aromatic)], which was consistent with the nmr analysis of an authentic sample of **6**.[12]

5-Bromo-2,5-di-*tert*-butyl-4-[1-(bromomethyl)-2,2-dichlorovinyl]-2-cyclopenten-1-one (5).—After the irradiation of **1a** in bromotrichloromethane with 300-nm light, the solvent was removed from the reaction mixture, and the residue was recrystallized five times from absolute ethanol to give **5** (0.28 g, 13.5%) as white needles: mp 180–182°; ir (KBr) 1710 (cyclopentenone carbonyl group) and 1630 cm^{-1} ($C{=}CCl_2$); uv max (CH_2Cl_2) 237 nm (log ϵ 4.18); mass spectrum m/e 460 (M^+ with two bromines and two chlorines); nmr ($CDCl_3$) δ 1.15 (9 H, s, *t*-Bu), 1.30 (9 H, s, *t*-Bu), 4.35 (1 H, d, J = 3.0 Hz, *t*-H), 7.30 (1 H, d, J = 3.0 Hz, vinyl proton), and 3.35 and 4.25 (2 H, 2 d, $J_{HA} = J_{HB}$ = 11.0 Hz, CH_AH_BBr).

Anal. Calcd for $C_{16}H_{22}Br_2Cl_2O$ (460.74): C, 41.67; H, 4.77; Br, 34.69; Cl, 15.39. Found: C, 41.78; H, 4.84; Br, 34.27; Cl, 15.43.

The residue which remained after evaporation of the combined filtrates from the recrystallizations of **5** was dissolved in 10 ml of petroleum ether and eluted through a silica gel column with additional petroleum ether. The first 20 ml of the petroleum ether fraction contained about 0.01 g of low-melting (35–45°) material, shown by its nmr spectrum to be a mixture of 10% of **1a** and about 90% of a second component. The following spectroscopic data are consistent with the assignment of the **2,5-di-*tert*-butyl-4-methyl-4-(trichloromethyl)-2,5-cyclohexadien-1-one (9a)** structure to the major component of this mixture: ir (neat) 1650 and 1670 cm^{-1} (double strong bands, cyclohexadienone carbonyl group[13]); nmr ($CDCl_3$) δ 1.25 (18 H, s, 2 *t*-Bu), 6.70 (2 H, s, two vinyl protons), and 1.62 (3 H, s, CH_3); mass spectrum m/e 336 (M^+ with three chlorines), major fragments at m/e (rel intensity) 219 (96), 189 (13), 177 (42), 163 (17), 57 (100), and 41 (37); an intense metastable peak was observed at an apparent mass of 143 which results from the transition of M^+ (336) $\rightarrow$ M_1^+ (219) + Cl_3C^+ (117). After the elution of the first 20-ml fraction, an additional 100 ml of petroleum ether was added to the column to remove the rest of **1a** and **12a**. Then 50 ml of methylene chloride was passed through the column. Evaporation of the methylene chloride gave a brown tar which was refluxed in 90% ethanol for 30 min. On cooling, white crystals were formed and were identified as **3,5-di-*tert*-butyl-4-hydroxybenzaldehyde** (0.11 g, 10.5%), mp 188–189° (lit.[14] mp 189°). The aldehyde was assumed to result from the hydrolysis of **7** with 90% ethanol.[15] The column was again eluted, this time with 50 ml of methanol, and 0.15 g (8.8%) of **4** was isolated.

2,6-Di-*tert*-butyl-4-(dichloromethylene)-2,5-cyclohexadien-1-one (8).—After the irradiation of **1b** in bromotrichloromethane with 300-nm light, the solvent was removed from the reaction mixture, and the residue was recrystallized five times from absolute ethanol to give **8** as light yellow leaflet crystals (0.30 g, 30%): mp 91–93°; ir (KBr) 1630 (C=O) and 1590 cm^{-1} (conjugated $C{=}CCl_2$); uv max (CH_2Cl_2) 323 nm (log ϵ 4.15); nmr ($CDCl_3$) δ 1.40 (18 H, s, 2 *t*-Bu) and 7.30 (2 H, s, two vinyl protons); mass spectrum m/e 286 (M^+ with two chlorines).

Anal. Calcd for $C_{15}H_{20}Cl_2O$ (286.91): C, 62.74; H, 6.97; Cl, 24.72. Found: C, 62.59; H, 6.92; Cl, 24.58.

A mixture of **8** in methanol containing 1 *N* HCl was stirred at room temperature for 1 hr. The white precipitate formed was identified as **methyl(3,5-di-*tert*-butyl-4-hydroxy)benzoate (10)**, mp 156–158° (lit.[16] mp 159°).

2,4,6-Tri-*tert*-butyl-4-(trichloromethyl)-2,5-cyclohexadien-1-one (9b).—After the irradiation of **1b** in carbon tetrachloride with 300-nm light, the solvent was removed from the reaction mixture, and the residue was recrystallized three times from absolute ethanol to give **9b** as white needles (0.32 g, 56%): mp 69–71; ir (KBr) 1660 and 1640 cm^{-1} (double strong bands, carbonyl group of cyclohexadienone[13]); uv max (CH_2Cl_2) 248 nm (log ϵ 3.95) and 322 (3.87); nmr ($CDCl_3$) δ 1.24 (9 H, s, *t*-Bu), 1.26 (18 H, s, 2 *t*-Bu), and 6.95 (2 H, s, two vinyl protons).

Anal. Calcd for $C_{19}H_{29}Cl_3O$ (379.38): C, 60.10; H, 7.64; Cl, 28.04. Found: C, 59.95; H, 7.65; Cl, 27.97.

Attempted Thermal Reaction of 2,6-Di-*tert*-butyl-4-alkylphenol with Bromotrichloromethane.—A mixture of 5 mmol of **1a** or **1b** and 15 ml of bromotrichloromethane was sealed in a Pyrex tube and heated at 160°. After 10 hr, the solution was dark brown, but no product, other than some chloroform which was identified by glpc, could be isolated. When a similar mixture was heated at 80° in the presence of either AIBN or benzoyl peroxide, no reaction occurred, even after 2 days.

Registry No.—**1a**, 128-37-0; **1b**, 732-26-3; **3**, 34982-09-7; **4**, 34957-03-4; **5**, 34959-60-9; **8**, 34959-61-0; **9a**, 34959-62-1; **9b**, 34959-63-2.

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The Chemistry of Flavandiones. Reaction with Diazomethane[1a]

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Flavonols **1** are oxidized by periodic acid, 1 mol of oxidant being consumed.[2,3] When methanol is the solvent, the products are the methyl 3-hemiketals of 2-methoxy-3,4-flavandiones **2**.[4] Solutions of these hemiketals are an equilibrium mixture of **2** and the free dione, this being responsible for the solutions' yellow color.

When the hemiketals **2a–d** are mixed with an ethereal solution of diazomethane, they are converted to the epoxides **3**. This formulation is supported by elemental analysis, spectra, and chemical reactivity.

Before the advent of routine ir and nmr spectra, α-diketones were generally believed to form 1,3-dioxoles with diazomethane.[5] Later work by Eistert[6] established that these products were generally epoxides, although exceptions are known.[7] However, the products from diazomethane and **2a–d** all have strong bands in the carbonyl region and this renders a dioxole structure most unlikely.

With monoketones and diazomethane, epoxide formation competes with methylene insertion. This has been observed with α-diketones also. Diazomethane in ether converts phenanthraquinone into an epoxide, but, in the presence of much methanol, a ring-expanded product is found.[8] However, the spectral properties of the diazomethane products from **2a–d** are hardly consistent with those expected for any ring-expanded product. In our case, such a product could be either of a pair of α-diketones or a β-diketone. In the ketone form, any of these diketones would have two bands in

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[1] (a) Supported in part by the National Institute of General Medical Sciences, National Institutes of Health, U. S. Public Service (Grant No. 11830). (b) National Science Foundation Undergraduate Research Participant, summer, 1966.

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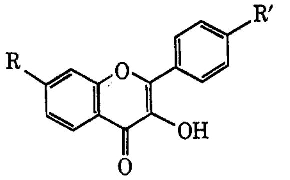
the carbonyl region of the ir spectrum. This is not the case; only a single band is found. Were these α-diketones in an enolic form, a band should be detected in the hydroxyl region of the ir spectra, There are no bands above 3070 cm^{-1} in any of the spectra. Had these enols undergone methylation, this would have doubled the methoxyl analysis.

Therefore, it is clear that the ir spectra of these products are incompatible with both the dioxole and the ring-expanded structures. The ir spectra and the nmr spectra do fit the epoxy structures **3a–d**.



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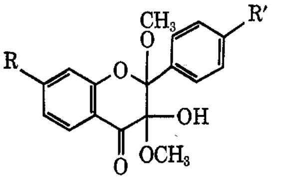

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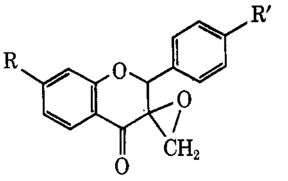

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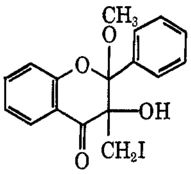

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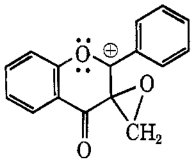

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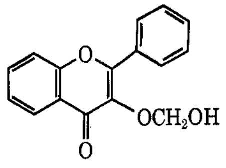

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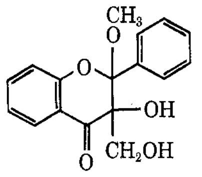

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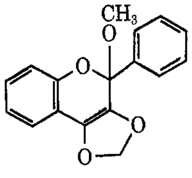

8

a, R = R′ = H c, R = OCH$_3$; R′ = H
b, R = H; R′ = OCH$_3$ d, R = R′ = OCH$_3$

In the earlier work[4] on the flavandione 3-hemiketals **2**, the position of the hemiketal methoxyl was expected to be at C-3, the carbonyl band in the ir spectrum being assigned to a carbonyl at C-4. This was confirmed by measuring the position of the ν_{CO} band with and without a methoxyl at C-7, *i.e*, para to the C-4 carbonyl. A similar study on **3a–d** has established that the oxymethylene group is also at C-3. The relevant data are recorded in Table I. The ν_{CO} for **3c** and **3d**, the pair with methoxyls at C-7, is significantly lower than the ν_{CO} for **3a** and **3b**. A methoxyl group at C-7 would be expected to have a bathochromic effect on the band for a carbonyl at C-4.

TABLE I

CARBONYL STRETCHING FREQUENCIES OF THE EPOXIDES 3a–d

Compd	ν_{CO}, cm^{-1} [a]
3a, R = R′ = H	1705
3b, R = H; R′ = OCH$_3$	1703
3c, R = OCH$_3$; R′ = H	1693
3d, R = R′ = OCH$_3$	1692

[a] Spectra recorded on a Perkin-Elmer 337 grating spectrophotometer, CCl$_4$ solution. Calibration was against the 1601-cm^{-1} line of polystyrene.

The epoxy structures **3a–d** receive additional support from the nmr spectra. A three-proton singlet near 3.2 ppm is common to all the spectra of **3a–d**. This is attributed to the 2-methoxyl group. This chemical shift is somewhat upfield from most methoxyl signals but it seems to be characteristic for 2-methoxyl groups in the flavandione compounds (see Table II).

TABLE II

NMR DATA (δ)[a]

	Epoxides			
	3a	**3b**	**3c**	**3d**
Aryl[b]	7–8	6.8–8.1	6.5–8.0	6.6–8.0
Aryl OCH$_3$[d]		4.01	3.88	3.81, 3.88
2-OCH$_3$[d]	3.19	3.21	3.23	3.21
Oxymethylene[c]	2.62, 3.49	2.65, 3.48	2.61, 3.45	2.62, 3.44
	Flavandione Hemiketals			
	2a	**2b**	**2c**	**2d**
Aryl[b]	7–8	7–8	6.6–8	6.6–8
COH[d]	4.73	4.74	4.87	4.78
Aryl OCH$_3$[d]		3.84	3.87	3.82, 3.85
2-OCH$_3$ / Hemiketal OCH$_3$[d]	2.94, 3.03	3.00, 3.07	2.97, 3.10	2.98, 3.07

[a] Varian A-60A, CDCl$_3$, in parts per million from TMS. [b] Complex multiplet. [c] Doublets (J = 6 Hz). [d] Singlets.

The aryl methoxyls of **3b–d** are unexceptional, giving rise to singlets between 3.8 and 3.9 ppm. The methylene protons of the epoxide ring are diastereiomeric. In all cases, these protons appear as a pair of doublets (J = 6 cps), one centered near 3.5 ppm, the other near 2.6.

Chemical evidence for the epoxide formula for **3a** is found in its facile conversion to an iodohydrin **4** by an acetic acid–potassium iodide mixture. The structure of **4** is amply supported by elemental analysis and spectra. Sodium methoxide reacts with **4** to regenerate the epoxide **3a**. The nmr spectrum of the iodohydrin **4** contained a nine-proton aryl multiplet between 6.9 and 7.9 ppm. The 2-methoxyl manifested itself as a singlet at 3.24 ppm, very near an OH singlet at 3.42 ppm. The diasteriomeric methylene protons appeared as a pair of AB doublets at 3.65 and 3.75 ppm (J = 22 cps). The direction of ring opening was as expected. The tertiary nature of the alcohol group in **4** was demonstrated when **4** gave a negative test with Bordwell's chromic acid reagent.[9]

We attempted to isomerize **3a** to an aldehyde with boron trifluoride. This well-known rearrangement[5] had been carried out by Eistert[6] on the epoxides of phenanthraquinone and benzil. In both cases the expected aldehyde was obtained. However, this reagent converts the epoxide **3a** into the corresponding flavonol. The same conversion is effected by aqueous acids. This transformation involves cleavage of the carbon–carbon bond of the epoxide.

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Several mechanisms can be envisaged to account for this transformation. Protonation of **3** followed by loss of methanol could lead to the carbonium ion **5**. Such a cation should be stabilized by the heterocyclic oxygen as well as the aromatic ring. An attack on the methylene group by water could cleave the carbon–carbon bond and lead to **6**, a hemiacetal of formaldehyde, which would then hydrolyze to flavonol **1**. Alternately, water could open the oxirane ring to the diol **7** which might then undergo fragmentation to flavonol **1**. A third possibility would be a rearrangement of **3** to a dioxole **8** followed by hydrolysis.

Experimental Section

Spectra.—Except for the data reported in Table I, all ir spectra were taken as Nujol mulls on a Perkin-Elmer Infracord, Model 137 (NaCl prism).[10] All nmr spectra were obtained in $CDCl_3$ using a Varian A-60A spectrometer.[10]

All melting points are uncorrected. Analyses were carried out by Schwarzkopf Microanalytical Laboratory.

Diazomethane.—This was prepared from *N*,*N*′-dimethyl-*N*,*N*′-dinitrosoterephthalamide (**8**) according to the procedure of Moore and Reed.[11] When running 1-g batches of the flavandione hemiketals **2a–d**, we used 7.2 g of the 70% suspension of **8** in mineral oil, adding this to 120 ml of ether, 18 ml of 2-(2′-ethoxyethoxy)ethanol, and 24 ml of 30% aqueous NaOH. This should produce about a tenfold excess of CH_2N_2. In practice the CH_2N_2–ether was distilled directly into a flask containing **2a–d** suspended in a little ether.

Flavonols (1a–d).—The flavonols **1a** and **1b** were prepared directly from *o*-hydroxyacetophenone and the corresponding benzaldehydes according to the procedure of Smith, Neuman and Webb.[12] This procedure is erratic for flavonols with methoxyls in the *o*-hydroxyacetophenone. However, alkaline hydrogen peroxide converts the corresponding 2′-hydroxychalcones into flavonols in yields of 40–50% using essentially the procedure of Algar and Flynn.[13] **1c** and **1d** were made this way.

2-Methoxy-3,4-flavandione Methyl 3-Hemiketals (2a–d).[10]—These were prepared as reported previously.[4] For nmr data, see Table II.

2-Methoxy-3,3-oxymethyleneflavanone (3a).—A 1.0-g sample of **2a** was treated with diazomethane at room temperature over night. The reaction was followed qualitatively by tlc on SiO_2 ($CHCl_3$), **2a** being much less mobile than the epoxide **3a**. Upon standing overnight **2a** had substantially disappeaerd. A trace of a second product was detected but not isolated. Evaporation of the filtered ether solution yielded a mixture of oil and solid. Crystallization from 15 ml of methanol afforded 0.58 g (62%) of **3a**, mp 133–134°.

Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00; OCH_3, 10.99. Found: C, 72.62; H, 5.19; OCH_3, 10.71.

2,4′-Dimethoxy-3,3-oxymethyleneflavanone (3b).—A 1-g sample, treated twice with diazomethane, yielded a tough residue upon evaporation of the solvent. This was crystallized from 20 ml of methanol to give 0.61 g (64%) of rodlike crystals, mp 138–139°.

Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16; OCH_3, 19.88. Found: C, 69.00; H, 5.16; OCH_3, 20.90.

2,7-Dimethoxy-3,3-oxymethyleneflavanone (3c).—A 1-g sample, treated twice with diazomethane, yielded a solid upon evaporation of the solvent. When recrystallized from 15 ml of MeOH, it afforded a 47% yield of white crystals melting at 135–137°. The analytical sample melted at 139–140° (MeOH).

Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16; OCH_3, 19.87. Found: C, 69.13; H, 5.26; OCH_3, 19.34.

2,4′,7-Trimethoxy-3,3-oxymethyleneflavanone (3d).—A 1-g sample of **2d** was treated with two portions of diazomethane, tlc indicating incomplete reaction after the first one. Both the starting hemiketal **2d** and the product **3d** have limited solubility in ether. At the end of the second treatment, there was 400 mg of a solid which was **3d** mixed with some polymer. Evaporation of the filtrate from this yielded an oil–solid mixture. This mixture yielded 180 mg (21%) of crystalline **3d**, mp 185–187° from 40 ml of MeOH. The analytical sample melted at 187.5–189°.

Anal. Calcd for $C_{19}H_{18}O_6$: C, 66.69; H, 5.30; OCH_3, 27.20. Found: C, 66.67; H, 5.38; OCH_3, 27.45.

3-Hydroxy-3-iodomethyl-2-methoxyflavanone (4).—A 500-mg sample of **3a** was rapidly converted to **4** in a hot mixture of 15 ml of acetic acid and 750 mg of KI. Tlc (SiO_2, $CHCl_3$) showed that reaction was complete in 10 min. The hot, brown solution was poured into 200 ml of water containing 1 g of sodium bisulfite. A formless solid separated. After drying, it was crystallized from 15 ml of petroleum ether (bp 60–110°), fine crystals separating. The yield of **4** was 450 mg (63%), mp 124–125°, nmr, see discussion. When treated with sodium methoxide in methanol, **4** was converted to the epoxide **3** in high yield.

Anal. Calcd for $C_{17}H_{15}O_4I$: C, 49.80; H, 3.79; I, 30.94. Found: C, 50.00, 50.87; H, 3.28, 3.67; I, 29.39, 30.3.

Conversion of Epoxide to Flavonol. With Boron Trifluoride Etherate.—**2a** (150 mg) was heated at 65° for 1 hr with a mixture of 20 ml of benzene and 2 ml of $BF_3 \cdot Et_2O$. The addition of 60 ml of ether afforded a copious precipitate of flavonol, 70 mg (47%), mp 168–170° (from MeOH).

With Sulfuric Acid.—**2a** (200 mg) was stirred with 40 ml of 50% H_2SO_4 for 1 hr at 100–120°. The resulting yellow solution was filtered through charcoal and diluted with 20 ml of water. After standing, the flavonol (**1a**) was collected by filtration, 120 mg (71%), mp 169°, ir identical with that of an authentic sample.

Registry No.—**1a**, 577-85-5; **2a**, 1603-46-9; **2b**, 1808-05-5; **2c**, 2047-54-3; **2d**, 1808-02-2; **3a**, 34917-93-6; **3b**, 34887-89-3; **3c**, 34887-90-6; **3d**, 34887-91-7; **4**, 34887-92-8; diazomethane, 334-88-3.

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[10] The ir and nmr spectra of hemiketal **2a**, epoxide **3a**, and iodohydrin **4** will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-2774. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

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2-Thiocyanobenzimidazoles. The Synthesis of 13*H*-[1,3,5]Thiadiazino[3,2-*a*:5,6-*a*′]-bisbenzimidazole-13-thiones

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We recently reported[1] that 2-thiocyanomethylbenzimidazoles (**1**) cyclized readily to yield 1-imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazoles (**2**). These results encouraged us to investigate the utility of 2-thiocyanobenzimidazole (**3**) for the synthesis of novel fused benzimidazole ring systems. Thus, it was hoped that the reaction of **3** with carbon disulfide in basic medium would furnish[2] A. However, the yellow crystalline product isolated in 86% yield from the reaction mixture (reaction time 5 min) showed no exchangeable proton (D_2O) in the nmr but exhibited only aromatic protons, with a one-proton multiplet significantly downfield from the remaining three protons. We have observed similar chemical shifts for 3,4-dihydropyrimido-

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