Synthesis of the Cyclic Oxalates of 1,2-Glycols by Controlling the Formation of the Cyclic Carbonates

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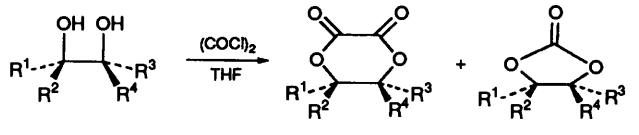
Cyclic oxalates **2** have been efficiently synthesized by the reaction of 1,2-glycols **1** with oxalyl chloride in the presence of pyridine or 2,4,6-trimethylpyridine, rather than triethylamine, or by reaction with 1,1'-oxalyldiimidazole.

Few compounds with a 1,4-dioxane-2,3-dione ring have been reported[1] probably because of their instability: in this structure, two unstable *E*-ester units[2] are linked to form the 1,2-dicarbonyl system, which cannot exist as the stable s-*trans* conformer.[3] We have already disclosed that oxalyl chloride reacts with acyclic 1,2-glycols **1a–j** in tetrahydrofuran (THF) in the presence of triethylamine to form the cyclic oxalates **2** together with the cyclic carbonates **3** (see Scheme 1): unsubstituted, **1a**, monosubstituted, **1b**, **c**, and *erythro*-1,2-disubstituted ethylene glycols **1d–f** provided **2** or polymeric oxalates as the major products, while the *threo*-isomers **1g–i** and pinacol **1j** afforded **3** as the major products. However, we failed to isolate **2e–i** owing to their instability, especially under conditions employed for chromatographic separation.[1] We report here three different methods for the synthesis of compounds **2** from a variety of compounds **1**.



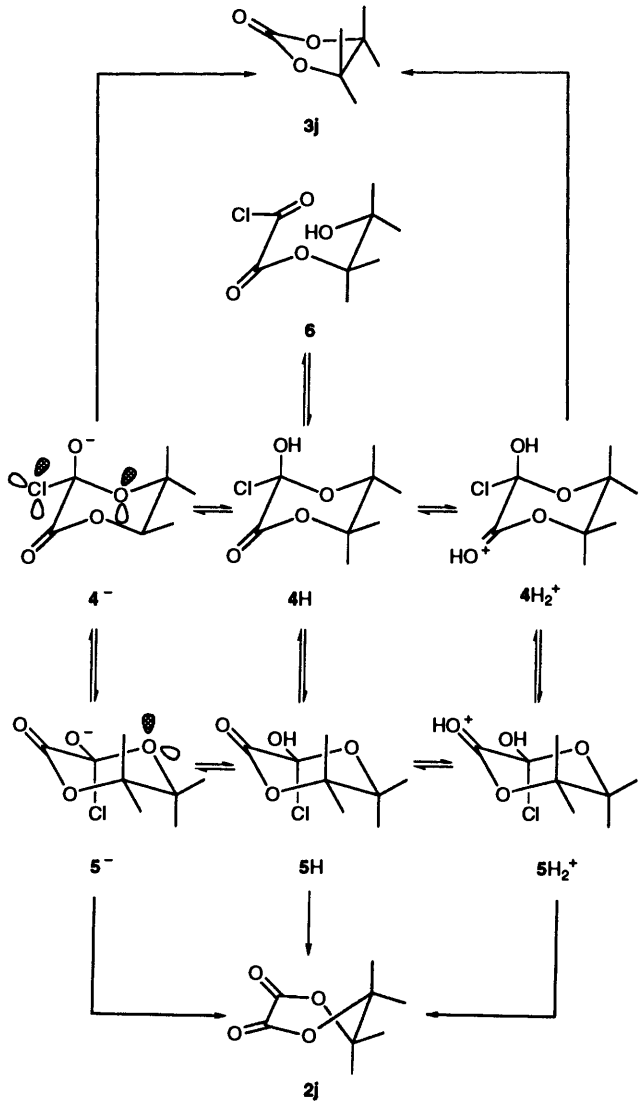
1 **2** **3**

a $R^1 = R^2 = R^3 = R^4 = H$
b $R^1 = R^2 = R^3 = H$, $R^4 = Me$
c $R^1 = R^2 = R^3 = H$, $R^4 = Ph$
d $R^1 = R^3 = H$, $R^2 = R^4 = Me$
e $R^1 = R^3 = H$, $R^2 = R^4 = Ph$
f $R^1 = R^3 = H$, $R^2 = Ph$, $R^4 = Pr^j$
g $R^1 = R^4 = H$, $R^2 = R^3 = Me$
h $R^1 = R^4 = H$, $R^2 = R^3 = Ph$
i $R^1 = R^4 = H$, $R^2 = Ph$, $R^3 = Pr^j$
j $R^1 = R^2 = R^3 = R^4 = Me$
k $R^1 = R^3 = H$, $R^2R^4 = (CH_2)_3$
l $R^1 = R^3 = H$, $R^2R^4 = (CH_2)_4$
m $R^1 = R^3 = H$, $R^2R^4 = (CH_2)_6$
n $R^1 = R^4 = H$, $R^2R^3 = (CH_2)_4$
o $R^1 = R^4 = H$, $R^2R^3 = (CH_2)_6$

Scheme 1

According to the mechanism exemplified for the reaction of **1j** in Scheme 2, the formation of **3** has been interpreted in terms of the stereochemically controlled formation of the tetrahedral intermediate **4H**, followed, successively, by deprotonation and stereoelectronically controlled cleavage (the nonbonding electron pairs contributing to bond cleavage are shown as shaded lobes). In the absence of a base, **3** may be produced through the protonated species $4H_2^+$. The cyclic oxalate **2** can be formed only after **4** conformationally changes into **5**.[1]

Logically, the formation of **3** may be controlled in three different ways. First, the tetrahedral intermediate (type **4H**, OH for Cl) in the reaction with oxalic acid requires no conformational change to be converted into **2**. Azeotropic distillation[4] of a mixture of **1h** and oxalic acid, however, resulted in complete recovery of **1h**. Secondly, the formation of **3** may be inhibited by the use of an appropriately weaker base, which prevents the formation of either 4^- or $4H_2^+$. Indeed,



Scheme 2

replacement of triethylamine by pyridine[5] afforded **2j** (85% yield), which had been obtained in 0.8% yield.[1] The dramatic reversal of the product ratio was also realised in the reactions with the *threo*-compounds **1g–i**, **o**. Yields of **3** were markedly diminished in all other reactions as shown in Table 1. Unfortunately, the reactions of compounds with an *erythro* configuration, **1d–f**, produced large amounts of the polymers at the cost of reduced yields of **2**; although **2d** was obtainable by

Table 1 Reactions of oxalyl chloride and 1,2-glycols **1** in THF in the presence of pyridine

		Reaction conditions[a]			Yield (%)[b]		
Entry	Diol	Solvent[c] Volume (cm^3)	Temp. (°C)	Time (min)	**2**	**3**	Polymers
1	**1a**	5	0	20	—[d] (90[e])	0	—[d]
2	**1b**[f]	5	0	25	26 (71[e])	0	74
3	**1c**[f]	110	0	30	81 (48)	0	19
4	**1d**	110	0	40	49 (49[e])	0[g]	51
5	**1e**	24	0	15	27 (—[h])	2	—[d]
6	**1f**[f]	24	0	15	25 (—[h])	1	74
7	**1g**[f]	110	0	40	92 (50[e,i])	0	8
8	**1h**[f]	24	0	15	93 (69[i])	7	0
9	**1i**[f]	26	0	15	>96 (75[i])	<4	0
10	**1j**	24	RT	480	—[d] (85)	—[d]	—[d]
11	**1k**	110	0	40	88 (31[e,i])	—[j]	9
12	**1l**	110	0	40	79 (58[e])	0	14
13	**1m**	110	0	40	64 (38[e,i])	3	33
14	**1n**[f]	110	0	40	78 (74[e])	0	9
15	**1o**[f]	110	0	40	92 (82[e,i])	3	5

[a] Except for entries 4, 7 and 11, the diol **1** (1 mmol) was treated with oxalyl chloride (1.1 mmol) and pyridine (5 mmol); compounds **1d, g, k** (1 mmol) were treated with oxalyl chloride (1.5 mmol) and pyridine (7.6 mmol). [b] Determined by means of ^1H NMR spectroscopy on the basis of relative areas of the O-CH or O-CH_2 signals. The broad signals of the polymers are much more deshielded than the corresponding ones of **2**. Figures in parentheses denote isolated yields. [c] Volume (cm^3) per mmol of **1**. [d] Not determined. [e] Obtained by Kugelrohr distillation of a mixture of the products. [f] Racemic modification. [g] Determined by means of thin-layer chromatography. [h] Could not be isolated. [i] Satisfactory analytical and spectroscopic data have been obtained for the new compound. [j] A trace, if any.

pyrolytic distillation, isolation of the benzylic compounds **2e, f** was unsuccessful. The formation of the polymers was completely suppressed by the use of 2,4,6-trimethylpyridine instead of pyridine: **2f** was obtained in 76% yield. We failed, however, to remove **3e** from a 95:5 mixture of **2e** and **3e**, obtained by this procedure, by means of recrystallisation. The strategy we finally adopted to obtain **2e** was to cancel the stereoelectronic effect from the chlorine atom in the intermediate (type **4H** or $\mathbf{4}^-$): replacement of oxalyl chloride by 1,1′-oxalyldiimidazole[6] produced **2e** almost exclusively; this compound was isolated in 64% yield.

In conclusion, the cyclic oxalates **2** of various 1,2-glycols **1** have become accessible by the present procedures, which have potential utility as a new method for protecting 1,2-glycols.[7] The results obtained in this work also support the correctness of the mechanism[1] proposed for the reaction of 1,2-glycols with oxalyl chloride.

Experimental

Typical Procedures.—Preparation of **2h**. A solution of oxalyl chloride (0.19 cm^3, 2.2 mmol) in THF (8 cm^3) was added to a solution of **1h** (429 mg, 2 mmol) and pyridine (0.80 cm^3) in THF (40 cm^3) at 0 °C. The mixture was stirred for 15 min and then concentrated under reduced pressure. The residue was partitioned between ethyl acetate (50 cm^3) and water (20 cm^3). The organic phase was separated, washed successively with 5% aqueous citric acid and saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was recrystallised from hexane–dichloromethane (2:1, v/v) to afford **2h** (370 mg, 69%), m.p. 160.5–163.5 °C. Further recrystallisation of **2h** afforded an analytical sample as colourless prisms, m.p. 164–165 °C (Found: C, 71.75; H, 4.4%; M^+ 268. $C_{16}H_{12}O_4$ requires C, 71.6; H, 4.5%; *M*, 268).

Preparation of **2e**. Oxalyl chloride (0.17 cm^3, 1.99 mmol) and a solution of **1e** (429 mg, 2 mmol) in THF (20 cm^3) were added successively to a solution of imidazole (545 mg, 8.01 mmol) in THF (20 cm^3) under nitrogen at 0 °C. After the mixture had been stirred at room temperature for 24 h, the resulting precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was partitioned between ethyl acetate and water. The organic phase was separated, washed successively with aqueous citric acid, water, aqueous sodium hydrogen carbonate and water, dried and concentrated to leave **2e** (342 mg, 64%), m.p. 125–128 °C. Recrystallisation of **2e** from hexane–ethyl acetate (1:1, v/v) afforded an analytical sample as colourless prisms, m.p. 128–129.5 °C (Found: C, 71.7; H, 4.5%; M^+ 268. $C_{16}H_{12}O_4$ requires C, 71.6; H, 4.5%; *M*, 268).

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