

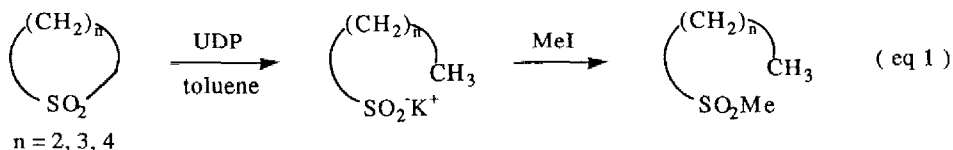
Ultrasonically Dispersed Potassium in Organic Synthesis. Water-Acceleration in Reductive C-S Bond Cleavage Reactions

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Abstract. The slow addition of a pre-measured amount of water in THF can greatly enhance the UDP induced C-S bond cleavage reactions of cyclic sulfones. This reaction can be used in the synthesis of open chain sulfones with γ -, δ - or ϵ -deuteration.

Ultrasound has been known to promote a variety of organic reactions, especially those involving metals.¹ Among the many useful applications of ultrasound, the use of ultrasonically dispersed potassium (UDP)² to cleave the carbon-sulfur bond of cyclic sulfones has been found to be high-yielding and regioselective.³ The intermediate sulfinate needs not be isolated and can be treated directly with an electrophile such as methyl iodide to give an open-chain sulfone (eq 1). This reaction normally requires prolonged ultrasound irradiation (4 hr for 1 mmol scale reaction) and it would be very nice to discover a condition under which the irradiation period can be greatly reduced.



In the procedure reported earlier,^{3a} the reactions were performed under anhydrous conditions. Since the C-S bond cleavage reaction requires a proton, the solvent toluene, a very weak acid (pK_a about 37)⁴ has to be the source of proton. In order to understand more about the proton transfer, a reaction of sulfolane **1** with UDP (3 mole equiv) was carried out in d₈-toluene for 1 hr of ultrasound irradiation. After treatment with MeI, the product was analyzed by ¹H NMR. It was found that the product, butyl methyl sulfone **6** (53% in yield) was incorporated with 22% of deuterium at the δ -position. The δ -deuteration indicates proton transfer from toluene to sulfolane during the reaction process, whereas the extent of deuteration indicates that it was not a direct transfer. The most likely medium for the indirect proton transfer is the α -position of the sulfolane. It was therefore thought that the introduction of a better source of proton during the reaction would probably accelerate this reaction.

Thus, when a sonicated mixture of sulfolane **1** (1 mole equiv) and UDP (3 mole equiv) in anhydrous toluene was added dropwise a solution of water in THF (containing 3 mole equiv of H₂O), sulfolane **1** was consumed within a few minutes. Heating this crude intermediate, presumably the sulfinate, with

MeI gave butyl methyl sulfone **6** (91%) as the only product (Table I). Water induced acceleration was observed in the reactions of pentamethylene sulfone **2** and trimethylene sulfone **3** with UDP (entries 2 and 3 in Table I). In these accelerated reactions, the slow addition of H₂O/THF has no adverse effect on the yield of products. When H₂O/THF was added too rapidly as in one portion, significant destruction of the potassium took place so that the C-S bond cleavage reaction was virtually blocked.

Table I. Water-accelerated Bond Cleavage Reactions of Cyclic Sulfones with UDP

Entry	Cyclic Sulfone	Amount of UDP (mole equiv)	Product ^a	Yield %
1	1	3	6	91 (91) ^b
2	2	3	7	92 (91) ^b
3	3	3	8	80 (84) ^b
4	4	3	9	73 (0) ^{b,c}
5	5	3	10	50 (0) ^{b,d}

a. The products were obtained after treatment with MeI (10 equiv) under reflux.

b. The yields in the parentheses are those obtained under anhydrous conditions without added H₂O/THF (see ref 3a).

c. Starting material was recovered in 75% yield under anhydrous conditions.

d. Starting material and some minor products were obtained in 55% yield under anhydrous conditions.

One very important feature of the addition of H₂O/THF to the reactions of UDP is that it causes the C-S bond cleavage reactions to take place for those sulfones of which the bond does not break under anhydrous conditions. For example, treatment of 2,2,5,5-tetramethylsulfolane **4**⁵ or norbornadienyl sulfone **5**⁶ with UDP under anhydrous conditions for more than 6 hr at up to 55°C gave mainly recovered starting material along with some unidentified compounds. Whereas by adding H₂O/THF to the sonicated mixture, C-S bond cleavage reaction took place immediately (entries 4 and 5 in Table I). The lack of acidic protons on **4** and **5** makes it impossible for indirect proton transfer during the reaction. Therefore, an exotic proton source is essential for their C-S bond cleavage.

The proton transfer from the introduced H₂O to sulfolane is basically a direct process. When a mixture of **1** and UDP in toluene was treated with D₂O/THF (3 equiv mole with respect to **1**), the product was 4-deuterobutyl methyl sulfone **14** with essentially 100% of deuteration (eq 2). This is easily understood since water (pK_a 16) is a much better proton source than a sulfone-stabilized proton (pK_a 25-29).⁴

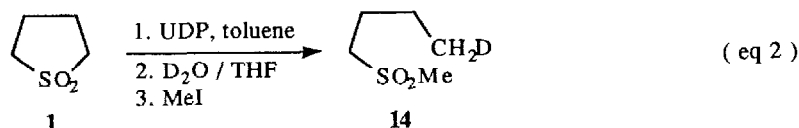


Table II. Preparation of Deuterated Sulfones from Cyclic Sulfones

Entry	Cyclic Sulfone	Amount of UDP (mole equiv)	Additive (mole equiv)	Product ^a	Yield % ^c
1	1	3	D ₂ O/THF (3)	14	92
2	2	3	D ₂ O/THF (3)	15	80
3	3	6	D ₂ O/THF (6)	16	64
4	11	3	H ₂ O/THF (3)	17 ^b	70
5	12	4	H ₂ O/THF (4)	18 ^b	93
6	13	6	H ₂ O/THF (6)	19 ^b	72
7	11	3	D ₂ O/THF (3)	20 ^b	90
8	12	6	D ₂ O/THF (6)	21 ^b	84
9	13	6	D ₂ O/THF (6)	22 ^b	52

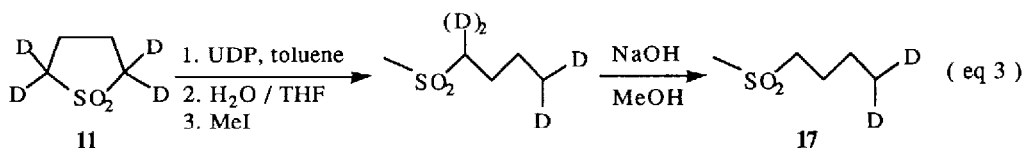
a. The products were obtained by treatment of the sulfinates with MeI (10 equiv).

b. These products were obtained after treatment of the crude product with 2N NaOH/MeOH under reflux for 2 hr

c. The numbers indicate isolated yields. The conditions were not optimized.

The quantitative δ -deuteration of **14** illustrates a useful application of the H₂O accelerated C-S bond cleavage reaction in the preparation of deuterium-labelled sulfone compounds. In principle, deuterium can be introduced at various remote positions by using different cyclic sulfones as starting materials. Multi-

deuteration should also be possible. For example, the H_2O induced bond cleavage reaction of tetradeuterosulfolane **11** with UDP, after MeI treatment, should give a polydeuterated butyl methyl sulfone of which the δ -position is dideuterated. Since the protons on the α -position are exchangeable under basic conditions, treatment of the crude product with methanolic NaOH produced **17** as a clean, dideuterated product (eq 3).



The application of the deuteration technique for the preparation of regiospecifically labelled sulfones are summarized in Table II.

In our early report where anhydrous conditions were exercised,^{3a} we found that the use of toluene as the solvent was essential for the success of C-S bond cleavage with UDP. Having known that H_2O can enhance such reactions, we performed the reaction of sulfolane **1** with UDP in benzene under sonication with the slow addition of H_2O /THF. This reaction proceeded as well as in toluene (91% yield). On the other hand, under the conditions where exotic H_2O is introduced, the importance of ultrasound irradiation is decreased. The reaction of **1** with finely chopped potassium in the presence of slowly added H_2O /THF proceeded well by simple stirring to give **6**, but in a much lower yield (61%).

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References and Notes

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