The Chemistry of 1,3-Glycol Derivatives. III. The Preparation of 1,1-Bis(1-hydroxyalkyl)cyclopropanes and Their Halogenation

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By the reduction of 1,1-diacylcyclopropanes and their related compounds, several kinds of 1,1-bis(1-hydroxyalkyl)cyclopropanes have been prepared. Some of the stereoisomers were separated, and their configurations were determined by the NMR study of the 1,3-dioxanes prepared by the acetallization of the diols. The diols were subjected to halogenation. Although the reactions of *meso*- and *dl*-bis(1-hydroxyethyl)cyclopropanes with thionyl chloride and phosphorus pentachloride gave normal dichlorides, accompanied by slight skeletal rearrangements, the stereospecificities were rather low. With $ZnCl_2$–HCl, the specificities were lost completely and large amounts of the homoallyl derivative were formed. The reaction mechanism is discussed.

Stereoisomers of several kinds of aliphatic 1,3-glycol and their derivatives, including cyclic orthoacetates, were prepared and their reactions reported previously.[1] In this paper, an extension of the study to 1,3-glycols, whose C-2 carbons are cyclopropane-ring carbons, will be reported, since the preparation of this type of compound has not yet been reported except for one case of 1,1-bis(hydroxymethyl)cyclopropane.[2]

The glycols have been prepared by the reduction of 1,1-diacylcyclopropanes. Some of the stereoisomers have been separated and their conformations have been determined by the ^{1}H and ^{13}C NMR study of the glycols and their corresponding acetals. The diols were subjected to halogenation under various conditions to examine the stereospecificities and the skeletal rearrangements.

The starting materials and the glycols obtained (including several kinds of related compounds) are listed in Table 1.

According to conventional methods, the reductions were carried out with lithium aluminium hydride in tetrahydrofuran at 0 °C, with sodium borohydride in methanol at room temperature, and with aluminium isopropoxide in 2-propanol under reflux. Normal results were obtained, and no unusual phenomena such as those observed in the case of spiro-diketone[3] were encountered.

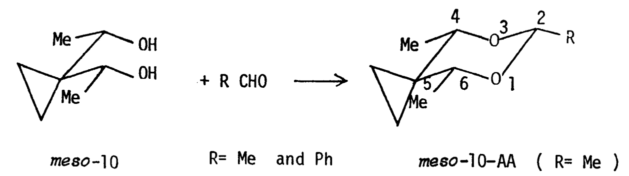
By reducing the reagent/substrate ratio, mono alcohols could be obtained. In the Meerwein-Pondorf-Verly reduction of the reference compound **6**, only glycol was obtained; no mono-alcohol could be isolated, not even with a smaller ratio of reagent/substrate (2/3) and with a shorter reaction time (0.5 h). No detectable amount of any by-product was obtained except 2-methyl-2,4-pentanediol, which was the aldol condensation product of acetone from the reducing reagent.[4] The results of the reduction are summarized in Table 2.

Since glycol **10** contains two asymmetric carbons, there should be *meso*- and *dl*-isomers. These were separated successfully by the following procedure. When a carbon tetrachloride solution of **10** was kept in a refrigerator at about −16 °C overnight, crystals (found to be *meso*-**10**, as will be described later) were formed. After filtration and evaporating the solvent, the liquid part of **10** (*dl*-**10**) was obtained. However, NMR analysis showed that the purity of the liquid part was as low as 70%. Since the solubility of *meso*-**10** was found to be slightly greater than that of the *dl*-form in water, the liquid portion was shaken with an ether–water mixture to remove the *meso*. After repeating the procedure, a *dl*-form with a purity of more than 80% was obtained.

Glycol **12** also has two asymmetric carbons and has *erythro*- and *threo*-forms. From crude **12**, crystals were formed after it had stood at room temperature for three months. Using the crystals as the seeds, a crystalline isomer of **12** (found to be *erythro*-**12**, as will be described later) were obtained from the ethereal solution of crude **12** at −30 °C. The residual part was *threo*-**12**, containing about 25% *erythro*-form.

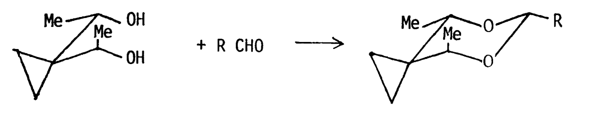
Glycol **13** has *cis*- and *trans*-isomers in addition to *meso*- and *dl*-isomers, and all attempts at separation were unsuccessful. The isomer separation of *meso*- and *dl*-**15** was unsuccessful too, although the NMR assignments could be made in this case.

The structural assignments of the isomers of **10** and **12** were carried out by NMR analyses of the corresponding acetals obtained by the reactions with acetaldehyde and benzaldehyde (in the presence of calcium chloride and catalytic amounts of *p*-toluenesulfonic acid[5]) in the same way as was reported previously.[1]



meso-10 R= Me and Ph *meso*-10-AA (R= Me)

meso-10-BA (R= Ph)

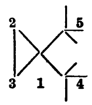


dl-10 *dl*-10-AA (R= Me)

dl-10-BA (R= Ph)

The physical properties of the acetals obtained are listed in Table 3.

The discussion of the NMR data of 1,3-dioxanes

Table 1. Physical properties of the diols obtained 

Starting material	Diol	Bp °C/mmHg (Mp/°C)	NMR data of diol in $CDCl_3$, δ/ppm: Ring CH_2	H on C^4	H on C^5	CH_3 on C^4	CH_3 on C^5	OH	Others
1	**7**	111—115/6	0.5, s, 4H	3.59, s, 4H				3.84, s, 2H	
2	**8**	91—92/4.7	0.32, m, 4H	3.45, q, 1H J=6.3	3.19, d, 1H J=11.3 4.02, d, 1H J=11.3	1.26, d, 3H J=6.3		3.28, s, 2H	
2	**9**	89—91/11.3	0.84—1.27 m, 4H	3.72, q, 1H J=7.0		1.26, d, 3H J=7.0		3.40, s, 2H	3.66, s, 3H (CH_3O)
3	*meso*-**10**	118—121/11 (62.8—63.0)	0.5, s, 4H	3.91, q, 2H J=6.8		1.15, d, 6H J=6.8		2.56, s, 2H	
3	*dl*-**10**	118—121/11	0.48, m, 4H	3.85, q, 2H J=6.8		1.13, d, 6H J=6.8		3.03, s, 2H	
3	**11**	110/15	0.86—1.29 m, 4H	3.90, q, 1H J=7.2		1.38, d, 3H J=7.2	1.91, s, 3H	3.60, 1H	
4	*erythro*-**12**	146—156/6 (84.5—85.1)	0.09—0.63 m, 4H	3.79, q, 1H J=6.0	4.84, s, 1H	0.95, d, 3H J=6.0	Ph, 7.20 s, 5H	3.14, 2H	
4	*threo*-**12**		0.09—0.63 m, 4H	1,00, d, 1H J=6.0	4.74, s, 1H	3.61, q, 1H J=6.0	Ph, 7.25 s, 5H	3.61, 2H	
5	**13**	164—170/11.5							
5	**14**	167/14	1.20—1.40 m, 2H PhCH 1.89, d of d, J=14, 7 } 1H 2.71, d of d, J=17, 14 } 1H	3.43, q J=6 4.23, q J=6 } 1H		1.24, d J=6 1.31, d J=6 } 3H	1.53, s 1.54, s } 3H	2.95, 1H	7.17, m, 5H Ph

1: 1,1-Bis(ethoxycarbonyl)cyclopropane,**2** : 1-acetyl-1-(methoxycarbonyl)cyclopropane, **3**: 1,1-diacetylcyclopropane, **4**: 1-acetyl-1-benzoylcyclopropane, **5**: 1,1-diacetyl-2-phenylcyclopropane, **6**: 1,1-diacetyl-2-phenylethylene, **7**: 1,1-bis(hydroxymethyl)cyclopropane, **8**: 1-(1-hydroxyethyl)-1-(hydroxymethyl)cyclopropane, **9**: 1-(1-hydroxyethyl)-1-(methoxycarbonyl)cyclopropane, **10**: 1,1-bis(1-hydroxyethyl)cyclopropane, **11**: 1-(1-hydroxyethyl)-1-(acetyl)cyclopropane, **12**: 1-(1-hydroxyethyl)-1-(1-hydroxybenzyl)cyclopropane, **13**: 1,1-bis(1-hydroxyethyl)-2-phenylcyclopropane, **14**: 1-acetyl-1-(1-hydroxyethyl)-2-phenylcyclopropane, **15**: 1,1-bis(1-hydroxyethyl)-2-phenylethylene which were obtained by the reactions of aliphatic 1,3-glycols with orthoacetate[1] can be applied to the present case without any change except that the cyclopropane ring anisotropy shifts the signals of equatorial hydrogens and methyl hydrogens at C^4 and C^6 to higher magnetic fields. The data in Table 3 can be explained reasonably in terms of the configurations described in the table. In the case of **8**, the NMR data showed that the acetallization gave a mixture of isomers due to axial and equatorial methyl derivatives in a ratio of 12:88.

The following characteristic features of the NMR signals of benzaldehyde acetals can be pointed out. 1. Acetal-ring methylene protons give signals at about δ=4.21—4.31 for axial ones, and at δ=3.21—3.39 for equatorial ones. 2. Methine protons at C^4 and C^6 give signals at δ=4.16—4.54 for axial ones, and at δ=3.21—3.68 for equatorial ones. 3. Methyl protons at C^4 and C^6 give signals at δ=1.32—1.61 for axial ones, and at δ=0.90—1.05 for equatorial ones. These facts can be explained by the anisotropic effects of cyclopropane and phenyl rings.

The structures of *meso*- and *dl*-**10** were confirmed further by ^{13}C NMR. The *meso*-form gave signals at δ=4.4 and 9.0 (ring CH_2), 20.0 (CH_3), 29.5 (ring head C), and 71.2 (CHOH). The *dl*-form gave signals at δ=7.7 (ring CH_2), 18.9 (CH_3), 28.6 (ring head C), and 71.2 (CHOH) ppm downfield from the internal TMS. The major differences between the spectra of the two isomers are those due to the ring methylene carbons. The fact that the ring methylene carbons of *meso*-**10** gave two signals, while those of *dl*-**10** gave only one signal, shows that the former carbons are not equivalent, while the latter is equivalent, and that all can be well understood in terms of their structures.[6]

Among the physical properties of **10**, it should be

TABLE 2. THE RESULTS OF THE REDUCTION

Substrate	Reducing reagent and Substrate/reagent mol ratio in mmol	Product (yield)
1	$LiAlH_4$ in THF 63/63	**7** (88%)
2	$LiAlH_4$ in THF 21/56	**8** (84%)
2	$NaBH_4$ in MeOH 70/53	**9** (70%)
3	$LiAlH_4$ in THF 380/330	**10** (77%) (*meso*:*dl*=63:37)
3	$LiAlH_4$ in THF 80/50	**3**+**10**+**11** (8:74:18)
3	Al(*i*-PrO)$_3$ in *i*-PrOH 25/82	**10** (88%) (*meso*:*dl*=79:21)
3	Al(*i*-PrO)$_3$ in *i*-PrOH 25/17	**11** (30%)
4	$LiAlH_4$ in THF 145/87	**12** (93%) (*threo*:*erythro*=1:1)
5	Al(*i*-PrO)$_3$ in *i*-PrOH 25/82	**13** (65%) mixture of 4 isomers
5	Al(*i*-PrO)$_3$ in *i*-PrOH 25/17	**14** (20%)
6	Al(*i*-PrO)$_3$ in *i*-PrOH 25/82	**15** (31%)

TABLE 3. PHYSICAL PROPERTIES OF THE ACETALS OBTAINED BY THE REACTIONS

Acetal	Bp °C/mmHg (Mp/°C)	e-H on C^4	a-H on C^4	e-H on C^6
7-AA	60/25	3.21, d, 1H J=11.6	4.21, d, 1H J=11.6	3.21, d, 1H J=11.6
7-BA	150/25	3.39, d, 1H J=11.8	4.31, d, 1H J=11.8	3.39, d, 1H J=11.8
8-BA-a			4.41, q, 1H J=7.0	3.34, d, 1H J=12.0
8-BA-b		3.68, q, 1H J=7.0		3.29, d, 1H J=12.0
meso-**10-AA**	80/23		4.16, q, 1H J=6.0	
dl-**10-AA**	68/22		4.37, q, 1H J=6.0	3.37, q, 1H J=6.0
meso-**10-BA**	98—104/4		4.30, q, 1H J=6.0	
dl-**10-BA**	100—104/4		4.50, q, 1H J=6.0	3.48, q, 1H J=6.0
erythro-**12-AA**	(88.5—89.0)		5.04, s, 1H	
threo-**12-AA**			5.15, s, 1H	3.44, q, 1H J=6.5
erythro-**12-BA**	180/5		5.24, s, 1H	
threo-**12-BA**	162/3		5.34, s, 1H	3.59, q, 1H J=7.0

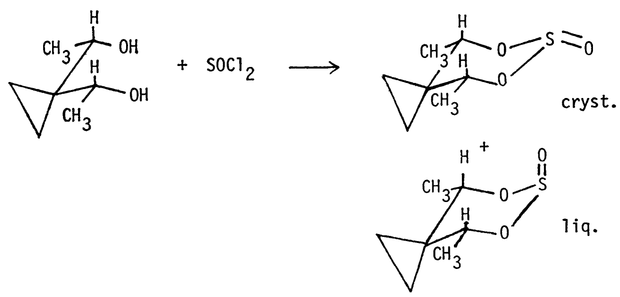
noted that the *meso*-form is crystalline and that the *dl*-form is liquid, while Pritchard reported that the crystalline form (mp 48—49 °C) was *dl* and the liquid one was *meso* in the case of 2,4-pentanediol.[7)]

It is well known that the halogenation of cyclopropylalkanols is accompanied by skeletal rearrangements. For example, the reaction of cyclopropylmethanol with thionyl chloride gave cyclopropylmethyl chloride, cyclobutyl chloride, and homoallyl chloride.[8)] We examined whether or not the behavior of bis(1-hydroxyalkyl)cyclopropanes is the same as that of mono-(1-hydroxyalkyl)cyclopropanes.

Thionyl chloride is the most frequently used reagent in the chlorination of a cyclopropylalkanol system. Therefore, the reaction with this reagent has been examined first.

Cyclic Sulfite Formation. Pritchard and his coworkers demonstrated that the reaction of 2,4-pentanediol with thionyl chloride gave a cyclic sulfite.[7)] Similarly, **10** gave cyclic sulfites. In pyridine at 0 °C, *meso*-**10** formed two kinds of sulfite, crystalline and liquid (7:3).

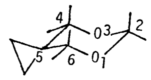
Six-membered cyclic sulfites have stereoconformers, as in the case of cyclohexane derivatives. Since the C–O bonds of the glycol are not broken in the sulfite formation, the configurations of the carbons of C–O in the sulfites should be the same as those in the starting glycol. The two methyl groups at C-4 and C-6 of the cyclic sulfites from *meso*-**10** should both be equatorial or both axial. Apparently, the diaxial conformer should be much more unstable, and the product should have a di-equatorial conformation. The fact that the two kinds of product were obtained appears to have resulted from the axial and equatorial forms of S=O bond. Since the S=O bond shows an anisotropic effect,[9)] NMR data can be used to clarify the structures. The axial S=O should shift the signals of the axial protons at C-4 and C-6 to lower fields, but not the equatorial S=O. All NMR data can be explained reasonably in terms of the structures depicted; they exclude the possibility of the twisted boat form.



There are two conflicting reports on the IR spectra of S=O. Pritchard and his coworkers assigned the absorptions of cyclic sulfite of 2,4-pentanediol at 1240 and 1188 cm^{-1} to axial and equatorial S=O respectively,[7)] while Hellier and his coworkers assigned the absorptions of the same compound at 1230 and 1190 cm^{-1} to equatorial and axial respectively.[9,10)] Our conclusion agreed with the latter assignment. *dl*-**10** gave only one cyclic sulfite, and the S=O bond was found to be axial from the NMR and IR data.

The cyclic sulfites obtained are listed in Table 4.

WITH ACETALDEHYDE (AA) AND BENZALDEHYDE (BA)



NMR data in $CDCl_3$, δ/ppm				
a-H on C^6	e-CH_3 on C^4	a-CH_3 on C^4	e-CH_3 on C^6	a-CH_3 on C^6
4.21, d, 1H J=11.6				
4.31, d, 1H J=11.8				
4.33, d, 1H J=12.0			0.95, d, 3H J=7.0	
4.32, d, 1H J=12.0		1.43, d, 3H J=7.0		
4.16, q, 1H J=6.0	0.91, d, 3H J=6.0		0.91, d, 3H J=6.0	
	0.90, d, 3H J=6.0			1.40, d, 3H J=6.0
4.30, q, 1H J=6.0	0.93, d, 3H J=6.0		0.93, d, 3H J=6.0	
	0.95, d, 3H J=6.0			1.44, d, 3H J=6.0
4.30, q, 1H J=6.0	C_6H_5–, 7.20		0.98, d, 3H J=6.0	
	C_6H_5–, 7.18			1.50, d, 3H J=6.5
4.54, q, 1H J=7.0	C_6H_5–, 6.82 —7.45, m		1.05, d, 3H J=7.0	
	C_6H_5–, 7.14 —7.32, m			1.61, d, 3H J=7.0

Table 4. Physical properties of the

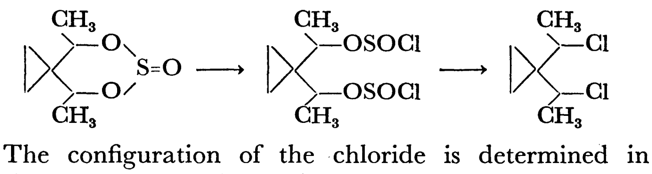
Sulfite	Bp °C/mmHg (Mp/°C)	e-H on C^4	a-H on C^4	e-H on C^6
7-S	78—82/13 (72.4—73.4)	3.04, d, 1H J=12.0	5.24, d, 1H J=12.0	3.04, d, 1H J=12.0
	IR of S=O, 1178 cm^{-1}, axial			
8-S-a	65/24	4.22, q, 1H J=6.5		3.72, d, 1H J=12.0
	IR of S=O, 1230 cm^{-1}, equatorial			
8-S-b			5.61, q, 1H J=7.5	3.00, d, 1H J=12.0
	IR of S=O, 1180 cm^{-1}, axial			
meso-**10-S**-e	(80.8—81.2)		5.01, q, 1H J=6.0	
	IR of S=O, 1230 cm^{-1}, equatorial			
meso-**10-S**-a			5.63, q, 1H J=6.0	
	IR of S=O, 1190 cm^{-1}, axial			
dl-**10-S**	112—120/22	3.89, q, 1H J=7.5		
	IR of S=O, 1180 cm^{-1}, axial			

Diol **8** gave the sulfite containing two conformers.

Reaction of Cyclic Sulfite with Thionyl Chloride. The reaction of alkyl sulfite with thionyl chloride is believed to proceed according to the following equation.[11)]

$$(RO)_2SO + SOCl_2 \longrightarrow 2ROSOCl \longrightarrow 2RCl$$

In the present case, the equation is as follows:



The configuration of the chloride is determined in the second step of the above equation, since the first step does not involve the breaking of the C–O bond.

The results of the reaction of sulfites with thionyl chloride are listed in Table 5.

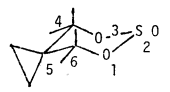
The sulfite of *meso*-**10** (*meso*-**10-S**) reacted much slower than that of *dl*-**10**. Since the rates of the second step should be the same in both the stereoisomers, the difference must have resulted from the first step. The results can reasonably be explained by considering that the backsides of both O–SO bonds are blocked by two methyl groups to S_N2 attack on O in the case of the *meso*-isomer, while one of the backsides is open in the case of the *dl*-isomer.

The final dichloride (**10-Cl**) has stereoisomers of *meso* and *dl*, whose structural assignments will be described later. In a chloroform solution, *meso*-**10-S** gave *meso*-**10-Cl** and *dl*-**10-S** gave *dl*-**10-Cl** predominantly, but the stereospecificities were about 70%. If the reactions of the two C–O–SO groups are of the S_Ni type (which is believed to be the case in the absence of a base), the specificities should be 100%. The addition of pyridine changes the reaction to S_N2, but the results should be the same by double inversion. The formation of 5-chloro-3-(1-chloroethyl)-2-pentene (homoallyl-**Cl**), although the yields were very low, appears to show that the cyclopropylmethyl cation intervenes in the reaction, as in the chlorination of the usual cyclopropylmethanol. The addition of pyridine to the reaction system resulted in the further loss of the specificity and in the larger yield of homoallyl-**Cl**. These results will be discussed in the following section.

Halogenation of meso- *and* dl-***10*** *under Various Conditions.* The results of the halogenation of *meso*- and *dl*-**10** are listed in Table 6.

It is difficult to reach a clean-cut conclusion as to the steric course of the reactions with thionyl chloride and phosphorus pentachloride except that slight retentions of configuration were observed. It has been pointed out that the stereospecificity of the chlorination of alcohol with thionyl chloride depends on the experimental technique.[12)] Therefore, we reexamined the reaction of *meso*-2,4-pentanediol reported by Pritchard[7)] and confirmed that the reaction gave a product with a stereospecificity of more 98%, showing that the above results had not resulted from our experimental technique.

The formation of a homoallyl derivative, which indicates the intervention of the cyclopropylmethyl cation, was observed in all cases. Its yields were higher in a chloroform solution than in donor solvents such as benzene, dioxane, ether, carbon disulfide, and acetonitrile, but not pyridine. These results may be explained on the assumptions that the cyclopropylmethyl cation is stabilized by solvation with the basic solvent and that the rearrangement to the homoallyl derivative is suppressed. In the presence of pyridine, the hydrogen chloride formed reacts to form ionic pyridine hydrochloride, which may favor the formation of the cation and the rearrangement to the homoallyl

CYCLIC SULFITE OF THE DIOLS 

NMR data in $CDCl_3$, δ/ppm				
a-H on C^6	e-CH_3 on C^4	a-CH_3 on C^4	e-CH_3 on C^6	Propane ring
5.24, d, 1H J=12.0				0.43—0.87, m
4.64, d, 1H J=12.0		1.51, d, 3H J=6.5		0.25—0.75, m
5.30, d, 1H J=12.0	0.98, d, 3H J=7.5			0.25—0.75, m
5.01, q, 1H J=6.0	1.12, d, 3H J=6.0		1.12, d, 3H J=6.0	0.20—1.10, m
5.63, q, 1H J=6.0	1.00, d, 3H J=6.0		1.00, d, 3H J=6.0	0.15—1.10, m
5.49, q, 1H J=6.0		1.59, d, 3H J=7.5	1.11, d, 3H J=6.0	0.23—0.96, m

TABLE 5. REACTIONS OF *meso*- AND *dl*-**10** SULFITES WITH THIONYL CHLORIDE IN CHLOROFORM

Sulfite	Temp / °C	Time / h	Isomer distribution *meso*-**10-Cl**	*dl*-**10-Cl**	homoallyl-**Cl**
meso-**10-S** crystal	60	8	71	29	trace
meso-**10-S** liquid	25	90	70	30	trace
dl-**10-S**	25	1	27	73	trace
dl-**10-S**[a)]	25	1	46	50	4

a) Pyridine was added to the chloroform.

derivative. The loss of the stereospecificity in the normal dichloride formation appears also to have resulted from the formation of the cation. Another possible reason for the loss of specificity might be that one of the two chlorine atoms is introduced by S_N2, and the other by S_N1. This possibility, however, appears to be excluded by the fact that the changes in the medium did not change the results appreciably.

In the case of the $ZnCl_2$–HCl system, the stereospecificity was lost almost completely and a large amount of the homoallyl product was formed, showing the formation of the cyclopropylmethyl cation.

The bromination of the same substrates resulted in further losses of specificity than in the case of chlorination and in larger yields of the homoallyl product.

Structural Assignments of meso- *and* dl-***10-X*** *and Homoallyl Chloride.* Attempts at the structural assignments of *meso*- and *dl*-**10** by PMR and IR were unsuccessful. However, ^{13}C NMR could clearly discriminate the two isomers by analogy with the case of diols mentioned in the early part of this paper. The cyclopropane-ring methylene carbons of the *dl*-isomer were equivalent (δ:11.3), but not those of the *meso*-isomer (δ:12.4 and 15.5).

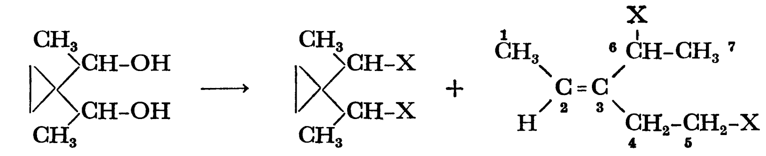
The NMR data of homoallyl-**10-Cl** show that the structure should be the one depicted in Table 4. [δ: 1.60 (d, J=7.0, 3H, C^7H_3), 1.69 (d, J=7.0, 3H, C^1H_3), 2.66 (t, J=8.0, 2H, C^5H_2), 3.58 (m, 2H, C^4H_2), 4.59 (q, J=7.0, 1H, C^6H), and 5.73 (q, J=7.0, 1H, C^2H)]. Whether this compound has the structure of E or that of Z could not be determined, however.

Experimental

Materials. According to the method reported by Dox and Yoder,[13)] **1** was prepared by the reaction of diethyl malonate with 1,2-dibromoethane in the presence of sodium ethoxide. The use of 2 M NaOH instead of the previously reported *n*-$BuNH_2$ to remove the unreacted diethyl molonate from the reaction product gave better results. Compounds **2—5** were prepared by the reaction of oxymercuration products of olefins with β-diketo compounds followed by demercuration, as had been reported previously.[14)] Compound **6** was prepared from benzaldehyde and acetylacetone in the presence of picoline.[15)]

Reduction. The reductions were carried out by the conventional methods;[3)] no special technique was used except in the product isolations of **7**, **11**, and **14**. The reported poor yields of **7**[2)] was greatly improved by the following procedure. After the hydrolysis of the reduction mixture, the aluminium hydroxide was filtered and washed

TABLE 6. HALOGENATION OF *meso*- AND *dl*-**10**[a)]



meso- and *dl*-**10** *meso*- and *dl*-**10-X** (X=Cl or Br) homoallyl-**X**

Diol-**10**	Reagent	Solvent	Temp °C	Time h	Isomer distribution of the product *meso*-**10-X**	*dl*-**10-X**	homoallyl-**X**
meso	$SOCl_2$	$CHCl_3$	0	1	50	45	5
dl	$SOCl_2$		0	1	44	52	4
meso	$SOCl_2$	$CHCl_3$+Py[b)]	0	1	50	34	16
dl	$SOCl_2$	$CHCl_3$+Py[b)]	0	1	42	49	9
meso	$SOCl_2$	$CHCl_3$	−70	1	63	25	12
meso	$SOCl_2$	C_6H_6	0	1	60	40	trace
dl	$SOCl_2$	C_6H_6	0	1	50	50	trace
meso	$SOCl_2$	dioxane	60	20	68	32	trace
dl	$SOCl_2$	dioxane	60	20	41	59	trace
meso	$SOCl_2$	CH_3CN	25	1	62	38	trace
meso	$SOCl_2$	Et_2O	25	1	65	35	trace
meso	$SOCl_2$	CS_2	25	1	57	43	trace
meso	$SOCl_2$	CCl_4	25	1	51	49	trace
meso	PCl_5	C_6H_6	0	2	73	22	5
dl	PCl_5	C_6H_6	0	2	36	60	4
meso	$ZnCl_2$-HCl	concd HCl	0	1	37	33	30
dl	$ZnCl_2$-HCl	concd HCl	0	1	27	26	47
meso	$SOBr_2$	$CHCl_3$	0	2	40	35	25
dl	$SOBr_2$	$CHCl_3$	0	2	45	45	10
meso	PBr_3	$CHCl_3$	25	1	57	39	4
dl	PBr_3	$CHCl_3$	25	1	42	48	10

a) The *dl*-**10** substrate contained 20% *meso*. The combined yields of the halides were about 80—90%. b) The ratio of $CHCl_3$:pyridine:$SOCl_2$=6.7:0.38:0.42 (mol).

TABLE 7. ANALYTICAL DATA

Compound	Calcd for	C, %	H, %	Cl, Br, or S, %	Found C, %	H, %	Cl, Br, or S, %
8	$C_6H_{12}O_2$	62.04	10.41		61.87	10.66	
9[a)]	$C_7H_{12}O_3$	58.31	8.39		57.81	8.35	
meso-**10**	$C_7H_{14}O_2$	64.58	10.84		64.62	11.11	
dl-**10**	$C_7H_{14}O_2$	64.58	10.84		64.40	11.11	
11	$C_7H_{12}O_2$	65.59	9.44		63.86	9.69	
erythro-**12**[a)]	$C_{12}H_{16}O_2$	74.97	8.37		74.29	8.38	
threo-**12**	$C_{12}H_{16}O_2$	74.97	8.37		75.30	8.66	
13	$C_{13}H_{18}O_2$	75.69	8.80		75.50	8.86	
14	$C_{13}H_{16}O_2$	76.44	7.90		76.29	8.18	
15	$C_{12}H_{16}O_2$	74.97	8.39		75.10	8.11	
meso-**10-BA**	$C_{14}H_{18}O_2$	77.03	8.11		77.00	8.14	
dl-**10-BA**	$C_{14}H_{18}O_2$	77.03	8.11		77.02	8.24	
erythro-**12-AA**	$C_{14}H_{18}O_2$	77.03	8.11		77.07	8.29	
threo-**12-BA**	$C_{19}H_{20}O_2$	81.39	7.19		81.25	7·30	
7-S[b)]	$C_5H_8O_3S$	40.52	5.44	21.63	39.90	4.96	
8-S-(a+b)[b)]	$C_6H_{10}O_3S$	44.44	6.22	19.74	44.77	6.35	19.12
meso-**10-S**-a	$C_7H_{12}O_3S$	47.72	6.87	18.17	47.19	6.88	17.54
dl-**10-S**	$C_7H_{12}O_3S$	47.72	6.87	18.17	47.88	7.00	17.91
meso-**10-Cl**	$C_7H_{12}Cl_2$	50.32	7.24	42.44	50.04	7.19	41.91
meso-**10-Br**	$C_7H_{12}Br_2$	33.84	4.73	62.43	33.12	4.69	62.14

a) Very hygroscopic. b) Unstable to atmospheric moisture and light.

with water. When the water was removed from the filtrate by the use of rotatory evaporator, aluminium hydroxide precipitated again. After filtering again, the filtrate was distilled under reduced pressure. It appears that the second removal of aluminium hydroxide improved the isolation yield.

In order to isolate **11** (IR, $\nu_{C=O}$ at 1670 cm^{-1}), the distillate which had been obtained by the usual work-up was subjected to column chromatography (Wakogel C-200 $2\phi \times 20$ cm; 1. hexane-ethyl acetate (95 : 5), 2. hexane-ethyl ether (70 : 30), 3. ethyl ether). Similarly, **14** (IR, $\nu_{C=O}$ at 1680 cm^{-1}) was isolated by column chromatography (Silicic acid, Mallinckrodt, $2\phi \times 15$ cm; 1. hexane-ethyl ether (95 : 5), 2. hexane-ethyl ether (70 : 30), 3. ethyl ether).

Acetallization. The acetaldehyde acetal and benzaldehyde acetals were prepared by the method by Eliel and his coworkers.[16]

Cyclic Sulfite. The following example shows a typical experimental procedure. Into a pyridine (20 ml) solution of diol **10** (2.6 g, 20 mmol), we stirred thionyl chloride (4.76 g, 40 mmol), drop by drop in an ice bath. After 1 h, the crystalline pyridine hydrochloride formed was removed by filtration, and then pyridine was removed by distillation under reduced pressure. Ether was added to the residue, which was then washed with 6 M HCl, a saturated $NaHCO_3$ solution, and then with water, and dried over Na_2SO_4. After the ether had been removed, the residue (2.5 g, 71% yield) was recrystallized from CCl_4 to give crystalline *meso*-**10-S** (mp 80.8—81.2 °C). The liquid part was purified by column chromatography with Wakogel C-200, using $CHCl_3$ as the solvent (bp 112—120 °C). The ratio of the crystalline to the liquid part was 7 : 3. The same procedure gave the cyclic sulfite of **8** (bp 65 °C/24 mmHg).

Formation of Dihalides. The experimental procedure is shown by the following example. Into a chloroform (800 g) solution of diol **10** (29.6 g, 0.374 mol) we stirred a pyridine (29.6 g, 0.374 mol) solution of thionyl chloride (50.0 g, 0.42 mol) in an ice bath. After 10 h, the reaction mixture was washed with 2 M HCl, saturated $NaHCO_3$ and then water, and dried over Na_2SO_4. After the chloroform had then been removed, the residue was distilled under reduced pressure to give a mixture of *dl*- and *meso*-dichloride and homoallyl chloride (bp 84—86 °C/20 mmHg; yield, 90%), which was analyzed by GLC. Upon cooling in a dry ice-acetone bath, the mixture gave crystalline *meso*-**10-Cl**. The liquid part was *dl*-**10-Cl**, containing a small amount of homoallyl-**Cl**.

*Reaction of Diol-**10** with $ZnCl_2$–HCl.* Into concd hydrochloric acid (1 ml) containing $ZnCl_2$ (0.22 g) we stirred **10** (0.3 g) at 0. °C. After 5 h, the product was extracted with benzene, washed with saturated $NaHCO_3$ and water, dried over Na_2SO_4, and analyzed by GLC.

The analytical data are shown in Table 7.

The IR spectra were recorded on a HITACHI EPI-G2 apparatus. The NMR spectra (in deuteriochloroform, with TMS as the internal standard) were recorded on a Varian Associates HR-220 apparatus at 220 MHz at room temperature. The ^{13}C NMR spectra (in deuteriochloroform, with TMS as the internal standard) were obtained by the use of a JNM FX-100 spectrometer.

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