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Formaldehyde Polymers. 22.[1] Reaction Products of 6,8-Dimethyl-4-chromanone with Formaldehyde—On the Dimeric Products—

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The reaction of 6,8-dimethyl-4-chromanone with formaldehyde has been carried out in 96% sulfuric acid. From the mother liquors after obtaining 5-hydroxymethyl-6,8-dimethyl-4-chromanone, the methylene and oxydimethylene dimers of 6,8-dimethyl-4-chromanone, 6,6′,8,8′-tetramethyl-5,7′-methylenedichroman-4,4′-dione and bis(6,8-dimethyl-4-oxochroman-5-ylmethyl) ether, respectively, were isolated by recrystallization. ^{1}H- and ^{13}C-NMR spectra of 5-hydroxymethyl-6,8-dimethyl-4-chromanone in 96% sulfuric acid show the existence of 6,8-dimethyl-4-oxochroman-5-ylmethyl cation. The intermediate ion is stable, not reacting in sulfuric acid.

In a previous paper,[1] a report was given on the reactions of 4-chromanones with formaldehyde carried out in the presence of sulfuric acid or polyphosphoric acid. The reaction products of 4-chromanone, 6- as well as 8-methyl- and 5,7-dimethyl-4-chromanone with formaldehyde were the polymers linked by methylene bridges, while 6,8-dimethyl-4-chromanone gave only 5-hydroxymethyl-6,8-dimethyl-4-chromanone.

In this paper, the isolation of dimeric products from the reaction products of 6,8-dimethyl-4-chromanone with formaldehyde in the presence of sulfuric acid and the spectral characteristic of 5-hydroxymethyl-6,8-dimethyl-4-chromanone in sulfuric acid are reported.

Results and Discussion

Isolation of the Dimeric Compounds. The reaction of 6,8-dimethyl-4-chromanone (**1**) with formaldehyde was carried out in different mol ratios of the reactants in the presence of 96% sulfuric acid. The products are given in Table 1.

TABLE 1. REACTION OF 6,8-DIMETHYL-4-CHROMANONE WITH FORMALDEHYDE AT 60 °C

Exp. No.	Reactant (mol)		CH_2O/**1** (mol ratio)	H_2SO_4 (g)	Time (hr)	Products and Yield (%)		
	1	CH_2O				**2**	**3**	**4**
1	0.10	0.05	0.5	38	4	—	3.1	—
2	0.20	0.10	0.5	80	4	0.5	—	—
3	0.20	0.10	0.5	80	8	0.15	0.9	—
4	0.28	0.28	1.0	230	6	36.	1.2	—
5	0.50	0.60	1.2	1000	4	55.	—	—
6	0.80	1.17	1.5	3000	4	60.	—	0.3

The reaction products of **1** with formaldehyde in a 2: 1 molar ratio in sulfuric acid were 5-hydroxymethyl-6,8-dimethyl-4-chromanone (**2**) and 6,6′,8,8′-tetramethyl-5,7′-methylenedichroman-4,4′-dione (**3**). The low yield of **2** is due to a lower fractionation of **2** from a mixture of unreacted **1** and **2**, and the solubility of **2** in aqueous sulfuric acid solution. With increase of the mol ratio the yield of **2** increased, another dimeric compound, bis(6,8-dimethyl-4-oxochroman-5-ylmethyl) ether (**4**) being obtained with **2** from the reaction product (6, Table 1).

Structures of the Dimeric Compounds. The ^{1}H-NMR spectra of the methylene dimer **3** and the oxydimethylene dimer **4** are given in Table 2.

TABLE 2. ^{1}H-NMR SPECTRA OF METHYLENE DIMER **3** AND OXYDIMETHYLENE DIMER **4**

	Methylene dimer **3** (CCl_4; 1.0%)	Oxydimethylene dimer **4** (CCl_4; 5.0%)
Aromatic	7.08(1H, s)	6.98(2H, s)
	6.17(1H, s)	
Methylene between two aromatic rings	4.20(2H, s)	4.85(4H, s)
Pyrone ring	4.45(2H, t^a)	4.41(4H, t^b)
	4.40(2H, t^a)	2.67(4H, t^b)
	2.69(2H, t^a)	
	2.65(2H, t^a)	
Methyl	2.65(3H, s)	2.30(6H, s)
	2.20(3H, s)	2.11(6H, s)
	2.04(3H, s)	
	1.96(3H, s)	

a) J=6.7 Hz. b) J=6.7 Hz.

The ^{1}H-NMR spectrum of **3** shows two sharp singlet of aromatic protons, four sharp singlet of methyl protons and four sets of triplet of pyrone ring protons, while that of **4** shows a sharp singlet of aromatic protons, two sharp singlet of methyl protons and two sets of triplet of pyrone ring protons. The ^{1}H-NMR spectrum of the oxydimethylene dimer **4** is very similar to that of the symmetrical methylene dimers of 6- and 8-methyl-4-chromanone.[2] It is thought that an oxydimethylene bridge of **4** is formed between 5- and 5′-positions of 6,8-dimethyl-4-chromanones and a methylene bridge of **3** between 5- and 7′-positions of 6,8-dimethyl-4-chromanones.

Reactivity of 5-Hydroxymethyl-6,8-dimethyl-4-chromanone. Reactions of **2** with **1** or *p*-cresol which is more active than **1**[3] were carried out in the presence of sulfuric acid.

TABLE 3. REACTION CONDITIONS FOR THE REACTION OF 5-HYDROXYMETHYL-6,8-DIMETHYL-4-CHROMANONE WITH 6,8-DIMETHYL-4-CHROMANONE OR *p*-CRESOL

Reactant (mmol)			H_2SO_4 (g)	Temp (°C)	Time (h)
2	**1**	*p*-Cresol			
25.0	50.0	—	40.0	60	4
1.0	2.0	—	16.6	80	6
1.0	—	2.0	16.6	80	6

Table 4. ^{1}H-NMR spectra of 5-hydroxymethyl-6,8-dimethyl-4-chromanone in 96% sulfuric acid and carbon tetrachloride

Solvent	Conc. (wt %)	2-H	3-H	5-CH_2	6-CH_3	8-CH_3	7-H	OH
H_2SO_4	2.1	4.39(t)[a]	3.09(t)[a]	5.68(s)	1.86(s)	1.82(s)	7.30(s)	c)
CCl_4	5.7	4.45(t)[b]	2.78(t)[b]	4.46(s)	2.32(s)	2.14(s)	7.05(s)	3.38(s)

a) J=7.4 Hz. b) J=6.6 Hz. c) Not observable in 96% H_2SO_4.

Table 5. ^{13}C-NMR spectra of 6,8-dimethyl-4-chromanone and 5-hydroxymethyl-6,8-dimethyl-4-chromanone in 96% sulfuric acid and deuteriochloroform[a]

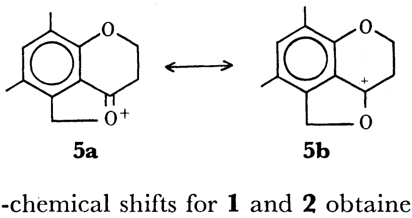
Chromanones	Solvent	Conc. (wt %)	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	6-CH_3	8-CH_3	CH_2OH
1	H_2SO_4	11.9	65.7	31.4	202.7	125.0	133.9	151.9	129.9	168.0	114.6	19.5	14.3	—
	$CDCl_3$	36.5	66.5	37.2	190.8	123.6	129.1	137.0	126.0	157.6	120.2	19.7	14.9	—
	Δ	—	−0.8	−5.8	11.9	1.4	4.8	14.9	3.9	10.4	−5.6	−0.2	−0.6	—
2	H_2SO_4	7.7	68.3	28.1	206.5	144.0	128.6	152.6	127.5	160.6	120.7	16.8	12.9	89.4
	$CDCl_3$	13.5	66.3	39.0	196.0	138.0	129.4	139.4	126.8	160.0	120.2	18.8	15.7	59.5
	Δ	—	2.0	−10.9	10.5	6.0	−0.8	13.2	0.7	0.6	0.5	−2.0	−2.8	29.9

a) Chemical shifts are reported in ppm relative to Me_4Si. $\Delta=(H_2SO_4-CDCl_3)$ is the chemical shift difference.

The reaction conditions are given in Table 3. **2** was recovered from the reaction mixtures under these reaction conditions.

NMR Spectra of 5-Hydroxymethyl-6,8-dimethyl-4-chromanone in Sulfuric Acid. ^{1}H-NMR spectra of **2** in carbon tetrachloride and 96% sulfuric acid as solvents are given in Table 4. The chemical shift of the methylene protons of 5-hydroxymethyl group in 96% sulfuric acid moves towards lower magnetic fields relative to carbon tetrachloride. The remarkable ^{1}H-NMR down field shift of the absorption of the methylene protons on the 5-position of **2** together with the data in carbon tetrachloride suggest that **5a** is a more suitable representation for the ion **5b**. This chemical shift difference resembles that reported for 2-methyl-1-oxonia-1-cyclopentene hexachloroantimonate[5] and for 5-hexen-2-one in sulfuric acid.[6]

The spectrum of **2** in sulfuric acid remained unchanged even after being heated at 80 °C for 3 h. This indicates that five-menbered oxonium ion **5a** is very stable in sulfuric acid.


5a **5b**

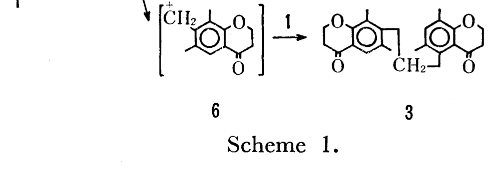
The ^{13}C-chemical shifts for **1** and **2** obtained in 96% sufuric acid and deuteriochloroform, as well as the chemical shift difference, Δ, between these two solvents are given in Table 5. Chemical shifts were assigned by comparison with the spectra of 4-chromanone,[7] and by consideration of the known substituent effects of methyl,[8] and hydroxymethyl groups.[9] All the assignments are supported by off-resonance decoupling experiments. A positive Δ indicates that the resonance is deshielded in sulfuric acid relative to deuteriochloroform.

Larger deshielding patterns ($+\Delta$) of **2** except the aromatic carbons are observed for C-4 and CH_2OH with the shift of CH_2OH larger than that of C-4. The observed chemical shift trends for **2** are interpreted to result predominantly from 5-methylene cation. Larger contribution from resonance form **5a**, which places positive charge on oxygen of ketone, can be used to rationalize the deshielding noted for this carbon.

The chemical shift change of C-4 for **2** is smaller than that observed for **1** which is protonated in 96% sulfuric acid.[10] Chemical shift changes associated with the aromatic ring seem to result from further inductive and positive charge delocalization effects on these carbons.

Reaction of 1 with Formaldehyde in Sulfuric Acid. The orientation of **1** of the cationic substants appears to be 5- and 7-positions on account of the inductive effects of two methyl groups.[1] In an acid catalyzed reaction of aromatic compounds with formaldehyde, it is probable that the hydroxymethyl cation (CH_2OH^+) is generated at first to react with **1**. Accordingly, 5- and 7-hydroxymethyl derivatives of **1** should be generated. 5-Hydroxymethyl derivative **2** was isolated from the reaction products. 5,7′-Methylene dimer **3** was obtained, but not 7-hydroxymethyl derivative.

The oxonium ion **5a** formed from 5-hydroxymethyl derivative is very stable, not reacting with **1** in 96% sulfuric acid. After being poured into water, **2** was regenerated.



Scheme 1.

It seems that 5,7'-methylene dimer **3** arises from 7-hydroxymethyl derivative by a benzyl cation process. It is proposed that a hydroxide ion is first abstracted yielding the 7-methylene cation **6**, which then attacks on 5-position of **1** to give **3**.

4 might be formed from **2** during post-treatment of the reaction mixture.

A reasonable reaction mechanism might be as shown in Scheme 1.

Experimental

General. Melting points are uncorrected. IR spectra were obtained as KBr pellets on a Hitachi EPI-G2 spectrophotometer. Mass spectra were obtained on a Hitachi RMU-6 mass spcetrometer at 70 eV, and ^1H-NMR spectra on a JEOL Model PS-100 spectrometer with tetramethylsilane (Me_4Si) as an internal standard. Chemical shift values are given in terms of δ (ppm). ^{13}C-NMR spectra were obtained on a JNM-FX60 spectrometer. Chemical shifts in deuteriochloroform were measured using Me_4Si as an internal standard. Chemical shifts in 96% sulfuric acid were obtained relative to external deuteriochloroform and converted to the Me_4Si scale by the relationship $\delta Me_4Si = \delta CDCl_3 + 77.1$.

Materials. 6,8-Dimethyl-4-chromanone (**1**) was prepared by the previous method,[2] bp 108—110 °C/2 mmHg [lit,[2] bp 121.5—122 °C/7 mmHg]. Commercial 1,3,5-trioxane and 96% sulfuric acid were used.

Reactions of 1 with Formaldehyde. The general procedure is as follows. A mixture of **1** (0.10—0.80 mol) and 1,3,5-trioxane (0.05—1.17 mol) in 96% sulfuric acid (38—3000 g) was stirred at 60 °C.

After completion of the reaction, the reaction mixture was poured into ice water. Crystalline material was obtained by filtration. Benzene solution of the filtrate was washed successively with sodium hydroxide solution and water, dried over anhydrous sodium sulfate, and then condensed to a yellow paste. Both products were dissolved in hot ligroin and allowed to stand at room temperature. The first precipitate was **2**. Concentration and cooling of the mother liquor gave **3** or **4**. These products were purified as follows.

5-Hydroxymethyl-6,8-dimethyl-4-chromanone (2): The first product separated from the hot ligroin solution of the reaction products was recrystallized from ligroin. Colorless needle crystals were obtained; mp 95—97 °C (lit,[2] mp 94—95 °C). The structure of this product was confirmed by IR, ^1H-NMR and MS spectra.

6,6',8,8'-Tetramethyl-5,7'-methylenedichroman-4,4'-dione (3): The compound soluble in the mother liquor after obtaining **2**, was fractionally recrystallized from hexane to give colorless needle crystals; mp 195—197 °C. IR; 1675 (ν C=O) and 885 (δ CH, aromatic, isolated H) cm^{-1}. MS; m/e 364 (M^+, 70.3%), 349 ($M^+ - CH_3$, 55.0%), 346 ($M^+ - H_2O$, 100%), and 189 ($M^+ - C_{11}H_{11}O_2$, 72.0%). Found: C, 75.64; H, 6.48%. Calcd for $C_{23}H_{24}O_4$: C. 75.80, H, 6.64%. ^1H-NMR spectrum of **3** is shown in Table 2.

Reduction of **3**; Reduction of **3** was carried out by the Clemmensen method.[11] To a mixture of 5.0 g of amalgamated zinc, 6.0 ml of water, 0.31 ml of concentrated hydrochloric acid and 20 ml of toluene was added 0.5 g of **3**. The mixture was refluxed briskly for 24 h, during which time a 3.0 ml portion of concentrated hydrochloric acid was added every 8 h. The solution was cooled to room temperature and the aqueous layer was separated and extracted with benzene. The combined benzene and toluene solutions were washed with water and dried over calcium chloride. After removal of the solvents, the residue was chromatographed on silica gel (Merk, silica gel 60 pre-paked column for LC size B) with benzene as an eluent to give 0.2 g of 6,6,'8,8'-tetramethyl-5,7'-methylenedichroman. Colorless oil. IR(neat); 1100 (ν C–O–C) and 875 (δ CH, aromatic, isolated H) cm^{-1}, the absorption at 1675 cm^{-1} disappearing. MS; m/e 336 (M^+, 19.5%) and 174 ($M^+ - C_{11}H_{13}O$, 100%). Found: C, 81.85; H, 8.08%. Calcd for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39%. ^1H-NMR (CCl_4; 6.0%); 6.68 (1H, s, Ph), 5.95 (1H, s, Ph), 3.61 (2H, s, $PhC\underline{H}_2Ph$), 4.03 (4H, t, J=5.8 Hz, 2- and 2'-CH_2), 2.63 (2H, t, J=6.9 Hz, 4- or 4'-CH_2), 2.45 (2H, t, J=6.9 Hz, 4'- or 4-CH_2), 1.87 (2H, m, 3- or 3'-CH_2), 1.79 (2H, m, 3'- or 3-CH_2), 2.14 (3H, s, CH_3), 2.10 (3H, s, CH_3), 2.01 (3H, s, CH_3), and 1.91 (3H, s, CH_3).

Bis(6,8-dimethyl-4-oxochroman-5-ylmethyl) Ether (4): The product separated from the ligroin solution (6, Table 1) was recrystallized repeatedly from ligroin to give **4**. mp 177—179 °C. IR; 1680 (ν C=O) and 1075 (ν C–O–C) cm^{-1}. MS; m/e 349 (M^+, trace), 205 ($M^+ - C_{12}H_{13}O_2$, 100%), and 190 (54.7%). Found: C, 73.08; H, 6.64%. Calcd for $C_{24}H_{26}O_5$: C, 73.08; H, 6.64%. ^1H-NMR spectrum of **4** is shown in Table 2.

Reactions of 2 with 1 or p*-Cresol.* A typical procedure is as follows. A mixture of **2** (0.21 g) and *p*-cresol (0.21 g) in sulfuric acid (16.6 g) was stirred at 80 °C for 6 h. The reaction mixture was then poured into ice water and extracted with chloroform. The chloroform layer was washed with aqueous sodium hydroxide solution and water, successively. After removal of the solvent, the residue was confirmed by IR and ^1H-NMR spectra.

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3) The reactivity of *p*-cresol towards electrophilic reagents appears to be higher than that of **1**. The reaction rate of **1** with formaldehyde in dioxane in the presence of perchloric acid at 60 °C was 1/2 of that of *m*-xylene with formaldehyde[1] and the reaction rate of *m*-xylene with formaldehyde catalyzed by perchloric acid in acetic acid at 60 °C was 1/1650 of that of *p*-cresol with formaldehyde.[4]

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