Synthesis and Polymerization of 2,6,7-Trioxabicyclo[2.2.2]octane and Its Derivatives

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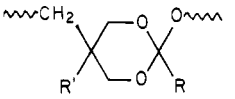
Received March 23, 1981

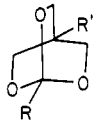
ABSTRACT: Ten new 2,6,7-trioxabicyclo[2.2.2]octane derivatives, $RC(OCH_2)_3CR'$ [where R = H, R′ = NO_2 (**5**); R = H, R′ = NH_2 (**6**); R = H, R′ = $N(CH_3)_2$ (**7**); R = H, R′ = $NHCOCH_3$ (**8**); R = H, R′ = $COOC_2H_5$ (**9**); R = H, R′ = $CH_2OSO_2C_7H_7$ (**10**); R = CH_3, R′ = $COOCH_3$ (**13**); R = CH_3, R′ = $COOC_2H_5$ (**14**); R = CH_3, R′ = NO_2 (**15**); and R = CH_3, R′ = NH_2 (**16**)], were synthesized, and six other derivatives, **1**–**4**, **11**, and **12**, were prepared by literature directions. Each of these bicyclic compounds was polymerized with boron trifluoride etherate as initiator at 0 °C. The polymers were usually obtained as highly crystalline white powders with high melting points accompanied by decomposition. These polymers were not soluble in any solvent without decomposition. Initiation with deliberately high initiator concentration gave soluble oligomers with η_{inh} ca. 0.1 g/dL, indicating that most of the polymers had fairly high molecular weights. From IR and NMR spectroscopic results (of the oligomers) they possessed the structure



Introduction

With the objective of synthesizing linear stereoregular, high molecular weight analogues of polysaccharides, we have studied bicyclic orthoesters 2,6,7-trioxabicyclo-[2.2.1]heptane,[1] 2,7,8-trioxabicyclo[3.2.1]octane,[2] and 2,8,9-trioxabicyclo[3.3.1]nonane.[2] However, no stereoregular propagation has been observed. The molecular weight of these polymers has been low, and the polymers have all been liquid rubbers.

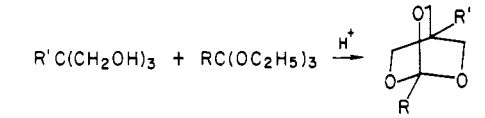
The highly symmetrical 2,6,7-trioxabicyclo[2.2.2]octane system (**1**) has not been studied extensively before. Steuck[3] showed that the 4-methyl derivative **2** underwent cationic polymerization. Bailey, Endo, and Saigo[4] polymerized several derivatives of **1** with boron trifluoride at elevated temperatures to open both rings, causing volume expansion. In the present paper, we describe the synthesis and polymerization of 2,6,7-trioxabicyclo[2.2.2]octane (**1**) and its derivatives **2**–**16**.



1, R = H; R′ = H (ref 7)
2, R = H; R′ = CH_3 (ref 8)
3, R = H; R′ = CH_2Br (ref 9)
4, R = H; R′ = CH_2OH (ref 9)
5, R = H; R′ = NO_2
6, R = H; R′ = NH_2
7, R = H; R′ = $N(CH_3)_2$
8, R = H; R′ = $NHCOCH_3$
9, R = H; R′ = $COOC_2H_5$
10, R = H; R′ = $CH_2OSO_2C_7H_7$
11, R = CH_3; R′ = CH_3 (ref 10)
12, R = CH_3; R′ = CH_2OH (ref 9)
13, R = CH_3; R′ = $COOCH_3$
14, R = CH_3; R′ = $COOC_2H_5$
15, R = CH_3; R′ = NO_2
16, R = CH_3; R′ = NH_2

Results

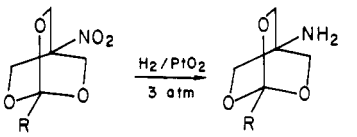
Synthesis of Bicyclic Orthoesters. By the interchange reaction of acyclic triol and acyclic orthoester, unsubstituted and substituted 2,6,7-trioxabicyclo[2.2.2]-octanes were prepared, eq 1. The procedure of Hall and De Blauwe[1,5,6] was used for each of these syntheses. In this procedure triol and orthoester are heated under vacuum with stirring in solution in a high-boiling oil. The bicyclic orthoester distills or sublimes under these conditions, which protects it from unwanted oligomerization and permits monomer isolation and purification.



(1)

1-5, 7, 11, 12, 15

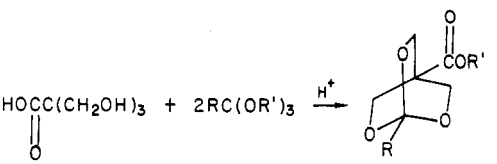
2-Amino-2-(hydroxymethyl)-1,3-propanediol and triethyl or trimethyl orthoformate gave no bicyclic compounds. In contrast, by repeated treatment the dimethylamino derivative **7** could be prepared in moderate yield. The primary amino derivatives **6** and **16** were prepared by the reduction of **5** and **15**, respectively, in good yields.



(2)

5, R = H; **15**, R = CH_3 — **6**, R = H; **16**, R = CH_3

(Alkoxycarbonyl)-2,6,7-trioxabicyclo[2.2.2]octanes **9**, **13**, and **14** were prepared from 1 mol of 2-carboxy-2(hydroxyethyl)-1,3-propanediol and 2 mol of acyclic orthoester, eq 3.[11] The yield for the preparation of 4-(methoxycarbonyl)-2,6,7-trioxabicyclo[2.2.2]octane was too low to be useful. Polymeric material with a melting point higher than 300 °C was formed.



(3)

9, R = H; R′ = C_2H_5
13, R = CH_3; R′ = CH_3
14, R = CH_3; R′ = C_2H_5

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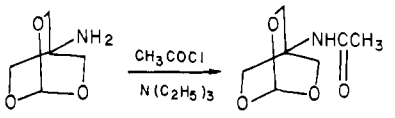
Table I
Melting Points and Elemental Analyses of the New Bicyclic Orthoester Monomers

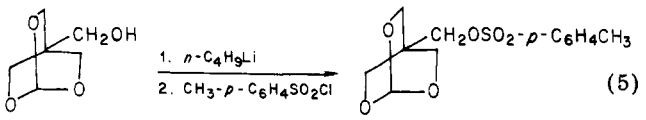
compound	mp, °C	calcd			found		
		% C	% H	% N	% C	% H	% N
5	124-126	37.3	4.4	8.7	36.1	4.3	8.9
6	110-114	45.8	6.9	10.7	44.7	6.7	10.5
7	37-41	52.8	8.2	8.8	52.6	8.1	8.6
8	143-147	48.6	6.4	8.1	49.4	6.3	7.9
9	43	51.1	6.4		51.2	6.7	
10	76-83	52.0	5.4		51.2	5.5	
13	98-100	51.1	6.4		50.4	5.9	
14	55	53.5	7.0		53.4	7.2	
15	98-99	41.2	5.2	8.0	41.1	5.1	7.8
16	100-103	49.7	7.6	9.7	49.7	7.5	9.5

4-Amino-2,6,7-trioxabicyclo[2.2.2]octane is derivatized to 8 in good yield.



6 8 (4)

The *p*-toluenesulfonate of 4-(hydroxymethyl)-2,6,7-trioxabicyclo[2.2.2]octane is conveniently prepared in high yield.



4 10 (5)

Characterization of the 2,6,7-Trioxabicyclo[2.2.2]-octane Monomers. The melting points and elemental analyses for the new bicyclic compounds are listed in Table I. The bicyclic orthoesters showed reasonable ^1H NMR spectra (Table II). The difference in the chemical shifts of the ring protons of the unsubstituted and the substituted 2,6,7-trioxabicyclo[2.2.2]octanes (Δppm) was plotted against the Taft σ_I value for the substituents at C_4 (Figures 1 and 2). The following σ_I values were used: CH_3, 0.0; CH_2Br, 0.18; CH_2OH, 0.14; NO_2, 0.63; NH_2, 0.10; $N(CH_3)_2$, −0.10; $NHCOCH_3$, 0.28; $COOC_2H_5$, 0.30.[12,13] A good correlation was obtained for the ring methylene protons of all compounds except **4** and **7** (Figure 1); for the ring methine protons a good correlation was also obtained (Figure 2).

The results of the IR studies are summarized in Table III.

Polymerization. The polymerization results are shown in Table IV. The bicyclic orthoesters **1–5**, **8–10**, **12**, and **15** gave polymers under acidic conditions at 0 °C. The polymers are white and crystalline. All the polymers except poly-**3**, -**8**, -**10**, and -**12** are insoluble in ordinary organic solvents such as dimethyl sulfoxide, *N,N*-dimethylformamide, acetone, nitromethane, alcohols, ethers, and hydrocarbons. Hexafluoroisopropyl alcohol dissolved the polymers with slow decomposition. Poly-**8** and -**12** are soluble in water and dimethyl sulfoxide. The viscosity in dimethyl sulfoxide at 30 °C is not high. However, **1** and **5** were polymerized under abnormally high initiator concentration (5–10 mol %) to yield dimethyl sulfoxide soluble polymers.

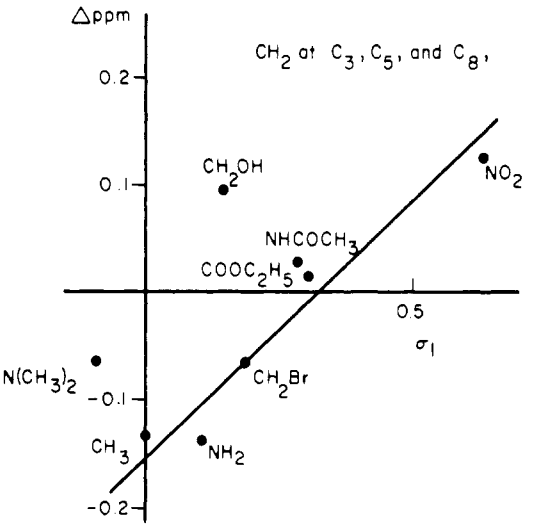


Figure 1. Correlation between Δppm in ring methylene protons and Taft σ_I value.

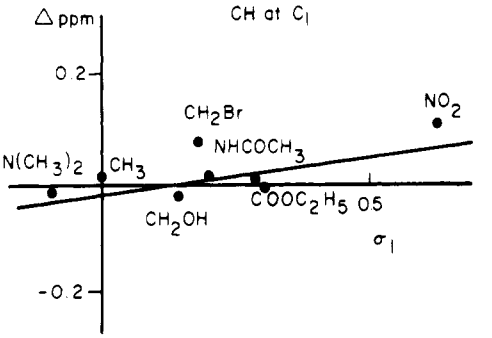
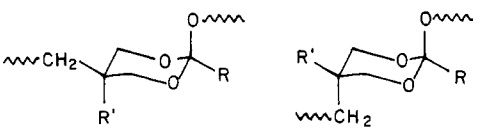


Figure 2. Correlation between Δppm in ring methine proton and Taft σ_I value.

The elemental analyses and IR data of the polymers are shown in Tables V and VI, respectively. In their IR spectra, all the polymers except poly-**9** showed negligible carbonyl stretching bands at 1730 cm^{-1}. This means that these polymers are mainly composed of monocyclic units **17** and/or **18**.



17 18

Table II
Proton Chemical Shifts (ppm) and Coupling Constants (Hz)[a]

compound	ring protons: CH at C_1	ring protons: OCH_2	ring protons: CH at C_4	substituents
1	5.53 (d, J_{CHOCCH} = 1.5)	4.18 (d, J_{CH_2CH} = 1.9)	2.10 (m)	
2	5.54 (s)	3.91 (s)		0.81 (CH_3, s)
3	5.61 (s)	4.05 (s)		3.15 (CH_2Br, s)
4	5.51 (s)	3.99 (s)		3.42 (CH_2O, s), 2.15 (OH, s)
5	5.64 (s)	4.43 (s)		
6	5.54 (s)	3.90 (s)		1.1 (NH_2, br)
7	5.52 (s)	4.05 (s)		2.26 ($N(CH_3)_2$, s)
8	5.54 (s)	4.24 (s)		6.9 (NH, br), 1.94 (CH_3CO, s)
9	5.53 (s)	4.21 (s)		4.19 ($COOCH_2$, q, J = 7.1), 1.25 (CH_3, t, J = 7.1)
10	5.53 (s)	3.94 (s)		7.84 and 7.45 (C_6H_4, q, J = 8.8), 3.70 (CH_2, s), 2.47 (CH_3, s)
11		3.92 (s)		1.43 (CH_3 at C_1, s), 0.80 (CH_3 at C_4, s)
12		4.00 (s)		3.42 (CH_2O, H, J = 4.8), 2.29 (OH, t, J = 4.8), 1.43 (CH_3)
13		4.24 (s)		3.73 ($COOCH_3$, s), 1.45 (CH_3, s)
14		4.24 (s)		4.19 ($COOCH_2$, q, J = 7.2), 1.26 (CH_3, t, J = 7.2), 1.48 (CH_3, s)
15		4.42 (s)		1.50 (CH_3 at C_1, s)
16		3.88 (s)		1.44 (CH_3 at C_1, s), 1.1 (NH_2, br)

[a] Solvents, $CDCl_3$; room temperature.

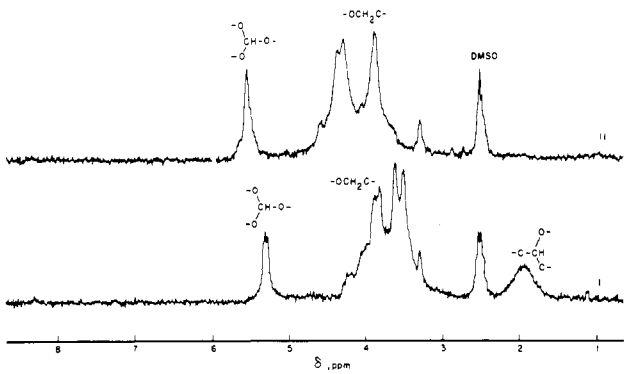
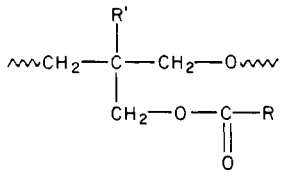


Figure 3. NMR spectra of poly(orthoesters): sample no. I, poly-1; sample no. II, poly-5 (solvent, Me_2SO-d_6).

^1H NMR spectra of poly-1 and -5 are shown in Figure 3. The assignments of each signal are summarized in Table VII along with those for poly-3, -8, and -12. In the NMR spectra, no formate proton (HCOO–) is observed. Again, these results show that very few, if any, monomer units 19 are present in the polymer chain.



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^{13}C NMR data of poly-1 and -5, obtained with high initiator concentration, are shown in Table VII. Poly-1 shows one signal, at δ 109.04, for the orthoester carbon, even though the viscosity of the polymer is 0.10 dL/g. On the other hand, poly-5 (η_{inh} 0.07–0.10 dL/g) shows two signals, at δ 108.65 and 106.37 (peak ratio ca. 1:9), for the orthoester carbon. These data suggest high stereoregularity in both poly-1 and poly-5, along with an end group visible in the latter.

Discussion

Synthesis. The monomer synthesis of Hall and De Blauwe[1,5,6] proved to be very effective for the synthesis of the required bicyclic monomers. Reasonable yields of these reactive monomers were obtained in almost all cases.

One of the two exceptions was that of the amino derivatives, doubtless because the amino group neutralized the *p*-toluenesulfonic acid catalyst. Even here the dimethylamino derivative 7 could be obtained by repeated treatment, and the primary amino derivatives were obtained by catalytic hydrogenation of the corresponding nitro derivatives 5 and 15.

The other cases in which low yields were obtained were those of the alkoxycarbonyl derivatives, 9, 13, and 14. Because of the several steps involved with these syntheses, evidently side reactions, especially oligomerization, can occur. This will be especially prominent if the carboxyl group has not been completely esterified when the bicyclic monomer forms and can catalyze its oligomerization.

NMR Studies of 2,6,7-Trioxabicyclo[2.2.2]octanes. As shown in Figures 1 and 2, the chemical shifts of the ring protons (except for compounds 4 and 7) are in good correlation with Taft's σ_I values for the substituents at C_4. The results show that the chemical shifts are affected by the direct electrostatic effect and/or the inductive effect of the substituents. The significant downfield shifts of ring methylene protons in 4 and 7 may be due to van der Waals effects. The chemical shifts of the C_1 proton also show good correlation between the Δppm and Taft's σ_I values (Figure 2). In this case, mesomeric effects, hybridization, and van der Waals effects may be of less importance. Roberts and Moreland[14] and Baker, Parish, and Stock[15] concluded from their study of the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and related compounds that the field effect is the dominant contribution to the total substituent effect. The chemical shifts at C_1 in 4-substituted 2,6,7-trioxabicyclo[2.2.2]octanes may also be dominantly affected by the field effect.

Polymerization. The new poly(orthoesters) were pre-

Table III
IR Data of Bicyclic Orthoesters in Chloroform

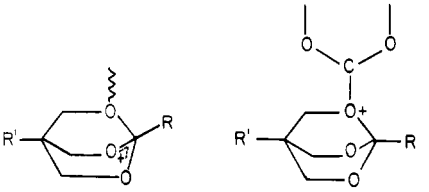
compound	frequency, cm^{-1}
1	3040, 2950, 2900, 1375, 1325, 1210, 1160 (max, ν_{C-O-C}), 1115, 1100, 1090
2	3040, 2970, 2945, 2890, 1460, 1400, 1370, 1215, 1200, 1190, 1160 (max, ν_{C-O-C}), 1055, 1000
3	2950, 2890, 1475, 1430, 1375, 1290, 1160 (max, ν_{C-O-C}), 1015, 990, 935, 860
4	3630 and 3450 (m, ν_{O-H}), 2960, 2900, 1610 (w), 1385, 1170, 1040, 1005 (max, ν_{C-O-C}), 940, 870
5	2900, 1555-1520 (max, $\nu_{as}(NO_2)$), 1370, 1190, 1165 (s, ν_{C-O-C}), 1000, 940
6	3680, 3580, and 3390 (w, ν_{N-H}), 3000, 2950, 2890, 1610 (w, δ_{N-H}), 1480, 1375, 1160 (max, ν_{C-O-C}), 1020, 1000, 925
7	3000, 2950, 2900, 2850, 2810, 1470, 1375, 1160, 1100, 1020 (max, ν_{C-O-C}), 985, 930, 895
8	3440 (m) and 3400 (w, ν_{N-H}), 3045, 2950, 2900, 1695 (s, $\nu_{C=O}$), 1610, 1510, 1370, 1300, 1250, 1160 (max, ν_{C-O-C}), 1040, 990
9	2975, 2905, 1735 (max, $\nu_{C=O}$), 1610, 1480, 1425, 1400, 1380, 1300, 1270, 1220, 1165 (s, ν_{C-O-C}), 1120, 1020, 990, 930, 860
10	3050, 2950, 2900, 1920, 1730, 1605 (m, $\nu_{C=O}$), 1460, 1375 (s, $\nu_{as}(SO_2)$), 1370, 1300, 1220, 1200, 1185 (max, ν_{C-O-C}), 1105 (s, $\nu_s(SO_2)$)
11	3035, 2975, 2950, 2900, 1410, 1390, 1365, 1270, 1260, 1220, 1200, 1140 (max, ν_{C-O-C}), 1065, 1000
12	3620 and 3430 (m, ν_{O-H}), 3000, 2895, 1610, 1410, 1360, 1310, 1185, 1135 (max, ν_{C-O-C}), 1070, 1040, 1000, 920, 860
13	2900-3010, 1740 (s, $\nu_{C=O}$), 1600, 1410, 1360, 1320, 1190-1280 (s), 1135 (max, ν_{C-O-C}), 1020-1080, 1000, 875
14	3050, 3000, 2890-2960, 1735 (s, $\nu_{C=O}$), 1610, 1410, 1380, 1360, 1190-1290 (s), 1135 (s, ν_{C-O-C}), 1080, 875
15	3000-3060, 2960, 2900, 1520-1555 (s, $\nu_{as}(NO_2)$), 1480, 1410, 1390, 1360, 1310, 1190, 1130 (max, ν_{C-O-C}), 1030, 1000, 870 (s)
16	3380 (w, ν_{N-H}), 3000-3100, 2950, 2890, 1610 (w, ν_{N-H}), 1410, 1360, 1305, 1190, 1135 (max, ν_{C-O-C}), 1040-1065, 870

pared by ring-opening polymerization of the bicyclic orthoesters. The polymers except poly-**3**, -**8**, and -**12** are insoluble in common organic solvents. The structure of the polymer and the fact that no swelling of these polymers occurs in common organic solvents lead us to ascribe this low solubility not to cross-linking but to high crystallinity and/or to a highly stereoregular structure.

Under abnormally high initiator concentration, **1** and **5** gave dimethyl sulfoxide soluble polymers (η_{inh} in Me_2SO, 0.07–0.10 dL/g). The results show that the molecular weights of polymers prepared under normal conditions are high and that the rate constant of propagation is higher than that of the initiation.

^1H and ^{13}C NMR spectra of low molecular weight poly-**1** (η_{inh} 0.10 dL/g) show one signal at δ 5.28 and 109.04 for the orthoester proton and carbon, respectively. The results suggest that the stereoregularity of this polymer is extremely high (probably trans). The ^{13}C NMR spectrum of poly-**5** shows two signals, at δ 108.65 and 106.37 (peak ratio 1:9), for the orthoester carbon. It is not clear if the minor signal is due to the end group or to the configuration of the polymer. However, the IR spectrum also suggests that the stereoregularity of the polymer is high.

From these results, it is suggested that the polymerization intermediate is **24**. The weak dipole–dipole interaction between the 1,3-dioxan-2-ylium ion and the chain oxygen atom contributes to the stereoregular propagation. The alternative oxonium ion **25** is not stable because four oxygen atoms are situated at the β position of a positively charged oxygen atom.



24 **25**

It is very interesting that only one ring opens to form the poly(orthoesters) (kinetically controlled polymers) under the mild conditions (in solution, $BF_3{\cdot}OEt_2$, 0 °C) even when 10 mol % initiator is used. On the other hand, two rings react to form the polyethers (thermodynamically controlled polymers) under more drastic conditions (in bulk, $BF_3{\cdot}OEt_2$, 5 and 70 °C).[4,16] The difference suggests that the polymerization intermediates are the corresponding 1,3-dioxan-2-ylium ions which react with nucleophiles to form two kinds of products depending on the reaction conditions.[1,17]

Experimental Section

Instrumentation. ^1H NMR spectra were obtained with a Varian T60 spectrometer. Infrared spectra were recorded with Perkin-Elmer 710A and 337 spectrophotometers. Elemental analyses were performed by the University of Arizona Analytical Center (Tucson, Ariz.). Melting points were taken with a Fischer-Johns melting point apparatus. The viscosity of the polymers was determined on 0.5% dimethyl sulfoxide solutions at 30 °C with a Cannon-Fenske viscosimeter.

Solvents. All solvents for synthesis were reagent grade. Trimethyl orthoformate, triethyl orthoformate, trimethyl orthoacetate, and triethyl orthoacetate were purified by distillation over calcium hydride. All triols were reagent grade. Polymerization solvent dichloromethane was purified by distillation over calcium hydride. Nitromethane was dried over calcium chloride and distilled.

2,6,7-Trioxabicyclo[2.2.2]octane (1). 2-(Hydroxymethyl)-1,3-propanediol (1.12 g, 10.6 mmol) and triethyl orthoformate (1.57 g, 10.6 mmol) were dissolved in 10 mL of dioctyl phthalate (DOP). The solution was heated at 120 °C for 2.5 h. Some ethanol distilled out. DOP (10 mL) and a trace of anhydrous *p*-toluenesulfonic acid were added, and the temperature was increased to 140 °C at 0.15 mmHg. Compound **1** was distilled out of the reaction flask. Recrystallization from *n*-pentane gave 0.51 g of pure **1**: yield 42%; mp 68–74 °C[18] (lit.:[7] yield 5%; mp 90–92 °C).

4-Methyl-2,6,7-trioxabicyclo[2.2.2]octane (2). Equimolar amounts of 2-(hydroxymethyl)-2-methyl-1,3-propanediol and triethyl orthoformate (0.03 mol) were mixed in 10 mL of DOP and heated at 130 °C. Some ethanol was distilled out. A trace of *p*-toluenesulfonic acid was added and the reaction was continued at 130 °C at 0.1 mmHg. Compound **2** distilled out of the reaction flask. Recrystallization from acetone gave 2.7 g of **2**: yield 50%; mp 96–100 °C (lit.[8] mp 105–106 °C).

4-(Bromomethyl)- (3), 4-(Hydroxymethyl)- (4), and 4-(Hydroxymethyl)-1-methyl-2,6,7-trioxabicyclo[2.2.2]octane (12). These compounds were prepared as described.[9]

4-Nitro-2,6,7-trioxabicyclo[2.2.2]octane (5). 2-(Hydroxymethyl)-2-nitro-1,3-propanediol (7.55 g, 0.05 mol) and triethyl orthoformate (8.14 g, 0.055 mol) were mixed and heated at 90–100 °C in a sublimation apparatus equipped with a side arm until 6

Table IV
Polymerization of Bicyclic Orthoesters[a]

monomer	amt of monomer, g	amt of $BF_3 \cdot OEt_2$, mol %	vol of CH_2Cl_2, mL	time, h	yield, %	character of polymer: mp, °C	character of polymer: solubility in water	character of polymer: η_{inh},[b] dL/g
1	0.1002	1.0	0.25	1	98	208-210	–	
1	0.1434	5.2	2.0	2	43	~155[c]	–	
1	0.1520	9.9	2.0	2	38	~124[c]	–	0.10
2	0.2024	1.0	1.0	0.25	69	225-226	–	
2	0.2030	1.0	1.0	1	76	225-226	–	
3	0.2112	1.5	0.5	0.25	52	88-91	–	0.08
3	0.4240	1.5	1.0	1	78	93-95	–	
4	0.2042	1.1	1.0	0.25	76	240-241	–	
4	0.2019	1.1	1.0	4	82	241-244	–	
5	0.3998	1.2	3.5	1	83	~250[c,d]	–	
5	0.2209	4.7	2.0	2	72	234-241[d]	–	0.07
5	0.1915	10.9	2.0	2	78	220-239[d]	–	0.07
6	0.2005	1.0	0.5	24	0		–	
7	0.2023	1.0	2.0	72	0		–	
8	0.1029	0.9	1.5	1	31	125-134	+	
8	0.2019	1.0	2.0	24	53	150-156	+	0.10
9	0.200	1.4	1.0	24	35	267-269	–	
9	0.2098	1.4	1.0	48	27	264-267	–	
10	0.1291	2.0	1.0	24	17	163-165	–	
11	0.2025	0.8	2.0	72	0		–	
12	0.2040	1.2	1.0	36	42	~225	+	0.09
12	0.2120	1.0	2.0	48	50	~248	+	
13	0.2023	1.0	2.5	24	0		–	
14	0.2038	1.0	2.5	24	0		–	
15	0.1084	0.9	1.0	0.25	88	224-227	–	
15	0.2088	0.9	2.5	1	82	219-222[d]	–	
16	0.1005	0.8	1.0	24	0		–	

[a] Temperature 0 °C. [b] Dimethyl sulfoxide, 30 °C, concentration 50 mg/10 mL. [c] Melting point and decomposition point are not clear. [d] Polymers decompose.

Table V
Elemental Analysis of Poly(orthoesters)

	calcd			found		
	% C	% H	% N	% C	% H	% N
poly-1	51.7	6.9		50.9	7.2	
poly-2	55.4	7.7		55.4	7.9	
poly-3	34.5	4.3		34.4	4.4	
poly-4	49.3	6.9		48.7	4.0	
poly-5	37.3	4.4	8.7	37.4	4.6	8.7
poly-8	48.5	6.4	8.1	47.2	6.7	7.1
poly-9	51.1	6.4		49.7	6.3	
poly-10	52.0	5.4		50.3	5.4	
poly-12	52.5	7.6		50.6	8.2	
poly-15	41.1	5.2	8.0	41.1	5.4	8.2

mL of ethanol was eliminated. DOP (120 mL and a trace of *p*-toluenesulfonic acid were added. Heating was continued at 150 °C for 2 h at 0.5 mmHg. The crude sublimed product was dissolved in 20 mL of ether. The insoluble material was filtered off. Evaporation of the ether gave 3.3 g of **5**, which was purified by recrystallization from acetone; yield 41%.

4-Amino-2,6,7-trioxabicyclo[2.2.2]octane (6). Compound **5** (1.02 g, 6.33 mmol) was reduced in 20 mL of ether with platinum oxide (0.135 g, 0.593 mmol) at room temperature at 3 atm of hydrogen pressure for 40 h. Solids were removed by passing the solution through a column (aluminum oxide, Woelm neutral, Waters Associates Inc.). Evaporation of the ether gave 0.58 g of **6**, which was purified by recrystallization from 1:1 (v/v) pentane–acetone; yield 69%.

5-(Hydroxymethyl)-1-aza-3,7-dioxabicyclo[3.3.0]octane and 2-(Dimethylamino)-2-(hydroxymethyl)-1,3-propanediol. 5-(Hydroxymethyl)-1-aza-3,7-dioxabicyclo[3.3.0]octane was prepared by the method of Senkus:[19] yield 97.3%; mp 59–60 °C (lit.[19] mp 65 °C). The bicyclic compound was reduced to 2-(dimethylamino)-2-(hydroxymethyl)-1,3-propanediol with Raney Ni by the method of Senkus:[19] yield 85%; mp 85 °C (lit.[19] mp 90 °C).

4-(Dimethylamino)-2,6,7-trioxabicyclo[2.2.2]octane (7). 2-(Dimethylamino)-2-(hydroxymethyl)-1,3-propanediol (2.98 g, 0.02 mol) was suspended in triethyl orthoformate (2.96 g, 0.02 mol) and heated at 120 °C for 1 h. Some ethanol was collected. Catalytic amounts of *p*-toluenesulfonic acid were added and the solution was heated at 160–170 °C at 0.1 mmHg for 1 h. Compound **7** distilled out of the reaction mixture onto the wall of the distillation apparatus. Some of the precursor 2-ethoxy-5-(hydroxymethyl)-5-(dimethylamino)-1,3-dioxane [NMR ($CDCl_3$) δ 5.51 and 5.37 (CHO_3, 1 H, 2 s), 4.3–3.4 (OCH_2, 8 H, m), 2.7 (OH, 1 H, b), 2.38 and 2.26 ($N(CH_3)_2$, 6 H, 2 s), and 1.25 (CH_3, 3 H, t)] distilled out. The precursor was put back in the reaction flask and again heated at 160–170 °C at 0.1 mmHg. The procedure was repeated three times. The crude product was collected and recrystallization from 2:1 (v/v) pentane–ether gave 1.46 g of **7**; yield 46%.

4-Acetamido-2,6,7-trioxabicyclo[2.2.2]octane (8). Acetyl chloride (1.0 mL, 14.1 mmol) was added slowly to a solution of 4-amino-2,6,7-trioxabicyclo[2.2.2]octane (0.817 g, 6.23 mmol) in 50 mL triethylamine; the temperature was kept below 5 °C. Stirring was continued for 1 h. Diethyl ether (100 mL) was added. The precipitated solid was removed by filtration and the solvent was evaporated. The crude product was recrystallized from chloroform. Recrystallization gave 0.5 g of **8**; yield 46%.

4-(Ethoxycarbonyl)-2,6,7-trioxabicyclo[2.2.2]octane (9). 2-Carboxy-2-(hydroxymethyl)-1,3-propanediol (3.00 g, 0.02 mol) was suspended in triethyl orthoformate (5.93 g, 0.04 mol) and heated at 120 °C for 2 h; 4.5 mL of ethanol and ethyl formate distilled out. A trace of *p*-toluenesulfonic acid was added. Temperature was increased to 190 °C during 1 h at 0.1 mmHg. Heating was continued for 20 h. Monomer crystallized on the wall of the distillation apparatus. The crude product was recrystallized from acetone; yield 0.70 g (19%).

4-[[(*p*-Toluenesulfonyl)oxy]methyl]-2,6,7-trioxabicyclo-[2.2.2]octane (10). Compound **4** (1.00 g, 6.85 mmol) was dissolved in 50 mL of ether. A 1.6 M *n*-hexane solution (4.5 mL) of *n*-butyllithium (7.20 mmol) was added dropwise during 15 min at a temperature below 10 °C. Stirring was continued for 1 h. A solution of *p*-toluenesulfonyl chloride (1.7 g, 8.93 mmol) in 50 mL of ether was added at a temperature below 5 °C. Stirring was continued for 2 h at 0 °C. Ether (100 mL) was added and the precipitated solid was filtered off. Evaporation of ether gave the

Table VI
IR Data (KBr) of Poly(orthoesters)

polymer	frequency, cm^{-1}
poly-1	3400 (w, ν_{O-H}), 2950, 2880, 1725 (vw, $\nu_{C=O}$), 1470, 1380, 1300, 1250, 1200, 1160 (s), 1140 (max, ν_{C-O-C}), 1060 (s), 1000 (s), 980, 960
poly-2	3500 (w, ν_{O-H}), 2960, 2900, 1730 (vw, $\nu_{C=O}$), 1620, 1480, 1465, 1395, 1350, 1300, 1270, 1235, 1190 (s), 1155 (s), 1065 (max, ν_{C-O-C}), 1020 (s), 1000 (s), 935 (s), 820, 760
poly-3	3520 (w, ν_{O-H}), 2960, 2900, 1730 (w, $\nu_{C=O}$), 1485, 1470, 1440, 1410, 1395, 1350, 1260, 1165 (s), 1120 (s), 1090 (s), 1075 (s), 1030 (max, ν_{C-O-C}), 1000 (s), 940, 860, 810, 755, 660
poly-4	3400 (s, ν_{O-H}), 2950, 2890, 1720 (vw, $\nu_{C=O}$), 1620, 1480, 1395, 1100 (s), 1070 (s), 1030 (max, ν_{C-O-C}), 940
poly-5	3450 (w, ν_{O-H}), 2970–2900, 1555 (max, $\nu_{as}(NO_2)$), 1475, 1455, 1400, 1360, 1330, 1270, 1160 (s), 1080 (s, ν_{C-O-C}), 1040 (s), 1000 (s), 940, 880, 860
poly-8	3550 (s, ν_{N-H}), 3100 (w), 2950, 2900, 1720 (w, $\nu_{C=O}$), 1660 (max, $\nu_{C=O}$ of amide), 1550 (s, δ_{N-H} and ν_{C-N}), 1470, 1380, 1315, 1220, 1160 (s), 1080 (s, ν_{C-O-C}), 1040, 1000, 945
poly-9	3450 (w, ν_{O-H}), 2980, 2910, 1730 (s, $\nu_{C=O}$), 1490, 1470, 1400, 1380, 1355, 1315, 1245 (s), 1220, 1175 (s), 1110 (s), 1075 (s), 1060 (s), 1025 (max, ν_{C-O-C}), 990 (s), 940
poly-10	3520 (vw, ν_{O-H}), 3060 (w, ν_{C-H} of aromatic), 3000–2870, 2750, 1710, 1640, 1605 (m, $\nu_{C=C}$), 1480, 1465, 1365 (s, $\nu_{as}(SO_2)$), 1230, 1185 (max, $\nu_s(SO_2)$), 1105, 1025, 1045, 990 (s, ν_{C-O-C}), 850, 820, and 800 (m, δ_{C-H} of aromatic), 675
poly-12	3370 (s, ν_{O-H}), 2960, 2900, 1710 (negligible), 1620, 1480, 1460, 1415, 1390, 1285, 1240, 1140, 1050, 1020 (max, ν_{C-O-C}), 1000, 880
poly-15	3400 (negligible, ν_{O-H}), 3000–2900, 1750 (w), 1555 (max, $\nu_{as}(NO_2)$), 1485, 1450, 1400, 1360, 1330, 1275, 1220, 1160 (s), 1125 (s), 1060 (s, ν_{C-O-C}), 1040 (s), 1010, 950, 900, 860

Table VII
NMR Data (in Me_2SO-d_6) of Poly(orthoesters)

polymer	chemical shift (δ) and assignment
poly-1[a]	5.28 (CHO_3, 1 H), 3.8 and 3.5 (OCH_2, 6 H), 1.91 (CHC_3, 1 H)
poly-3	5.41 (CHO_3, 1 H), 3.6 (OCH_2 and CH_2Br, 8 H)
poly-5[b]	5.55 (CHO_3, 1 H), 4.3 and 3.9 (OCH_2, 6 H)
poly-8	5.39 (CHO_3, 1 H), 3.9 (OCH_2, 6 H), 1.80 (CH_3CO, 3 H), 7.8 (NHCO, 1 H)
poly-12	4.19 (OH and OCH_2, 3 H), 3.4 (OCH_2, 6 H), 3.33 (CH_3, 3 H)

[a] ^{13}C NMR (Me_2SO-d_6) for poly-1 (η_{inh} 0.10 dL/g) δ 109.04 (CHO_3), 62.76 (OCH_2), 33.19 (CHC_3). [b] ^{13}C NMR (Me_2SO-d_6) for poly-5 (η_{inh} 0.07 dL/g) δ 108.65 and 106.37 (CHO_3, peak ratio ca. 1:9), 84.93 and 84.41 (CNO_2), 64.84 (OCH_2), 62.31 and 60.30 (OCH_2 in ring).

crude product. Recrystallization from ether gave 1.46 g of **10**; yield 71%.

1,4-Dimethyl-2,6,7-trioxabicyclo[2.2.2]octane (11). Equimolar amounts of 2-(hydroxymethyl)-2-methyl-1,3-propanediol and triethyl orthoformate (0.03 mol) were mixed in 10 mL of DOP and heated to 120 °C. The theoretical amount of ethanol (3.5 mL) distilled out. A trace of *p*-toluenesulfonic acid was added. The solution was allowed to react at 120 °C at 0.1 mmHg. Immediately white crystalline product sublimed out of the reaction mixture. Recrystallization from acetone gave 2.82 g of pure **11**: yield 65%; mp 82–90 °C (lit.[10] mp 85–90 °C).

4-(Methoxycarbonyl)-1-methyl-2,6,7-trioxabicyclo[2.2.2]-octane (13). 2-Carboxy-2-(hydroxymethyl)-1,3-propanediol (3.00 g, 0.02 mol) was suspended in a mixture of DOP (10 mL) and trimethyl orthoacetate (4.24 g. 0.04 mol) and heated at 100 °C for 30 min. Some methanol and methyl acetate distilled out. DOP (20 mL) and a trace of *p*-toluenesulfonic acid were added. Temperature was increased to 120 °C at 0.2 mmHg. White crystalline product sublimed out very quickly on the wall of the distillation apparatus. Crystallization from *n*-pentane gave 2.60 g of **13**; yield 69%.

4-(Ethoxycarbonyl)-1-methyl-2,6,7-trioxabicyclo[2.2.2]octane (14). 2-Carboxy-2-(hydroxymethyl)-1,3-propanediol (3.00 g, 0.02 mol) was suspended in a mixture of DOP (10 mL) and triethyl orthoacetate (6.49 g, 0.04 mol) and heated at 120 °C for 1 h; 5.1 mL of ethanol and ethyl acetate distilled out. DOP (20 mL) and a trace of *p*-toluenesulfonic acid were added. Temperature was increased to 140 °C during 2 h at 0.2 mmHg. White crystalline product sublimed out on the wall of the distillation apparatus. Crystallization from *n*-pentane gave 2.72 g of **17**; yield 67%.

1-Methyl-4-nitro-2,6,7-trioxabicyclo[2.2.2]octane (15). 2-(Hydroxymethyl)-2-nitro-1,3-propanediol (6.04 g, 0.04 mol) was suspended in a mixture of DOP (20 mL) and triethyl orthoacetate (6.49 g, 0.04 mol) and heated at 120 °C for 2 h; 3.6 mL of ethanol distilled out. DOP (10 mL) and a catalytic amount of *p*-toluenesulfonic acid were added. Temperature was increased to 150 °C at 0.3 mmHg. White crystals sublimed onto the wall of the distillation apparatus during 4 h. Crystallization from *n*-pentane gave 3.13 g of **15**; yield 45%.

4-Amino-1-methyl-2,6,7-trioxabicyclo[2.2.2]octane (16). Compound **15** (5.79 g, 35.9 mmol) was reduced to **16** in 50 mL of diethyl ether at room temperature for 48 h under 3 atm of hydrogen pressure using platinum oxide (0.495 g, 2.18 mmol). Removal of catalyst and diethyl ether and recrystallization from tetrahydrofuran gave 3.66 g of **16**; yield 70%.

Polymerization. The required amounts of monomer and solvent were weighed into a small glass ampule, the ampule was chilled in a dry ice–methanol mixture, and a dichloromethane solution of initiator was added. The ampule was cooled, evacuated, sealed off, and transferred to the desired temperature. Polymerization was terminated by addition of a few milliliters of 4:1 (v/v) methanol–triethylamine and the solution was poured into a large amount of methanol to precipitate the polymers. Polymer was collected by filtration and washed with methanol. Polymer **8** was precipitated into a large amount of diethyl ether. Nitromethane was also used as a solvent for the polymerization of **10**. Polymers were dried under vacuum to constant weight.

Acknowledgment. We are deeply indebted to the National Institutes of Health, Grant GM18595, for support of this work, to Dr. M. W. Barnes of Thiokol, who kindly supplied us with 2-(hydroxymethyl)-1,3-propanediol, and to Dr. J. R. Schaeffer of Eastman Kodak, who provided 2-carboxy-2-(hydroxymethyl)-1,3-propanediol.

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Synthesis of Polyamides from Active Diacyl Derivatives of 2-Mercaptobenzoxazole and Diamines under Mild Conditions

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ABSTRACT: New active dithioesters and diamides derived from 2-mercaptobenzoxazole were prepared for use in polyamide synthesis. The active thioester and amide reacted readily with amines to give excellent yields of the corresponding amides. The high reactivity of these active thioesters and amides is discussed in relation to the electron-withdrawing effect on the leaving group and intramolecular general-base catalysis. Solution polycondensation of new active dithioesters and amides with aliphatic and aromatic diamines proceeded rapidly under mild conditions to produce polyamides with inherent viscosities up to 1.6 dL/g.

Introduction

The polycondensation of diamines with active dicarboxylic acid derivatives to form polyamides under mild conditions has received considerable attention.[1,2] On the other hand, it is recognized that the increasing reactivity order of carboxylic acid derivatives toward nucleophiles may be roughly correlated with the order of increasing stability of the leaving group anions, that is, pK_a of the leaving group.

From this point of view, we have exploited a series of good leaving groups for the syntheses of active esters and amides and demonstrated that the active ester and amide methods are useful in the preparation of high molecular weight polyamides under mild conditions.[3]

In our foregoing paper,[3e] we described the synthesis of polyamides from active 2-benzothiazolyl dithioesters and diamines. This prompted us to study analogous dithioesters derived from 2-mercaptobenzoxazole, which was expected to be a good leaving group of carboxylic acid derivatives. We have found that the *N*- or *S*-acyl products from the acylation of 2-mercaptobenzoxazole reacted very rapidly with various amines to give excellent yields of the corresponding amides.

This article describes a successful synthesis of polyamides through active dithioesters or diamides obtained from acylation of 2-mercaptobenzoxazole.

Experimental Section

Materials. Solvents and Diamines. *N*-Methyl-2-pyrrolidone (NMP) (supplied by Mitsubishi Chemical Industries Ltd.) and hexamethylphosphoramide (HMPA) were purified by vacuum distillation and stored over 4-Å molecular sieves. Reagent grade hexamethylenediamine (HMDA) was used as received. Bis(4-aminophenyl)methane (MDA) and bis(4-aminophenyl) ether (ODA) (supplied by Sumitomo Chemical Co.) were purified by recrystallization from benzene and tetrahydrofuran (THF), respectively. Other reagents, including 2-mercaptobenzoxazole (MB) and solvents, were obtained commerically and used as received.

***S*-(2-Benzoxazolyl) Thiobenzoate (1).** To a cold solution (−30 °C) of MB (15.1 g, 0.1 mol) and triethylamine (TEA, 14 mL) in THF (300 mL) was added dropwise a solution of benzoyl chloride (14 g, 0.1 mol) in THF (30 mL). The solution was stirred at a temperature lower than −20 °C for 20 min and poured into ice water (100 mL). The precipitate was collected by filtration and dried in vacuo; yield 23 g (90%). Recrystallization from cyclohexane afforded pale yellow needles, mp 83–85 °C. The IR (KBr) spectrum showed an absorption at 1695 cm^{-1} (C=O). Anal. Calcd for $C_{14}H_9NO_2S$: C, 65.87; H, 3.55; N, 5.48. Found: C, 66.0; H, 3.8; N, 5.5.

3-Benzoylbenzoxazoline-2-thione (2). Compound **2** was prepared as described above using acetone as a solvent at 15 °C for 30 min; yield 93%. Recrystallization from ethanol gave yellow needles, mp 117–118 °C (lit.[4] mp 117 °C). The IR (KBr) spectrum showed absorptions at 1695 (C=O) and 1340 cm^{-1} (C=S).

***S,S'*-Bis(2-benzoxazolyl) Dithioisophthalate (3).** A solution of MB (4.0 g, 0.03 mol) and TEA (4.2 mL, 0.03 mol) in THF (80 mL) was cooled in a dry ice–acetone bath. To this solution was added at −30 °C with stirring a solution of isophthaloyl chloride (3.0 g, 0.015 mol) in THF (20 mL). After 20 min of stirring at the above temperature the mixture was poured into water (300 mL). The precipitate formed was collected by filtration, washed with water, and dried in vacuo over P_2O_5. It was thoroughly washed with acetone to give 23 g (77%) of white powder, mp 129–131 °C. The IR (KBr) spectrum showed an absorption at 1700 cm^{-1} (C=O). Anal. Calcd for $C_{22}H_{12}O_4N_2S_2$: C, 61.10; H, 2.80; N, 6.48. Found: C, 61.1; H, 3.0; N, 6.6.

***S,S'*-Bis(2-benzoxazolyl) Dithioadipate (4).** Compound **4** was prepared from adipoyl chloride and MB as previously described. The crude product, which was washed with acetone, was obtained in a yield of 73%. The temperature of thermal rearrangement was 115 °C (by DTA). The IR spectrum (KBr) showed an absorption at 1720 cm^{-1} (C=O). Anal. Calcd for $C_{20}H_{16}N_2O_4S_2$: C, 58.24; H, 3.91; N, 6.79. Found: C, 58.2; H, 4.1; N, 6.8.

***N,N'*-Isophthaloylbis[benzoxazoline-2-thione] (5).** Compound **5** was prepared from isophthaloyl chloride and MB in acetone at room temperature as previously described. The yield was 70%. It was recrystallized from benzene to give yellow needles, mp 201–202 °C. The IR spectrum showed absorptions at 1720 (C=O) and 1380 cm^{-1} (C=S). Anal. Calcd for $C_{22}H_{12}N_2O_4S_2$: C, 61.10; H, 2.80; N, 6.48. Found: C, 61.0; H, 3.0; N, 6.6.

***N,N'*-Adipoylbis[benzoxazoline-2-thione] (6).** Compound **6** was prepared from adipoyl chloride and MB as previously described. The yield was 85%. It was recrystallized from toluene to give white leaflets, mp 242–244 °C. The IR spectrum showed

0024-9297/82/2215-0017$01.25/0