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Reaction of Sulfoximines with Diazomalonate in the Presence of Cu-salt. A New Synthesis and Stereochemistry of Optically Active Oxosulfonium Ylids

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In the course of the study on the chemistry of sulfoximine, we found that $CHCl_3$ decomposes violently when it is treated with NaOH in dimethyl sulfoximine. However when the decomposition was carried out in the presence of cyclohexene, 7,7-dichlorobicyclo[4.1.0]heptane was obtained only in 5% yield with a concomitant decomposition of the sulfoximine. This observation suggests that dichlorocarbene is generated during the reaction, but consumed by a competing reaction with the sulfoximine thus lowering the yield of the carbene adduct.

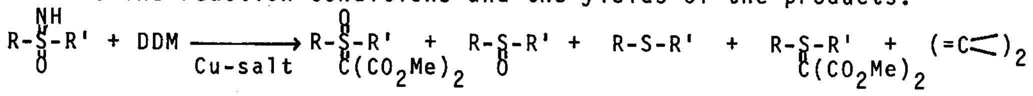
In order to clarify the reaction of carbenes with sulfoximines, a few typical sulfoximines1) were treated with dimethyl diazomalonate(DDM) in the presence of Cu-salt as catalyst. In these reactions, the NH group of the sulfoximines was eventually displaced by dimethyl malonate group and the corresponding oxosulfonium ylids were obtained as the major products.

This paper describes the reactions of sulfoximines with diazomalonate in the presence of Cu-salt, paying special attentions on the synthesis and the stereochemistry of an optically active oxosulfonium ylid along with the mechanistic implications of the new type of substitution reaction on the sulfur atom.

A typical experiment of methyl phenyl sulfoximine with DDM was carried out in a following way: a mixture of the sulfoximine (0.594g,3.83mmol) and DDM (0.653g, 4.13mmol) was refluxed in the presence of CuCl(0.101mmol) in benzene for 6.5 hr. Then, the products were separated by passing the reaction mixture through a silica gel column with $CHCl_3$ as the eluent and identified by their spectroscopic and elemental analyses. Methylphenyloxosulfonium ylid was obtained in 25% yield.

mp.88-89°C, nmr(δ)3.57(s,6H),3.70(s,3H),7.60(m,5H).ir 1690,1625cm^{-1}(C=O).mass 270(M$^+$).Analysis Calcd for $C_{12}H_{14}O_5$ C,53.32;H,5.22.Found C,53.41;H,5.16. The other sulfoximines were treated similarly. The products and their yields are summarized in Table 1.

Table 1. The reaction conditions and the yields of the products.



$$R-\underset{O}{\overset{NH}{S}}-R' + DDM \xrightarrow[\text{Cu-salt}]{} R-\underset{C(CO_2Me)_2}{\overset{O}{S}}-R' + R-\underset{O}{S}-R' + R-S-R' + R-\underset{C(CO_2Me)_2}{S}-R' + (=C\lessdot)_2$$

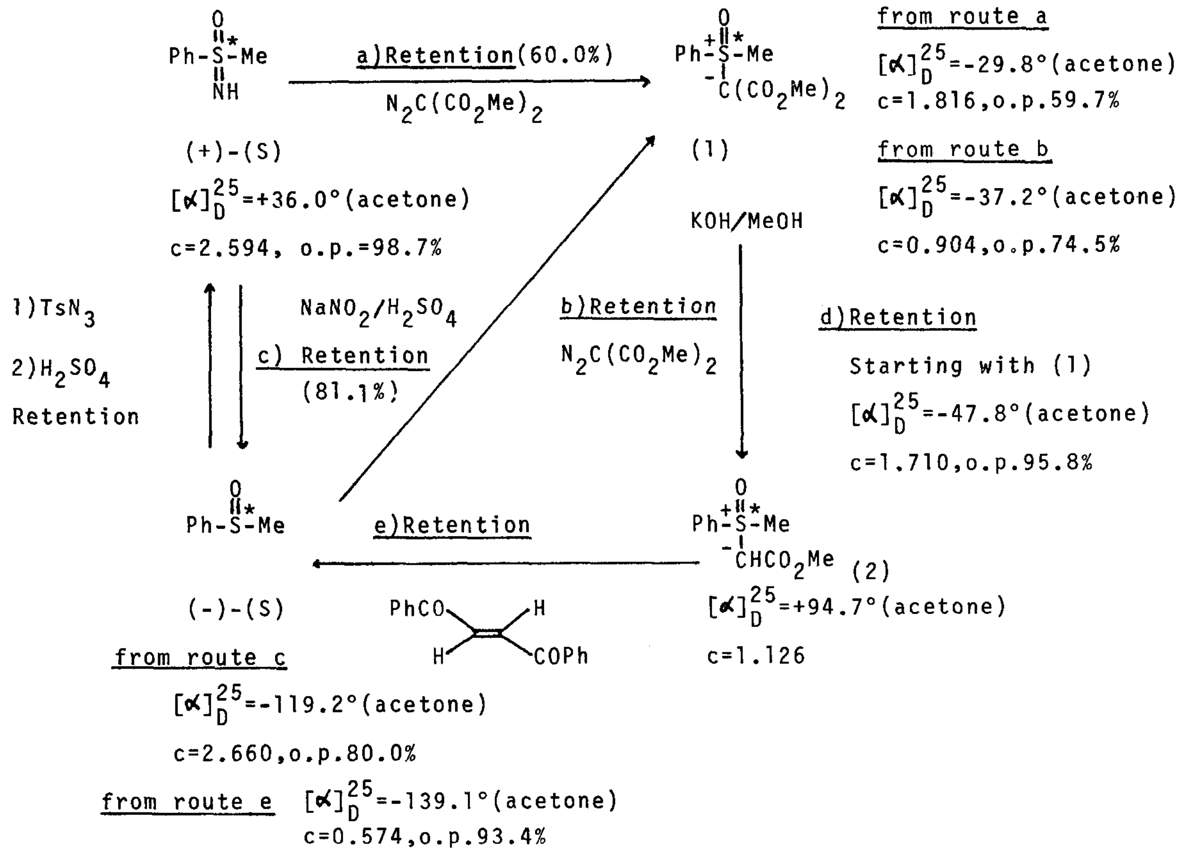
(I) (II) (III) (IV) (V)

Sulfoximine		Cu-salt	Solv.	Time	(I)	(II)	(III)	(IV)	(V)
R	R'								
CH_3	CH_3	CuCl	neat	1min.	16	--	--	--	--
"	"	$CuSO_4$	C_6H_6	12hr	53	--	--	trace	--
CH_3	C_6H_5	CuCl	"	6.5hr	25	11	1.5	--	13
"	"	$CuSO_4$	"	20hr	39	16	2.4	12	12
C_6H_5	C_6H_5	$CuSO_4$	neat	12hr	60	19	5.8	--	16

These experimental results reveal the following charactristic features of the reaction: (1) the products isolated are the recovered sulfides, sulfonium ylids, sulfoxides, dimer of DDM and oxosulfonium ylids which are the major products in the reactions. Recently, preparation of a few oxosulfonium ylids both by photolysis and thermolysis of DDM in corresponding sulfoxides was reported.$^{2)}$

(2) photolysis of a mixture of the sulfoximine and DDM in benzene with high pressure Hg lamp did not proceed at all and the sulfoximine was recovered nearly quantitatively implying that the Cu-carbene complex is the key intermediate for the reaction. (3) at the initial stage of the reactions, the color of the solution changed to deep green (methyl phenyl sulfoximine) and in the case of dimethyl sulfoximine blue crystalline precipitates were formed. Although the structure of these complexes was not determined, apparently a complex is formed between DDM, Cu-salt and sulfoximines.

In order to understand the stereochemistry of the reaction, we prepared an optically active methyl phenyl sulfoximine$^{3,4)}$ and treated it under the similar reaction condition. Then the oxosulfonium ylid was separated carefully in order to avoid further fractionation of the products. The typical results obtained both in this experiment(route a) and in the reaction of the optically active methyl phenyl sulfoxide and DDM(route b) are shown in the following scheme.



The optical rotation of the oxosulfonium ylid(1) was increased by several repeated recrystallizations of the crude compound from ether-hexane and eventually attained the constant value of $[\alpha]_D^{25}$=-49.9°(c=1.616,acetone) mp.145-146°C. If we assume this value to be 100% optically pure, the optical purity obtained by this reaction is 60%(route a). Meanwhile, the optically active methyl phenyl sulfoxide, upon reaction with DDM, afforded the ylid (1) which has an optical purity of more than 93% (route b) without any treatment. In order to determine the absolute configuration of the oxosulfonium ylid (1) and the stereochemistry of the reactions of both the routes a) and b), the compound (1) was hydrolyzed at first by KOH in MeOH to the oxosulfonium ylid (2)$^{5)}$ since (1) was so stable that it could not be degraded directly to the sulfoxide(having known configuration). The ylid(2) thus obtained is less stable and hence was found to react with dibenzoyl ethylene affording methyl phenyl sulfoxide and methyl 2,3-dibenzoylcyclopropane carboxylate.6) Therefore the reaction cycle between sulfoxide,(1) and (2) was performed starting from the sulfoxide. In this cycle, the path d) should be a retention process since the reaction in route d) does not perturb the optically active center. The reaction of route e) should also be another retention process, since the similar reaction of sulfoximinium ylid and olefin afforded the sulfinyl amide with retention of configuration around the sulfur atom.4) The experimental results which start from (1) having $[\alpha]_D^{25}$=-47.8°(o.p. 95.8%) to afford initially the ylid(2) having $[\alpha]_D^{25}$=+94.7° and finally methyl phenyl sulfoxide of $[\alpha]_D^{25}$=-139.1°, indicate clearly that the sulfoxide obtained by this reaction cycle retaines 93.4% optical purity with (S)-configuration. Therefore, the absolute configurations of both oxosulfonium ylids(1) and (2) can be assigned as (R)-configuration. Consequently, both routes to afford the ylid (1) namely routes a) and b) can safely be assumed to proceed via retention of configurations around the sulfur atom.7)

References and Footnotes

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2) W.Ando,T.Yagihara,S.Tozune,S.Nakaido and T.Migita,Tetrahedron Lett.,1969,1979. M.Takebayashi,T.Kashiwada,M.Hamaguchi and T.Ibata,Chem.Lett.,1973,809;F.Dost, and J.Gosselck,Tetrahedron Lett.,1970,5091.
3) R.Fusco and F.Tericoni, Chim.Ind.,1965,47,61.
4) C.R.Johnson and C.W.Schroeck, J.Am.Chem.Soc.,1973,95,7418.
5) The ylid(2) was obtained in 35% yield. mp.97-98°C. ir.1635cm^{-1}(C=O).nmr(δ) 3.45(3H,s,O-CH_3),4.05(1H,CH),3.53(3H,s,S-CH_3),7.65-8.00(5H,Ph-H).mass,(M^++1) 213(C.I.).
6) The compound was obtained in 53% yield and identified by comparing its nmr with that cited in the reference. P.Bravo,G.Fronza,G.Gaudiano,C.Ticozzi and M.G.Zubiani, Tetrahedron,1971,27,3563.
7) The detailed mechanism for the route a), namely the causes of a partial racemization of the ylid(1), is not known, however the mechanism involving the initial formation of the sulfoxide followed by the reaction of it with DDM seems to be ruled out since the ratios of the racemization in routes a) and b) are quite different. Furthermore, the sulfoxide recovered was found to retain 87% optical purity (route a). Thus further experiments are necessary to clarify the mechanism of the reaction.