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2-Oxo-1,3,2-dioxathianes. I. Preparation of the Alkyl-substituted Derivatives

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2-Oxo-1,3,2-dioxathiane, all methyl- and several other alkyl-substituted 2-oxo-1,3,2-dioxathianes have been synthesized by condensing 1,3-alkanediols and thionyl chloride. The amount of the S=O-axial and S=O-equatorial isomers can be controlled by adding pyridine to the reaction mixture.

2-Oxo-1,3,2-dioxathianes are cyclic sulfurous acid esters, cyclic sulfites. The parent compound, 2-oxo-1,3,2-dioxathiane has been shown to exist in a chair conformation with the S=O group axially oriented.[1,2] An axial S=O group has been found to be about 15 kJ mol^{-1} more stable than an equatorial S=O group.[2] Substituted derivatives exist preferentially in a chair conformation with an axial or equatorial S=O group, or in a mixture of two interconverting chair forms.[1,2]

2-Oxo-1,3,2-dioxathianes can be synthesized by condensing an appropriate 1,3-alkanediol and thionyl chloride (Fig. 1). They are easily hydrolyzed by base to the corresponding diols. Since diastereoisomeric 2-oxo-1,3,2-dioxathianes are relatively easy to separate from each other they offer a useful method for the preparation of the diol isomers.

In order to carry out a thorough and definite structural analysis of this ring system 2-oxo-1,3,2-dioxathiane, all methyl- and several other alkyl-substituted derivatives have been synthesized. In the present paper two variations of the preparation method are briefly discussed.

2-Oxo-1,3,2-dioxathianes can be prepared by refluxing the ethereal solution of diol and thionyl chloride or by adding thionyl chloride dissolved in benzene to a diol–pyridine solution. In the first

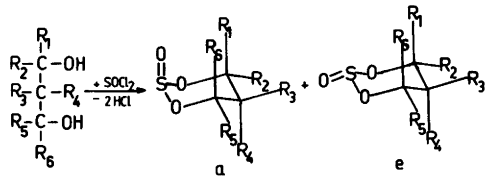

Fig. 1. Preparation of 2-oxo-1,3,2-dioxathianes.

method the liberated hydrogen chloride equilibrates isomers *a* and *e* (Fig. 1) and the final product consists mainly of the more stable isomer *a*. In the other method pyridine reacts with hydrogen chloride forming pyridine hydrochloride and the proportion of isomer *e* depends on the pyridine–diol ratio and the reaction time (Fig. 2). When the pyridine–diol ratio is close to two, the mol fraction of isomer *e* decreases with the increasing reaction time. When this ratio is equal to or greater than eight the mol fraction of isomer *e* is time-independent since the concentration of the hydrogen chloride is

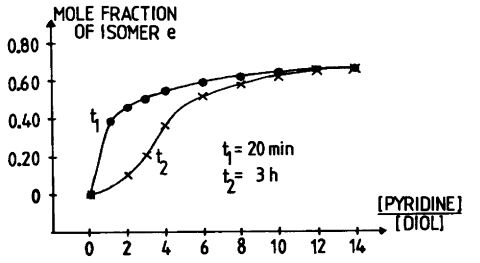

Fig. 2. Dependence of the mol fraction of S=O-equatorial isomer *e* on the pyridine–diol ratio and reaction time (reactants 0.03 mol butanediol and 0.03 mol thionyl chloride in benzene, 273 K, determinations were made by gas chromatography).

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Table 1. 2-Oxo-1,3,2-dioxathianes prepared in this study.

	Substitution in 2-oxo-1,3,2-dioxathianes	B.p./K kPa^{-1} or m.p./K	n_D^{293}
1	–	343/2.3	1.4529
2	*r*-2-*t*-4-Me	343 – 344/1.3	1.4563
3	*r*-2-*c*-4-Me	351 – 353/1.3	1.4550
4	*r*-2-*c*-5-Me	331 – 333/1.2	1.4482
5	*r*-2-*t*-5-Me	338 – 342/1.1	1.4520
6	4,4-Me_2	343/1.1	1.4500
7	5,5-Me_2	331/1.2	1.4451
8[a,b]	*r*-2-*t*-4,*c*-5Me_2	359 – 361/1.6	1.4509
9	*r*-2-*t*-4,*t*-5-Me_2		
10[a,b]	*r*-2-*c*-4,*c*-5-Me_2	376 – 378/1.8	1.4668
11	*r*-2-*c*-4,*t*-5-Me_2		
12	*r*-2-*t*-4,*t*-6-Me_2	343 – 347/1.6	1.4410
13	*r*-2-*c*-4,*c*-6-Me_2	320	
14	*r*-2-*c*-4,*t*-6-Me_2	353 – 355/1.6	1.4495
15[a,b]	*r*-2-4,4,*c*-5-Me_3	363/1.6	1.4583
16	*r*-2-4,4*t*-5-Me_3		
17	*r*-2-4,4,*t*-6-Me_3	353/1.3	1.4450
18	*r*-2-4,4,*c*-6-Me_3	315	
19[a,b]	*r*-2-*t*-4,5,5-Me_3	373/2.3	1.4523
20	*r*-2-*c*-4,5,5-Me_3		
21[a,b]	*r*-2-*t*-4,*c*-5,*t*-6-Me_3		
22	*r*-2-*t*-4,*t*-5,*t*-6-Me_3	363 – 383/1.5	1.4525
23	*r*-2-*c*-4,*c*-5,*t*-6-Me_3		
24	*r*-2-*c*-4,*t*-5,*t*-6-Me_3		
25[c]	4,4,5,5-Me_4	381/2.3	
26	4,4,6,6-Me_4	360/1.3	1.4488
27[a,b]	*r*-2-4,4,*c*-5,*t*-6-Me_4		
28	*r*-2-4,4,*t*-5,*t*-6-Me_4	353 – 355/1.3	1.4483
29	*r*-2-4,4,*t*-5,*c*-6-Me_4		
30	*r*-2-4,*c*-5,4*c*-6-Me_4		
31[a,b]	*r*-2-*t*-4,5,5,*t*-6-Me_4		
32[d]	*r*-2-*c*-4,5,5,*c*-6-Me_4	353-361/1.1	1.4563
33	*r*-2-*c*-4,5,5,*t*-6-Me_4		
34	*r*-2-4,4,5,5,*t*-6-Me_5	393 – 396/2.3	1.4566
35	*r*-2-4,4,5,5,*c*-6-Me_5	355	
36[a,b]	*r*-2-4,4,*t*-5,6,6-Me_5	388 – 393/2.0	1.4508
37	*r*-2-4,4,*c*-5,6,6-Me_5		
38	4,4,5,5,6,6-Me_6	402	
39[b,e]	*r*-2-*c*-5-isoPr	371 – 372/2.1	1.4535
40	*r*-2-*t*-5-isoPr		1.4602
41	*r*-2-*c*-5-t-Bu	371 – 372/1.2	1.4608
42	*r*-2-*t*-5-t-Bu	309	
43[a,b]	*r*-2-*c*-5-Ph	423 – 427/0.9	1.5466
44	*r*-2-*t*-5-Ph		
45[b,e]	*r*-2-*t*-4-isoPr	365 – 367/1.6	1.4459
46	*r*-2-*c*-4-isoPr		1.4607
47	*r*-2-*t*-4-t-Bu	373 – 378/1.2	1.4638
48	*r*-2-*c*-4-t-Bu	312	
49	*r*-2-*t*-4-Ph	408 – 413/1.1	1.5488
50	*r*-2-*t*-4-t-Bu-,*c*-4-Me	388 – 390/1.3	1.4543

[a] Boiling point and refractive index determined for a mixture of isomers. [b] Isomers were separated with a preparative gas chromatograph. [c] M.p. 363 K. [d] This isomer was not isolated. [e] Boiling point determined for a mixture of isomers.

Table 2. 1,3-Alkanediols prepared in this study.

Diol	B.p./K kPa^{-1} or m.p./K	n_4^{293}	Yield/%	Method[b] of preparation
1,3-propanediols				
2-Me-	373–374/0.9	1.4420	35	R
2-isoPr-	383–388/09	1.4495	82	R
2-t-Bu-	330		67	R
2-Ph-	443/1.3	1.5468	46	R
3-Ph-	437/0.8	–[a]	60	R
1,3-butanediols				
2-Me-	375-379/0.9	1.4500	63	R
3-Me-	363-365/0.9	1.4423	40	R
2,2-diMe-	375/1.1	1.4497	55	R
2,3-diMe-	369/0.9	1.4455	66	R
2,2,3-triMe	400		86	R
1,3-pentanediols				
4-Me-	385–388/1.2	1.4486	77	R
4,4-diMe-	333–334		87	R
3,4,4-triMe	333		99	R
2,3-pentanediols				
2,3-diMe-	362–367/0.9	1.4469	63	G
2,4-diMe-	365/1.2	1.4335	59	G
3,3-diMe	378/0.9	1.4498	55	R
2,3,3-triMe-	358		90	G
2,3,4-triMe-	355–357/0.9	1.4350	44	G
2,3,3,4-tetraMe	340–341		46	G

[a] Refractive index not determined (a viscous liquid). [b] R = reduction. G = Grignard reaction.

too low to cause the equilibration. Besides pyridine, other amines can also be used. The efficiency of an amine and the proportion of isomer *e* depend on the pK_a-value: the amine with higher pK_a gives higher proportion of isomer *e*. Since protonation is faster than the equilibration the latter method is kinetically controlled when the pyridine–diol ratio is eight or more.

The 2-oxo-1,3,2-dioxathianes presented in Table 1 were prepared using the latter of the above methods. The pyridine–diol ratio was generally close to two. When *cis*-4-methyl (*3*), *trans*-5-methyl (*5*), *cis*-4,*cis*-5-dimethyl (*10*) and *cis*-4,*trans*-5-dimethyl (*11*) and *cis*-4,*cis*-6-dimethyl (*13*) derivatives were prepared the amount of pyridine was ten times the amount of diol. In each case the method used appared to be an easy and excellent way to prepare the title compounds. Since the proportion of isomers *a* and *e* can be controlled by adding amine to the reaction mixture, the reaction gave not only a good yield of 2-oxo-1,3,2-dioxathianes but also the highest yield of the less stable isomer *e*.

EXPERIMENTAL

Materials. 2-Oxo-1,3,2-dioxathianes were prepared by adding dropwise, with stirring and external cooling, thionyl chloride (0.013–0.061 mol) in anhydrous benzene (10 cm^{-3}) to the solution of diol (0.012–0.055 mol) and pyridine (0.024–0.110 mol; see also text) in anhydrous benzene. The reaction was allowed to run 1–3 h. After filtering off the hydrochloride formed and neutralizing the traces of hydrogen chloride with dilute bicarbonate solution the organic layer was separated, washed with water and dried over $MgSO_4$. The solvent was evaporated and the product was distilled under reduced pressure. The stereoisomers were separated by distillation or with a preparative gas chromato-

graph using XE-60 and Carbowax 20 M columns. The yields varied generally from 60 to 75 %. The characterization of the compounds was performed by gas chromatography and ^{1}H NMR spectroscopy,[1,2] partly also by mass spectroscopy.[4]

The starting materials, 1,3-alkanediols, were prepared by $LiAlH_4$-reduction or by the Grignard reaction from 1,3-alkanediones or ethyl 3-hydroxyalkanoates using the methods described earlier.[5]

Apparatus. The refractive indices were determined with an Abbe refractometer at 293 K. The GLC analyses were performed with a Perkin Elmer F 11 analytical gas chromatograph using columns containing 10 % Carbowax 20M and 5 % XE-60 on Chromosorb G (60/80 mesh). The stereoisomers were separated with a Perkin Elmer F 21 preparative gas chromatograph equipped with the columns containing 10 % Carbowax 20M and XE-60 on Chromosorb G (60/80 mesh). The ^{1}H NMR spectra were recorded with a Jeol PMX-60 spectrometer at 303 K using 10 % (w/v) CCl_4-solutions and TMS as internal standard.

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