Procedure.—The procedure described here for the preparation of 2-butylheptanoic acid is typical of the method used for all the acids mentioned in Table I.

2-Butylheptanoic Acid.—Anhydrous THF (35 ml) and diisopropylamine (4.9 g, 0.049 mol) was added to a dry, nitrogen-flushed flask under an atmosphere of nitrogen. *n*-Butyllithium in hexane (30 ml of 1.6 M, 0.048 mol) was added to the magnetically stirred solution at such a rate as to maintain the temperature below 0°. *n*-Heptanoic acid (2.95 g, 0.0227 mol) was then added to the cold basic solution and again the temperature was kept below 0°. After 15 min, HMPA (9 ml, 0.050 mol) was added to the milky white solution, which became transparent and light yellow after 5 min of stirring at 5°. The solution was stirred for an additional 15 min at 5°, and *n*-butyl bromide (3.3 g, 0.024 mol) was added at once at 0°. The reaction temperature immediately rose to 18°. After 2 hr of additional stirring at room temperature, the reaction was worked up in the following manner. Dilute hydrochloric acid (10%) was added at 0° until the mixture became acidic. The aqueous layer was separated and extracted with petroleum ether (bp 30–60°). The combined organic layers were washed five times with 100-ml portions of dilute hydrochloric acid, H_2O, and saturated sodium chloride solutions. The organic layer was then dried and the solvent was stripped off. The residue was distilled through a 5-in. Vigreux column to give 4.06 g (96%) of a colorless oil, bp 175–177° (30 mm). Examination of this oil on a gas chromatographic column (0.25 in. × 6 ft, 25% DEGA, phosphoric acid treated 60–80 Chromosorb A) at 180° showed this product to be 96.5% 2-butylheptanoic acid and 3.5% *n*-heptanoic acid.

An Improved Synthesis of 2,4,6-Octatriene

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The title compound has been prepared previously *via* a coupling reaction followed by a dehydration.[1] The yields are low (20–40%) and the product is often contaminated with its isomers.[1c,d,h] Recently, 1,3,6- and 1,3,7-octatriene (I and II, respectively) have become available in high yield by the metal-catalyzed dimerization of the butadiene.[2] Attempts at converting I and II to 2,4,6-octatriene (III) have shown that the bases studied which are strong enough to isomerize II will catalyze a cyclization of the octatrienyl anion, forming a mixture of methylcycloheptadienes.[3,4]

We wish now to report that some hydroxide bases in dimethyl sulfoxide (DMSO) are specific for the isomerization of I and II, giving 70–85% yields of III with little or no accompanying cyclization. Triton B and

tetramethylammonium hydroxide catalyze the reaction smoothly, and <5% cyclic products are obtained even with prolonged reaction times. Cyclization is obtained with KOH; however, the reaction time may be controlled to give an 84% yield of 95% pure 2,4,6-octatriene. Other alkali metal hydroxides give a less clear-cut reaction.

Thus, 2,4,6-octatriene may be obtained as a mixture of stereoisomers[3] in 70% overall yield from butadiene.

Experimental Section

All boiling points are uncorrected. Analyses by gas–liquid partition chromatography (glpc) were performed on an F & M Model 720 chromatograph using a 20-ft column packed with 20% tris(cyanoethoxy)propane on 35/80 mesh Chromosorb P. The octatrienes were prepared by the dimerization of butadiene in the presence of a zero-valent nickel complex and a hydroxylic solvent,[2c] and consisted of a 1:3 mixture of 1,3,6-octatriene and 1,3,7-octatriene contaminated with *ca*. 6% of 4-vinylcyclohexene and 1–2% of other unidentified materials.

Preparative Isomerization of the Octatriene Mixture. A. With Triton B in DMSO at 90°.—The octatriene mixture (0.82 g) and DMSO (10.0 ml) were sealed under N_2 in a glass-walled pressure vessel equipped with a septum through which liquids could be injected. After the mixture had equilibrated at 90°, 0.25 ml of Triton B (40% benzyltrimethylammonium hydroxide in methanol, K & K Laboratories) was added. The reaction mixture was stirred for 10 min, cooled briefly, and quenched in 20 ml of ice-water. Following work-up, 0.67 g (81.8%) of material was distilled at 58° (30 mm). Glpc analysis showed the presence of 2,4,6-octatriene (85.3%), methylcycloheptadienes (3.6%), 4-vinylcyclohexene (5.8%), 1,3,7-octatriene (1.3%), and unidentified materials (4.0%). Fractional distillation may be employed to give III in >95% purity

B. With KOH in DMSO at 80°.—Potassium hydroxide pellets (5.0 g) and DMSO (30 ml) were sealed in a pressure vessel. When equilibrium was established, 2.28 g of octatrienes was added *via* a syringe and stirring was continued for 2 hr at 80°. The reaction vessel was allowed to cool at room temperature for 30 min, at which time the contents were quenched in 150 ml of ice-water. After work-up, 1.91 g (84%) of 95% pure 2,4,6-octatriene was distilled at 66° (44 mm). In a separate experiment the reaction temperature and time were extended to 105° and 4 days, respectively, and a 53% yield of methylcycloheptadienes[3] (96% pure) was obtained.

(1) (a) R. Kuhn and C. Grundmann, *Chem. Ber.*, **71**, 442 (1938); (b) P. Nayler and M. C. Whiting, *J. Chem. Soc.*, 3037 (1955); (c) G. F. Woods and A. Viola, *J. Amer. Chem. Soc.*, **78**, 4380 (1956); (d) K. Alder and H. von Brachel, *Ann.*, **608**, 195 (1957); (e) J. Normant, *Bull. Soc. Chim. Fr.*, 1868 (1963); (f) V. L. Bell, *J. Polym. Sci.*, *Part A*, **2**, 5291 (1964); (g) E. N. Marvell, G. Caple, and B. Schatz, *Tetrahedron Lett.*, 385 (1965); (h) C. W. Spangler and R. D. Feldt, *Chem. Commun.*, 709 (1968).

(2) (a) S. Takahashi, T. Shibano, and N. Hagihara, *Tetrahedron Lett.* 2451 (1967); *Bull. Chem. Soc. Jap.*, **41**, 454 (1968); (b) E. J. Smutney, *J. Amer. Chem. Soc.*, **89**, 6793 (1967); E. J. Smutney and H. Chung, *Preprints*, *Div. Petrol. Chem.*, *Amer. Chem. Soc.*, **14**, No. 2, B112 (1969); (c) see, for example, J. Feldman, O. Frampton, B. Saffer, and M. Thomas, *ibid.*, **9**, No. 4, A55 (1964).

(3) E. A. Zuech, D. L. Crain, and R. F. Kleinschmidt, *J. Org. Chem.*, **33**, 771 (1968).

(4) H. Takahasi, T. Kimata, and M. Yamaguchi, *Tetrahedron Lett.*, 3173 (1964).

The Meerwein–Ponndorf–Verley Reduction of 1,2-Cyclopentanedione. Stereochemical Evidence for Dual Reductive Paths

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Reduction of 1,2-cyclohexanedione[1] with aluminum isopropoxide in toluene has been shown to produce *cis*- and *trans*-1,2-cyclohexanediols in a stoichiometrically

(1) Although both 1,2-cyclohexanedione and 1,2-cyclopentanedione have been shown to exist largely as the tautomeric enolones (footnote 14, ref 2), the dione nomenclature will be used here because both compounds behave as diones in this study.

dependent ratio.[2] Although an excess of the *cis* isomer is invariably obtained, this excess decreases to a limiting minimum of 54% *cis* as the dione alkoxide ratio approaches zero. To differentiate among a number of proposed mechanisms for the dione reduction,[2] the study has been extended to 1,2-cyclopentanedione, a system containing more severe conformational requirements than 1,2-cyclohexanedione.

Results of 15 reductions, carried out as described earlier,[2] are presented in Table I. Figure 1 shows the

TABLE I

YIELDS AND STEREOCHEMICAL COMPOSITIONS
OF 1,2-CYCLOPENTANEDIOLS AS A FUNCTION OF
$Al(O-i-Pr)_3$ STOICHIOMETRY

Run[a]	$Al(O-i-Pr)_3$,[b] mmol	1,2-Cyclo-pentane-diols, %	cis^c-Glycol, %	Solids, g
1[d]	40	59	91.6	None
2	40	80	91.4	Trace
3	40	71	90.4	Trace
4	20	33	90.6	2.30
5[d]	20	32	90.4	2.25
6	20	28	87.8	3.19
7	10	9	80.0	2.87
8[d]	10	12	79.8	2.24
9[d]	10	8	79.0	2.42
10[d]	6.7	2	70.0	2.15
11	5	2	70.4	2.20
12[d]	5	1	70.0	1.88
13	5	1	67.2	1.55
14[e]	40	7	88.3	1.95
15[f]	40	62	93.8	None

[a] Acetone distilled unless otherwise indicated. [b] Ten millimoles of dione were used in all reductions. [c] As per cent total glycol. [d] Total reflux. [e] Thirty-minute reaction time. [f] Ten-hour reaction time.

relation between the molar dione/aluminum alkoxide ratio and the stereochemical compositions of recovered glycols in this and the earlier study. Ranges of glycol compositions appear as vertical bars. Results of runs 14 and 15 of the present study are so labeled in Figure 1. As reported earlier, reductions involving dione/alkoxide ratios of 0.5 or larger produce significant amounts of amorphous solids when the reaction mixtures are shaken with aqueous tartrate. The solids appear to be derived directly from unreduced dione (*vide infra*).

Because particularly low yields were obtained in runs 7–13 (runs 14 and 15 were carried out under non-standard conditions), greater confidence was placed in the stereochemical results of the first six runs. To test the reliability of entries 7–13, least-squares analyses of runs 1–9, 1–10, and 1–13 were carried out. These results, together with a similar analysis of the combined data of ref 2, are presented in Table II. Good values for the correlation coefficient, r, support both

TABLE II

LEAST-SQUARES FIT OF DATA OF TABLE I AND REF 2 TO % *cis*
= % cis_0 + m(DIONE/ALKOXIDE)

Data	% cis_0	m	r
Runs 1–9	96.1	−16.0	0.965
Runs 1–10	96.6	−17.1	0.981
Runs 1–13	94.6	−13.5	0.974
Ref 2	54.4	10.4	0.983

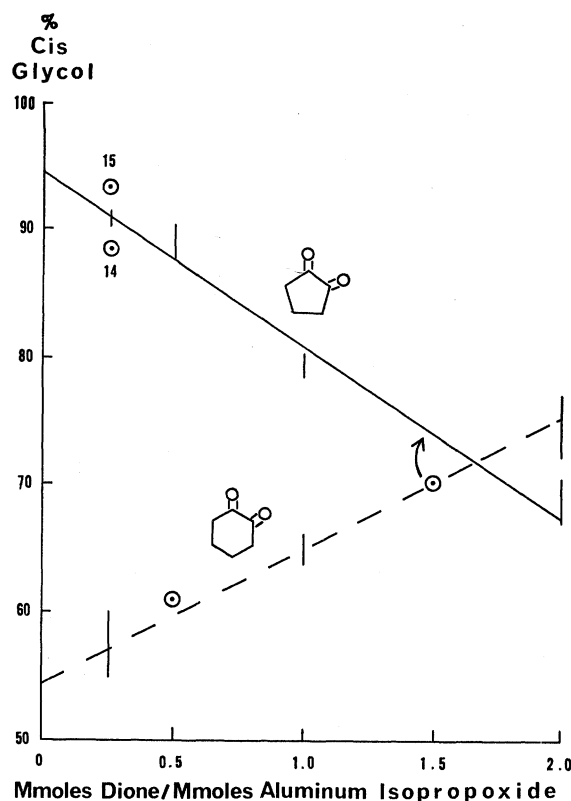(2) C. H. Snyder, *J. Org. Chem.*, **31**, 4220 (1966).

Figure 1.—Isomeric glycol composition as a function of $Al(O-i-Pr)_3$ stoichiometry for 1,2-cyclopentanedione (solid line) and 1,2-cyclohexanedione (broken line, ref 2). Circles represent individual reductions.

inclusion of all data of Table I and the graphical linearity shown in Figure 1.

As in the previous study, mechanistic significance of the results depends on demonstrations not only of the correlation just indicated, but also of kinetic product control and of absence of isomeric fractionation in solids formation, e.g., by selective inclusion of one stereoisomer or its immediate precursor.

Reflux of individual 1,2-cyclopentanediols with aluminum isopropoxide in toluene under reduction conditions revealed that the *cis*-glycol is stable under these conditions but the *trans*-glycol slowly isomerizes to the *cis* form. Since this isomerization appears to be significant only in the presence of acetone, reductions themselves were carried out with two different modes of reflux: total reflux and reflux with a condenser "coolant" consisting of water at 75–80°. This second mode insured that while toluene would be returned to the reaction mixture, acetone necessary for the equilibration would be removed as it formed. The data of Table I show clearly that the two modes give identical stereochemical results within experimental error and thus support kinetic control. Additional evidence for substantial kinetic control is provided by results of runs 14 and 15 which, although suggesting a slight enrichment in *cis* isomer as reflux time is increased, appear commensurate with experimental error, as indicated by the graphical scatter of Figure 1.

Selective fractionation in solids formation can also be ruled out as a contributing factor. As reported earlier,[2] dissolving the solids in aqueous alkali and extracting with chloroform gives only traces of glycols. Addition of these glycols to the yields reported in Table I pro-

duces no significant changes in the data. Since the solids are obtained on replacing aluminum isopropoxide by the nonreducing aluminum *t*-butoxide, they are not derived from the glycols or their immediate precursors. Appearance of a large quantity of solids in run 14 represents the only occasion in which significant solids formation was observed with a dione/alkoxide ratio of 0.25. The accompanying yield of 7% glycols suggests that the solids result from interaction of unreduced dione, aluminum isopropoxide, and aqueous tartrate. To test this, a solution of 1,2-cyclopentanedione and aluminum isopropoxide in toluene was kept at room temperature for 1 minute. Formation of copious solids on shaking the solution with aqueous sodium potassium tartrate confirms the conclusion. Investigation of the solids is continuing.

Discussion

Two remarkable differences between reductions of the two diones appear in Figure 1. First, at the limit dione/alkoxide = 0, reduction of 1,2-cyclopentanedione takes place with high stereoselectivity, while reduction of 1,2-cyclohexanedione shows very little selectivity. Second, an increase in the dione/alkoxide ratio produces a decrease in stereoselectivity in the cyclopentanedione reduction, but an increase with cyclohexanedione. Neither isomerization nor formation of solids can be used to explain stereochemical results in either system or, more importantly, the *differences* in two systems. These differences are readily explained by modification of mechanistic routes discussed in ref 2.

Since ring size constitutes the only significant difference between the two diones, it presumably accounts for the observed stereochemical differences. In the cyclohexyl system the aluminum of the intermediate obtained after reduction of one carbonyl of the dione (or reduction of the carbonyl of the enone, then tautomerism) can easily eclipse the carbonyl oxygen (1). However, torsional requirements prohibit similar eclipsing in the cyclopentyl system[3] (2). This difference between the two systems can be used to explain the observed results if, as Moulton, Van Atta, and Ruch[4] have suggested, the reduction can proceed by either the commonly accepted path or one which involves coordination of the carbonyl oxygen by one aluminum isopropoxide molecule but hydride transfer by another.


1   2
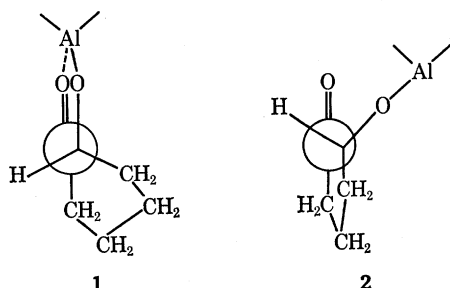
At very low ratios, with a large amount of aluminum isopropoxide available for reduction of both carbonyls, a "two-aluminum" path may be followed. Steric

requirements of the isopropoxyaluminate substituent of 2 would force the second aluminum alkoxide to approach from the opposite side, as in 3, to produce almost exclusively the *cis*-glycol.[5] The more symmetrically oriented aluminate substituent in 1 should permit equal approach from either side. The small excess of cis-1,2-cyclohexanediol observed at dione/alkoxide = 0 may result from the difference in steric requirements of the hydrogen and the ring methylene in the intermediate, favoring slightly the approach shown in 4 to give the *cis*-1,2-cyclohexanediol.

3   4
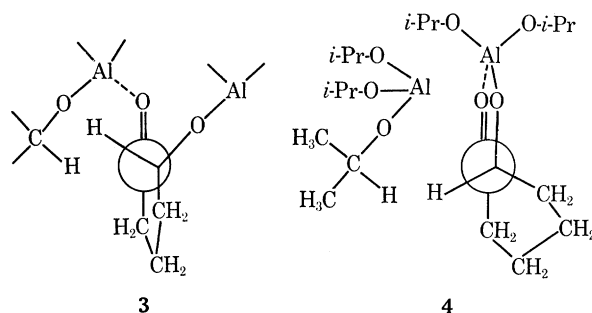
As the amount of aluminum isopropoxide available for the second reduction is decreased (*i.e.*, dione/alkoxide is increased), the second carbonyl may be increasingly reduced by the same aluminum which effected the first reduction. The geometry of the cyclopentyl system would force a reduction which must result in a *trans* product, 5, lowering the per cent of *cis* product. Although *trans* fusion of two five-membered carbocyclic rings involves introduction of a considerable amount of strain, the equivalent process in a heterocyclic analog is surprisingly facile.[6]

The increase in stereoselectivity in the cyclohexyl system may be explained if the difference in steric requirements of the carbinol hydrogen and the geminal

5

ring methylene is of minimal significance in the intermediate of a "two-aluminum" reduction, 4, which includes five rather crowded isopropoxy groups. With incursion of a "one-aluminum" mechanism as the dione/alkoxide ratio increases, 6, the methylene–hydrogen difference may grow in stereochemical significance, since it increasingly represents the only significant steric demand in the transition state. In other words, with incursion of the "one-aluminum" mechanism, steric requirements in transition states leading to both *cis*- and *trans*-glycols decrease, but

(3) L. Joris and P. von R. Schleyer, *J. Amer. Chem. Soc.*, **90**, 4599 (1968), have noted the significance of eclipsing in intramolecular hydrogen bonding in α-hydroxy ketones.

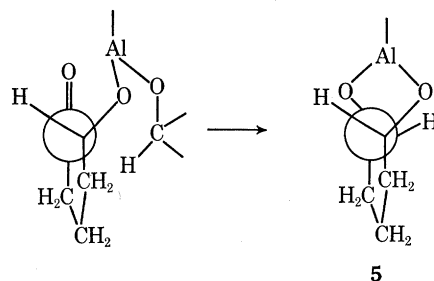(4) W. N. Moulton, R. E. Van Atta, and R. R. Ruch, *J. Org. Chem.*, **26**, 290 (1961).

(5) Operation of Cram's rules and subsequent modifications [G. J. Karabastos, *J. Amer. Chem. Soc.*, **89**, 1367 (1967), and references cited therein] is implicit in this discussion. Karabastos' modification does not seem applicable to this study because of the absence of free rotation about the carbinol–carbonyl bond in these cyclic systems.

(6) E. L. Eliel, "Stereochemistry of Organic Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 10, pp 273–274.

those in the transition state leading to the *cis*-glycol, 6 (*cf.* 4), decrease more rapidly.

6
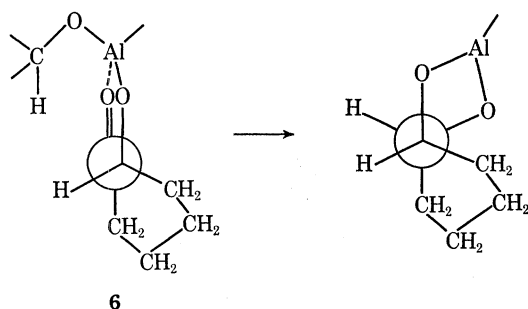
Experimental Section

Materials.—Commercial toluene was distilled before use. Commercial aluminum isopropoxide was distilled and the solidified distillate was fused before each use. Weighing and transfer of aluminum isopropoxide were accomplished in a dry nitrogen atmosphere. 1,2-Cyclopentanedione was prepared by the method of Acheson,[7] except that the dione was extracted with chloroform rather than ether. 1,2-Cyclopentanedione was recrystallized from low-boiling petroleum ether before each use: mp 55–56° (lit.[7] mp 55–56°). Authentic *cis*- and *trans*-1,2-cyclopentanediols, used for identification of glycolic products, were prepared by the methods of Owen and Smith.[8]

Representative Reduction.—A solution of 4.1 g (20 mmol) of fused aluminum isopropoxide and 0.98 g (10 mmol) of 1,2-cyclopentanedione in 25 ml of toluene was heated in a 50-ml one-neck round-bottomed flask attached to a condenser capped by a drying tube. After 5 hr at 105°, the dark, red-brown reaction mixture was shaken with an equal volume of saturated, aqueous potassium sodium tartrate. Filtration removed 2.30 g of dark brown solids, which separated when the reaction mixture was shaken with the tartrate solution. The liquid phases of the filtrate were separated and the aqueous phase was extracted continuously with chloroform for 48 hr. Organic phases were combined and their volume was adjusted for glpc analysis. Analysis was accomplished with external standards of the authentic glycols and a 3-m column of 5% Carbowax 20M on 60/80 mesh, HMDS-treated Chromosorb W. A column temperature of 120° and a helium inlet pressure of 20 psi gave a satisfactory resolution of the isomeric glycols. Results are reported in Table I.

(7) R. M. Acheson, *J. Chem. Soc.*, 4232 (1956).
(8) L. N. Owen and P. N. Smith, *ibid.*, 4026 (1952).

3-(5-Methylfuryl-2)cycloalkanones. A Synthesis of Bicyclic Dionenes

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Although the reaction involving the condensation of α,β-unsaturated ketones with furan and its homologs is a well documented one,[1-4] there are no reports con-

(1) S. M. Sherlin, A. Y. Berlin, T. A. Serebrennikova, and F. E. Rabinovich, *Zh. Obshch. Khim.*, **8**, 7 (1938); *Chem. Abstr.*, **32**, 5397 (1938).
(2) K. Alder and S. Schmidt, *Chem. Ber.*, **76**, 183 (1943).
(3) Lambiotte and Co., French Patent 972,652 (1951); *Chem. Abstr.*, **47**, 1744 (1953).

cerned with its use as a starting point in the synthesis of molecules containing condensed ring systems. Therefore, we wish to report a two-step synthesis of 5,6-dihydro-7-methyl-1,4-indandione (**10**) and 2,3,4,6,7,8-hexahydro-8-methyl-1,5-naphthalenedione (**11**), in which the first step of each involves the condensation of 2-cyclopenten-1-one (**1**) or 2-cyclohexen-1-one (**2**) with 2-methylfuran.
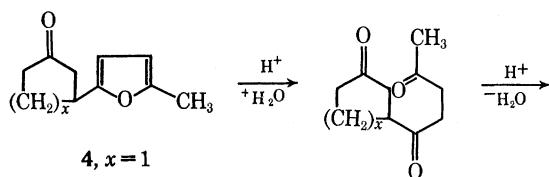

$$ \text{(1)} $$
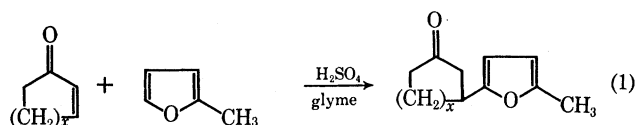
1, x = 1   4, x = 1
2, x = 2   5, x = 2
3, x = 3   6, x = 3

4, x = 1
5, x = 2
6, x = 3

7, x = 1
8, x = 2
9, x = 3

$$ \text{(2)} $$
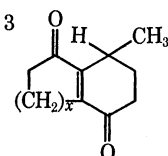
10, x = 1
11, x = 2
12, x = 3

When the alicyclic α,β-unsaturated ketones **1**, **2**, and **3** were allowed to react with 2-methylfuran in refluxing glyme containing a catalytic amount of sulfuric acid (eq 1), the 3-(5-methylfuryl-2)cycloalkanones **4**, **5**, and **6** were produced in yields of 36, 40, and 32%, respectively. Preparation of the dionenes **10** (47%) and **11** (35%) (eq 2) was best accomplished by refluxing **4** or **5** for 48 hr in aqueous acetic acid containing a trace of sulfuric acid. Although extended treatment (72 hr) of **6** under the same conditions yielded triketone **9**, no bicyclic dionene **12** could be isolated from this reaction.

When **5** was subjected to variations in the amount of time that it was heated under these acidic conditions, significant changes in the product composition from this reaction occurred. For example, while treatment for 24 hr yielded almost equal amounts of **8** and **11**, refluxing for 72 hr afforded both **11** and a single keto phenol **13**. Heating **5** for 96 hr produced a tarry reaction mixture from which only traces of **8** and **11** could be isolated, but from which a 20% yield of **13** was obtained.

The identification of **13** as 3,4-dihydro-5-hydroxy-8-methyl-1-(2H)-naphthalenone and not the alternative 3,4-dihydro-4-methyl-5-hydroxy-1-(2H)-naphthalenone (**16**) was based on the fact that the nmr spectrum of the isolated keto phenol displayed a methyl singlet at δ 2.45, and not the higher field methyl doublet anticipated for **16**. Additional proof for the structure of **13** was

(4) Y. K. Yur'ev, N. S. Zefirov, A. A. Shteinman, and V. I. Ruboedov *Zh. Obsch. Khim.*, **30**, 3755 (1960); *Chem. Abstr.*, **55**, 19890 (1961).