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A New Rearrangement of α-Keto Sulfoxide and Thiolsulfinate with Acetic Anhydride

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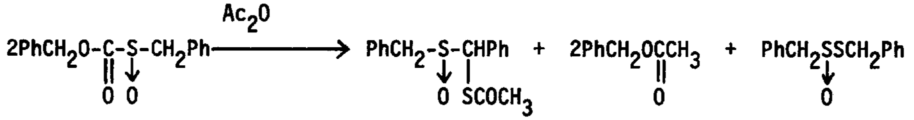
α-Keto sulfoxides having a general structure, $R-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{S}}-R'$, are interesting but unknown class of organic sulfur compounds which were thought to exist as unstable intermediates.$^{1)}$ However, recently Barton and his co-workers reported the preparation of stable α-keto sulfoxides by oxidizing monothiocarbonates ($R-O-\overset{O}{\overset{\|}{C}}-S-R'$) or thiocarbamates ($R_2N-\overset{O}{\overset{\|}{C}}-S-R'$) with m-chloroperbenzoic acid, and also their physical properties and some chemical behaviors.$^{2)}$

In order to explore chemical properties of α-keto sulfoxide further, we prepared benzyl benzyloxycarbonyl sulfoxide (1) and treated it with acetic anhydride expecting to see the Pummerer rearrangement of the α-keto sulfoxide.$^{3)}$ However, unexpectedly, we obtained a new rearranged product 1-(acethylthio)benzyl benzyl sulfoxide (2) in moderate yield together with other products, shown in Scheme 1. The rearranged product (2) would be formed via an initial formation of benzyl phenylmethanethiolsulfinate (4), since treatment of the thiolsulfinate (4) with acetic anhydride actually afforded the compound (2).

In this communication, we wish to report this new rearrangement reaction of either the α-keto sulfoxide (1) or the thiolsulfinate (4) with acetic anhydride to afford (2) and to discuss the mechanism of the rearrangement.

For a typical run, the keto sulfoxide (1) (550 mg,2.01 mmol) was treated with 10 ml of acetic anhydride at 60 °C for 2hr. After (1) was consumed, the products were separated by preparative tlc or column chromatography, using benzene/ethyl acetate=8/1 mixed solvent as the eluent, and their structures were determined by both spectroscopic and elemental analyses. The products and their yields are shown in Scheme 1.

The compound (2) is nearly 1:1 mixture of two isomers which can be separated nicely by



(1) (2) A and B 65% (3) 44% (4) trace

Scheme 1. The reaction of α-keto sulfoxide with acetic anhydride

preparative tlc on silica gel. The configurations of the two isomers (2) are not determined but one (A) has mp. 110.5-111.5°C and the other(B), 85.0-86.0°C, respectively. Their spectroscopic and analytical data are following. (A); nmr(δppm in $CDCl_3$) 2.47(s,3H),3.82(d, J=5.5Hz,2H),5.63(s,1H),7.20-7.40(m,10H).ir(νcm^{-1}KBr) 1690(C=O),1040(S-O).mass(m/e) 165 ($PhCHSCOCH_3^+$),122($PhCH{=}S^+$),91($C_7H_7^+$base peak). Elemental Analysis Calcd.for $C_{16}H_{16}O_2S_2$;C,63.13; H,5.30;S,21.06. Found C,63.06;H,5.30;S,20.69. (B);nmr(δppm in $CDCl_3$)2.40(s,3H),3.71(broad s,2H), 5.50(s,1H),7.20-7.40(m,10H).ir(νcm^{-1}KBr) 1702(C=O),1040(S-O).mass(m/e) 165($PhCHSCOCH_3^+$),122 ($PhCH{=}S^+$),91($C_7H_7^+$ base peak). Elemental Analysis Calcd.for $C_{16}H_{16}O_2S_2$; C,63.13;H,5.30;S,21.06 Found C,62.96;H,5.24;S,20.66.

When both (A) and (B) were oxidized separately with hydrogen peroxide in acetic acid, they afforded the same compound (5) in 74% yield which was assigned as the corresponding sulfone based on the following spectroscopic data. nmr(δppm in $CDCl_3$) 2.40(s,3H),4.22(s,2H),5.76 (s,1H),7.20-7.60(m,10H). ir(νcm^{-1} KBr) 1710(C=O),1310,1307(SO_2),1135,1125(SO_2).mass(m/e) 165($PhCHSCOCH_3^+$),122($PhCH{=}S^+$),91($C_7H_7^+$base peak).

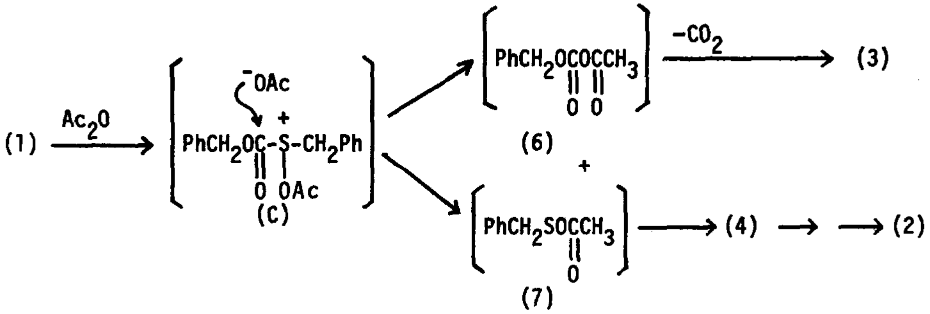
$$(1) \rightarrow (2)[\text{A and B}] \xrightarrow{[O]} PhCH_2S(O)_2CH(SCOCH_3)Ph$$

(5) mp.104.0-105.0°C

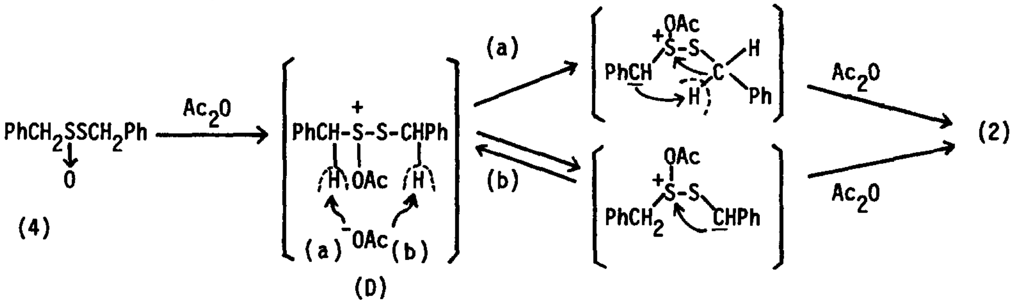
This reaction is considered to proceed via an initial acetylation of the sulfoxide (1) affording the intermediate (C) which is cleaved off to yield two mixed anhydrides, namely (6) and (7). The decarboxylation of (6) should lead to the product (3). Meanwhile, the compound (7) would disproportionate to afford the thiolsulfinate (4) which is the important key intermediate for the rearrangement of (1) to (2), since during the rearrangement of (1) to (2) a small amount of (4) was detected by nmr.

Recently, a similar intermediate like (C) was postulated for the reaction of (1) with thionyl chloride.[4)]

In order to confirm the above postulated pathways, namely if the rearrangement should proceed via the thiolsulfinate (4), we prepared the thiolsulfinate (4) separately by oxidation

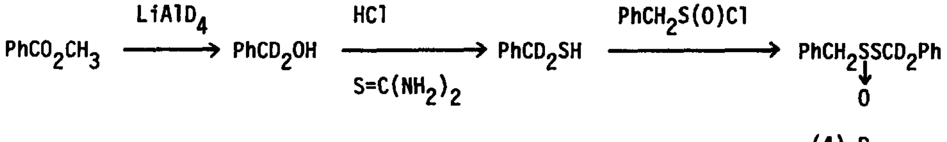


of the corresponding disulfide with m-chloroperbenzoic acid and treated it with acetic anhydride under the same reaction condition. The major products obtained were the rearranged sulfoxide (2) having nearly 1:1 mixture of the isomers (A) and (B) in 37% yield.[5] Thus, one can postulate the following two mechanisms for the rearrangement of (4) to (2) as shown below.



The route (a) involves the initial proton abstraction by acetate anion from the methylene group attached to the sulfinyl sulfur, followed by the intramolecular proton abstraction from the methylene protons attached to the sulfenyl sulfur just like the Ei reaction of some quarternary ammonium or sulfonium salts.[6] The carbanion once formed may attack the sulfinyl sulfur affording the rearranged α-thiolsulfoxide which is then acetylated with acetic anhydride to give the compound (2). The route (b) involves the initial proton abstraction from the methylene group attached to the sulfenyl sulfur followed by the similar rearrangement like route (a).

In order to make a choice between these two routes, we prepared the thiolsulfinate labeled with deuterium at the methylene attached to the sulfenyl sulfur as shown below,



$$PhCO_2CH_3 \xrightarrow{LiAlD_4} PhCD_2OH \xrightarrow[S=C(NH_2)_2]{HCl} PhCD_2SH \xrightarrow{PhCH_2S(O)Cl} PhCH_2\underset{\overset{\downarrow}{O}}{S}SCD_2Ph$$

(4)-D_2

and treated it with acetic anhydride similarly. After the reaction, (2)-D was isolated and both the position and the amount of D-content were determined by nmr. The results revealed that the product (2) had only deuterium atoms at the methine position and not at all at the methylene position. Moreover, the ratio of the D:H at the methine position was 60:40 indicating that the route (a) can be ruled out completely, since if the reaction proceeds via the route (a), H-D ratio of at least 50:50 should be observed in the methylene group of the sulfoxide (2)-D. Furthermore, the compound (2)-D did not undergo any H-D exchange at either the methylene or the methine position of (2) under the same experimental condition. Thus, the presence of proton in the methine group is very likely to be due to the equilibrium between (D) and the carbanion intermediate. This is also in keeping with the observation that when (4)-D_2 recovered after the reaction, the original D-label in (4)-D_2 was found to have lost substantially.

References and Footnotes

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5) When the thiolsulfinate (4) was treated with acetic anhydride which was purified carefully, the yield of (2) decreased to only 4%. Furthermore, when a small amount of acetic acid was added to the purified anhydride, the yield of (2) increased to about 65%.
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