The Acid-catalyzed Reaction of Cycloalkanones with Formaldehyde

Fukumi Hirano and Shoji Wakabayashi
Department of Chemistry, Faculty of Science, Okayama College of Science, Okayama 700

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The acid-catalyzed reactions of several cycloalkanones, such as cyclopentanone (**1a**), 2-methylcyclopentanone (**1b**), cyclohexanone (**1c**), 2-methylcyclohexanone (**1d**), and 2-isopropyl-5-methylcyclohexanone (**1e**), with formaldehyde were investigated. These reactions involved an aldol condensation analogous to the Prins reaction, and they afforded methylol derivatives and cyclic ethers. It was found that the formation of the products is strongly influenced by the skeletal structure and by the substituent on the cycloalkanones. That is, **1a**, **1c**, and **1d** gave mainly 1,3-dioxanes, while **1b** and **1e** formed only methylol derivatives. The reaction of cycloalkanone enol esters with formaldehyde was also studied.

The base-catalyzed reaction of cycloalkanones with formaldehyde has already been studied by many workers.[1–4] However, only a few papers have been reported on the acid-catalyzed reaction. For example, Olsen[5] has shown that cyclohexanone in sulfuric acid gave mono- and *bis*-1,3-dioxanes. Lumma[6] has recently reported the formation of methylol derivatives in the reaction of 2-methylcyclohexanone in trifluoroacetic acid. However, the details of the products have not been described.

In this investigation, the reaction of cycloalkanones and their enol esters with formaldehyde in the presence of an acid-catalyst was examined in considering the effects of the skeletal structure and of the substituents on the cycloalkanones.

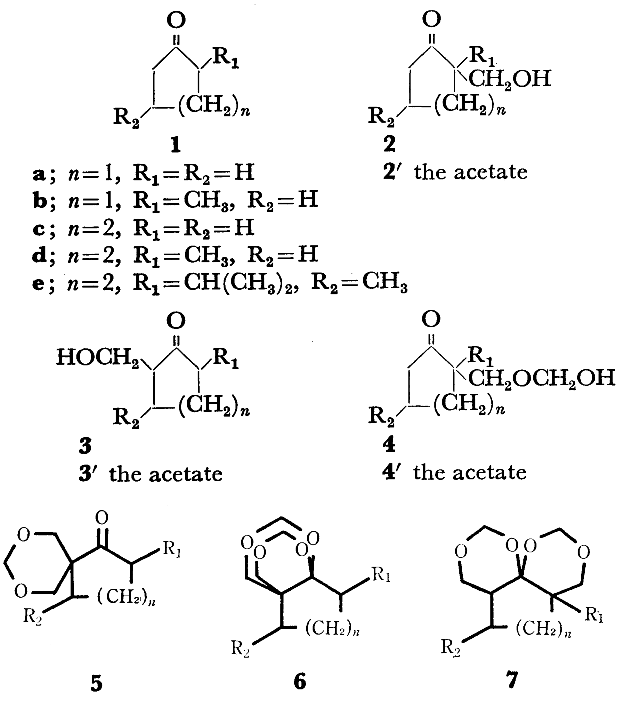
Results and Discussion

These reactions were mainly carried out in a mixture of acetic acid and acetic anhydride in the presence of phosphoric acid.

The reaction of cyclopentanone (**1a**) with formaldehyde gave 2-hydroxymethylcyclopentanone (**2a**), the acetate (**2′a**), 2-[(acetoxymethoxy)methyl]cyclopentanone (**4′a**), and 2,4,8,10-tetraoxatricyclo[4.4.3.0^{1,6}]tridecane (**6a**) as the main products.

Table 1. Reactants and products in the acid-catalyzed reaction of cycloalkanones with formaldehyde

Reactants	Products
1a	**2a, 2′a, 4′a, 6a**
1b	**2b, 2′b, 3b, 3′b**
1c	**2c, 2′c, 4′c, 5c, 6c, 7c**
1d	**2d, 2′d, 3′d, 4′d, 6d, 7d**
1e	**2e, 2′e, 3e, 3′e**



a; $n=1$, $R_1=R_2=H$
b; $n=1$, $R_1=CH_3$, $R_2=H$
c; $n=2$, $R_1=R_2=H$
d; $n=2$, $R_1=CH_3$, $R_2=H$
e; $n=2$, $R_1=CH(CH_3)_2$, $R_2=CH_3$

Scheme 1.

The reaction of 2-methylcyclopentanone (**1b**) with formaldehyde yielded 2-hydroxymethyl-2-methylcyclopentanone (**2b**), the acetate (**2′b**), 5-hydroxymethyl-2-methylcyclopentanone (**3b**), and the acetate (**3′b**) mainly. In this reaction, no formation of a bis-1,3-dioxane, such as **6a**, was detected.

The reaction of cyclohexanone (**1c**) with formaldehyde afforded 2-hydroxymethylcyclohexanone (**2c**), the acetate (**2′c**), 2-[(acetoxymethoxy) methyl] cyclohexanone (**4′c**), 2,4-dioxa-7-oxospiro[5.5]undecane (**5c**), 2,4,8,10-tetraoxatricyclo[4.4.4.0^{1,6}]tetradecane (**6c**), and 2,4,12,-14-tetraoxatricyclo[8.4.0.0^{1,6}]tetradecane (**7c**) mainly.

Similarly, the reaction of 2-methylcyclohexanone (**1d**) gave 6-methyl-2,4,12,14-tetraoxatricyclo[8.4.0.0^{1,6}]-tetradecane (**7d**), along with small amounts of 2-hydroxymethyl-2-methylcyclohexanone (**2d**), the acetate (**2′d**), 6-acetoxymethyl-2-methylcyclohexanone (**3′d**), 2-[(acetoxymethoxy)methyl]-2-methylcyclohexanone (**4′d**), and 11-methyl-2,4,8,10-tetraoxatricyclo[4.4.4.0^{1,6}]tetradecane (**6d**).

The reaction of 2-isopropyl-5-methylcyclohexanone (**1e**) with formaldehyde gave 2-hydroxymethyl-2-isopropyl-5-methylcyclohexanone (**2e**), the acetate (**2′e**) 6-hydroxymethyl-2-isopropyl-5-methylcyclohexanone (**3e**), and the acetate (**3′e**) as the main products. Methylol derivatives (**2e** and **3e**) when heated to 160—210 °C decomposed to **1e** and formaldehyde. A similar treatment of the acetates (**2′e** and **3′e**) yielded 2-isopropyl-5-methyl-1-cyclohexenyl acetate and formaldehyde.

The methanolysis of bis-1,3-dioxanes (**6c** and **7d**) gave the methylol compounds, (**2c** and **2d** respectively).

The spectral data of these products are summarized in Tables 2 and 3.

Table 2. Spectral data of methylol derivatives

Compd.	IR, cm^{-1} a)	NMR (δ, in CCl_4)
2a	3450, 1730, 1250	1.5—2.5(m, 7H), 3.6—3.8(m, $-\overset{\vert}{C}HCH_2$ OH, 2H), 4.14(s, 1H)
2′a	1730, 1230	1.5—2.4(m, 7H), 1.98(s, 3H), 4.0—4.3(m, $-\overset{\vert}{C}HCH_2OAc$, 2H)
2b	3500, 1735, 1030	1.08(s, 3H), 1.5—2.7(m, 6H), 2.90(s, 1H), 3.2—3.8(m, $-\overset{\vert}{\underset{\vert}{C}}CH_2OH$, 2H)
2′b	1735, 1230, 1160, 1070, 1030	1.02(s, 3H), 1.5—2.5(m, 6H), 2.00(s, 3H), 4.00(s, $-\overset{\vert}{\underset{\vert}{C}}CH_2OAc$, 2H)
2c	3500, 1700, 1020	1.0—2.7(m, 9H), 3.20(broad s, 1H), 3.2—3.9(m, $-\overset{\vert}{C}HCH_2OH$, 2H)
2′c	1740, 1710, 1230	1.0—2.7(m, 9H), 2.04(s, 3H), 3.9—4.3(m, $-\overset{\vert}{C}HCH_2OAc$, 2H)
2d	3400, 1700, 1125, 1040	1.12(s, 3H), 1.5—2.7(broad, 8H), 2.86(s, 1H), 3.43(s, $-\overset{\vert}{\underset{\vert}{C}}CH_2OH$, 2H)
2′d	1735, 1705, 1235, 1125, 1035	1.10(s, 3H), 1.6—2.6(broad, 8H), 1.99(s, 3H), 4.03(AB-q centered at 4.03, J=11 Hz, $-\overset{\vert}{\underset{\vert}{C}}CH_2OAc$, 2H)
2e	3500, 1700, 1040, 1020	0.8—1.1(m, $-CH_3$, 9H), 1.7—2.7(m, 8H), 3.02(s, 1H), 3.62(AB-q centered at 3.62, J=12 Hz, $-\overset{\vert}{\underset{\vert}{C}}CH_2OH$, 2H)
2′e	1740, 1700, 1230, 1030	0.7—1.2(m, $-CH_3$, 9H), 1.5—2.5(m, 8H), 2.00(s, 3H), 4.20(AB-q centered at 4.20, J=12 Hz, $-\overset{\vert}{\underset{\vert}{C}}CH_2OAc$, 2H)
3b	3500, 1740, 1040	0.97(d, J=3.0 Hz, 3H), 1.5—2.8(m, 6H), 3.5—3.8(m, $-\overset{\vert}{C}HCH_2OH$, 2H), 4.02(s, 1H)
3′b	1740, 1735, 1235, 1160, 1095, 1030	0.98(d, J=3.0 Hz, 3H), 1.5—2.7(m, 6H), 1.92(s, 3H), 3.8—4.1(m, $-\overset{\vert}{C}H-CH_2OAc$, 2H)
3′d	1740, 1715, 1235, 1130, 1035	1.00(d, J=3.0 Hz, 3H), 1.4—2.7(m, 8H), 1.98(s, 3H), 3.4—4.5(m, $-\overset{\vert}{C}H-CH_2OAc$, 2H)
3e	3500, 1700, 1220, 1060, 1020	0.7—1.1(m, $-CH_3$, 9H), 1.5—2.5(m, 8H), 2.92(s, 1H), 3.40(q, centered at 3.40, J=12 Hz, $-\overset{\vert}{C}HCH_2OH$, 2H)
3′eb)	1740, 1700, 1230, 1030	0.7—1.2(m, $-CH_3$, 9H), 1.4—2.5(m, 8H), 1.98(s, 3H), 4.12(q, centered at 4.12, J=12 Hz, $-\overset{\vert}{C}HCH_2OAc$, 2H)

a) Neat liquid film. b) IR spectrum was determined in Nujol.

Table 3. Spectral data of ether derivatives

Compd.	IR, cm^{-1}	NMR (δ, in CCl_4)
4′a	1745, 1730, 1220, 1110	1.5—2.4(m, 7H), 2.06(s, 3H), 3.6—3.9(m, $-\overset{\vert}{C}HCH_2O-$, 2H), 5.15(s, $-OCH_2O-$, 2H)
4′c	2780, 1740, 1710, 1215, 1160	1.0—2.7(m, 9H), 2.07(s, 3H), 3 3—3.7(m, $-\overset{\vert}{C}HCH_2O-$, 2H), 5.25(s, $-OCH_2O-$, 2H)
4′d	1735, 1710, 1230, 1155, 1120, 1030	1.05(s, 3H), 1.7—2.5(m, 8H), 2.10(s, 3H), 3.65(AB-q, centered at 3.65, J=9.8 Hz, $-\overset{\vert}{\underset{\vert}{C}}CH_2O-$, 2H), 5.25(s, $-OCH_2O-$, 2H)
5c	2770, 1710, 1160, 1030	1.5—2.4(m, 8H), 3.78(s, $-CH_2O-$, 4H), 4.62(AB-q centered at 4.62, J=6.0 Hz, $-OCH_2O-$, 2H)
6a	2780, 1145, 1130, 1090	1.5—2.3(m, 6H), 3.54(AB-q centered at 3.54, J=11 Hz, $-CH_2O-$, 4H), 4.82(AB-q centered at 4.82, J=5.6 Hz, $-OCH_2O-$, 4H)
6c	2780, 1170, 1080	1.3—2.1(broad, 8H), 3.3—4.3(broad, $-CH_2O-$, 4H), 4.94(AB-q centered at 4.94, J=5.5 Hz, $-OCH_2O-$, 4H)
6d	2800, 1170, 1090, 1040, 980	0.82(d, J=6.2 Hz, 3H), 1.0—2.6(m, 7H), 3.43(AB-q centered at 3.43, J=11 Hz, $-CH_2O-$, 2H), 3.67(AB-q, J=11 Hz, $-CH_2O-$, 2H), 4.80(s, $-OCH_2O-$, 2H), 4.82(AB-q, J=5.6 Hz, $-OCH_2O-$, 2H)
7c	2800, 1160, 1070	1.0—2.6(m, 8H), 3.2—4.3(m, $-CH_2O-$, 4H), 4.5—5.1(m, $-OCH_2O-$, 4H)
7d	2790, 1165, 1095, 985	0.84(s, 3H), 1.1—2.7(m, 7H), 2.9—3.9(m, $-CH_2O-$, 4H), 4.78(AB-q centered at 4.78, J=5.7 Hz, $-OCH_2O-$, 2H), 4.81(AB-q, J=5.7 Hz, $-OCH_2O-$, 2H)

Effect of the Skeletal Structure. The reaction products in the condensation of **1a** and of **1c** with formaldehyde were compared. The reaction of **1c** afforded a spiro-type 1,3-dioxane (**5c**), along with a bis-1,3-dioxane (**6c**), in good yields. On the contrary, in the case of **1a**, the yield of bis-1,3-dioxane was remarkably less than that in the case of **1c**, and a spiro-type 1,3-dioxane was not formed at all. These results indicate that the formation of a 1,3-dioxane ring involving the adjacent two carbon atoms of cyclopentane and that of a spiro-type 1,3-dioxane involving the α-carbon atom to the carbonyl group of cyclopentanone are attended with various difficulties, because of the consequent internal strain and the steric hindrance respectively.

Effect of the Substituent. In the reaction of **1d**, which has the methyl group in the α-position to the carbonyl group, with formaldehyde, bis-1,3-dioxane (**7d**) was produced in a greater yield than in the case of **1c**, but no spiro-type 1,3-dioxane such as **5c** was formed. On the other hand, the α-substituted cyclopentanone (**1b**) did not give any 1,3-dioxane derivatives. Moreover, the reaction of **1e**, with a bulky substituent such as an isopropyl group, also did not give 1,3-dioxanes at all. These results suggest that a methyl or isopropyl substituent attached at the α-position of cycloalkanones plays an important role in the formation of the 1,3-dioxane ring, in combination with the effect of the skeletal structure.

Effect of the Reaction Temperature. In all cases, the reactions carried out at temperatures between 40 and 60 °C provided products in good yields. At temperatures below 30 °C, these reactions scarcely proceeded at all. Above 90 °C, the reaction mixture gave a large amount of a polymer, along with the other products which could be isolated with difficulty from the reaction mixture.

Effect of the Catalyst. The effects of catalyst in these reactions were examined using several inorganic and organic acids, and also such Lewis acids as zinc chloride. Phosphoric acid and *p*-toluene sulfonic acid were found to be most effective catalysts. The use of hydrochloric acid, sulfuric acid, and *d*-10-camphorsulfonic acid gave rise to the polymerization of reactants, resulting in the formation of the products in lower yields. Lewis acids had little catalytic effect. The effect in the reaction of **1d** with formaldehyde is shown in Fig. 1 as an example.

Effect of the Solvent. It was found that the ratio and constitutions of the products are largely dependent on the solvents employed. The results shown in Tables 4 and 5 indicate that the reaction is affected markedly by the character of the solvents. Especially, the use of aliphatic alcohol caused a remarkable reduction in the yields of the products. When the reaction was carried out in halogen-substituted alkanes under reflux, the only products were 1,3-dioxanes. The reaction proceeded hardly at all in the same solvents at a lower temperature. In acetonitrile, lower aliphatic acids, and ethers, the reaction gave 1,3-dioxanes mainly.

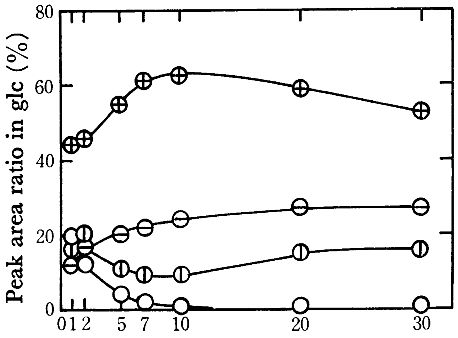


Fig. 1. Effect of supported amount of acid-catalyst, H_3PO_4 in the reaction of **1d** with formaldehyde Reaction conditions: Reactants, **1d** 10 mmol; $(CH_2O)_n$ 30 mmol; Solvent, AcOH 10 ml; Reaction temperature, 60 °C; Time, 15 hr.

○: **2d**; ⊖: **2′d**; ⦶: **6d**; ⊕: **7d**

TABLE 4. SOLVENT EFFECT OF THE VARIOUS ALIPHATIC ACIDS IN THE REACTION OF **1d** WITH FORMALDEHYDE

Reactant (mmol)		Solvent (ml)	Peak area ratio in glc (%)			
1d	$(CH_2O)_n$		**2d**	**6d**	**7d**	others
10.0	30.0	HCOOH(10)	5.7	9.0	55.2	30.1
10.0	30.0	AcOH(10)	2.6	8.6	62.5	26.3
10.0	30.0	Ac_2O(10)	20.6	12.0	33.5	33.9
10.0	30.0	Ac_2O–AcOH (5—15)	8.4	18.1	42.5	31.0
10.0	30.0	C_2H_5COOH (10)	3.1	8.8	62.5	25.6
10.0	30.0	*n*-C_3H_7COOH (10)	4.6	22.5	43.0	29.9

Reaction conditions: Catalyst, H_3PO_4 10.0 mmol; Reaction temperature, 60 °C; Time, 15 hr.

TABLE 5. SOLVENT EFFECT IN THE REACTION OF **1b** WITH FORMALDEHYDE

Reactant (mmol)		Solvent (mmol)	Catalyst (mmol)	Time (hr)	Peak area ratio in glc (%)	
1b	$(CH_2O)_n$				**2b**+**2′b**	**3b**+**3′b**
25.0	75.0	AcOH(125)	4.2	10	28	72
25.0	75.0	Ac_2O(125)	3.8	10	92	8
25.0	75.0	AcOH–Ac_2O (125—25)	2.6	21.5	21	79
25.0	75.0	*n*-Hex–Ac_2O (125—25)	5.2	7.5	14	86
25.0	75.0	EtOH–Ac_2O (125—25)	6.4	10	47	53
25.0	75.0	AcOEt–Ac_2O (125—25)	6.4	8.5	11	89
25.0	75.0	C_6H_6–Ac_2O (125—25)	4.2	7	9	91

Reaction conditions: Reaction temperature, 70 °C; Catalyst, PTS.

Reaction of Cycloalkanone Enol Esters with Formaldehyde. The acid-catalyzed reaction of cycloalkanone enol esters (acetates and propionates) with formaldehyde was investigated under the same reaction conditions as those used for cycloalkanones. The reactions of cycloalkanones and of its enol esters with formaldehyde afforded quite similar products, but in the latter reaction the yields of 1,3-dioxanes increased remarkably. Especially, the reaction of the enol esters of cycloalkanones (**1c** and **1d**) with formaldehyde led preferentially to the formation of 1,3-dioxanes, even under milder reaction conditions. Therefore, it may be considered that the 1,3-dioxane derivatives are produced through the enolization of cycloalkanone, followed by a mechanism analogous to the Prins reaction.

Experimental

All the melting points are uncorrected. The IR spectra were measured with a JASCO Model IR-G spectrometer. The NMR spectra were recorded on a JEOL LMN-MH-60 II spectrometer (60 MHz) in CCl_4, using TMS as an internal standard.

Materials. *2-Methylcyclopentanone (**1b**)* was prepared by the method of van Rysselberge[7] from adipic acid. bp 138.0—138.5 °C; d_4^{25} 0.9127; n_D^{25} 1.4330. *2-Isopropyl-5-methylcyclohexanone (**1e**)* was prepared by the oxidation of 2-isopropyl-5-methylcyclohexanol with sodium bichromate,[8] bp 66—67 °C/4 mmHg; d_4^{25} 0.8950; n_D^{25} 1.4499; α_D^{25} −26.62 °. The other cycloalkanones, solvents, and catalysts were commercial materials.

The enol acetates of cycloalkanones were prepared by the method of Goodman *et al.*[9] *1-Cyclopentenyl acetate*: bp 47—49 °C/15 mmHg; d_4^{25} 1.0115; n_D^{25} 1.4480. *2-Methyl-1-cyclopentenyl acetate*: bp 62.5—63.0 °C/9 mmHg; d_4^{25} 0.9864; n_D^{25} 1.4476. *1-Cyclohexenyl acetate*: bp 178—179 °C; d_4^{25} 1.0082; n_D^{25} 1.4547. *2-Methyl-1-cyclohexenyl acetate*: bp 67—68 °C/14 mmHg; d_4^{25} 0.9901; n_D^{25} 1.4568. *2-Isopropyl-5-methyl-1-cyclohexenyl acetate*: bp 88—90 °C/3 mmHg; d_4^{25} 0.9465; n_D^{25} 1.4550; α_D^{25} +66.35 °.

The enol propionates of cycloalkanones (**1c** and **1d**) were prepared by the method described in the literature.[10] *1-Cyclohexenyl propionate*: bp 194—195 °C; d_4^{25} 0.9783; n_D^{25} 1.4548. *2-Methyl-1-cyclohexenyl propionate*: bp 73—75 °C/3 mmHg; d_4^{25} 0.9649; n_D^{25} 1.4539.

*Reaction of Cycloalkanones (**1a**—**1e**) with Formaldehyde.* To a mixture of paraformaldehyde (0.30 mol), acetic anhydride (0.10 mol), glacial acetic acid (1.00 mol), 85% phosphoric acid (0.05 mol), and cycloalkanone (0.10 mol) was added in several portions, under moderate cooling, after which the mixture was stirred at 40 or 60 °C for 10 or 15 hr. The reaction mixture was poured into cold water (30 ml), neutralized with 5% sodium carbonate, and then extracted with ether. After the ether had been evaporated, the residual oil was subjected to fractional distillation under reduced pressure. From these fractions, the individual products were isolated by preparative glpc using a DEGSP column at 160 °C.

The reaction of the enol ester of cycloalkanone with formaldehyde was carried out similarly.

The structures of the products were identified on the basis of the elemental analysis, and the MS, IR, and the NMR spectra. Tables 2 and 3 show some pertinent spectral data on the products.

*2-Hydroxymethylcyclopentanone (**2a**)*: Bp 95—96 °C/10 mmHg (lit,[11] 104 °C/13 mmHg); d_4^{25} 1.0823; n_D^{25} 1.4629; MR: 29.042. Calcd for $C_6H_{10}O_2$: 29.244. MS: *m/e* 114 (M^+).

Found: C, 63.10; H, 9.00%. Calcd for $C_6H_{10}O_2$: C, 63.13; H, 8.83%.

*2-Acetoxymethylcyclopentanone (**2′a**)*: Bp 100—102 °C/10 mmHg (lit,[11] 120—121 °C/15 mmHg); d_4^{25} 1.0886; n_D^{25} 1.4502; MR: 38.570. Calcd for $C_8H_{12}O_3$: 38.609. EV: 359. Calcd 359.3.

Found: C, 61.54; H, 7.94%. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75%.

*2-[(Acetoxymethoxy)methyl]cyclopentanone (**4′a**)*: Bp 109—110 °C/5 mmHg; d_4^{25} 1.1136; n_D^{25} 1.4513; MR: 45.046. Calcd for $C_9H_{14}O_4$: 44.870. EV: 296. Calcd: 301.3. MS: *m/e* 186 (M^+).

Found: C, 57.91; H, 7.49%. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58%.

*2,4,8,10-Tetraoxatricyclo[4.4.3.0^{1,6}]tridecane (**6a**)*: Bp 102—102.5 °C/10 mmHg: d_4^{25} 1.1920; n_D^{25} 1.4741. MR: 43.907. Calcd for $C_9H_{14}O_4$: 43.734. MS: *m/e* 186 (M^+).

Found: C, 58.02; H, 7.61%. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58%.

*2-Hydroxymethyl-2-methylcyclopentanone (**2b**)*: n_D^{25} 1.4677 (lit,[12] n_D^{20} 1.4681).

Found: C, 65.54; H, 9.45%. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44%.

*2-Acetoxymethyl-2-methylcyclopentanone (**2′b**)*: Bp 194—195 °C*; d_4^{25} 1.0558; n_D^{25} 1.4485. MR: 43.196. Calcd for $C_9H_{14}O_3$: 43.277. EV: 327. Calcd: 329.7.

Found: C, 63.50; H, 8.23%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

*5-Hydroxymethyl-2-methylcyclopentanone (**3b**)*:

Found: C, 65.52; H, 9.40%. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44%.

*5-Acetoxymethyl-2-methylcyclopentanone (**3′b**)*: Bp 206—207 °C*; d_4^{25} 1.1080; n_D^{25} 1.4692. MR: 42.794. Calcd for $C_9H_{14}O_3$: 43.277. EV: 322. Calcd: 329.7.

Found: C, 63.48; H, 8.34%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

*2-Hydroxymethylcyclohexanone (**2c**)*: d_4^{25} 1.0660; n_D^{25} 1.4735 (lit,[13] n_D^{11} 1.4780). MR: 33.759. Calcd for $C_7H_{12}O_2$: 33.862. MS: *m/e* 128 (M^+).

Found: C, 65.70; H, 9.43%. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44%.

*2-Acetoxymethylcyclohexanone (**2′c**)*: n_D^{25} 1.4628 (lit,[14] n_D^{20} 1.4632). EV: 321. Calcd for $C_9H_{14}O_3$: 330.0. MS: *m/e* 170 (M^+).

Found: C, 63.51; H, 8.32%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

*2-[(Acetoxymethoxy)methyl]cyclohexanone (**4′c**)*: d_4^{25} 1.1466; n_D^{25} 1.4818. MR: 49.768. Calcd for $C_{10}H_{16}O_4$: 49.488. EV: 283. Calcd: 280.2. MS: *m/e* 200 (M^+).

Found: C, 60.02; H, 8.22%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

*2,4-Dioxa-7-oxospiro[5.5]undecane (**5c**)*: d_4^{25} 1.1532; n_D^{25} 1.4848. MR: 42.284. Calcd for $C_9H_{14}O_3$: 42.659. MS: *m/e* 170 (M^+).

Found: C, 63.32; H, 8.13%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

*2,4,8,10-Tetraoxatricyclo[4.4.4.0^{1,6}]tetradecane (**6c**)*: d_4^{25} 1.1720; n_D^{25} 1.4852. MR: 48.981. Calcd for $C_{10}H_{16}O_4$: 48.352. Mp 86.5—87.0 °C (from i-C_3H_7OH). MS: *m/e* 200 (M^+).

Found: C, 59.92; H, 8.23%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

*Methanolysis of Bis-1,3-dioxane (**6c**)*: A solution of **6c** (25 mmol) in methanol (10 ml) was refluxed with two drops of conc. sulfuric acid for 15 hr, and then the solvent was evaporated. The residual mixture was extracted with ether, and the extract was washed with water, dried, and evaporated. The distillation of the residue gave a methylol derivative (**2c**) including a small amount of cyclohexanone (**1c**).

*2,4,12,14-Tetraoxatricyclo[8.4.0.0^{1,6}]tetradecane (**7c**)*: Mp 59—60 °C (from i-C_3H_7OH).

Found: C, 59.84; H, 8.18%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

*2-Hydroxymethyl-2-methylcyclohexanone(**2d**)*: Bp 85.0—85.5 °C/3 mmHg (lit,[13] 107—108 °C/11 mmHg); d_4^{25} 1.0310; n_D^{25} 1.4702. MR: 38.492. Calcd for $C_8H_{14}O_2$: 38.470. MS: *m/e* 142 (M^+).

Found: C, 67.23; H, 9.98%. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93%.

*2-Acetoxymethyl-2-methylcyclohexanone (**2′d**)*: Bp 103—104 °C/3 mmHg; d_4^{25} 1.0600; n_D^{25} 1.4598. MR: 47.585. Calcd for $C_{10}H_{16}O_3$: 47.845. EV: 304. Calcd: 304.6. MS: *m/e* 184 (M^+).

Found: C, 64.87; H, 8.93%. Calcd for $C_{10}H_{16}O_3$: C,

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* Measured by a capillary method.

65.19; H, 8.75%.

The saponification of the acetate (**2′d**) did not produce the methylol (**2d**), but a polymer with a glass-like gloss.

6-Acetoxymethyl-2-methylcyclohexanone (3′d): d_4^{25} 1.0540; n_D^{25} 1.4602. MR: 47.891. Calcd for $C_{10}H_{16}O_3$: 47.845. EV: 302. Calcd: 304.6.

Found: C, 65.37; H, 8.68%. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.

2-Methyl-2-[(acetoxymethoxy)methyl]cyclohexanone (4′d): d_4^{25} 1.0971; n_D^{25} 1.4661. MR: 54.097. Calcd for $C_{11}H_{18}O_4$: 54.106. EV: 252. Calcd: 261.9.

Found: C, 61.64; H, 8.38%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%.

11-Methyl-2,4,8,10-tetraoxatricyclo$[4.4.4.0^{1,6}]$*tetradecane (6d)*: d_4^{25} 1.1410; n_D^{25} 1.4762. MR: 52.980. Calcd for $C_{11}H_{18}O_4$: 52970. Mp 74—75 °C (from *i*-C_3H_7OH).

Found: C, 61.73; H, 8.54%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%.

6-Methyl-2,4,12,14-tetraoxatricyclo$[8.4.0.0^{1,6}]$*tetradecane (7d)*: Bp 104.5—105.0 °C/3 mmHg; d_4^{25} 1.1464; n_D^{25} 1.4818. MR: 53.262. Calcd for $C_{11}H_{18}O_4$: 52.970. Mp 79—80 °C (from *i*-C_3H_7OH). MS: *m/e* 214 (M^+).

Found: C, 61.58; H, 8.53%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%.

Methanolysis of Bis-1,3-dioxane (7d): By the use of the procedures described for the methanolysis of **6c**, **7d** was treated with methanol to afford a methylol derivative (**2d**) including a small amount of 2-methylcyclohexanone (**1d**).

2-Hydroxymethyl-2-isopropyl-5-methylcyclohexanone (2e):

Found: C, 71.63; H, 10.92%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

2-Acetoxymethyl-2-isopropyl-5-methylcyclohexanone (2′e): Bp 130—131 °C/2 mmHg; d_4^{25} 1.0182; n_D^{25} 1.4635. MR: 61.276. Calcd for $C_{13}H_{22}O_3$: 61.699. EV: 243. Calcd: 247.9. MS: *m/e* 226 (M^+).

Found: C, 68.80; H, 9.99%. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%.

6-Hydroxymethyl-2-isopropyl-5-methylcyclohexanone (3e):

Found: C, 71.62; H, 11.03%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

6-Acetoxymethyl-2-isopropyl-5-methylcyclohexanone (3′e): Bp 138—139 °C/2 mmHg; mp 39—40 °C (from *i*-C_3H_7OH). EV: 242. Calcd for $C_{13}H_{22}O_3$: 247.9. MS: *m/e* 226 (M^+).

Found: C, 69.02; H, 9.87%. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%.

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