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Alkene synthesis: elimination of arenesulfinic acid from alkyl aryl sulfones using potassium trimethylsilanolate as base

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Abstract—The use of potassium trimethylsilanolate as base to induce elimination of potassium arenesulfinate from alkyl aryl sulfones to produce *E*-alkenes is described. The reaction was appropriate for substrates containing a benzyl or allyl group α to the sulfone residue.

Lithium, sodium and potassium trimethylsilanolates are stable solids, which are commercially available either as solids or in solution, and are recognized as hydroxide anion equivalents soluble in organic solvents. Despite this unique property, there are relatively few reports describing their use. The most frequently encountered application of potassium trimethylsilanolate is in the preparation of anhydrous carboxylate salts from esters and acid chlorides introduced by Laganis and Chenard in 1984.[1] This procedure has recently found application in the racemization-free hydrolysis of the base sensitive α-hydroxy amido acid BMS-270394[2] and the hydrolysis of delicate dienoate esters.[3] The use of trimethylsilanolates has been extended to the conversion of *N*-(trifluoromethylsulfonyl)trifluoromethanesulfinimidoyl chlorides to the corresponding moisture sensitive sulfinimidic acid salts,[4] and to the displacement of fluoride from activated aromatic rings to produce phenols by nucleophilic aromatic substitution.[5] Another application of potassium trimethylsilanolate, reported by one of us, involves the diastereoselective nucleophilic Michael-type addition to 1-(phenylthio)-1-nitroalkenes, which on ozonolysis of the intermediate nitronate produced the corresponding α-hydroxy thioester in excellent yield.[6] Other functional group manipulations involve the conversion of nitriles to primary amides reported by Merchant,[7] and the cleavage, under mild conditions, of oxazolidinones and benzyloxycarbonyl protecting groups reported by us.[8] More recently, the Denmark group has used silanolates in the palladium-catalyzed fluoride-free cross-coupling of organosilanols to aryl iodides,[9] and also in the Sonogashira reaction.[10] Two more reports describe the use of sodium trimethylsilanolate as a base to promote elimination of methanol from β-methoxyketones,[11] and the deprotonation of propyne iminium salts.[12] Herein, we report a new application of potassium trimethylsilanolate as a base to mediate the E_2 elimination of aryl sulfones.

The elimination of sulfinic acid from sulfones bearing an electron-withdrawing group such as a nitrile β to sulfone is a relatively well-known reaction.[13] Elimination of arenesulfinate from homoallylic sulfones in the presence of potassium *tert*-butoxide was first described by Julia and Arnould[14] and has been the cornerstone of a number of polyene syntheses, such as vitamin A,[15–17] and the ionophore antibiotic X-14547A.[18] Elimination of arenesulfinate from phenethyl sulfones in the presence of sodium ethoxide was first reported by Fenton and Ingold[19] in 1930, however, this transformation has not been used in synthesis, presumably due to the very high temperature (235 °C) required for the elimination. Uguen reported the use of potassium *tert*-butoxide at room temperature to mediate the elimination of sulfinate from α-carbamido sulfones,[20] however, this reaction remained not widely used. Finally, there are two

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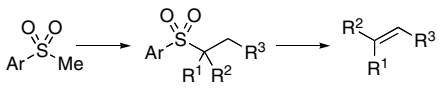
reports of the cleavage of unactivated sulfones, such as 2-pentyl methyl sulfone[21] and phenyl 2-pentyl sulfone[22] to give alkenes under extreme conditions.

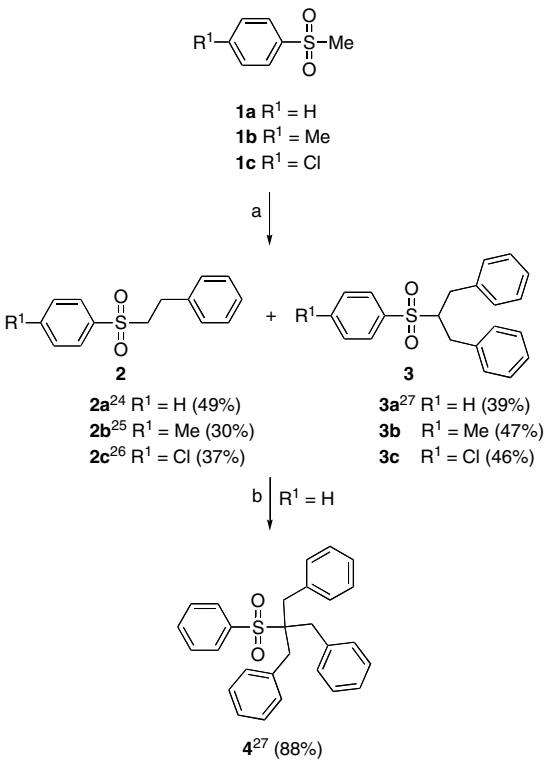
We envisaged the preparation of alkenes from aryl alkyl sulfones by elimination of arenesulfinate using potassium trimethylsilanolate instead of potassium *tert*-butoxide. The pK_a of trimethylsilanol is 12.7, which is less basic than water, and much less basic than *tert*-butanol (pK_a = 19).[23] These comparisons are consistent with the expectation of elimination of arenesulfinic acid from sulfones under the milder basic conditions, which might be selective, or less likely to cause racemization in the case of susceptible chiral sulfones under basic conditions. Furthermore, if a methyl aryl sulfone were alkylated with three different alkyl groups, then depending on the nature of the β-substituent of each alkyl group, selectivity may possibly be observed (Scheme 1).

Treatment of the appropriate methyl aryl sulfone **1** with 1 equiv of potassium bis(trimethylsilyl)amide, followed by benzyl bromide, led to a mixture of mono- and di-alkylated products, **2** and **3**,[24–27] which were readily separated by chromatography (Scheme 2). Alkylation of **3a** under the same reaction conditions provided the tri-alkylated product **4**. Sulfone **4** was allowed to react with 2 equiv of KO^{t}Bu in THF at room temperature and the course of the reaction was followed by LCMS. The starting material was seen to undergo 80% conversion after 30 min. In contrast, treatment of the same sulfone with 2 equiv of potassium trimethylsilanolate at room temperature did not result in any reaction, even after extended reaction time (>24 h). However, on heating the reaction to 70 °C the elimination proceeded with 60% conversion after 12 h. The reaction in the presence of 5 equiv of $KOSiMe_3$ at 70 °C gave the arenesulfinate **5a**[28] in quantitative yield and the alkene **6**[29] (82%) (Scheme 3). Using these conditions, the elimination reaction[30] was extended to the sulfones **2a**, **3a**, **2b**, **3b**, **2c**, **3c** and **4** with the extent of reaction being monitored over time (Scheme 4 and Table 1).

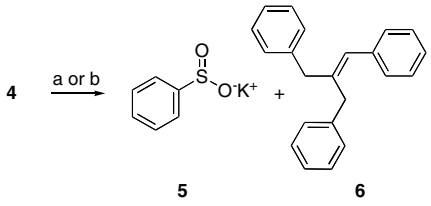
It was observed that the rate of elimination was consistent with the leaving ability of the arenesulfinic acid produced (pK_a Cl–$C_6H_4SO_2H$ = 1.14, pK_a $PhSO_2H$ = 1.35, pK_a $MeC_6H_4SO_2H$ = 1.48).[23] In all cases, the potassium arenesulfinate could be obtained by precipitation from the crude reaction mixture by addition of dichloromethane. Analysis by ^{1}H NMR and LCMS showed the presence of an impurity, attributed to the corresponding potassium arenesulfonate. Samples of alkene **7**,[31] produced from the elimination from sulfones **3a**, **3b** and **3c** were obtained exclusively as the *trans* isomer (^{1}H NMR analysis). Interestingly, it was observed that the elimination reaction was specific to potassium trimethylsilanolate. Attempted elimination reactions using the



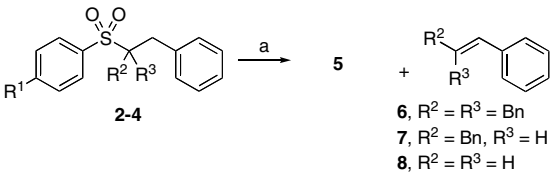
Scheme 1.



Scheme 2. Reagents and conditions: (a) $KN(SiMe_3)_2$, $PhCH_2Br$, THF, −78 °C, 3 h; (b) $KN(SiMe_3)_2$, $PhCH_2Br$, THF, −78 to 0 °C, 3 h.



Scheme 3. Reagents and conditions: (a) KO^{t}Bu (2 equiv), THF, 20 °C, 30 min; (b) $KOSiMe_3$ (2 equiv), THF, 70 °C, 12 h.



Scheme 4. Reagents and conditions: (a) $KOSiMe_3$ (5 equiv), THF, 70 °C.

lithium and sodium trimethylsilanolates with sulfone **3c** at 70 °C failed to result in any significant conversion to the alkene.

In order to determine whether elimination was possible on unactivated sulfones, methyl *p*-tolyl sulfone was alkylated with 1-bromo-3-phenylpropane to provide sulfones **9**,[32] **10** and **11**. Compound **10** was found to be completely inert under the usual elimination condi-

Table 1. Elimination reactions of sulfones **2**–**4**

Entry	Sulfone	R^1	R^2	R^3	Alkene (% Yield)	Conversion (%) at time t hours		
						$t = 2$	$t = 5$	$t = 12$
1	**2a**	H	H	H	**8** (96)[a]	68	81	98
2	**2b**	CH_3	H	H	**8** (82)[a]	28	63	83
3	**2c**	Cl	H	H	**8** (75)[a]	40	70	78
4	**3a**	H	Bn	H	**7** (56)[b]	87	100	100
5	**3b**	CH_3	Bn	H	**7** (73)[a]	77	92	100
6	**3c**	Cl	Bn	H	**7** (94)[a]	91	99	100
7	**4**	H	Bn	Bn	**6** (82)[b]	65	75	83

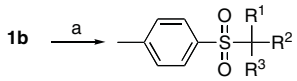
[a] Calculated from crude ^{1}H NMR analysis.
[b] Isolated yield.

tions even with the use of 10 equiv of $KOSiMe_3$ (Scheme 5). The reaction was repeated in the presence of KO^{t}Bu as base in order to determine whether a stronger base could cause elimination of the arenesulfinate. After 12 h of heating, with regular monitoring, almost all the sulfone **10** had been consumed, but no alkene products were observed in the intractable mixture of products (^{1}H NMR analysis).

Alkylation of sulfone **9** with allyl bromide gave the unsaturated sulfone **12**, which on treatment with $KOSiMe_3$ for 20 h gave diene **13**[33] (complete conversion by LCMS and ^{1}H NMR spectroscopy, 40% isolated yield). Again the product was obtained as the *E*-isomer (Scheme 6).

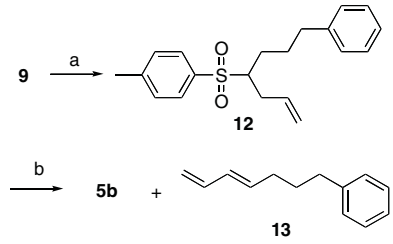
The sulfone triene **15**, obtained from methyl sulfone **14**, was subjected to the standard elimination reaction and this gave the corresponding tetraene **16** (Scheme 7). After 20 h, complete conversion of starting material had occurred, with alkene **16** detected as a single product by TLC and LCMS. Disappointingly, attempts to isolate tetraene **16** resulted in its complete decomposition upon evaporation of solvent. However, arenesulfinate **17** was isolated (56%) and its structure confirmed.

In order to probe the selectivity of the elimination reaction, sulfone **18** was prepared by alkylation of sulfone **2c** with allyl bromide (Scheme 8). In sulfone **18**, the presence of two sets of activated protons, the allylic and benzylic, allows the possibility of the formation of two possible regioisomeric alkene products on the elimination of arenesulfinate **5**. Abstraction of the benzylic proton would yield diene **19**, whereas loss of the allylic proton would result in the conjugated diene **20**. Reaction of sulfone **18c** with 5 equiv of $KOSiMe_3$ was complete after 5 h. ^{1}H NMR spectroscopic analysis of the crude product was consistent with the formation of

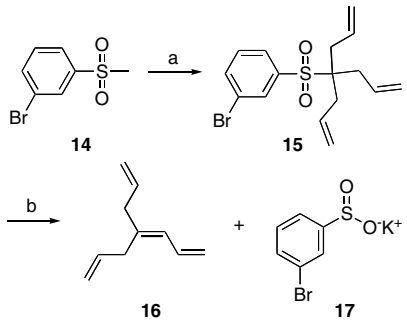


9, $R^1 = (CH_2)_3Ph$, $R^2 = R^3 = H$
10, $R^1 = R^2 = (CH_2)_3Ph$, $R^3 = H$
11, $R^1 = R^2 = R^3 = (CH_2)_3Ph$

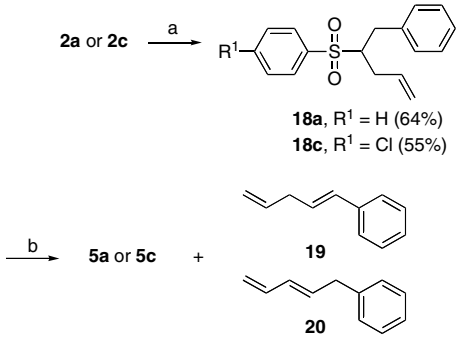
Scheme 5. Reagents and conditions: (a) $KN(SiMe_3)_2$, $Ph(CH_2)_3Br$, THF, −78 °C, 80 h, **9** (28%), **10** (14%), **11** (12%).



Scheme 6. Reagents and conditions: (a) $LiN(SiMe_3)_2$, allyl-Br, THF, −78 °C, 2 h (36%); (b) $KOSiMe_3$ (5 equiv), THF, 70 °C, 20 h (40%).



Scheme 7. Reagents and conditions: (a) $LiN(SiMe_3)_2$, allyl-Br, THF, −78 °C, 2 h (6%); (b) $KOSiMe_3$ (5 equiv), THF, 70 °C, 20 h.



Scheme 8. Reagents and conditions: (a) $LiN(SiMe_3)_2$, allyl-Br, THF, −78 °C, 3 h; (b) $KOSiMe_3$ (5 equiv), THF, 70 °C, 12 h.

one major alkene product, which was isolated and identified as the (*E*,*E*)-diene **21**,[34] presumably derived from the initially formed diene by isomerization of the double bonds into conjugation with the phenyl ring. Similarly, elimination of sulfone **18a** generated the corresponding

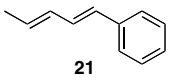


Figure 1.

conjugated (*E*,*E*)-diene **21** (95%) within 2 h (Fig. 1). Unfortunately, these results precluded us from determining the initial site for deprotonation and the selectivity of the reaction.

In conclusion, we have demonstrated the use of potassium trimethylsilanolate as base in the elimination of activated sulfones to generate the potassium arenesulfinate and corresponding alkene with exclusive *trans* geometry.

Acknowledgements

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30. General procedure: Sulfone (0.25 mmol) and $KOSiMe_3$ (1.25 mmol) in THF (5.0 mL) were heated to reflux (N_2) for the respective time. After rotary evaporation, CH_2Cl_2 (5 mL) was added and the precipitate of the arenesulfinate salt was filtered off, the filtrate evaporated and the residue analyzed by ^1H NMR and/or chromatographed.
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