The Reactions of a Variety of Diazo Compounds with Sulfur Dioxide in Ethanol

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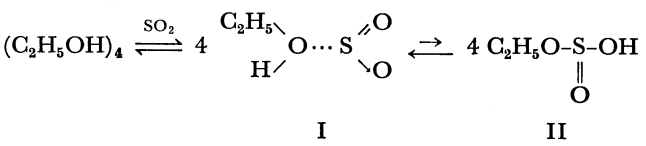
The reactions of several diazomethanes bearing a variety of substituents with sulfur dioxide were carried out in ethanol. The reaction of a diazomethane possessing an electron-releasing group gave the olefin as the major product. On the contrary, the ethyl ethers were predominantly afforded from the reactions of the diazomethanes containing an electron-withdrawing group. Moreover, the ethyl alkanesulfonates were obtained in the cases bearing the substituent of an intermediate electronic character. The observed product distribution is interpreted in terms of the nucleophilicity of the α-carbon atom of the diazomethane: the preference of the formation of sulfene by the electrophilic attack of SO_2 on the diazomethane to the acid-catalyzed decomposition by ethyl hydrogen sulfite reflects the nucleophilicity of the α-carbon atom in the diazomethane.

The reactions of diazoalkanes with sulfur dioxide in aprotic solvents are well known to lead to a sulfene intermediate *in situ* followed by the formation of episulfone, olefin, and the carbonyl compounds.[1] In a previous paper,[2] we demonstrated that this reaction certainly proceeds *via* sulfene by the use of enamine as a trapping reagent. Ethanol, one of the typical protic solvents, is also known to act as a trapping agent of the sulfene derived from alkanesulfonyl chloride and triethylamine.[3] However, in the system of diazoalkane and sulfur dioxide, contrary to the amine–chloride system, diazoalkane is liable to undergo decomposition by ethyl hydrogen sulfite, which is at equilibrium with ethanol and sulfur dioxide(Scheme 1, Route B). For example, Hesse and Majmudar[4] reported that ethyl ethoxyacetate was afforded from ethyl diazoacetate and that benzhydryl ethyl sulfite, whose structure had not yet been entirely established, was obtained from diphenyldiazomethane; therefore, the reaction proceeds not by a sulfene mechanism, but by a mechanism involving a protic acid.

In the present paper, we will describe how the possibility of an electrophilic attack of sulfur dioxide on the diazo compound to form sulfene(Scheme 1, Route A) can not be precluded as the initial stage of the reaction even in the system of ethanol and sulfur dioxide, depending on the substituents of diazomethane. Furthermore, as for the follow-up reaction of sulfene (formed *via* Route A), the reaction of sulfene with a new molecule of a diazo compound to give olefin (Route A_1) was found possibly to take place in competition with the trapping of sulfene by ethanol to yield the sulfonate(Route A_2).

Results and Discussion

NMR Study of the Interaction between Ethanol and SO_2. In order to obtain information on the interaction of ethanol and SO_2, the NMR spectra of these solvent mixtures at various ratios were measured, adding CCl_4 to keep the concentration of ethanol constant. The results are listed in the table. Upon an increase in the relative amount of SO_2, the signal of the hydroxylic hydrogen atom gradually shifts to a higher magnetic field, as may be seen in the table. This observation may be attributed to the cleavage of the hydrogen-bonding self association of ethanol by a weak interaction between the oxygen atom of ethanol and the sulfur atom of SO_2, like I as well as the methanol–SO_2 system which was previously reported.[5] If ethyl hydrogen sulfite(II), the OH-proton signal of



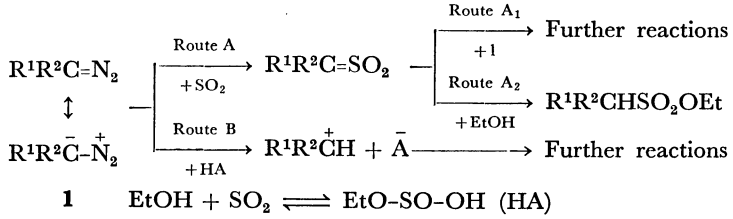
I II

which would appear in a very low field, were formed in an appreciable amount, the observed chemical shift (δOH) should go to a lower field because δOH must be the average chemical shift of two exchangeable hydroxylic protons of ethanol and II. Therefore, an

Table. The chemical shifts of protons of EtOH under the influence of SO_2

[EtOH] mol%	Molar ratio SO_2 : CCl_4	δOH ppm	δCH_2 ppm	δCH_3 ppm
83.1	0 : 100	5.01	3.38	0.93
84.0	25 : 75	5.00	3.38	0.93
82.8	39 : 61	4.95	3.33	0.88
82.3	58 : 42	4.95	3.36	0.92
84.2	82 : 18	4.89	3.31	0.88
82.6	100 : 0	4.84	3.32	0.88

Measured at 26° C; external standard, TMS.



1 $EtOH + SO_2 \rightleftharpoons EtO\text{-}SO\text{-}OH$ (HA)

Scheme 1.

$R^1R^2CN_2 + SO_2 + EtOH \longrightarrow R^1R^2C{=}CR^1R^2 + R^1R^2CHSO_2\text{-}OEt$

1a R^1=*p*-tolyl, R^2=H — *cis*-**2a** 21%[a] **3a** 23%; *trans*-**2a** 38%

$+ R^1R^2C{=}N\text{-}N{=}CR^1R^2 + R^1\text{-}CO\text{-}R^2$

4a 9% **5a** 4%

$R^1R^2CN_2 + SO_2 + EtOH \longrightarrow R^1R^2CHSO_2\text{-}OEt$

1b R^1=R^2=phenyl — **3b** 87%

1c R^1,R^2=fluorenylidene — **3c** 89%

$R^1R^2CN_2 + SO_2 + EtOH \longrightarrow R^1R^2CHO\text{-}SO\text{-}OEt + R^1R^2CH\text{-}OEt$

1d R^1=*p*-nitrophenyl, R^2=H — **6d** 4% **7d** 79%

1e R^1=ethoxycarbonyl, R^2=H — **7e** 81%

Scheme 2. The reactions of diazo compounds(**1**) with SO_2 in ethanol.

a) The yields are in mol% based on the **1** used for **3**, **5**, **6**, and **7**, and based on a half mole of the **1** used for **2** and **4**.

ethanol solution of SO_2 consists largely, if not entirely, of ethanol and SO_2 rather than of ethyl hydrogen sulfite.

Reactions of Diazo Compounds in Ethanol–SO_2 System. The reactions of diazoalkanes(**1**) bearing a variety of substituting groups were carried out by passing gaseous SO_2 through an ethanol solution of **1** for a period of 1 h at 20 °C. The results are summarized in Scheme 2.

In the reaction of **1a**, *cis*- and *trans*-di-*p*-tolylethylene (**2a**) were afforded as the major products in yields of 21 and 38% respectively, together with ethyl *p*-tolylmethanesulfonate(**3a**) (23%), *p*-tolualdehyde azine(**4a**) (9%), and *p*-tolualdehyde(**5a**) (4%). Moreover, there was no proton signal at around δ=5 ppm[6] which could be assigned to the methylidyne proton of the corresponding *cis*- and *trans*-episulfone, 2,3-di-*p*-tolylthiirane 1,1-dioxide. This result may be ascribed to the low stability of episulfone under these reaction conditions; they might undergo decomposition to yield stilbene derivatives.[1b,7]

When **1b** or **1c** was used, the corresponding sulfonate, ethyl diphenylmethanesulfonate(**3b**) or ethyl 9-fluorenesulfonate(**3c**), was predominantly afforded. As for the structure of the reaction product of **1b**, benzhydryl ethyl sulfite(**6b**) was proposed, though not fully established, by Hesse and Majmudar.[4] This product was identified as **3b** and not the isomeric **6b** from the evidence of the mass fragmentation and the IR spectrum, in which two characteristic absorption bands of $-SO_2-$ were observed at 1168 and 1345 cm^{-1}. These observations were also made in **3c**.

On the other hand, ethyl ether, **7d** or **7e**, was exclusively afforded from the reaction of **1d** or **1e** respectively, in which an electron-withdrawing substituent is attached. This type of product is commonly obtained from the acid-catalyzed decomposition of diazo compounds in ethanol and from the thermolysis and the photolysis of diazo compounds in ethanol. In the reaction of **1d**, *p*-nitrobenzyl ethyl sulfite(**6d**) was also obtained in a very low yield(4%). Further, in the case of **1e**, the reaction did not practically proceed under the condition described above; the reaction was, instead, carried out at 40 °C for 2 h.

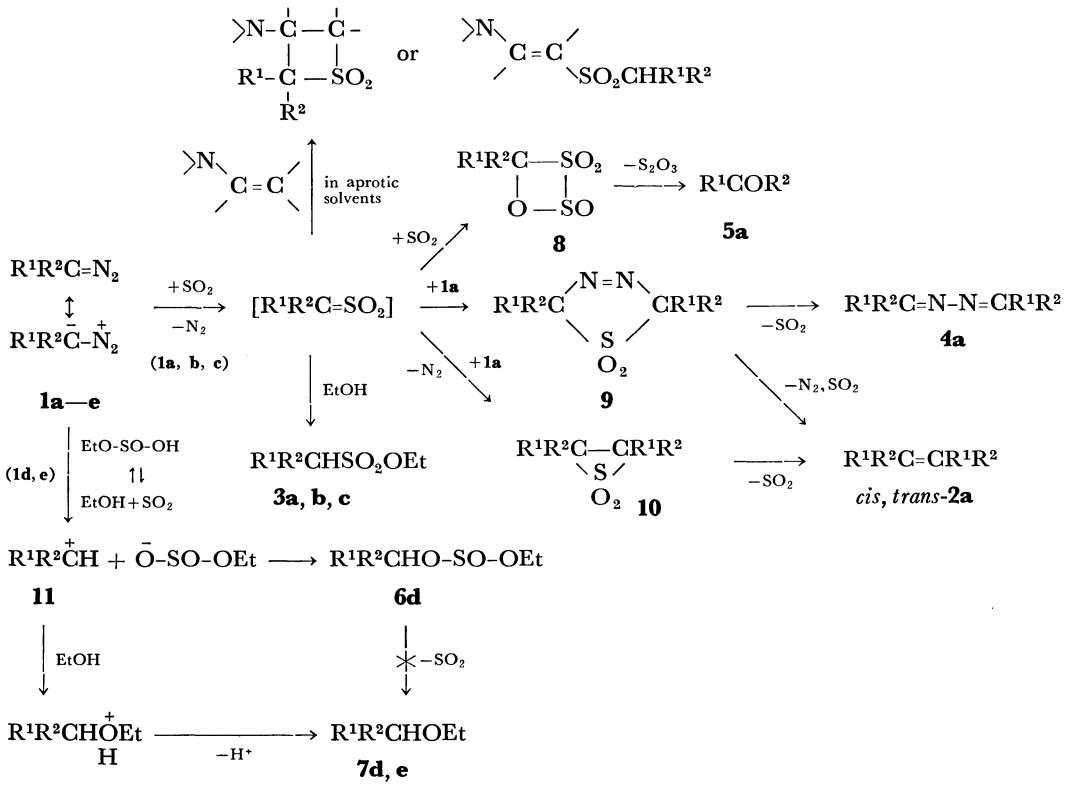
From the results presented above, it is clear that the product distribution was drastically varried with the electronic character of the substituent in **1**, that is, according to the nucleophilicity of the α-carbon atom in **1**.

Reaction Mechanism. Two different explanations are apparently possible to account for the decomposition of the diazo compounds(**1**) in the ethanol–SO_2 system and the formation of the various compounds, **2**—**7**: a reaction *via* sulfene[1] and an acid-catalyzed reaction.[8]

In the reaction of **1b**, the exclusive formation of **3b** is best explained by the process *via* the sulfene intermediate. If the decomposition proceeded by II, the reaction would result in the formation of benzhydryl ethyl ether, tetraphenylethylene, or benzhydryl ethyl sulfite as likely in a protic-acid decomposition. Hence, the possibility of acid catalysis can be ruled out. In this system, a sulfene intermediate was formed *in situ* by the electrophilic attack of SO_2 on **1b**, followed by the addition to ethanol, thus affording **3b**. This is also the case with the reaction of **1c**. As in these two cases, in the reaction of **1a**, which has a more electron-releasing substituent, sulfonate(**3a**) was also given in a 23% yield. In this instance, however, the major product was olefin, *cis*- and *trans*-**2a**(21 and 38% respectively). For the formation of this type of compound, both the sulfene process[1] and acid decomposition[8] are possible. If the latter process is involved in the present reaction, ethyl ether may be formed. Ethyl ether was not, however, obtained here. Furthermore, azine(**4a**) and aldehyde(**5a**) can not be afforded by acid decomposition.

As an alternative, the route involving a sulfene intermediate seems rather attractive as an explanation of the formation of **2a**, together with **4a** and **5a**. According to this process, sulfene was first generated *in situ* by the electrophilic attack of SO_2 on **1a**, with the loss of N_2. The further electrophilic attack of this sulfene intermediate on another, **1a**, rather than ethanol provides the transient 1,3,4-thiadiazoline 1,1-dioxide derivative(**9**), without the loss of N_2, or provides the thiirane 1,1-dioxide derivative(**10**), with the loss of N_2, which then lead to **2a** or **4a** (Scheme 3).[9] Furthermore, **5a** was afforded by the reaction of sulfene and SO_2.[1]

On the contrary, ethers are the major products in the cases bearing electron-withdrawing substituents like **1d** and **1e**. A sulfene mechanism can not give a satis-



Scheme 3.

factory explanation of the formation of **7d** and **7e**. If a sulfene intermediate is involved, the expected product is a sulfonate like **3**. Rather, **7d** or **7e** is the typical product of an acid-catalyzed decomposition of diazo compounds, as has already been mentioned. **1d** and **1e** did not show sufficient reactivity against SO_2 because of the low electron density on the α-carbon atom. Actually, **1d** showed a slower decolorization than the other diazomethanes(**1a**, **b**, and **c**). Especially, **1e** did not react against SO_2 positively under ordinary reaction conditions. Furthermore, **1e** was recovered in the reaction of **1e** with SO_2 at 20 °C in benzene in the presence of 1-morpholino-2-methylpropene, which traps the sulfene intermediate to afford the additive product.[2] Therefore, the most reasonable and acceptable mechanistic route for the formation of ether, **7d** or **7e**, is that the carbonium ion(**11**) is first formed by protonation to diazomethane with a small amount of ethyl hydrogen sulfite, which is at equilibrium with ethanol and SO_2; this is followed by the addition to ethanol, giving **7d** or **7e** in a catalytic manner. As for the formation of **7e**, Hesse and Majmudar[4] proposed a route involving the decomposition of sulfite(**6**), which is yielded by the collapse of **11** with the conuter-ion. In the current observation, **6d** was isolated in a very low yield(4%); this compound is too stable to undergo decomposition to afford **7d**.

According to the observed results and the discussions presented above, the mechanism of the decomposition of the diazomethanes and the follow-up reaction, in the ethanol–SO_2 system depend on the structures of the diazomethanes. An acid-catalyzed decomposition may be limited to the diazo compounds with a relatively strong electron-withdrawing group, while a sulfene formation is regarded as much more likely for the more nucleophilic diazomethanes: olefin or sulfonate was afforded *via* the sulfene from the diazomethane, in which the α-carbon atom has a comparatively high electron density, or from that of an intermediate electronic character, respectively. To clarify the scope and limitations of this reaction, further investigation will be necessary; however, it should be noted here that not all kinds of the diazomethanes are decomposed by a protic acid.

Experimental

The NMR spectra were recorded on a Varian EM-360 (60MHz) instrument in $CDCl_3$, with TMS as the internal standard. The IR spectra were measured with a Hitachi 215 spectrophotometer. The mass spectra were run on a VD-10001-A Hitachi spectrometer.

Materials. All the diazo compounds were prepared by known procedures: *p*-tolyldiazomethane(**1a**),[10] diphenyl diazomethane(**1b**),[11] 9-diazofluorene(**1c**),[12] *p*-nitrophenyldiazomethane(**1d**),[13] and ethyl diazoacetate(**1e**).[14] The sulfur dioxide was dried by passing it through $CaCl_2$ and P_2O_5 tubes. The ethanol was purified[15] and dried by refluxing it over magnesium metal. The carbon tetrachloride was purified by the ordinary method[15] and was dried over activated molecular sieves, MS-4A.

Procedure. *NMR Study*: The solutions to be studied were prepared by passing SO_2 slowly through ethanol until saturation. After determining the amount of SO_2, definite amounts of CCl_4 and ethanol were added to this solution. These operation were carried out under a good dry condition. The solution was then transferred into

an NMR tube, and the tightly cap-sealed tube was submitted to NMR analysis at 26 °C.

General Method for the Reaction of ***1*** *with SO_2 in Ethanol.* In a 100-ml, three-necked flask equipped with a magnetic stirrer, a gas inlet tube, a thermometer, and a calcium chloride drying tube we placed 5 mmol of **1** and 100 ml of anhydrous ethanol. Gaseous SO_2 was then introduced into this solution at 20 °C for a period of 1 h. After the decolorization of the solution and the evolution of N_2 was complete, the solvent and the excess SO_2 were removed *in vacuo* at room temperature. An aliquot of the residue was dissolved in $CDCl_3$ and analyzed by NMR; then the NMR solvent was removed, and the combined residue was separated by preparative silica gel column chromatography, if necessary. An analytically pure sample was obtained by recrystallization from suitable solvents.

The Reaction of ***1a.*** The reaction was carried out using twice the amount of **1a**. According to the NMR spectrum, five kinds of products were contained in the crude reaction mixture. These products were submitted to the preparative silica gel column chromatograph. *cis-* and *trans-***2a** were eluted first by benzene; these two geometric isomers were isolated by fractional recrystallization from ethanol. The isolated yields of *cis-* and *trans-***2a** were 21 and 38% respectively. *cis*-Di-*p*-tolylethylene (*cis-***2a**) was crystallized from ethanol; colorless prisms; mp 31—32 °C (lit, 32.3 °C).[16] NMR: δ 2.30(6H, s, methyl), 6.50(2H, s, vinyl), and 7.00 and 7.15(each 4H, d, J=8 Hz, phenyl). MS: m/e=208(M^+). *trans*-Di-*p*-tolylethylene(*trans-***2a**) was recrystallized from ethanol; colorless leaflets; mp 183—184 °C (lit, 179—180 °C).[17] NMR: δ 2.30(6H, s, methyl), 6.98 (2H, s, vinyl), and 7.10 and 7.37(each 4H, d, J=8Hz, phenyl). Found: C, 91.75; H, 7.74%. Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74%. *p*-Tolualdehyde azine(**4a**) was obtained as the second eluate by the use of benzene; its yield was estimated to be 9% from the intensity of the NMR spectrum of a reaction mixture. The recrystallization from acetone gave pale yellow prisms; mp 159—160 °C(lit, 157 °C).[18] IR(KBr): 1615 cm^{-1}(C=N). NMR: δ 2.40(6H, s, methyl), 7.26 and 7.77 (each 4H, d, J=8.5Hz, phenyl), and 8.65 (2H, s, methylidyne). Found: C, 81.32; H, 6.83; N, 11.66%. Calcd for $C_{16}H_{16}N_2$: C, 80.99; H, 6.85; N, 11.65%. *p*-Tolualdehyde(**5a**) and ethyl *p*-tolylmethanesulfonate(**3a**) were eluted by ether as the final fraction in yields of 4 and 23% respectively. The **5a** was identified by the comparison of its IR and NMR spectra with those of an authentic specimen. The **3a** was purified by further silica gel column chromatography and was recrystallized from ethanol; colorless plates; mp 40—41 °C. IR(KBr): 1170, 1175, 1350, and 1355 cm^{-1} (SO_2). NMR: δ 1.30(3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 2.37 (3H, s, CH_3), 4.12 (2H, q, J=7 Hz, $\underline{CH_2}CH_3$), 4.30 (2H, s, benzylic), and 7.25 (4H, broad s, phenyl). MS: m/e=214(M^+),105 (p-CH_3-C_6H_4-CH_2^+).

Reaction of ***1b.*** The white crystalline was obtained in a 87% yield by removing the solvent; subsequent recrystallization from ethanol gave colorless needles of ethyl diphenylmethanesulfonate (**3b**); mp 70—71 °C. IR (KBr): 1168 and 1345 cm^{-1}(SO_2). NMR: δ 1.15(3H, t, J=6Hz, CH_3), 4.00(2H, q, J=6Hz, CH_2), 5.50(1H, s, methylidyne), and 7.23—7.73(10H, m, phenyl). MS: m/e=276(M^+), 167(Ph_2CH^+). Found: C, 65.12; H, 5.77%. Calcd for $C_{15}H_{16}O_3S$: C, 65.21; H, 5.84%.

Reaction of ***1c.*** In the same manner as has been described above, a white powder, ethyl 9-fluorenesulfonate (**3c**), was obtained in a 89% yield; it was subsequently recrystallized from ethanol; colorless needles; mp 94.5—95.5 °C. IR(KBr): 1175 and 1355 cm^{-1}(SO_2). NMR: δ 0.93(3H, t, J=7Hz, CH_3),3.87(2H, q, J=7Hz, CH_2), 5.37(1H, s, methylidyne), and 7.2—8.1(8H, m, aromatic). MS: m/e=274(M^+), 165($M^+-C_2H_5SO_3$). Found: C, 65.96; H, 5.24%. Calcd for $C_{15}H_{14}O_3S$: C, 65.96; H, 5.15%.

Reaction of ***1d.*** The reaction was carried out using 10 mmol of **1d**. The crude reaction mixture was chromatographed over silica gel. *p*-Nitrobenzyl ethyl ether(**7d**), fractionated as the first eluate, was purified by further column chromatography; a pale yellow oil. IR: 1515 and 1345 cm^{-1}(NO_2), 1105 cm^{-1}(C-O-C). NMR: δ1.27(3H, t, J=7 Hz, CH_3), 3.60(2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 4.59 (2H, s, benzylic), and 7.50 and 8.18(each 2H, d, J=8.5Hz, phenyl). MS: m/e=181(M^+), 152(p-NO_2-C_6H_4-CH_2O^+), 136(p-NO_2-C_6H_4-CH_2^+), 106(p-O-C_6H_4-CH_2^+). *p*-Nitrobenzyl ethyl sulfite(**6d**) was also separated in a 4% yield by further elution with benzene; it was recrystallized from ethanol as colorless needles; mp 87—88 °C. IR(KBr): 1175 cm^{-1}(O-SO-O), 1345, 1355, 1515, and 1525 cm^{-1}(NO_2). NMR: δ 1.33(3H, t, J=7Hz, CH_3), 4.23(2H, q, J=7Hz, $O\underline{CH_2}CH_3$), 4.41(2H, s, benzylic), and 7.60 and 8.26(each 2H, d, J=8Hz, phenyl). MS: m/e=245(M^+), 152(p-NO_2-C_6H_4-CH_2O^+), 136(p-NO_2-C_6H_4-CH_2^+), 106(p-O-C_6H_4-CH_2^+).

Reaction of ***1e.*** Although the reaction did not practically proceed under ordinary conditions, it was accomplished at 40 °C for 2 h using 15 mmol of **1e** and 60 ml of ethanol. The oily crude product, obtained in an 81% yield by fractional distillation under reduced pressure, was identified as ethyl ethoxyacetate(**7e**); a colorless oil. IR: 1753 cm^{-1} (C=O), 1138 and 1205 cm^{-1}(C-O-C). NMR: δ 1.23(3H, t, J=6.5Hz, $OCH_2\underline{CH_3}$), 1.27(3H, t, J=7Hz, $CO_2CH_2\underline{CH_3}$),3.60(2H, q, J=6.5Hz, $O\underline{CH_2}CH_3$), 4.03(2H, s, OCH_2CO), and 4.21(2H, q, J=7Hz, $CO_2\underline{CH_2}CH_3$). MS: m/e= 103($M^+-C_2H_5$), 88($M^+-C_2H_4O$).

Reaction of ***1e*** *with SO_2 in the Presence of Enamine.* The reaction was tried using 10 mmol of **1e**, 10 mmol of 1-morpholino-2-methylpropene, and 50 mmol of SO_2 in 100 ml of benzene in the manner described in the previous paper,[2] but **1e** was recovered from the reaction mixture by distillation under reduced pressure.

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