Cyclohexadienyl Cations. IV. Methoxy Substituent Effects in the Dienone–Phenol Rearrangement

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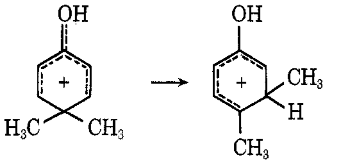
4-Methoxy-4-methylcyclohexadienone has been prepared and has been shown to undergo the dienone–phenol rearrangement in concentrated hydrochloric acid with >95% methyl migration. Rates of rearrangement of this dienone in concentrated perchloric acid from 37.9 to 71.1 wt % acid have been determined. These results, coupled with an estimate of the basicity of 4-methoxy-4-methylcyclohexadienone, are compared to similar data for 4,4-dimethylcyclohexadienone and are discussed in the context of the currently accepted mechanism of the dienone–phenol rearrangement.

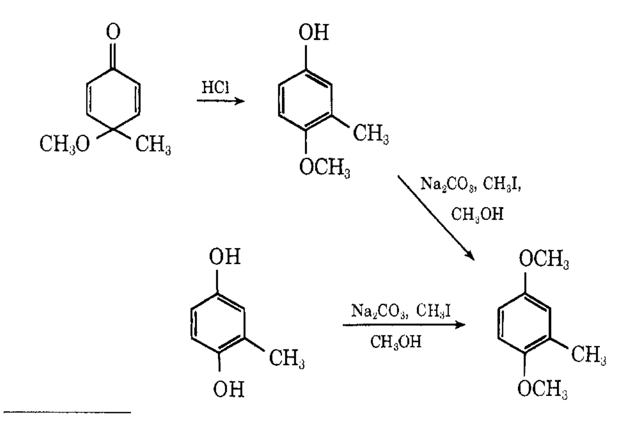
The dienone–phenol rearrangement provides an interesting and useful system for the study of the kinetic acidity dependence of a simple A1 reaction on the one hand while also functioning as a probe system which can be studied to increase our understanding of 1,2 migrations in carbonium ion reactions. For simple alkyl cyclohexadienones such as 4,4-dimethylcyclohexadienone previous work[1–6] has established the mechanism and acidity dependence for this reaction. For example, it has been shown[2] that the rate-determining step for this reaction is



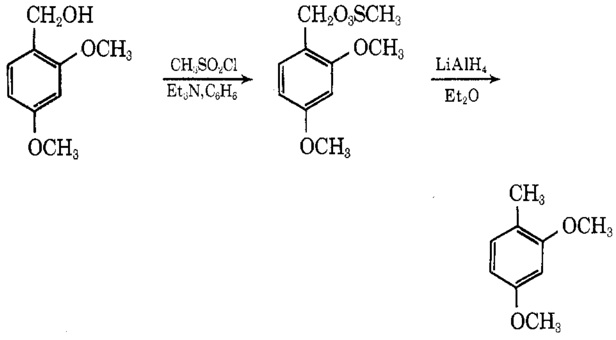
(1)

In this paper we address ourselves to another aspect of this transformation; the effect of a 4-methoxy substituent on the course of the reaction and its effect on individual steps of the reaction sequence.

Results. Product Identification.—4-Methoxy-4-methylcyclohexadienone (1) was prepared by the reaction of *p*-cresol with $Pb(OAc)_4$ in methanol as described by Hecker.[7] A sample was isolated by preparative glpc and rearranged in concentrated HCl. The rearrangement product was methylated with Na_2CO_3–CH_3I in methanol and the methylated product purified by glpc. The ir spectrum of this material was identical with that of authentic 2,5-dimethoxytoluene prepared from 2-methylhydroquinone.



A sample of 2,4-dimethoxytoluene was prepared as outlined below and a comparison of its ir spectrum with that of the methylated rearrangement product established that >95% methyl migration had occurred.



These results establish that the methyl group migrates in the acid-catalyzed rearrangement of **1**. Hecker[8] has reported similar results for the rearrangement of **1** in CF_3COOH.

Results. Kinetics.—Rates of rearrangement of **1** in solutions of perchloric acid of varying composition are presented in Table I and Figure 1. The rate is strongly dependent on the proton donating ability of the solvent as measured by the Hammett acidity function H_0. In fact, the first seven data points in Figure 1 provide a good linear relationship between log k_{obsd} and $-H_0$ with slope 0.92 ± 0.04. Historically, this kind of relationship (linear log k_{obsd} *vs.* $-H_0$ plot, slope ≈ 1) has been taken to be evidence for the operation of an A1 mechanism based on Hammett and Zucker's

Table I

Rates of Rearrangement of 4-Methoxy-4-methylcyclohexadienone in Aqueous Perchloric Acid at 25.2 ± 0.1°

$10^5 k_{obsd}$ (sec^{-1})	Wt % $HClO_4$	$-H_0$[a]
8510	71.06	8.06
3060	65.98	6.67
1420	63.17	5.97
330	59.72	5.20
87.0	55.00	4.28
28.9	52.83	3.92
5.90	48.13	3.24
2.54	44.70	2.83
1.58	41.53	2.50
0.601	37.93	2.18

[a] K. Yates and H. Wai, *Can. J. Chem.*, **43** 2131 (1965).

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(1) V. P. Vitullo, *J. Org. Chem.*, **34**, 224 (1969).

(2) V. P. Vitullo and N. Grossman, *Tetrahedron Lett.*, 1559 (1970).

(3) V. P. Vitullo, *Chem. Commun.*, 688 (1970).

(4) V. P. Vitullo, *J. Org. Chem.*, **35**, 3976 (1970).

(5) K. L. Cook and A. J. Waring, *Tetrahedron Lett.*, 1675 (1971).

(6) K. L. Cook and A. J. Waring, *ibid.*, 3359 (1971).

(7) E. Hecker and R. Lattrel, *Justus Liebigs Ann. Chem.*, **662**, 48 (1963).

(8) E. Hecker and E. Meyer, *Angew. Chem., Int. Ed. Engl.*, **3**, 329 (1964).

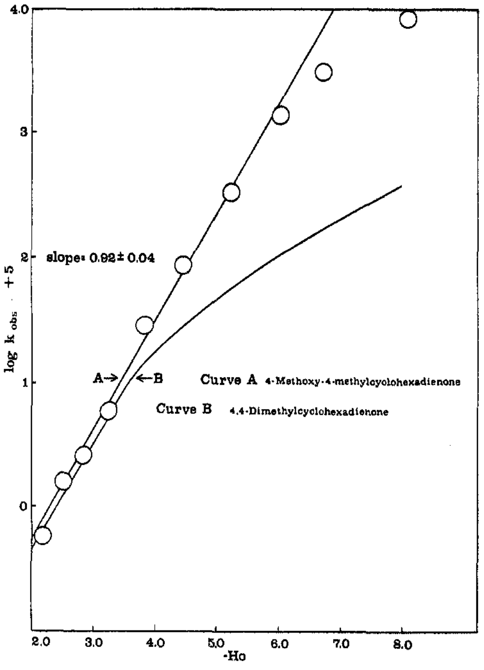

Figure 1.—Plot of log k_{obsd} *vs.* $-H_0$ for 4-methoxy-4-methylcyclohexadienone (upper curve) and 4,4-dimethylcyclohexadienone (lower curve) in perchloric acid at 25°.

original work.[9] Now the underlying assumption of the Zucker–Hammett hypothesis is that the reversible protonation of the substrate undergoing reaction is similar to the protonation of Hammett-type bases, *i.e.*, substituted anilines. However, cyclohexadienones have been shown *not* to be Hammett bases. For example, for six substituted cyclohexadienones thus far investigated[1,4-6]

$$\alpha = (\mathrm{constant})h_0^{0.6} \tag{2}$$

$$\mathrm{D} + \mathrm{H}^+ \rightleftharpoons \mathrm{DH}^+ \qquad \alpha = [\mathrm{DH}^+]/[\mathrm{D}] \tag{3}$$

In fact, it has been suggested[5,6] that the protonation of cyclohexadienones more nearly parallels the *amide* acidity function h_A[10] although the introduction of yet another unrelated acidity function hardly seems advisable. This is especially true since all acidity functions have been shown to be linear functions of H_0.[11]

Thus, while the dienone–phenol rearrangement is an example of an authentic A1 reaction,[2] the kinetic acidity dependence for the rearrangement of 4-methoxy-4-methylcyclohexadienone is considerably steeper than the equilibrium protonation acidity dependence of other cyclohexadienones.

In earlier work we suggested that over a range of acid concentrations similar to that used in this investigation the rate of the dienone–phenol rearrangement of 4,4-dimethylcyclohexadienone depended not only on the fraction of substrate protonated but also *inversely* on the water activity.

$$k_{\mathrm{obsd}} = k[\text{fraction protonated}]/a_{\mathrm{H_2O}} \tag{4}$$

Now

$$k_{\mathrm{obsd}} = \frac{k\alpha}{(\alpha + 1)a_{\mathrm{H_2O}}} \tag{5}$$

where α is as defined in eq 3. If the amount of substrate protonated is small (*vide supra*) then

$$k_{\mathrm{obsd}} = k\alpha/a_{\mathrm{H_2O}} \tag{6}$$

and

$$\log k_{\mathrm{obsd}} + \log a_{\mathrm{H_2O}} = \log k + \log \alpha \tag{7}$$

thus, ($\log k_{\mathrm{obsd}} + \log a_{\mathrm{H_2O}}$) is proportional to $\log \alpha$ and the slope of a plot of ($\log k_{\mathrm{obsd}} + a_{\mathrm{H_2O}}$) *vs.* $-H_0$ should be characteristic of cyclohexadienone protonation. A plot of ($\log k_{\mathrm{obsd}} + \log a_{\mathrm{H_2O}}$) against $-H_0$ for the first seven data points in Figure 1 yielded a slope of 0.66 ± 0.04 in excellent agreement with the equilibrium protonation data for several other dienones.[1,4-6]

Results. Basicity of 1.—To understand the effect of methoxy substitution on individual steps of the dienone–phenol rearrangement it is necessary to estimate the basicity of **1** in concentrated solutions of perchloric acid. For **1** this presents a problem since the half-life for rearrangement in 71% $\mathrm{HClO_4}$ is ~8 sec and the absorption spectrum of the fully protonated cyclohexadienone is difficult to obtain. Therefore, we measured the absorbance at zero time in three different perchloric acid solutions by monitoring the absorbance at 295 nm[1,4,5] (a wavelength characteristic of protonated cyclohexadienones of two other similar systems) as a function of time and back-extrapolating to $t = 0$. These results are recorded in Table II.

TABLE II

EQUILIBRIUM PROTONATION DATA FOR 1 IN PERCHLORIC ACID AT 25°

Absorbance[a]	N[b]	Wt % $\mathrm{HClO_4}$	$-H_0$[c]	$-a$[d]
0.598 ± 0.032	8	71.06	8.06	(3.60)
0.441 ± 0.044	5	65.98	6.67	3.64
0.310 ± 0.027	7	61.37	5.97	(3.60)

[a] Absorbance at 295 nm; total dienone = 2.68×10^{-4} M; path length = 1 cm. [b] Number of independent determinations. [c] Footnote *a* Table I. [d] From eq 10 in text.

In general, the protonation of a weak base in concentrated acid solutions can be expressed by eq 8. The value of m for various dienones[1,4-6] so far investigated is 0.6.

$$\log \alpha = -mH_0 - a \tag{8}$$

In particular the previous discussion of the kinetic acidity dependence for **1** suggests a similar value for this substrate as well. Now α can be related to the measured absorbance through eq 9 where A is the measured absorbance and A^+ is the absorbance of the fully protonated dienone at the same stoichiometric concentration of substrate. Thus

$$\alpha = A/(A^+ - A) \tag{9}$$

$$\log \frac{\mathrm{A}}{A^+ - A} = -0.6H_0 - a \tag{10}$$

Since there are two unknowns in this equation (A^+ and a) two independent measurements of A at two different acidities suffice to evaluate A^+ and a. The values of a and A^+ computed from the first and third entries in

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[9] For a review of acidity functions and their use in mechanistic organic chemistry, see C. H. Rochester in "Acidity Functions," Academic Press, New York, N. Y., 1970, pp 110–196.

[10] K. Yates, J. B. Stevens, and A. R. Katritzky, *Can. J. Chem.*, **42**, 1957 (1964).

[11] K. Yates and R. A. McClelland, *J. Amer. Chem. Soc.*, **89**, 2686 (1967).

Table II are −3.60 and 0.633, respectively. This value of A^+ yields an extinction coefficient for protonated **1** at 295 nm of 2360 M^{-1} cm^{-1} which is similar to the value of 3680 M^{-1} cm^{-1} reported by us earlier[1,4] for two other dienones differing only in the substituent at the 4 position. When this value of A^+ is used with the second entry in Table II and eq 10 a very similar value of a (−3.64) is obtained. This lends strong support to our assignment of this constant.[12]

In Table III we have summarized the available basicity data for a series of 4-methyl-4-X-cyclohexadienones. The trend is quite clear. As X becomes more electron withdrawing inductively the cyclohexadienyl cation becomes less stable and the parent dienone less basic. In fact there is a good linear relationship between $(-H_0)_{\text{half-protonation}}$ and σ^*.[13]

TABLE III

H_0 VALUES AT HALF-PROTONATION FOR 4-METHYL-4-X-CYCLOHEXADIENONES IN CONCENTRATED ACID AT 25°

X	H_0
$-CH_3$[a]	−3.66
$-CHCl_2$[b]	−5.54
$-OCH_3$[c]	−6.02
$-CCl_3$[d]	−6.12

[a] Reference 4. [b] Reference 1. [c] This work. [d] N. Grossman, unpublished results.

$$(-H_0)_{\text{half-protonation}} = (0.89 \pm 0.01)\sigma^* + 3.76 \pm 0.03$$

These results suggest that within this series of compounds the basicity of the cyclohexadienone is controlled primarily by the inductive effect of the 4-substituent. It should be noted in this context that a methoxy substituent in the 4 position can only exert a $-I$ effect since resonance stabilization of the cation by this substituent is not possible. The decreased basicity of **1** reflects this electron withdrawing inductive effect.

With $a = -3.62$ it can be estimated that <20% of **1** is protonated at the highest acidity for which the linear correlations discussed above were obtained. This would introduce at most a very modest correction to the computed slope and can be ignored.

Discussion

In Figure 1 along with kinetic data for the acid-catalyzed isomerization of **1** in perchloric acid the lower curve represents kinetic results for the acid-catalyzed rearrangement of 4,4-dimethylcyclohexadienone.[14] At an acidity of $H_0 = -2$ (both substrates are <10% protonated at this acidity) the effect of a methoxy substituent on the free energy of activation is very small; $k_{OCH_3}/k_{CH_3} = 1.2$. Assuming that the neutral dienone reactants have the same free energy this rate factor corresponds to a decrease in free energy of the transition state for methoxy *vs.* methyl of ~100 cal/mol.

It is, however, possible to estimate the relative rearrangement rates for the oxygen-protonated cyclohexadienyl cation intermediates from observed relative rates and an estimate of the fraction protonated for each substrate (eq 11 and 12). Here k_+^{X} is the specific

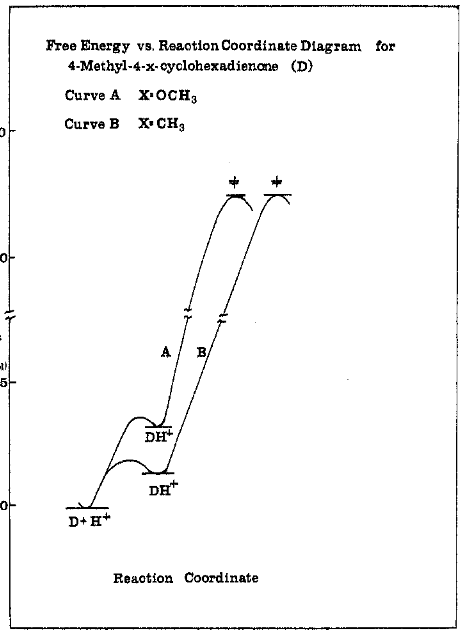
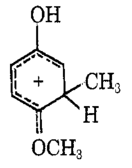


Figure 2.—A free energy *vs.* reaction coordinate profile for the dienone–phenol rearrangement ($H_0 = -2$).

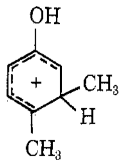
$$k_{\text{obsd}}^{CH_3O} = k_+^{CH_3O}F_{CH_3O}/a_{H_2O} \qquad (11)$$

$$k_{\text{obsd}}^{CH_3} = k_+^{CH_3}F_{CH_3}/a_{H_2O} \qquad (12)$$

rate of rearrangement of the X-substituted cyclohexadienyl cation and F_X is the fraction of X-substituted dienone protonated at this acidity. We estimate at $H_0 = -2$, $k_+^{CH_3O}/k_+^{CH_3} = 33$. Virtually this entire rate-enhancing effect originates from a destabilization of the intermediate (a factor of 27, 2.0 kcal/mol) by methoxy while only a small stabilization of the transition state is observed (a factor of 1.2, 0.1 kcal/mol). These results are summarized schematically in Figure 2. It is apparent that even though the intermediate cyclohexadienyl cation is destabilized by the electron withdrawing effect of the methoxy substituent this destabilization is not felt in the transition state. This is due to the fact that in the transition state there is some positive charge developed at C-4 and the methoxy substituent can stabilize this partial positive charge by resonance. Now while some positive charge development at C-4 is suggested by our results a very "product-like" transition state (*i.e.*, a transition state with a large fraction of the positive charge at C-4) is considered unlikely because of the small stabilizing effect observed for the methoxy substituent on the transition state.



1^+



2^+

From CH_3–CD_3 isotope effects[15] observed in the rearrangement of 4,4-dimethylcyclohexadienone (**2**) it

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[12] In fact, for reasonable variations of m in eq 10 the values of a calculated from the data in Table II are very similar. *E.g.*, for values of m = 0.59–0.63 the average value of a is −3.68 ± 0.09.

[13] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, pp 219–235.

[14] V. P. Vitullo and N. Grossman, *J. Amer. Chem. Soc.*, **94**, 3844 (1972).

[15] V. P. Vitullo and N. Grossman, unpublished results.

appears that the transition state for the rearrangement of this substrate is "product-like," *i.e.*, bearing a close structural resemblance to 2^+. The rearranged cations directly succeeding the transition state for these two substrate should markedly differ in stability with 1^+ being much more stable than 2^+. This should result in a shift in transition state structure[16] for 1^+ toward a more nearly "symmetrical" transition state with an attendant decrease in the amount of positive charge at C-4 in the transition state. This is consistent with the relatively small stabilizing effect of the methoxy group of **1** in the transition state.

Experimental Section

4-Methoxy-4-methylcyclohexadienone (1).—This material was prepared as described by Hecker.[7] The product was produced in 31% yield, purified by preparative glpc (130°, diethylene glycol succinate) and had the following properties: mp 61–61.5° (lit.[7] mp 62–63°); ir (CCl_4) 1675 (>C=O), 1640 (C=C), 1200 cm^{-1} ($COCH_3$); nmr δ 6.15 (d, CH=CHC=O), 6.65 (d, **CH**=CHC=O), 3.14 (s, OCH_3), 1.38 (s, CH_3).

Rearrangement of 1 in Concentrated Hydrochloric Acid.—A 50-mg portion of 1 was treated with 1 ml of concentrated HCl for 3 days with vigorous stirring. The yellowish solution was extracted with several portions of ether. The ether was dried (Na_2SO_4) and removed on a rotary evaporator. The residue was dissolved in 5 ml of methanol and treated with 106 mg of Na_2CO_3 and 114 mg of CH_3I. After refluxing for 3 days the solution was cooled, filtered, and diluted with ether. The ether solution was washed with water and dried over Na_2SO_4, and the ether removed on a rotary evaporator. The crude product was subjected to glpc analysis (10% diethylene glycol succinate, 140°) and one peak was observed. This peak was collected and its ir spectrum was shown to be virtually identical to that obtained from the methylation of 2-methylhydroquinone (Aldrich Chemical Co).

2,4-Dimethoxytoluene.—2,4-Dimethoxybenzyl mesylate was prepared by allowing 2,4-dimethoxybenzyl alcohol, triethylamine, and methanesulfonyl chloride in benzene to react at room temperature.[17] From 431 mg of 2,4-dimethoxybenzyl alcohol there was obtained 213 mg (35%) of mesylate ester, ir, no OH, 1380 cm^{-1} (sulfonate). The crude mesylate was reduced in refluxing ether for two days with an excess of $LiAlH_4$. A small sample of the reduction product was isolated by preparative glpc (10%, diethylene glycol succinate, 140°). An ir spectrum of this material was substantially different from that of the methylated rearrangement product. In fact, a comparison of ir spectra showed that <5% methoxy migration had occurred in the acid-catalyzed rerrangement of 1.

Kinetic Procedures.—All rate constants reported in this paper were obtained by monitoring the dissappearance of dienone of 240 nm[7] using either a Beckman DK-1A or Gilford Model 2400 spectrophotometer. The kinetic data were processed by using a nonlinear least-squares program written for the Wang 700 computer. Most of the results reported in Table I are average values based on three or more runs. A concentrated solution of dienone was prepared in ethanol and 2–5 μl of this solution was deposited in the end of a stirring rod. The reaction was initiated by plunging the stirring rod into a cuvette containing acid of the desired strength (previously equilibrated) and monitoring the absorbance as a function of time. Acid concentrations were determined by titrating weighed amounts of acid with previously standardized base.

Basicity of 1 in Perchloric Acid.—To estimate the degree of protonation of 1 we measured the absorbance of solutions of 1 in perchloric acid at 295 nm as a function of time and extrapolated back to the time of mixing either graphically or by using the nonlinear kinetics program. The cyclohexadienyl cations produced by the protonation of 4-dichloromethyl-4-methylcyclohexadienone[1] and 4,4-dimethylcyclohexadienone[2,4] have λ_{max} 295 nm. Neutral 1 has virtually no absorption at this wavelength. These results are presented in Table II.

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[16] G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).

[17] R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).

Structural Effects on the Acid–Base Properties of Some Closely Related Phosphinic Acids and Phosphine Oxides[1]

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Several isomeric cyclic and acyclic C_8 phosphinic acids and some isomeric cyclic and acyclic C_8 methylphosphine oxides have been synthesized, and their acidity and basicity, respectively, have been determined. The effect of structural branching is acid weakening with the phosphinic acids and base weakening with the phosphine oxides. The presence of a four-membered ring which includes the phosphorus heteroatom tends to be acid strengthening with the phosphinic acids, and it tends to be base weakening with the phosphine oxides. The reasons for these structural effects are discussed.

The acid–base properties of molecules are due to a combination of internal effects and environmental effects,[3] and the relative ability of these effects to stabilize the acids and their conjugate bases or the bases and their conjugate acids. The relative ability of these effects to stabilize the acid or base forms of a molecule are determined only by the structure of the molecule if one uses a constant solvent environment. The structural effects on acid and base properties of some isomeric aliphatic phosphinic acids and phosphine oxides are reported in this study. Since only aliphatic phosphinic acids and phosphine oxides are involved, the important internal effect is an inductive effect, and the important environmental effect is a solvation effect.

All but one of the phosphinic acids listed in Table I were synthesized by treatment of phosphorus oxychloride or phosphorus trichloride with the appropriate Grignard reagent followed by hydrolysis. The exception was cyclic phosphinic acid (**1**) which was produced by treating 2,4,4-trimethyl-2-pentene with phosphorus trichloride in the presence of aluminum chlo-

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[1] Based on work performed under the auspices of the U. S. Atomic Energy Commission.

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[3] E. J. King, "Acid-Base Equilibria," Pergamon Press, Oxford, 1965.