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The Acid-catalyzed Reaction of Alicyclic Ketones with Formaldehyde. III.[1] The Reaction of 3- and 3,5-Methyl-substituted Cyclohexanones with Formaldehyde

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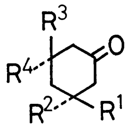
The reaction of 3- and 3,5-methyl-substituted cyclohexanones with formaldehyde in acid media has been studied. The acid-catalyzed reaction gave 2,4,12,14-tetraoxatricyclo[8.4.0.$0^{1,6}$]tetradecane, 2,4-dioxaspiro[5.5]undecan-7-one, and 2,4,8,10-tetraoxatricyclo[4.4.4.$0^{1,6}$]tetradecane derivatives. The effect of the methyl groups on the product distribution has been discussed.

In previous papers,[1,2] the acid-catalyzed reaction of cycloalkanones or alkyl-substituted cycloalkanones with formaldehyde has been reported. The reaction involved an aldol condensation analogous to the Prins reaction to afford spiro mono(1,3-dioxanes), fused di(1,3-dioxanes), and hydroxymethyl derivatives. The yield and distribution of the products were strongly influenced by the ring-size of the cycloalkanones, the alkyl-substituents on the alicyclic ketones and the reaction conditions. This paper deals with the reaction of 3- and 3,5-methyl-substituted cyclohexanones with formaldehyde, together with the effect of the methyl substituent affecting the distribution of the products in the acid-catalyzed reaction.

Results and Discussion

Reaction of Methylcyclohexanones with Formaldehyde. The reaction of 3-methylcyclohexanone(**1a**) with formaldehyde has been conducted in a mixture of acetic acid and acetic anhydride in the presence of phosphoric acid at 60—65 °C for 10 h. The resulting products were isolated by column chromatography over silica gel and purified by preparative gas chromatography. The reaction of **1a** gave 7-methyl-2,4,12,14-tetraoxatricyclo[8.4.0.$0^{1,6}$]tetradecane(**2a**), 9-methyl-2,4-dioxaspiro[5.5]undecan-7-one (**3a**), 14-methyl-2,4,8,10-tetraoxatricyclo[4.4.4.$0^{1,6}$]tetradecane (**4a**), 11-methyl-2,4-dioxaspiro[5.5]undecan-7-one (**5a**), and 12-methyl-2,4,8,10-tetraoxatricyclo[4.4.4.$0^{1,6}$]tetradecane (**6a**). 3,3-Dimethylcyclohexanone (**1b**), *cis*-3,5-dimethylcyclohexanone(**1c**), *trans*-3,5-dimethylcyclohexanone (**1d**), 3,3,5-trimethylcyclohexanone (**1e**) and 3,3,5,5-tetramethylcyclohexanone(**1f**) were similarly treated with formaldehyde to give the same type of products as those of the reaction of **1a**. The yields are summarized in Table 1.



1

1a: R^1=Me, R^2=R^3=R^4=H
1b: R^1=R^2=Me, R^3=R^4=H
1c: R^1=R^3=Me, R^2=R^4=H
1d: R^1=R^4=Me, R^2=R^3=H
1e: R^1=R^2=R^3=Me, R^4=H
1f: R^1=R^2=R^3=R^4=Me

Fig. 1.

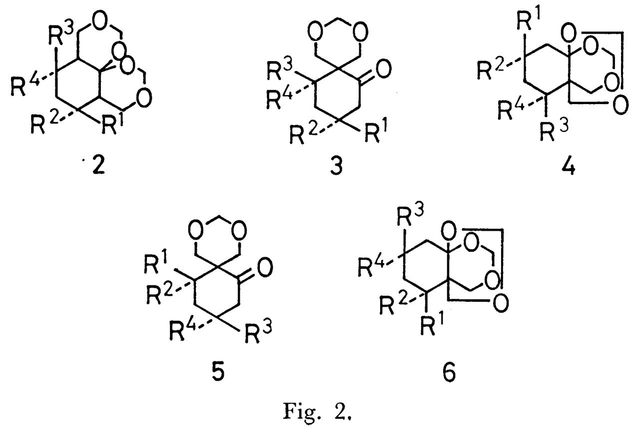


Fig. 2.

Structures of Reaction Products. The structure of the spiro mono(1,3-dioxane) (**3a**) has been identified by the synthesis of an authentic specimen from 2,4-dioxaspiro[5.5]undecan-7-one.[2] The structure of **3b** or **3e** has also been confirmed by direct comparison with an authentic specimen prepared from **3a** or **3d** (see Experimental). The spiro mono(1,3-dioxanes) (**5**) have been characterized as the structural isomers of **3**, which differ only from the substituted position of a spiro(1,3-dioxane) ring, on the basis of similar spectral data and elemental analyses.

The acid-catalyzed hydrolysis of fused di(1,3-dioxanes) (**4** or **6**) quantitatively afforded the corresponding spiro mono(1,3-dioxanes) (**3** or **5**), respectively (see Experimental). On this basis, the structure of the fused di(1,3-dioxanes) (**4** or **6**) has been characterized. Fused di(1,3-dioxanes) (**2**) were presumed to be the structural isomers of **4** or **6**, on the basis of similar spectral data and elemental analyses.

Methyl-substituent Effect. As seen in Table 1, the methyl groups adjacent to the reaction points (C_2- and C_6-positions in methyl-substituted cyclohexanones) play an important role in the individual reactions. When the C_5-position of cyclohexanone has no methyl groups, *e.g.*, **1a** or **1b**, the reactivity is the largest in the reactions studied. When both C_3- and C_5-positions are substituted by a methyl group, *e.g.*, **1c** or **1d**, the reactivity decreases to one-half of that of **1a** or **1b**. As the methyl group is further introduced, *e.g.*, **1e** or **1f**, the reactivity becomes very poor.

The substituent also influences the product distribution. The reaction of **1a** or **1c**, which has no C_3-

Table 1. Acid-catalyzed reaction of 3- and 3,5-methyl-substituted cyclohexanones (**1a**—**1f**) with formaldehyde

Alicyclic ketone **1**	Isolated yield (%) **2**	**3**	**4**	**5**	**6**	Total yield (%)	Recovered **1** (%)
3-Methylcyclohexanone (**1a**)	2	4	83	1	2	92	3
3,3-Dimethylcyclohexanone (**1b**)	—	30	59	6	—	95	3
cis-3,5-Dimethylcyclohexanone (**1c**)	3	5	42	—	—	50	48
trans-3,5-Dimethylcyclohexanone (**1d**)	26	25	3	—	—	54	41
3,3,5-Trimethylcyclohexanone (**1e**)	—	4	1	2	—	7	89
3,3,5,5-Tetramethylcyclohexanone (**1f**)	—	3	—	—	—	3	95

or C_3,C_5-axial substituents, mainly affords **4**; **1b**, which has two C_3-substituents, chiefly affords **4**, accompanied by **3**; **1d**, which has an axial and an equatorial substituent at each of the C_3- and C_5-positions, chiefly yields **2**, together with **3**, and very little **4**; **1e** or **1f** mainly affords **3**, although the yield is very low.

These results have been interpreted as follows; (i) The first step in the acid-catalyzed reaction is the enolization of the cyclic ketone, followed by the axial attack of a hydroxymethyl cation ($^+CH_2OH$) on the enolic double bond. The attack takes place predominantly at the α-methylene position where the steric interference caused by the C_3- or C_5-methyl substituent is very small (steric approach control). (ii) The resulting intermediate, a *cis* fused hemiacetal, attains equilibrium with the *trans* fused isomer as shown below. The hemiacetal is dehydrated preferentially according to the Sayzeff rule to give an olefin. The olefin is again attacked by the cation in an antiparallel attack[3] to give the fused di(1,3-dioxane) (**4**).

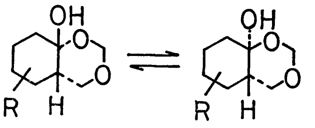


Fig. 3.

(iii) The axial methyl groups at C_3- or C_3,C_5-positions interfere with the formation of **4** and promote that of **3**, because of the 1,3-diaxial interactions between a 1,3-dioxane ring and the axial methyl groups (product development control). (iv) The formation of **5** is more unfavored than that of **3**. However, the reaction of **1e** affords **5e** in a fairly high ratio. This may be explained by the steric approach control and product development control described above, that is, there is no remarkable differences between the two controls on the formation of **3e** or **5e**. (v) In a series of this reaction, the fused di(1,3-dioxane) (**2**) is produced in only small quantities and has been attributed to the fact that **2** is more thermodynamically unstable than **4**, in addition to the reasons given in (ii). However, the reaction of **1d** gave **2d** in an exceptionally good yield but the explanation for this remains unknown.

Experimental

All the boiling and melting points are uncorrected. PMR spectra were taken with a JEOL LMN-MH-60 II spectrometer (60 MHz) with tetramethylsilane as an internal reference. IR spectra were recorded with a Japan Spectroscopic IR-A spectrophotometer. The molecular weight was determined by Rast's method. Preparative GLPC was performed with a Shimadzu GC-3AH using a 3 m×3 mmϕ column with 30% diethylene glycol succinate polyester on 60/80 kamelite operating at 160 °C with a H_2 pressure of 0.2 kg/cm^2. Preparative column chromatography was conducted over silica gel (Wakogel C-200) with a mixture of hexane and ether (5:1 v/v) as an eluent.

Materials. Commercial 3-methylcyclohexanone(**1a**) of analytical grade was used. 3,3-Dimethylcyclohexanone(**1b**),[4] *cis*-3,5-dimethylcyclohexanone(**1c**),[5] *trans*-3,5-dimethylcyclohexanone(**1d**),[5] 3,3,5-trimethylcyclohexanone(**1e**),[6] and 3,3,5,5-tetramethylcyclohexanone(**1f**)[7] were prepared according to reported methods. **1c** and **1d** were obtained as a mixture of their isomers and each isomer was isolated by preparative GLPC. **1b**: bp 51—52 °C/4 mmHg, n_D^{25} 1.4460. **1c**: n_D^{25} 1.4400. **1d**: n_D^{25} 1.4456 (mixture of **1c** and **1d**: bp 174—176 °C). **1e**: bp 72—73 °C/8 mmHg, n_D^{25} 1.4426. **1f**: bp 196—197 °C, n_D^{25} 1.4512.

*Reaction of Methylcyclohexanones(**1a**—**1f**) with Formaldehyde.* A mixture of methylcyclohexanone(10 mmol) and acetic anhydride (1.02 g, 10 mmol) was added to a stirred solution of 95% paraformaldehyde (1.58 g, 50 mmol) and 85% phosphoric acid (0.58 g, 5 mmol) in glacial acetic acid(10 ml) at room temperature, stirring being continued at 60—65 °C for 10 h. After the usual work-up, each product was isolated by column chromatography and subsequent preparative GLPC.

*Hydrolysis of Fused Di(1,3-dioxanes)(**4** or **6**).* A solution of the fused di(1,3-dioxane)(**4** or **6**) (10 mmol) in 10% aqueous hydrochloric acid(10 ml) and cyclohexane(10 ml) was stirred under reflux for 5 h. The mixture was extracted with ether (20 ml×3), the combined extracts washed with 5% aqueous sodium carbonate and saturated brine (10 ml×2), and dried. Removal of the solvent gave crude spiro mono(1,3-dioxane) (**3** or **5**), which was isolated by preparative GLPC. The yields of hydrolyzed products are given in Table 6.

*Authentic Sample of **3a**.* A solution of 2,4-dioxaspiro[5.5]undecan-7-one(**7**) (1.07 g, 10 mmol) in ethylene glycol (20 ml) was treated with bromine(1.60 g, 20 mg atom) according to the method of Garbisch Jr.[8] The work-up gave crude crystals of 8-bromo-2,4-dioxaspiro[5.5]undecan-7-one ethylene acetal(**8**), which were recrystallized from benzene-petroleum ether to give white crystals of **8**(2.87 g, 98%); mp 110.5—111.5 °C. PMR[C_6H_6-CCl_4(4 : 1 v/v)]: δ 1.1—2.7(br m, 6H), 3.2—4.2(m, 9H), 4.64 (AB-q, J=5.8 Hz, 2H). IR(Nujol): 2764(w), 1153(s), 1027(s), 748(w), 680(m) cm^{-1}. Found: C, 45.41; H, 5.84%; mol wt: 295. Calcd for $C_{11}H_{17}O_4Br$: C, 45.06; H, 5.85%; mol wt: 293.3. Ethylene acetal (**8**) (2.93 g, 10 mmol) was stirred with sodium methoxide(1.62 g, 30 mmol) in dimethyl sulfoxide(30 ml)

TABLE 2. PHYSICAL PROPERTIES OF FUSED DI(1,3-DIOXANES) (**2**, **4**, AND **6**)

Compd	n_D^{25} (mp)	Molecular formula	Found %		Calcd %		Molecular weight	
			C	H	C	H	Found	Calcd
2a	(82—84 °C)[a)]	$C_{11}H_{18}O_4$	61.82	8.41	61.66	8.47	216	214.3
2c	(76—78 °C)[a)]	$C_{12}H_{20}O_4$	63.02	8.85	63.13	8.83	231	228.3
2d	1.4887	$C_{12}H_{20}O_4$	63.41	8.87	63.13	8.83	229	228.3
4a	(73—74 °C)[a)]	$C_{11}H_{18}O_4$	61.27	8.43	61.66	8.47	218	214.3
4b	(86—88 °C)[a)]	$C_{12}H_{20}O_4$	63.55	8.91	63.13	8.83	227	228.3
4c	1.4874	$C_{12}H_{20}O_4$	63.40	8.68	63.13	8.83	228	228.3
4d	1.4887	$C_{12}H_{20}O_4$	63.38	8.87	63.13	8.83	224	228.3
4e	1.4862	$C_{13}H_{22}O_4$	64.80	9.38	64.44	9.15	245	242.3
6a	1.4926	$C_{11}H_{18}O_4$	61.95	8.46	61.66	8.47	215	214.3

a) Recrystallized from 2-propanol.

TABLE 3. PHYSICAL PROPERTIES OF SPIRO MONO(1,3-DIOXANES) (**3** AND **5**)

Compd	n_D^{25} (mp)	Molecular formula	Found %		Calcd %		Molecular weight	
			C	H	C	H	Found	Calcd
3a	1.4791	$C_{10}H_{16}O_3$	65.02	8.68	65.19	8.75	181	184.2
3b	(76—77 °C)[a)]	$C_{11}H_{18}O_3$	66.73	9.36	66.64	9.15	194	198.3
3c	1.4829	$C_{11}H_{18}O_3$	66.88	9.10	66.64	9.15	201	198.3
3d	1.4822	$C_{11}H_{18}O_3$	66.89	9.32	66.64	9.15	200	198.3
3e	(53—54 °C)[a)]	$C_{12}H_{20}O_3$	67.42	9.13	67.89	9.50	210	212.3
3f	(87—88 °C)[a)]	$C_{13}H_{22}O_3$	68.63	9.76	68.99	9.80	227	226.3
5a	1.4890	$C_{10}H_{16}O_3$	65.18	8.82	65.19	8.75	183	184.2
5b	(80—81 °C)[a)]	$C_{11}H_{18}O_3$	66.73	9.36	66.64	9.15	194	198.3
5e	1.4880	$C_{12}H_{20}O_3$	67.88	9.47	67.89	9.50	212	212.3

a) Recrystallized from 2-propanol.

TABLE 4. IR AND PMR SPECTRAL DATA OF FUSED DI(1,3-DIOXANES) (**2**, **4**, AND **6**)

Compd	IR (cm^{-1})	PMR (ppm in CCl_4)
2a[a)]	2779(w), 1164(s), 1064(s), 997(s)	0.77 (d, J=5.3 Hz, 3H), 0.9—2.5 (m, 7H), 3.14—4.07 (m, 4H), 4.60 (AB-q, J=6.0 Hz, 2H), 4.66 (AB-q, J=6.0 Hz, 2H)
2c[a)]	2766(w), 1163(s), 1063(s), 995(s)	0.82 (d, J=6.3 Hz, 3H), 1.01 (d, J=6.9 Hz, 3H), 1.2—2.7 (m, 6H), 3.4—4.3 (m, 4H), 4.86 (AB-q, J=5.3 Hz, 2H), 4.88 (AB-q, J=5.3 Hz, 2H)
2d	2769(w), 1172(s), 1153(s), 1092(s), 1044(s)	1.04 (d, J=7.2 Hz, 3H), 1.07 (d, J=7.2 Hz, 3H), 1.2—2.3 (m, 6H), 3.63 (s, 2H), 3.73 (AB-q, J=12 Hz, 2H), 4.87 (AB-q, J=6.0 Hz, 2H), 4.92 (AB-q, J=6.0 Hz, 2H)
4a[a)]	2770(w), 1160(s), 1040(s), 992(s)	0.93 (d, J=7.2 Hz, 3H), 1.0—2.7 (m, 7H), 3.39 (AB-q, J=11 Hz, 2H), 3.66 (AB-q, J=11 Hz, 2H), 4.78 (AB-q, J=5.7 Hz, 2H), 4.83 (s, 2H)
4b[a)]	2774(w), 1160(s), 1046(s), 953(s)	1.05 (s, 6H), 1.1—2.0 (m, 6H), 3.18—3.90 (br, 4H), 4.73 (AB-q, J=6.0 Hz, 4H)
4c	2769(w), 1161(s), 1041(s), 940(s)	0.72 (d, J=7.5 Hz, 3H), 0.94 (d, J=7.5 Hz, 3H), 1.1—2.8 (m, 6H), 3.50 (AB-q, J=12 Hz, 2H), 3.96 (AB-q, J=12 Hz, 2H), 4.91 (AB-q, J=6.0 Hz, 2H), 4.93 (s, 2H)
4d	2767(w), 1173(s), 1044(s), 946(s)	1.04 (d, J=6.9 Hz, 3H), 1.06 (d, J=7.2 Hz, 3H), 1.2—2.4 (m, 6H), 3.63 (s, 2H), 3.74 (AB-q, J=11 Hz, 2H), 4.88 (AB-q, J=6.0 Hz, 2H), 4.92 (AB-q, J=6.0 Hz, 2H)
4e	2766(w), 1164(s), 1044(s), 952(s)	0.82 (d, J=6.5 Hz, 3H), 0.97 (s, 3H), 1.15 (s, 3H), 1.3—2.9 (m, 5H), 3.49 (AB-q, J=12 Hz, 2H), 3.98 (AB-q, J=12 Hz, 2H), 4.93 (s, 2H), 4.95 (AB-q, J=5.6 Hz, 2H)
6a	2760(w), 1160(s), 1036(s), 936(s)	0.81 (d, J=7.5 Hz, 3H), 1.0—2.8 (m, 7H), 3.43 (AB-q, J=12 Hz, 2H), 3.83 (AB-q, J=12 Hz, 2H), 4.75 (AB-q, J=6.0 Hz, 2H), 4.80 (s, 2H)

a) IR spectrum was measured in Nujol.

Table 5. IR and PMR spectral data of spiro mono(1,3-dioxanes) (**3** and **5**)

Compd	IR ($\mathrm{cm^{-1}}$)	PMR (ppm in $\mathrm{CCl_4}$)
3a	2751(w), 1696(s), 1159(s), 1032(s)	1.02 (m, 3H), 1.2—2.7 (m, 7H), 3.67 (AB-q, J=11 Hz, 4H), 4.48 (AB-q, J=5.6 Hz, 2H)
3b[a]	2754(w), 1699(s), 1157(s), 1035(s)	0.97 (s, 6H), 1.3—2.2 (m, 6H), 3.70 (s, 4H), 4.53 (AB-q, J=5.6 Hz, 2H)
3c	2751(w), 1703(s), 1164(s), 1034(s)	1.02 (m, 3H), 1.24 (d, J=6.0 Hz, 3H), 1.4—2.4 (m, 6H), 3.92 (AB-q, J=12 Hz, 4H), 4.62 (AB-q, J=6.0 Hz, 2H)
3d	2758(w), 1704(s), 1150(s), 1032(s)	0.93 (d, J=7.5 Hz, 3H), 1.02 (d, J=4.5 Hz, 3H), 1.3—2.9 (m, 6H), 3.80 (AB-q, J=11 Hz, 2H), 3.90 (AB-q, J=11 Hz, 2H), 4.60 (AB-q, J=6.0 Hz, 2H)
3e[a]	2757(w), 1703(s), 1169(s), 1036(s)	0.90 (s, 3H), 1.07 (s, 3H), 1.22 (d, J=6.3 Hz, 3H), 1.4—2.5 (m, 5H), 3.97 (AB-q, J=12 Hz, 4H), 4.70 (AB-q, J=5.7 Hz, 2H)
3f[a]	2777(w), 1684(s), 1144(s), 1036(s)	1.06 (s, 12H), 1.55 (s, 2H), 2.18 (s, 2H), 3.91 (AB-q, J=11 Hz, 4H), 4.54 (s, 2H)
5a	2751(w), 1698(s), 1150(s), 1034(s)	0.98 (d, J=7.5 Hz, 3H), 1.3—2.9 (m, 7H), 3.84 (s, 2H), 3.92 (AB-q, J=11 Hz, 2H), 4.63 (AB-q, J=6.0 Hz, 2H)
5b[a]	2776(w), 1700(s), 1160(s), 1045(s)	0.97 (s, 6H), 1.2—2.1 (m, 4H), 2.13 (s, 2H), 3.78 (AB-q, J=12 Hz, 4H), 4.62 (AB-q, J=6.0 Hz, 2H)
5e	2754(w), 1711(s), 1175(s), 1041(s)	0.87 (s, 3H), 1.03 (m, 3H), 1.18 (s, 3H), 1.3—2.5 (m, 5H), 3.97 (AB-q, J=12 Hz, 4H), 4.68 (s, 2H)

[a] IR spectrum was measured in Nujol.

Table 6. Acid-catalyzed hydrolysis of fused di(1,3-dioxanes) (**4** or **6**)

Reactant	Product	Isolated yield (%)
4a	**3a**	98
4b	**3b**	95
4c	**3c**	97
4d	**3d**	94
4e	**3e**	98
6a	**5a**	97

at room temperature for 15 h. The mixture was then acidified with 10% aqueous hydrochloric acid and stirred at 50 °C for 1 h. The work-up gave crude crystals of *2,4-dioxaspiro[5.5]undec-8-en-7-one(**9**)*, which were recrystallized from benzene to give white crystals of **9**(1.53 g, 91%); mp 77.5—78.0 °C. PMR($\mathrm{CCl_4}$): δ 2.1—2.6(m, 4H), 3.80(s, 4H), 4.70 (AB-q, J=6.0 Hz, 2H), 5.82(d, J=10.2 Hz, of t, J=1.8 Hz, 1H), 6.91(m, 1H). IR(Nujol): 2762(w), 1654(s), 1610(w), 1153(s), 1054(s), 1027(s), 931(s), 924(s) $\mathrm{cm^{-1}}$. Found: C, 64.38; H, 7.17%; mol wt: 168. Calcd for $\mathrm{C_9H_{12}O_3}$: C, 64.27; H, 7.19%; mol wt: 168.2. A solution of α,β-unsaturated ketone(**9**) (1.68 g, 10 mmol) in absolute ether (50 ml) was treated with methylmagnesium iodide prepared from the reaction of magnesium turnings (0.48 g, 20 mg atom) and methyl iodide(2.84 g, 20 mmol) in absolute ether (20 ml) in the presence of anhydrous copper(I) bromide(0.29 g, 1 mmol) below −10 °C. The work-up gave crude *9-methyl-2,4-dioxaspiro[5.5]undecan-7-one(**3a**)* which was isolated by preparative GLPC as a colorless oil (1.80 g, 96%). The physical constants of the compound were consistent with those of **3a**, produced by the acid-catalyzed reaction of **1a** with formaldehyde.

*Authentic Sample of **3b**.* By a procedure similar to that for the preparation of **8**, **3a**(1.84 g, 10 mmol) reacted with bromine (1.60 g, 20 mg atom) to afford crystals of *8-bromo-9-methyl-2,4-dioxaspiro[5.5]undecan-7-one ethylene acetal (**10**)*, which was recrystallized from methanol to give white crystals of **10**(2.92 g, 95%); mp 135—136 °C. PMR($\mathrm{CCl_4}$): δ 1.03(d, J=6.5 Hz, 3H), 1.2—2.5(br m, 5H), 3.43—4.22 (m, 9H), 4.50(AB-q, J=5.7 Hz, 2H). IR(Nujol): 2769(w), 1166(s), 1117(s), 1085(s), 1025(s), 748(m), 680(m) $\mathrm{cm^{-1}}$. Found: C, 46.77; H, 6.02%; mol wt: 306. Calcd for $\mathrm{C_{12}H_{19}O_4Br}$: C, 46.92; H, 6.24%; mol wt: 307.2. Ethylene acetal(**10**)(3.07 g, 10 mmol) reacted with sodium methoxide (1.62 g, 30 mmol) by the same procedure as that for the preparation of **9** to afford crystals of *9-methyl-2,4-dioxaspiro[5.5]undec-8-en-7-one(**11**)*, which were recrystallized from methanol to give white needles of **11** (1.46 g, 80%); mp 102.0—102.5 °C. PMR($\mathrm{C_5H_5N}$): δ 1.73(s, 3H), 2.23(s, 4H), 3.95 (AB-q, J=12 Hz, 4H), 4.82(AB-q, J=6.0 Hz, 2H), 5.76(br s, 1H). IR(Nujol): 2773(w), 1638(s), 1624(s), 1154(s), 1025(s), 920(s) $\mathrm{cm^{-1}}$. Found: C, 66.18; H, 7.68%; mol wt: 181. Calcd for $\mathrm{C_{10}H_{14}O_3}$: C, 65.91; H, 7.74%; mol wt: 182.2. α,β-Unsaturated ketone(**11**) (1.82 g, 10 mmol) reacted with methylmagnesium iodide (20 mmol) to give crude crystals of *9,9-dimethyl-2,4-dioxaspiro[5.5]undecan-7-one(**3b**)*, which were recrystallized from 2-propanol to give white crystals of **3b**(1.92 g, 97%). The physical constants of the compound were identical with those of **3b**, produced by the acid-catalyzed reaction of **1b** with formaldehyde.

*Authentic Sample of **3e**.* By a procedure similar to that for the preparation of **8**, **3c**(1.98 g, 10 mmol) reacted with bromine (1.60 g, 20 mg atom) to afford crude crystals of *8-bromo-9,11-dimethyl-2,4-dioxaspiro[5.5]undecan-7-one ethylene acetal(**12**)*, which were recrystallized from methanol to give white crystals of **12**(3.08 g, 96%); mp 115.0—122.0 °C. PMR($\mathrm{CCl_4}$): δ 0.98(dd, J=3.0, 6.0 Hz, 3H), 1.25(d, J=6.8 Hz, 3H), 1.4—2.3(m, 4H), 3.60—4.18(m, 8H), 4.42(d, J=6.0 Hz, 1H), 4.58 (AB-q, J=6.0 Hz, 2H). IR(Nujol): 2760(w), 1184(s), 1160(s), 1114(s), 1034(s), 686(m) $\mathrm{cm^{-1}}$. Found: C, 48.73; H, 6.62%. Calcd for $\mathrm{C_{13}H_{21}O_4Br}$: C, 48.61; H, 6.59%. Ethylene acetal(**12**)(3.21 g, 10 mmol) reacted with sodium methoxide (1.62 g, 30 mmol) to give a dark brownish mixture. Column chromatographic separation (silica gel with a 3:1 mixture of hexane and chloroform) of the mixture gave crude *9,11-dimethyl-2,4-dioxaspiro[5.5]-*

*undec-8-en-7-one(**13**)* which was purified by preparative GLPC to give a colorless oil(1.63 g, 83%); n_D^{25} 1.5083. PMR (CCl_4) : δ 1.07(d, J=7.1 Hz, 3H), 1.92(s, 3H), 2.1—3.1 (m, 3H), 3.72(AB-q, J=12 Hz, 2H), 3.90(AB-q, J=12Hz, 2H), 4.68(AB-q, J=6.0 Hz, 2H), 5.64(m, 1H). IR(neat): 2751(w), 1652(s), 1146(s), 1026(s), 920(s) cm^{-1}. Found: C, 67.58; H, 8.20% ; mol wt: 200. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22%; mol wt: 196.2. α,β-Unsaturated ketone (**13**) (1.96 g, 10 mmol) reacted with methylmagnesium iodide(20 mmol) to give crude crystals of *9,9,11-trimethyl-2,4-dioxaspiro[5.5]undecan-7-one(**3e**)*, which were recrystallized from 2-propanol to give white crystals of **3e**(2.08 g, 98%). The physical constants of the compound were identical with those of **3e**, produced by the acid-catalyzed reaction of **1e** with formaldehyde.

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