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CHEMOSELECTIVE REACTIONS OF ULTRASONICALLY DISPERSED POTASSIUM WITH SOME BROMINATED HYDROTHIOPHENE S,S-DIOXIDES

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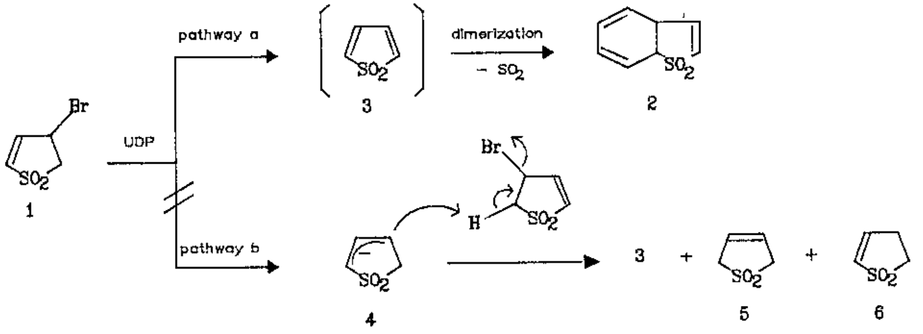
Abstract-*The reactions of ultrasonically dispersed potassium (UDP) with 4-bromo-2-sulfolenes resulted in chemoselective deprotonation at the C-5 position leading to the elimination-dimerization products. The possible C-S bond and C-Br cleavage reactions were not detected. The reaction of UDP with 3,4-dibromosulfolane resulted in dehydrobromination and double dehydrobromination.*

Ultrasonically dispersed potassium (UDP) has been recognized as a powerful reducing reagent for the cleavage of a C-S bond in cyclic sulfones[1,2] as well as for the promotion of cheletropic extrusion of SO_2 of substituted 3-sulfolenes.[2] On the other hand, UDP has been used as a deprotonation agent to induce Dieckmann condensation reactions.[3] In addition, we recently found that UDP was used to reductively cleave the C-Cl bond of alkyl halides, as most alkali metals do, so that the treatment of benzyl chloride with UDP gives bibenzyl in 70% yield.[4] Viewing that there are so many possible modes of reaction, we became interested in examining the reaction of UDP toward multiply functionalized molecules to see if there is any chemoselectivity. 4-Bromo-2-sulfolene, 1,[5] first came to our attention because it contains two types of carbon-sulfone bonds, a carbon-bromine bond, and acidic protons, all of which are reactive with UDP.

When 1 was treated with an excess of UDP (generated by sonicating finely-cut potassium in toluene at room temperature under N_2), a mixture containing mainly 2 and recovered starting material was obtained. Product 2 must have been formed from the well-established elimination-dimerization of 1 followed by a spontaneous extrusion of SO_2.[6] The result showed that primarily only one type of reaction took place selectively for 1 under the reaction conditions, ie. the elimination reaction.

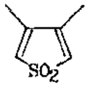
Scheme 1



The addition of excess of MeI to the reaction mixture before workup neither brought about additional by-proucts nor increased the weight of the crude product, indicating that C-S bond cleavage had not taken place in detectable amount. Otherwise, we would be able to trap the sulfinate intermediate with MeI and to obtain the corresponding methylsulfone.[1,2] The elimination product 3 can presumably be produced via two different pathways. The UDP may directly remove the proton at C-5 from the starting material similar to the reaction mode of the UDP promoted Dieckmann condensation reactions (pathway a). Alternatively, UDP may reductively cleave the C-Br bond similar to the reaction mode of the UDP induced coupling reaction of benzyl chloride (pathway b). The allylic carbanion intermediate 4 can in turn act as a base to induce the dehydrobromination of another molecule of 1. The two pathways can be differentiated because pathway a would result in a total conversion of 1 to the dimer 2 while pathway b would result in the formation of 50% of the dimer 2 at most since half of the starting material would become 3-sulfolene 5 or 2-sulfolene 6 (Scheme I). Based on the recovered starting material, dimer 2 was obtained over 50% yield (see Table I). Therefore, pathway a must have taken place. However, at this point, the possibility that both pathways a and b are taking place can not be strictly ruled out yet.

We further examined the reactions of 5 and 6 toward UDP[2] and found that approximately 25% of the starting material was consumed over a period of 10 min regardless of whichever being used. Therefore, should 5 or 6 have formed during the reaction of 1 as depicted in pathway b, we should have observed them in the product mixture in significant quantity. The fact that we did not detect the formation of 5 or 6 suggests that pathway b did not take place. The extreme ease of dehydrobromination of 1 as compared with other sulfone systems[1,2] might be due to the higher acidity of the C-5 hydrogen induced by the C-4 bromine.

Substituted 4-bromo-2-sulfolenes 7-9[7] were subjected to UDP treatment under similar conditions.[8] The products and their yields are summarized in Table I[9]. As can be seen in the Table, the predominant reaction products from the reaction of UDP toward these sulfolenes are from dehydrobromination and subsequent dimerization in all cases except that 3,4-dimethylated analogue 9 gave the corresponding thiophene S,S-dioxide 12 without dimerization (entry 4) . The other product 13 in this reaction is suspected to be the result of the double bond isomerization of 12. Such an isomerization is known to take place under basic conditions.[5a,10] In a test, 12 was subjected to UDP (4 equiv) treatment for 10 min to give 13, recovered starting material 12, and 3-sulfolene 14 in 10:4:1 ratio with 85% total yield. Similar treatment of UDP with 13 resulted in the complete recovery of the starting material in 87% yield. Thus, it is clear that under basic conditions, 12 can isomerize to 13 which does not isomerize back to 12. The formation of 3-sulfolene 14 under the reaction conditions suggests the possibility of 1,4-reduction of the thiophene dioxide 12. Prolonged treatment of the brominated 2-sulfolenes with UDP resulted in the complete consumption of starting materials as can be seen in Table I (entries 5-7). The aromatized products 15 and 16 are presumably obtained from the base-induced double bond isomerization of the dimers 2 and 10, respectively.



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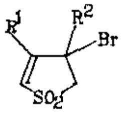
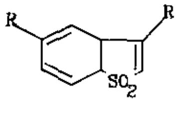
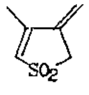


7 R^1=Me, R^2=H
8 R^1=Cl, R^2=H
9 R^1=R^2=Me



10 R=Me
11 R=Cl



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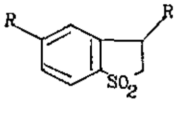

15 R=H
16 R=Me

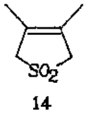

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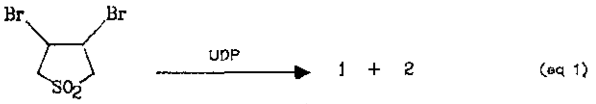
Table I. Reactions of 4-Bromo-2-sulfolenes with UDP

entry	compound	UDP	condition[8]	time	products and yields§
1	1	7 equiv	B	10 min	1 (12%) + 2 (52%) [55%]
2	7	4 equiv	A	10 min	7 (49%) + 10 (33%) [65%]
3	8	4 equiv	B	10 min	8 (38%) + 11 (46%) [75%]
4	9	4 equiv	B	10 min	12 (83%) + 13 (<2%) + 14 (4%)
5	1	4 equiv	A	7 hr	2 (48%) + 15 (8%)
6	7	3 equiv	A	7 hr	16 (43%)
7	9	3 equiv	A	3 hr	13 (70%) + 14 (3.5%)

§ The numbers in parentheses indicate isolated yields and those in brackets indicate yields based on the recovered starting material.

The reaction of 3,4-dibromosulfolane 17 with UDP (4 equiv) for 10 min (using condition A as described in Table I) resulted in dehydrobromination and some double-dehydrobromination giving 1 (7%) and 2 (54%), respectively (eq 1). Although debromination of 17 to form 3-sulfolene 5 appeared to be possible, we did not observe its formation. Apparently, deprotonation of the aforementioned brominated cyclic sulfones (1 and 7-9) with UDP is much more facile than the cleavage of C-Br bond. It is interesting to compare such a chemoselectivity with that of the reaction of 1 with Ag/Zn or Mg where the major reaction is C-Br bond scission.[11]



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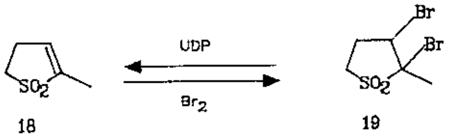
2,3-Dibromosulfolane 19, readily prepared by the bromination of 2-methyl-2-sulfolene 18 in CCl_4 under reflux, was also treated with UDP (10 equiv) for 5 h (using condition A as described in Table I) and then with an excess of MeI (eq 2). The only product obtained was the debrominated product **18** (85% in yield). Treatment of **19** with pyridine in acetone similarly resulted in debromination to give **18** in 98% yield. Dehydrobromination is difficult for **19** since there is no acidic proton adjacent to the bromine atom, and so C-Br bond scission took place instead.



(eq 2)

In summary, although the reactions of functionalized cyclic sulfones with UDP may take place in several possible modes, so far we have found that normally only one mode of reaction is observed for one type of cyclic sulfone. For example, bond cleavage between an sp^3 carbon and sulfur takes place on saturated cyclic sulfones;[1] bond cleavage between an sp^2 carbon and sulfur takes place on substituted 2-sulfolenes; cheletropic extrusion of SO_2 takes place on 3-sulfolenes; direct deprotonation takes place on 4-brominated 2-sulfolenes; and debromination takes place on a 2,3-dibromosulfolane as described herein. Therefore, the reaction of UDP with multiply functionalized cyclic sulfones is highly chemoselective.

ACKNOWLEDGMENT

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5. (a) T.S. Chou, S.C. Hung, and H.H. Tso, *J. Org. Chem.*, in press. (b) W.J. Bailey and E.W. Cummins, *J. Am. Chem. Soc.*, 76, 1932 (1954).

6. W.J. Bailey and E.W. Cummins, *J. Am. Chem. Soc.*, 76, 1936 (1954).

7. Substituted 4-bromo-2-sulfolenes 7-9 were all prepared from the corresponding 3-sulfolenes by a bromination-dehydrobromination sequence: The mixture of a 3-sulfolene (3 mmol) and bromine (3.3 mmol) in $CHCl_3$ (50 ml) was refluxed for 40 h. An additional amount of bromine (3 mmol) was then added to the mixture and refluxing was continued for another 24 h. Aqueous workup gave the crude dibromide which, without purification, was dissolved in anhydrous acetone and then pyridine (5 mmol) was added dropwise. The mixture was stirred at room temperature for 18 h. After the removal of the solid by filtration, the solution was concentrated and the crude oil was purified by column chromatography (silica gel column, eluted with hexane/EtOAc) to give the 4-bromo-2-sulfolene.

8. In fact, two slightly different conditions have been used in our laboratory. Condition A: The starting material was added to a suspension of UDP (see Ref. 1) in toluene and sonicated with a common ultrasound cleaning bath (Bransonic 220) at room temperature. The excess UDP was destroyed by careful addition of saturated NH_4Cl at 0°C. Extraction of aqueous layer with CH_2Cl_2 gave the crude product mixture which was purified by HPLC (LiChrosorb column, hexane/EtOAc). Condition B: The exactly same procedure was exercised except that sonication was performed with an ultrasonic disintegrator (MSE Soniprep 150).

9. The ^{1}H nmr spectral data of 8, 9, 11, 13, and 15 are: 8, δ 3.77 (dd, 1H, J = 3, 13.5 Hz), 4.04 (dd, 1H, J = 6.5, 13.5 Hz), 5.03 (dd, 1H, J = 3, 6.5 Hz), 6.84 (s, 1H); 9, δ 2.01 (s, 3H), 2.13 (s, 3H), 3.57 (d, 1H, J = 13.5 Hz), 3.99 (d, 1H, J = 13.5 Hz), 6.33 (s, 1H); 11, δ 4.14 (dd, 1H, J = 4, 11.5 Hz), 4.34 (dd, 1H, J = 4.5, 11.5 Hz), 5.89 (d, 1H, J = 4 Hz), 5.96 (dd, 1H, J = 4.5, 10 Hz), 6.25 (d, 1H, J = 10 Hz), 6.94 (s, 1H); 13, δ 2.04 (s, 3H), 3.92 (s, 2H), 5.36 (s, 1H), 5.51 (s, 1H), 6.45 (s, 1H); 15, δ 3.43 (s, 4H), 7.30-7.80 (m, 4H).

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