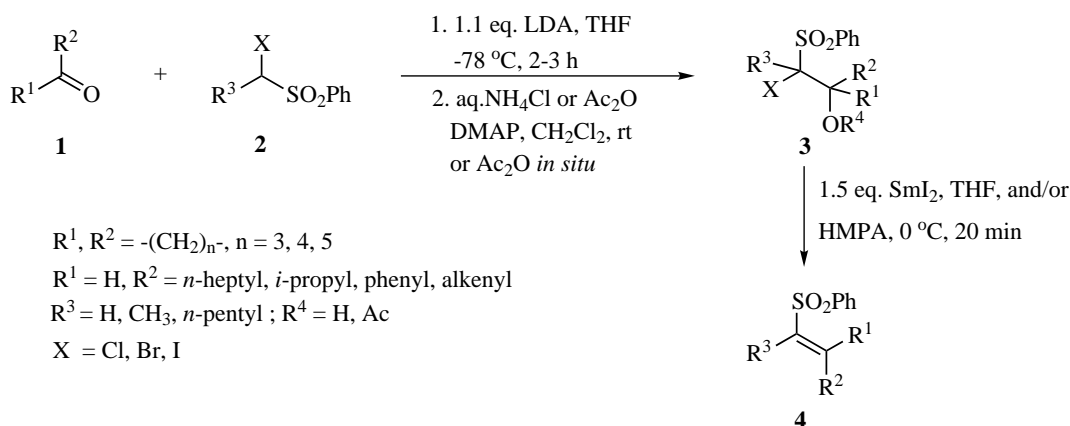
Abstract—Deoxygenative debromination of α-bromo-β-hydroxy (acetoxy) phenyl sulfones with samarium(II) iodide led to substituted α,β-unsaturated sulfones in good to excellent yields. The *E*-isomer is the major product. A possible mechanism via an α-sulfonyl radical pathway is proposed. © 2002 Elsevier Science Ltd. All rights reserved.

The reductive elimination reaction of β-oxygen substituted sulfones to olefins, known as the Julia–Lythgoe olefination, has been recognized as a very useful synthetic transformation and is commonly effected using sodium amalgam.[1] Recent modification of the reaction employing SmI_2–THF as the reducing agent has extended the scope of this reaction considerably.[2] As part of our continuing investigation on the utilization of the α-halomethyl phenyl sulfones as one-carbon building blocks,[3] we wish to report our studies on the deoxygenative debromination of α-bromo-β-hydroxy (acetoxy) phenyl sulfones with SmI_2–THF with or without HMPA leading to substituted α,β-unsaturated sulfones in good to excellent yields.[4,5] These results provide mechanistic insight and represent the first report[6] on the utilization of α-halomethyl phenyl sulfones for the synthesis of α,β-unsaturated sulfones (Scheme 1).

The α-haloalkyl-β-hydroxy (acetoxy) phenyl sulfone adducts **3** were prepared, in a straightforward manner, by the reaction of the aldehydes and ketones **1** with α-haloalkyl phenyl sulfones **2** employing LDA as the base. The yields of the corresponding β-hydroxysulfone

$R^1, R^2 = -(CH_2)_n-$, n = 3, 4, 5
$R^1 = H$, $R^2 = $ *n*-heptyl, *i*-propyl, phenyl, alkenyl
$R^3 = H$, CH_3, *n*-pentyl ; $R^4 = H$, Ac
$X = Cl$, Br, I

Scheme 1.

derivatives **3** (R^4=H) were in the range 64–84%. The corresponding β-acetoxysulfone derivatives **3** (R^4=Ac) were prepared by acetylation of the hydroxy derivatives under standard conditions. In the cases where R^3=CH$_3$ and *n*-pentyl, the β-acetoxysulfone derivatives could be prepared by in situ quenching of the incipient alkoxide adducts of compounds **1** and **2** with acetic anhydride. The yields of compound **3** (R^4=Ac) were in the range 50–98%. The key deoxygenative dehalogenation reaction was carried out using 1.5 equivalents of SmI$_2$ in THF with or without HMPA. Initial studies to find suitable halogen substituents, were carried out with the adducts **3** (X=Cl, Br, I); (R^1=R^2=-(CH$_2$)$_2$-; R^3=H; R^4=Ac). It was found that when X=Cl, the deoxy-

genative dechlorination was incomplete giving the corresponding vinyl sulfone in only 18% yield together with 64% recovery of the starting material. When X=I and Br, the deoxygenative dehalogenation gave the corresponding vinyl sulfone in a comparable yield (79%). Due to the fact that the bromo derivatives **3** (X=Br) are much easier to prepare and to handle, it was decided to use the bromosulfonyl derivatives **3** (X=Br) in the subsequent investigations. The results are summarized in Table 1.[7]

The results indicated that the deoxygenative debromination of the adducts **3** (R^4=Ac) gave higher yields of the α,β-unsaturated sulfones than the hydroxy deriva-

Table 1. Deoxygenative debromination of **3** with 1.5 equiv. SmI$_2$/THF/0°C/20 min with and without HMPA

Entry	Adduct 3 R^1, R^2 ; R^3 = H [*syn : anti* ratio][a]	R^4	Product 4, % yield (with HMPA) [*E : Z* ratio][a] R^3 = H	R^3 = CH$_3$	R^3 = *n*-C$_5$H$_{11}$
1	-(CH$_2$)$_3$-	H	52(56)	77(37)	82(82)
		Ac	79(79)	91(63)	93(89)
2	-(CH$_2$)$_4$-	H	83(66)	69(45)	88(75)
		Ac	88(79)	87(76)	-[b]
3	-(CH$_2$)$_5$-	H	72(63)	80(74)	-[b]
		Ac	90(86)	-[b]	-[b]
4	H, (CH$_3$)$_2$CH–[e]	H [46 : 54]	55(46) [86:14]	60(59) [86:14]	83(77) [75:25]
		Ac [41 : 59]	94(85) [96:4]	92(88) [96:4]	83(62) [87:13]
5	H, *n*-C$_7$H$_{15}$–[e]	H [35 : 65]	64(35) [87:13]	79(73) [86:14]	87(54) [60:40]
		Ac [36 : 64]	82(55) [92:8]	89(53) [96:4]	92(54) [87:13]
6	H, C$_6$H$_5$–[e]	H [39 : 61]	40(44) [97:3]	53(37) [90:10]	80(62) [69:31]
		Ac [-][c]	-[b]	50(32) [98:2]	80(62) [96:4]
7	H, CH$_3$CH=CH–[e]	H [30 : 70]	51(37)[d]	96(92)[d]	92(62)[d]
		Ac [26 : 74]	93[d](-)[f]	73(55)[d]	62(64)[d]
8	H, (CH$_3$)$_2$C=CH(CH$_2$)$_2$C(CH$_3$)=CH–[e]	H [48 : 59]	40(29) [90:10]	45(47) [82:18]	40(45) [57:43]
		Ac [48 : 59]	98(32) [93:7]	83(67) [95:5]	80(64) [93:7]

[a] The ratios were determined by ^{1}H-NMR (300 MHz). In the cases of product **4**, the *E:Z* ratio given was from the reaction without the addition of HMPA. The presence of HMPA gave the comparable *E:Z* ratio.
[b] The adduct **3** could not be prepared.
[c] Attempted acetylation of these compounds gave the eliminated product.
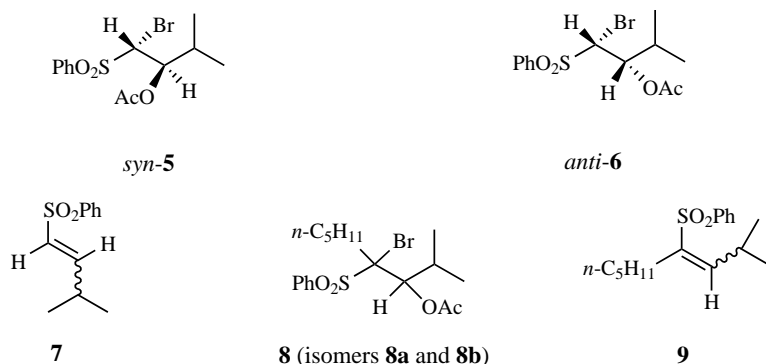[d] The product was unstable and did not permit the full characterization. The TLC of the product showed a single spot and ^{1}H-NMR data agreed with the assigned structure.
[e] The adduct **3** used is a mixture of diastereomers.
[f] The reaction gave a complex mixture and no product **4** could be isolated.

Scheme 2.

syn-**5**   *anti*-**6**

7   **8** (isomers **8a** and **8b**)   **9**
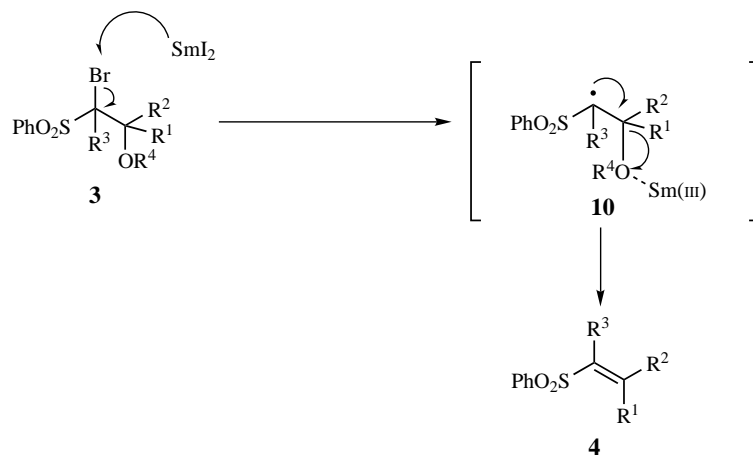
tives $R^4 = H$; except in entry 7. The addition of HMPA led to the lowering of the yields of products **4**. For the aldehyde entries 4, 5, 6 and 8, the product vinyl sulfones **4**, $R^3 = H$ and CH_3 showed high *E*-selectivity. When $R^3 = n\text{-}C_5H_{11}$, the product α,β-unsaturated sulfones **4** exhibit moderate to high *E*-selectivity.

The deoxygenative debromination of the diastereomers *syn*-**5** ($J = 1.6$ Hz) and the *anti*-**6** ($J = 7.6$ Hz) and the pair of diastereomers of **8** (isomers **8a** and **8b**) gave insight into the mechanism of the reaction.[8]

The reactions of *syn*-**5** and *anti*-**6** with SmI_2–THF gave the vinyl sulfone **7** (entry 4, $R^3 = H$) in 88% ($E:Z = 94:6$) and 96% ($E:Z = 96:4$) yields, respectively, with high *E*-selectivity. The deoxygenative debromination of isomers **8a** and **8b** under the same conditions gave the corresponding α,β-unsaturated sulfone **9** in 87% ($E:Z = 87:13$) and 84% ($E:Z = 82:18$) yields, respectively. With the currently accepted radical mechanism for the dehalogenation by SmI_2[9] and in view of the fact that only a slight excess of SmI_2 was used in the reaction, a radical mechanistic pathway can be proposed as shown in Scheme 2. The proposed radical intermediate **10** undergoes free radical elimination to give the thermodynamically more stable product.

In summary, our studies have provided preliminary mechanistic insight and illustrated the synthetic potential of the samarium-mediated deoxygenative debromination

for the synthesis of α,β-unsaturated sulfones and particularly sulfonyl substituted 1,3-dienes.[4d] Further investigation into the scope of the reaction is in progress.

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