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STEREOSELECTIVE FORMATION OF SOME THIETANE 1,1-DIOXIDES VIA SULFENES BY THE REACTION OF DIAZO COMPOUNDS WITH SULFUR DIOXIDE

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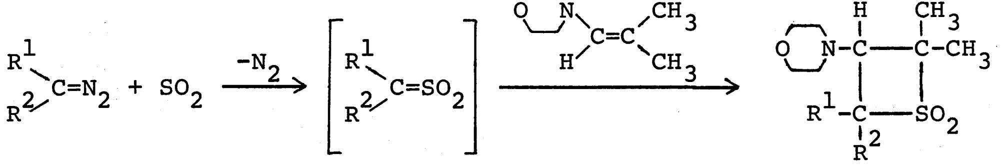
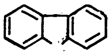
In the reaction of diazo compounds with sulfur dioxide, trapping experiment by enamines indicates the existence of sulfene as a reaction intermediate. The stereochemistry of the sulfene-enamine cycloadducts and the solvent effect upon the stereoselectivity gave a suggestive information on the mechanism of the cycloaddition reaction.

Recently sulfenes, generated by the action of amines on alkanesulfonyl chlorides, have received considerable attention.[1-4] We now wish to report the existence of sulfene as an intermediate in the reaction of diazo compounds, 9-diazofluorene(Ia), diphenyldiazomethane(Ib), and phenyldiazomethane(Ic), with sulfur dioxide.

A solution of Ia, Ib, or Ic in benzene was added dropwise to a solution of 2-methyl-1-morpholinopropene(MMP) and sulfur dioxide in benzene with stirring at 20°C. Decolorization of the solution was observed together with evolution of nitrogen. After the addition was complete, the reaction mixture was stirred at the same temperature for an additional 45 min. The removal of benzene, *in vacuo*, from the reaction mixture gave colorless crystals of IIa, IIb, or IIc(Scheme I). Structure of these products was determined by means of elemental analyses and measurements of IR and NMR spectra.

Scheme I



Ia R^1, R^2 = 
b R^1=R^2=Ph
c R^1=Ph, R^2=H

IIa 99 %*
b 95 %
c 62 %(cis and trans mixtures)

* The yields are in mol % based on I used.

2-Fluorenylidene-3-morpholino-4,4-dimethylthietane 1,1-dioxide(IIa): white leaflets, mp 156-157°C; NMR(60MHz,$CDCl_3$): δ 1.55-2.33(4H,broad m,NCH_2), 1.84(3H,s,CH_3), 2.01(3H,s,CH_3), 3.43(5H,m,OCH_2 and methine), and 7.3-8.1(8H,m,aromatic); IR(KBr): 1106 and 1315 cm^{-1}(SO_2).

2,2-Diphenyl-3-morpholino-4,4-dimethylthietane 1,1-dioxide(IIb): colorless plates, mp 136°C; NMR($CDCl_3$): δ 1.64(3H,s), 1.70(3H,s), 2.37(4H,m), 3.64(4H,m), 3.77(1H,s), 7.15-7.65(8H,m,C_6H_5 trans to morpholine ring and 3H of C_6H_5 cis to morpholine ring), and 7.8-8.2(2H,m,2H of C_6H_5 cis to morpholine ring); IR(KBr): 1112 and 1305 cm^{-1} (SO_2).

The formation of II, thietane 1,1-dioxide derivatives, suggests that the reaction involves "sulfene" as an intermediate. In the reaction with Ic, an isomeric mixture of cis and trans cycloadducts was obtained in the ratio of cis : trans=73 : 27 (determined by NMR analysis[3)] of the mixture). The isomeric mixture, furthermore, was separated by repeated fractional crystallization from a mixed solvent of petroleum ether and benzene into cis and trans isomers. The cis isomer: colorless prisms, mp 128-129°C; IR(KBr): 1098 and 1301 cm^{-1} (SO_2). On the other hand, stirring the methanol solution of the isomeric mixture in the presence of catalytic amounts of sodium methoxide gave almost quantitatively the trans isomer.[5)]

In order to study the effect of solvents on the stereoselectivity, the reaction of Ic was carried out in various solvents instead of benzene. The results are summarized in Table 1.

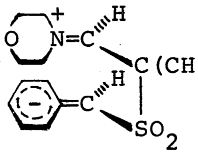
Table 1. The reaction of phenylsulfene with MMP in various solvents.

Solvents	Ratio of the Products[a)]		Yield(%)[b)]
	IIc-cis	IIc-trans	
cycl. C_6H_{12}	77	23	80
CCl_4	77	23	57
C_6H_6	73	27	62
CH_3CN	68	32	43
THF	63	37	50
DMF	64	36	77

a) The ratios were determined by the intensity measurement of the ring proton signals in the NMR spectra of the mixtures.

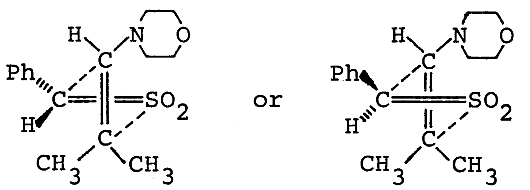
b) The yields are in mol % based on Ic used.

Although the predominant formation of less stable cis isomer can be explained by either (a) a stepwise process <u>via</u> a zwitter ionic intermediate(III) or (b) a concerted [$\pi 2a + \pi 2s$] process,[3)] increasing tendency of the trans isomer in the polar solvents as seen in Table 1 would support the former process(a).



III

(a) stepwise process



(b) concerted process

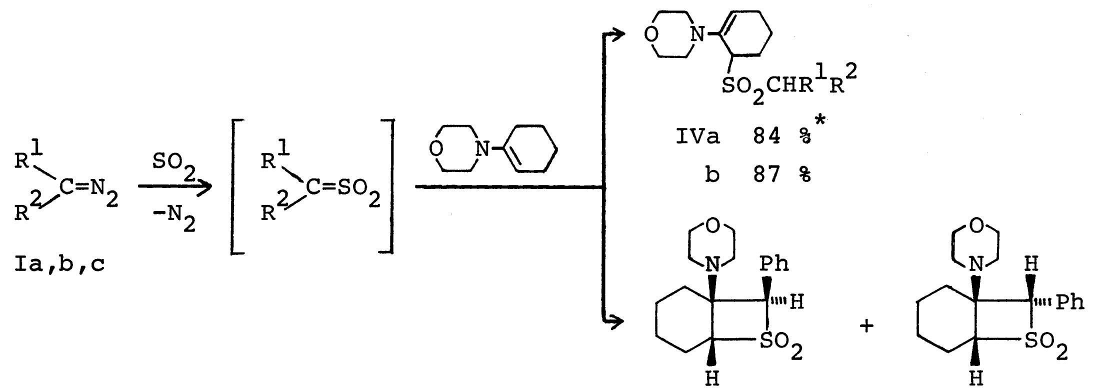
In the next place, the reaction of Ia and Ib with sulfur dioxide were carried out by the use of 1-morpholinocyclohexene(MCH) in benzene respectively.

The spectra of IR and NMR for these reaction products were in agreement with the structures of the acyclic sulfones IVa and IVb(Scheme II), instead of the cyclic sulfones(V).

3-Fluorenylsulfonyl-2-morpholinocyclohexene(IVa): colorless plates, mp 142-143°C; NMR($CDCl_3$): δ 1.25-2.75(6H,broad m), 2.58(4H,m), 3.48(5H,m,OCH_2 and $CHSO_2$), 5.28(1H,t,J=3Hz,vinyl), 5.58(1H,s,SO_2CH), and 7.2-8.1(8H,m); IR(KBr): 1120 and 1315 cm^{-1} (SO_2).

3-Diphenylmethylsulfonyl-2-morpholinocyclohexene(IVb): colorless plates, mp 150.5-151.5°C; NMR($CDCl_3$): δ 1.3-3.2(6H,broad m), 2.76(4H,m), 3.83(5H,m), 5.43(1H, t,J=4Hz), 6.02(1H,s), and 7.3-8.0(10H,m); IR(KBr): 1112 and 1305 cm^{-1} (SO_2).

Scheme II



	Vc-cis		Vc-trans	Yield(%)*
in C_6H_6	81	:	19	87
in THF	70	:	30	87

* The yields are in mol % based on I used.

On the contrary, the reaction of Ic with sulfur dioxide in a benzene solution of MCH gave a mixture of Vc-cis and Vc-trans in the ratio of cis : trans = 81 : 19 and in a THF solution its ratio was 70 : 30.[6] Each isomer was isolated and its configuration was determined by NMR using a shift reagent, $Eu(dpm)_3$.[7]

cis-1-Morpholino-8-phenyl-7-thiabicyclo[4,2,0]octane 7,7-dioxide(Vc-cis): white crystalline, mp 103-104.5°C; NMR($CDCl_3$): δ 1.2-2.8(8H,broad m), 2.50(4H,m), 3.30(4H,m), 4.44(1H,m), 4.92(1H,s), and 7.37(5H,m); IR(KBr): 1150 and 1314 cm^{-1} (SO_2).

trans-1-Morpholino-8-phenyl-7-thiabicyclo[4,2,0]octane 7,7-dioxide(Vc-trans): colorless prisms, mp 115-116°C; NMR($CDCl_3$): δ 1.2-2.6(8H,broad m), 2.63(4H,m), 3.80 (4H,m), 4.37(1H,m), 5.40(1H,s), and 7.2-7.7(5H,m); IR(KBr): 1140 and 1298 cm^{-1} (SO_2).

These facts can be also explained by the process(a). The extent of delocalization of carbanion in a zwitter ion like III seems to play the decisive role in the course of reaction. In the reactions with Ia and Ib, the carbanion of the zwitter ion might be stabilized by the fluorenyl or diphenylmethyl groups, and so, the mobile proton β to the morpholino moiety migrates to the carbanion to form IVa or IVb. In the reaction with Ic, however, cyclization of the zwitter ionic intermediate is favored because of the less stabilized carbanion, giving Vc.

Details of these reactions and mechanisms will be discussed in later papers.

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