BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 39 1785—1787 (1966)

Organic Sulfur Compounds. XI. The Reactions of the Cyclic Sulfites with the Aromatic Aldehydes

By Michio KOBAYASHI* and Akira YABE

Department of Chemistry, Yokohama City University, Mutsuura-machi, Kanazawa-ku, Yokohama

and Reiko KIRITANI

Department of Chemistry, Radiation Center of Osaka Prefecture, Sakai, Osaka

(Received January 5, 1966)

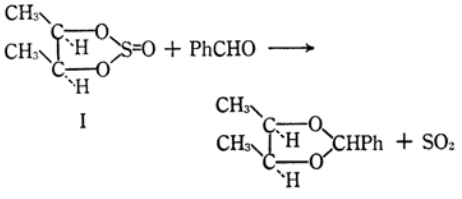
The reactions of the cyclic sulfites with aldehydes to give the cyclic acetals have been investigated with the stereochemical and with the ^{18}O tracer technique. Both groups of evidence have indicated that the bonds broken are the S–O, not the C–O bond, of the sulfites.

The formation of the acetals from the aldehydes and alkyl sulfites has long been known.[1] Recently, the reaction of ethylene sulfite with the carbonyl compounds to give the cyclic acetals or ketals has also been described.[2] These reactions are catalyzed with hydrogen chloride, without which no reaction has been observed. In order to clarify the mechanism of the latter reaction, the present investigation has been carried out.

Results and Discussion

Stereochemical Study.—The reaction of *meso*-2, 3-butylene sulfite (2-oxo-4, 5-dimethyl-1, 3, 2-dioxothiolane) (I) with benzaldehyde was examined in an attempt to find which bond in the cyclic sulfite was broken in the acetal formation. I was prepared from thionyl chloride and *meso*-2, 3-butanediol. There could exist two configurational isomers in I, one with sulfoxide oxygen in an axial position, Ia, and the other with that oxygen in an equatorial position, Ib. This kind of problem has attracted much interest recently, and several studies by means of infrared spectroscopy or NMR have been published.[3,4] In the case of *meso*-diphenylethylene sulfite, these two isomers have been isolated in the crystalline state.[4] Indeed, it has been pointed out that the ordinary I is a mixture of Ia and Ib, which could be separated incompletely by the gas liquid chromatography.[4] However, these two isomerides, the existence of which depends on the pyramidal configuration of the sulfoxide group, would be tautomerized to each other in the presence of the acid catalyst, since the optically active sulfoxides have been reported to undergo racemization very easily in the presence of hydrochloric acid.[5] Therefore, no effort was made to use the pure configurational isomer in the present investigation. (Incidentally, the configuration of *dl*-2, 3-butanediol has been shown not to change during the formation of the cyclic sulfite, *dl*-2, 3-butylene sulfite.[4])

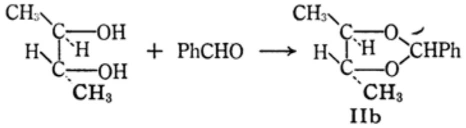
When I and benzaldehyde were refluxed in dioxane in the presence of hydrogen chloride, 2-phenyl-4, 5-dimethyl-1, 3-dioxolane (II) was obtained in a 50% yield. The identity of this product with 2-phenyl-*cis*-4, 5-dimethyl-1, 3-dioxolane IIa, prepared directly from *meso*-2, 3-butanediol and benzaldehyde, was established by the infrared spectroscopy and gas liquid chromatography. Symmetric structure of II was confirmed by NMR spectroscopy.



(1)

On the other hand, the reaction of *dl*-2, 3-butanediol with benzaldehyde gave 2-phenyl-*dl*-*trans*-4, 5-dimethyl-1, 3-dioxolane IIb, which exhibited the different NMR and infrared spectrum from those of the product II. The retention time of IIb in the gas liquid chromatography was shorter than that of II.

(2)



---

* To whom inquiries should be sent: Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Setagaya-ku, Tokyo.

[1] W. Voss, *Ann.*, **485**, 283 (1931).

[2] G. Hesse and M. Förderreuther, *Chem. Ber.*, **93**, 1249 (1960).

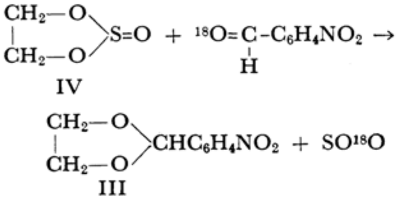
[3] J. G. Pritchard and P. C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961).

[4] Q. E. Thompson, M. M. Crutchfield and M. W. Dietrich, *J. Org. Chem.*, **30**, 2698 (1965).

[5] K. Mislow, T. Simmons, J. T. Melillo and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964).

Since it seems to be well understood that the C–O bond of the alcohols is retained in the acetal formation,[6] the above result may be considered to indicate the retention of the C–O bond in the cyclic sulfite in the reaction with aldehydes.

Isotope Tracer Study.—However, in the reaction described above, two successive inversions of the configuration around the asymmetric carbon atoms of the cyclic sulfite, one in each step involving C–O fission in the sulfite, could give *meso*-acetal from *meso*-sulfite. To confirm further the absence of the C–O bond fission of the sulfite in this type of reaction, the reaction of ethylene sulfite, IV, with *p*-nitrobenzaldehyde-[carbonyl-^{18}O] was examined. In the presence of hydrogen chloride, 2-*p*-nitrophenyl-1, 3-dioxolane III was produced in a 60% yield; this was found to contain no excess ^{18}O.



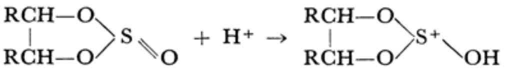
(3)

Consequently, from both of the stereochemical results and the isotope tracer study, it may be concluded that the C–O bond of the cyclic sulfite remained intact in the reaction with aldehydes to form the cyclic acetals.

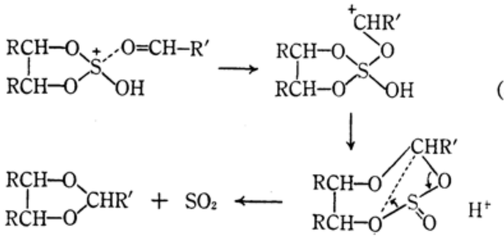
The mechanism of the hydrolysis of the cyclic sulfites has been investigated kinetically,[7-8] with the ^{18}O tracer technique[10] and stereochemically;[11] it is now firmly established that S–O bonds are broken in the reaction under acidic conditions, and that C–O bond fission has never been observed. Also, the reaction of alcohols with the carbonyl compounds to form acetals or ketals,[6] and the hydrolysis of the acetals or ketals to reverse the above reaction,[12] are both considered to involve the retention of the C-O bond in the alcohol part. The formation of the cyclic acetals from the sulfites investigated in the present research seems to conform with these findings regarding related reactions.

The reaction of IV with benzaldehyde was carried out in the presence of boron trifluoride etherate or trifluoroacetic acid in order to examine their catalytic properties. In the presence of boron trifluoride, IV gave no cyclic acetal; instead, a large amount of the polymeric substance was produced. With trifluoroacetic acid, the formation of acetal, 2-phenyl-1, 3-dioxolane (V), was observed, but the yield was not improved over that obtained with hydrogen chloride.

The following reaction mechanism may tentatively be considered as one possibility for the reaction investigated in this paper:



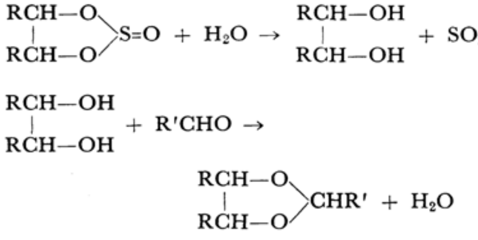
(4)



(5)

The addition of the proton to the cyclic sulfite (reaction 4) is a reversible, very fast step.[8] The attack on this protonated species by the nucleophilic reagent, somewhat as in the reaction 5, has been postulated to explain the catalytic property of the halides anion in the hydrolysis of the sulfites.[7,8]

Finally, it should be noticed that the following possibility can not be lightly excluded despite the denial of Hesse[2]—the possibility that the sulfite is hydrolyzed by a trace of water to give the glycols, which in turn react with aldehydes to form the cyclic acetals and to regenerate the equimolar water, with this water starting a new cycle. In the present stage of investigation, there is at least no definite evidence against this alternative.



Experimental

***meso*-2, 3-Butylene Sulfite** (**I**).—The starting material, *meso*-2, 3-butanediol, was a commercial product and was purified by distillation twice before use; b. p. 65°C/7 mmHg; lit.[13] 89°C/16 mmHg; 127°C/101 mmHg.[10] It gave di-*p*-nitrobenzoate, m. p. 188°C,

---

[6] J. Hine, "Physical Organic Chemistry," 2nd Ed., chapter 11, McGraw-Hill, N. Y. (1962).

[7] C. A. Bunton, P. B. D. de la Mare and J. G. Tillett, *J. Chem. Soc.*, **1958**, 4754.

[8] C. A. Bunton, P. B. D. de la Mare, A. Lennard, D. R. Llewellyn, R. B. Pearson, J. G. Pritchard and J. G. Tillett, *J. Chem. Soc.*, **1958**, 4761.

[9] R. E. Davis, *J. Am. Chem. Soc.*, **84**, 599 (1962).

[10] C. A. Bunton, P. B. D. de la Mare, P. M. Greaseley, D. R. Llewellyn, N. H. Pratt and J. G. Tillett, *J. Chem. Soc.*, **1958**, 4751.

[11] H. K. Garner and H. J. Lucas, *J. Am. Chem. Soc.*, **72**, 5497 (1950).

[12] M. M. Kreevoy, C. R. Morgan and R. W. Taft, Jr., ibid., **82**, 3064 (1960).

[13] C. E. Wilson and H. J. Lucas, ibid., **58**, 2396 (1936).

in a yield more than 80%. *meso*-2, 3-Butylene sulfite was prepared from 17 g. of the above glycol and 23 g. of thionyl chloride at 40°C, and a fraction boiling at 83—85°C/35 mmHg was collected (lit.[10] b. p. 67°C/8 mmHg; 181—189°C[14]). The infrared spectrum of the product coincided with that in the literature,[10] except for the presence of a 1059 cm^{-1} absorption instead of the 1099 cm^{-1} in that paper.

2-Phenyl-*cis*-4, 5-dimethyl-1, 3-dioxolane (IIa).—A mixture of 5 g. of *meso*-2, 3-butanediol, 6 g. of benzaldehyde and a few drops of 40% sulfuric acid was warmed on a water bath for 28 hr. and extracted with benzene; the product was purified by the vacuum distillation twice. B. p. 97—99°C/5 mmHg; lit.[15] 109—110°C/10 mmHg.

The Reaction of *meso*-2, 3-Butylene Sulfite with Benzaldehyde.—Hydrogen chloride was bubbled into a mixture of 6 g. of I, 5 g. of freshly-distilled benzaldehyde and 10 ml. of purified dioxane.[16] After it had been refluxed for 25.5 hr., the mixture was diluted with benzene, washed with a sodium hydrogen carbonate solution, water, and a sodium hydrogen sulfite solution, warmed with a sodium hydroxide solution, dried, and finally vacuum distilled to give a fraction boiling at 93—94°C/4 mmHg. Its infrared spectrum was superimposable upon that of IIa.

dl-2, 3-Butanediol was prepared from the *meso*-isomer by the following reaction sequence: *meso*-glycol→*meso*-2, 3-diacetate (b. p. 90—93°C/20 mmHg; lit.[13] 66°C/5.5 mmHg)→*dl-threo*-3-chloro-2-butanol (b. p. 52°C/28—30 mmHg; lit.[17] 52°C/30 mmHg)→*cis*-2, 3-epoxybutane[17]→*dl-trans*-2, 3-butanediol (b. p. 71°C/4 mmHg; lit.[13] 86°C/16 mmHg). It gave *dl*-di-*p*-nitrobenzoate, m. p. 130°C; lit. 128.5°C.

2-Phenyl-*dl-trans*-4, 5-dimethyl-1, 3-dioxolane (IIb).—A mixture of 1.2 g. of *dl*-2, 3-butanediol, 1.48 g. of benzaldehyde, and one drop of 40% sulfuric acid was heated on a water bath for 26 hr. The reaction mixture was then treated as in the case of *meso*-isomer, and finally purified by chromatography on alumina with petroleum ether, followed by vacuum distillation; this gave 90 mg. of IIb as a colorless liquid.

Found: C, 74.43; H, 8.19. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.91%.

The Preparation of *p*-Nitrobenzaldehyde-[carbonyl-^{18}O].—To a solution of *p*-nitrobenzylidenaniline (10 g.), and 10 g. of $H_2{}^{18}O$ (1.52 atom%) in 80 ml. of anhydrous dioxane, 5 ml. of concentrated sulfuric acid was added. After the mixture had been warmed on a water bath, two layers were separated. After it had been diluted with 150 ml. of benzene, the organic layer was washed with a sodium hydrogen carbonate solution and water, dried over magnesium sulfate, and evaporated. The crystalline residue was purified from petroleum ether to give 5.5 g. of the labeled aldehyde (84%). Its ^{18}O atom% was 0.61%.

Ethylene Sulfite.—Prepared from ethylene glycol and thionyl chloride; b. p. 72°C/22 mmHg. Lit. 94°C/43 mmHg, 84°C/38 mmHg[9]; 88°C/52 mmHg[10]; 86—88°C/38 mmHg[18]; 90°C/42 mmHg[19]; 63°C/13 mmHg[3].

The Reaction of Ethylene Sulfite with *p*-Nitrobenzaldehyde-^{18}O.—Hydrogen chloride was introduced into a solution of 5 g. of the labeled aldehyde and 4 g. of ethylene sulfite in 20 ml. of anhydrous dioxane, and the mixture was refluxed in an oil bath for 34 hr. Dioxane was removed in a vacuum, and the residue was dissolved in 100 ml. of benzene, washed with aqueous sodium hydrogen carbonate, dried, and evaporated. The remaining crystals were purified by chromatography on alumina with benzene and recrystallization from petroleum ether or carbon tetrachloride to give 3.10 g. of 2-*p*-nitrophenyl-1, 3-dioxolane (III), m. p. 89—91°C, in a 46% yield. Its ^{18}O atom % was normal (0.21%). The infrared spectrum of this specimen was the same as that of the product, m. p. 90°C, prepared by warming 20 g. of ethylene glycol, 3 g. of *p*-nitrobenzaldehyde, and a few drops of 40% sulfuric acid for 33 hr. The ^{18}O atom% of the unchanged *p*-nitrobenzaldehyde recovered in a low yield, contaminated with some acetal (III), was 0.35%.

Gas liquid chromatography measurements were performed on Hitachi KGL-2 using 6 m column packed with silicone KF 54. The column was operated at 206°C with a flow of 30 ml. nitrogen per minute. Retention times were: II and IIa, 14.2 min; IIb, 12.0 min.

NMR spectra were run on a Varian A 60A NMR Spectrometer operating 60 Mc./sec. TMS was used as an internal standard for solutions in carbon tetrachloride. The chemical shift values of II was as shown below:

Chemical shift (τ)	Number of H	Splitting	Assignment
8.83	6	Doublet J=6.0 c/s	Methyl
5.83	2	Multiplet	H at C_4 and C_5
2.72	5	Multiplet	Aromatic

Thanks are due to Mr. Shozo Masuda of the Department of Chemistry, The University of Tokyo, for his elemental analyses.

---

14) F. M. Robertson and A. Neish, *Can. J. Research*, **25B**, 491 (1947).

15) J. Kovář, J. Šteffková and J. Jarý, *Collection Czech. Chem. Commun.*, **30**, 2793 (1965).

16) A. Weissberger and E. S. Proskauer, "Organic Solvents," 2nd Ed. (1955).

17) H. J. Lucas and C. W. Gould, Jr., *J. Am. Chem. Soc.*, **63**, 2451 (1941).

18) W. W. Carlson and L. H. Cretcher, ibid., **69**, 1954 (1947).

19) P. B. D. de la Mare, W. Klyne, D. J. Millen, J. G. Pritchard and D. Watson, *J. Chem. Soc.*, **1956**, 1813.