was dried over calcium chloride and fractionally distilled, bp 155°, $n^{20}$D 1.5171 (lit.[42] bp 155°, $n^{20}$D 1.5179). Fractional distillation of fluorobenzene gave material of bp 85°, $n^{20}$D 1.4654 (lit.[42] bp 84.9°, $n^{20}$D 1.4658). Trifluoromethylbenzene purified by fractional distillation had bp 102°, $n^{20}$D 1.4136; less than 0.1% of impurities was detected by glpc. Reagent grade nitrobenzene was steam distilled, dried first over calcium chloride, then over phosphorus pentoxide, and fractionally distilled; bp 210°, $n^{20}$D 1.5522 (lit.[42] bp 211°, $n^{20}$D 1.5529).

Reaction tubes were made from 5-mm Pyrex or 6-mm Vycor glass cut into 10-cm lengths; the glass was cleaned with chromic acid, washed in aqueous sodium hydroxide, rinsed with deionized water, dried at 110°, and stored in a desiccator over phosphorus pentoxide.

Thermal kinetic runs were carried out with an oil bath maintained to ±0.03° by a proportional controller[43] at 129.6 ± 0.2°.

Ultraviolet radiation was provided by a low-pressure mercury lamp (No. RPR-2537A) in a Rayonet photochemical reactor. The reactor temperature did not rise above 45° during irradiations.

**Thermal Kinetic Runs.** Solutions for the "nitrene" runs were prepared by weighing benzene, a monosubstituted benzene, and ethyl azidoformate from a 50-$\mu$l syringe into a 10-ml volumetric flask; dilution to the 10-ml mark with "Freon" E-4 produced a solution 0.050 *M* in each aromatic component and 0.100 *M* in azidoformate. Solutions for the "carbene" runs were prepared by weighing benzene and a monosubstituted benzene into a 10-ml volumetric flask; dilution to the 10-ml mark with "Freon" E-4 produced a solution 0.050 *M* in each aromatic component. Ethyl diazoacetate was weighed into a 5-ml volumetric flask and diluted to the 5-ml mark with the "Freon" E-4 solution of two aromatics to give a solution 0.100 *M* in diazoacetate and 0.0497 *M* in each aromatic component.

Reaction tubes were filled with about 0.38 ml of a "carbene" or "nitrene" solution and sealed. Sets of tubes were immersed in the reaction bath in wire-screen baskets. The tubes were quenched at −80° upon removal from the bath. In the "nitrene" runs, the reaction was terminated at several points within 1 hr after immersion; the "time-zero" set of tubes in these runs was removed after 5 min in the bath. In the "carbene" runs, a set of tubes containing the ethyl diazoacetate–aromatics solution was allowed to react for a minimum of 9 hr; the "time-zero" set of tubes in the "carbene" study contained only the two aromatics in "Freon" E-4 and was simply set aside until analyzed.

Analysis of the contents of each tube for benzene and the monosubstituted benzene was accomplished by glpc, carried out with a Wilkins Aerograph Model A-90-P chromatograph in conjunction with a Brown "Electronik" recorder and disk integrator. The linearity of the thermal conductivity detector response was confirmed for the appropriate components and concentration range.

The columns used were 25% di-*n*-decyl phthalate or Apiezon L on Chromosorb W (nonacid washed) at temperatures between 85 and 145°. Each determination was carried out at least in triplicate; three reaction tubes were used for each determination. The relative rate ratios found are given in Table I.

The analyses of two "Freon" E-4 solutions of anisole, 0.050 *M*, one of which contained ethyl azidoformate, 0.10 *M*, were identical. When an analogous experiment was performed on the "carbene" system, as much as 12% of the anisole disappeared in the presence of ethyl diazoacetate.

The refractive index of each of the aromatic substrates was shown to remain unchanged after heating in sealed tubes for 12 hr at 135 ± 25°. Irradiating "Freon" E-4 solutions of monosubstituted benzene in sealed Vycor tubes placed in a Rayonet reactor caused between 21 (anisole) and 84% (trifluoromethylbenzene) decomposition of the aromatics.

**Acknowledgment.** We thank Professor K. Hafner and Professor W. Lwowski for helpful suggestions.

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[42] C. D. Hodgman, Ed., "Handbook of Chemistry and Physics," 43rd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1961.

[43] R. Anderson, *J. Chem. Educ.*, in press.

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# 7,12-Dihydropleiadenes. V. Transannular 1,4-Hydride Rearrangements in 1-Substituted 7-Hydroxy-12(7H)-Pleiadenones

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*Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214.* *Received November 29, 1966*

Abstract: 1-Chloro-7-hydroxy-12(7H)-pleiadenone (I) rearranges by intramolecular 1,4-hydride migration to 1-chloro-12-hydroxy-7(12H)-pleiadenone (IV) when treated with alkali metal *t*-butoxides in dimethyl sulfoxide. The rate-determining step is the transannular hydride rearrangement of the initially formed alkoxide and has $E_a \sim 24$ kcal/mole for the potassium salt in 95:5 DMSO–*t*-butyl alcohol. The primary deuterium isotope effect and metal cation effects on the rearrangement are also reported. The isomeric reactant and product hydroxy ketones both exhibit ring–chain tautomerism in solution.

We have recently studied several aspects of 7,12-dihydropleiadene chemistry, including the free energy barriers for "boat-to-boat" ring inversion[2,3] and the conformational preferences of alkyl[4] and other[5] substituents on the 7 position. Because of the close proximity of the 7- and 12-carbon atoms, it seemed probable that transannular rearrangements involving these positions might occur. In this paper, we report on the 1,4-hydride shift that occurs when 1-chloro-7-hydroxy-12(7H)-pleiadenone (I) is converted to the alkali metal salt (IIa–d) in dimethyl sulfoxide (DMSO) which leads to the isomeric alkoxide (IIIa–d) of 1-chloro-12-hydroxy-7(12H)-pleiadenone (IV). Although other transannular hydride shifts have been investigated by deuterium labeling and product studies,[6] no kinetic investigations have been reported from which activation parameters for the rearrangement step could

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[1] (a) Alfred P. Sloan Foundation Fellow, 1963–1967. (b) Du Pont Predoctoral Teaching Fellow, 1966–1967.

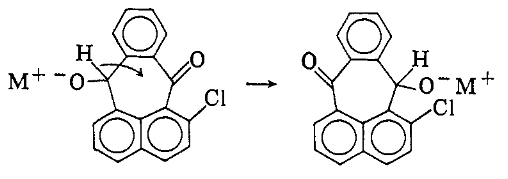
[2] P. T. Lansbury, J. F. Bieron, and M. Klein, *J. Am. Chem. Soc.*, **88**, 1477 (1966).

[3] P. T. Lansbury and F. D. Saeva, *Tetrahedron Letters*, 5991 (1966).

[4] P. T. Lansbury and A. J. Lacher, *J. Am. Chem. Soc.*, **88**, 3877 (1966).

[5] P. T. Lansbury, J. F. Bieron, and A. J. Lacher, *ibid.*, **88**, 1482 (1966).

[6] For a recent review and further references, see A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.* (London), **20**, 119 (1966).



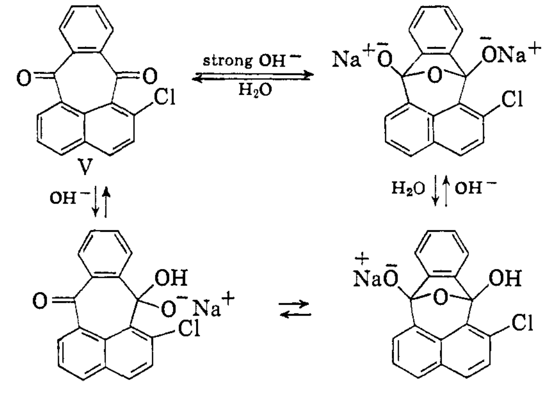
IIa-d IIIa-d

$M^+$
a = Li
b = Na
c = K
d = Cs

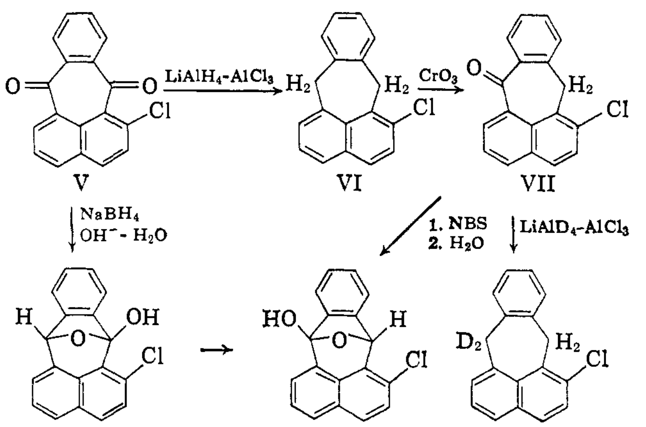
be obtained. We have studied the rates of intramolecular hydride shift for IIa-d, the primary deuterium isotope effect, and the variation of metal ion on rate. An additional aspect of interest is the ketol-cyclic hemiketal tautomerism exhibited in solution by I and IV (k and h subsequently denote ketol and hemiketal, respectively).

## Results and Discussion

1-Chloro-7,12-pleiadione[7] (V) served as the precursor of the essential compounds used in this investigation. By reducing V with sodium borohydride in sodium hydroxide solution, it was possible to isolate I-h in high yield (when recrystallized from benzene), rather than the *trans*-diol, which is the major product in neutral medium. It is not known what intermediate is undergoing the selective reduction; however V and concentrated base actually produce the disodium salt of the bicyclic hydrate[8] as a crystalline product which regenerates V when dissolved in water. Perhaps the open form of the monosodium salt is the actual substrate for reduction when borohydride is added. In this way, the more reactive carbonyl group is protected while the less reactive one is reduced.



Postponing the question of tautomerism in I for the time being, it is necessary to prove that I and IV do, in fact, have the structures assigned above, rather than the reverse. This was accomplished by selective chromic acid oxidation of 1-chloro-7,12-dihydropleiadene (VI) to 1-chloro-7(12H)-pleiadenone (VII) and subsequent benzylic bromination, followed by hydrolysis, to provide authentic IV. The structure of VII was verified by lithium aluminum deuteride–aluminum chloride reduction to VI-7,7-$d_2$, the position of deuterium being proven by nmr spectroscopy. In VI, the $C_7$-methylene signal under fast exchange conditions appears at 265 Hz (downfield from TMS at 60 MHz), whereas the $C_{12}$ protons appear as a singlet at 283 Hz,[3] being deshielded by neighboring chlorine.[9] In addition, the $C_7$ protons show an AB quartet with $\Delta\nu_{AB} = 67$ Hz at *ca.* −20° (compared with 71 Hz for 7,12-dihydropleiadene itself[2]), whereas the $C_{12}$ protons, in the slow exchange situation, show $\Delta\nu_{AB} = 17$ Hz. The decrease of $\Delta\nu_{AB}$ for $C_{12}$-methylene protons in 1-substituted 7,12-dihydropleiadenes has been observed in the low-temperature nmr spectra of a number of such compounds.[3] The fact that $LiAlD_4$–$AlCl_3$ reduction of VI gives VII, showing a single methylene peak at 283 Hz at room temperature, which separates into a quartet with $\Delta\nu_{AB} = 17$ Hz on cooling, therefore confirms the site of oxidation of VI. Ketol IV prepared from VII was different from its isomer I and, in fact, proved identical with the base-induced rearrangement product resulting from transannular hydride shift.



V VI VII

I-h IV-h VI-7, 7-$d_2$

It is now appropriate to consider the tautomerism of I and IV, which may be conveniently studied in solution by nmr. Both nonaromatic protons in I-k and IV-k are doublets in DMSO ($J \simeq 3$ Hz), whereas they appear as singlets in I-h and IV-h, the chemical shifts being as indicated below. The tautomeric equilibrium constants for I and IV in DMSO and dioxane were determined at several temperatures by integration of the appropriate proton signals and $\Delta F$, $\Delta H$, and $\Delta S$ calculated from the temperature dependence of $K_{eq}$. The data are summarized in Table I, together with information on 12-hydroxy-7(12H)-pleiadenone, which exists largely in the ketol form, in contrast with I and IV. Apparently, the $C_1$-Cl substituent in I and IV sterically favors the ring-closed hemiketal much like *ortho* substituents in *o*-benzoylbenzoic acids produce greater proportions of pseudo-acid in equilibrium with keto acid.[10] A $C_1$-$CH_3$ group (as in IX) has the same effect. Because of possible experimental error, it is not certain if the indicated solvent effects on $\Delta S$ are real; the major point is that the ketol structures have greater rotational freedom than the noninverting bicyclic hemiketals.

Most experiments involving rearrangement of I dealt with the potassium salt IIc, which was generated rapidly and quantitatively from I and potassium *t*-butoxide in DMSO. The addition of 0.1 equiv of alkoxide to I-k and I-h resulted in immediate disappearance of the

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[7] M. P. Cava and R. H. Schlessinger, *Tetrahedron*, 21, 3073 (1965).

[8] An even more stable bridged hydrate is formed from 1,8-(1′,8′-naphthalyl)naphthalene [W. C. Agosta, *Tetrahedron Letters*, 3635 (1966)].

[9] R. C. Fort, Jr., G. W. H. Cheeseman, and E. C. Taylor, *J. Org. Chem.*, 29, 2440 (1964).

[10] M. S. Newman and C. W. Muth, *J. Am. Chem. Soc.*, 73, 4627 (1951).

Table I. Ketol–Hemiketal Equilibrium of Hydroxypleiadenones

| Compd | Solvent | Temp, °K | $K^a$ | kcal/mole<br>$\Delta F$ | <br>$\Delta H^b$ | $\Delta S$, eu |
|---|---|---|---|---|---|---|
| I | DMSO | 313 | 0.58 | 0.34 | | |
| | | 353 | 1.08 | −0.06 | 3.1 | 9.1 |
| | | 393 | 1.78 | −0.45 | | |
| | | 433 | 2.34 | −0.73 | | |
| | Dioxane | 307 | 0.62 | 0.29 | | |
| | | 339 | 0.83 | 0.13 | | |
| | | 354 | 0.97 | 0.02 | 2.2 | 6.1 |
| | | 370 | 1.16 | −0.11 | | |
| IV | DMSO | 353 | 0.79 | 0.17 | | |
| | | 373 | 0.91 | 0.07 | | |
| | | 393 | 1.01 | −0.01 | 1.7 | 4.4 |
| | | 413 | 1.13 | −0.10 | | |
| | Dioxane | 309 | 0.35 | 0.65 | | |
| | | 336 | 0.50 | 0.46 | | |
| | | 347 | 0.60 | 0.35 | 2.9 | 7.6 |
| | | 360 | 0.70 | 0.26 | | |
| 1-Methyl-12-hydroxy-7(12H)-pleiadenone | DMSO | 309 | 0.43 | 0.52 | | |
| 12-Hydroxy-7(12)-pleiadenone | DMSO | 309 | 4.30 | −0.90 | | |

[a] $K$ = [ketol]/[hemiketal], determined from an average of four integrations of the peaks due to each tautomer (see Discussion). The solutions used were *ca.* 1.4 $M$ in each solvent. [b] From graphical analysis.

four nonaromatic proton signals and appearance of a single resonance peak at *ca.* 390 Hz, due to rapid time averaging of the protons in I-h, I-k, and IIc, as a consequence of chemical exchange. This peak moved upfield linearly as increasing amounts of alkoxide up to 1.0 equiv were added, whereupon the signal, now due entirely to $C_7$–H in IIc,(11) appeared at 373 Hz and remained unchanged when excess *t*-butoxide was present. The rate-determining rearrangement of IIc to IIIc in DMSO containing *ca.* 5 mole % *t*-butyl alcohol was then studied by nmr spectroscopy (details in Experimental Section), using the disappearing $C_7$–H signal and the developing $C_{12}$–H signal of IIIc(11) at 401 Hz (note deshielding effect of $C_1$–Cl(8)) to monitor the rate. From duplicate runs at four temperatures (Table II) approximate values of the activation parameters were calculated using the Arrhenius and Eyring equations: $\Delta F^*_{321^\circ} \simeq$ 24.0 kcal/mole; $\Delta H^*_{321^\circ} \simeq$ 24.5 kcal/mole, and $\Delta S^*_{321^\circ} \simeq -1$ eu.(12) The effect of changing metal ion from $Li^+$ to $Cs^+$, under otherwise identical experimental conditions (being especially careful to maintain constant DMSO:*t*-butyl alcohol ratios), on the rate of hydride transfer in IIa–d was also determined, pertinent data being summarized in Table III.

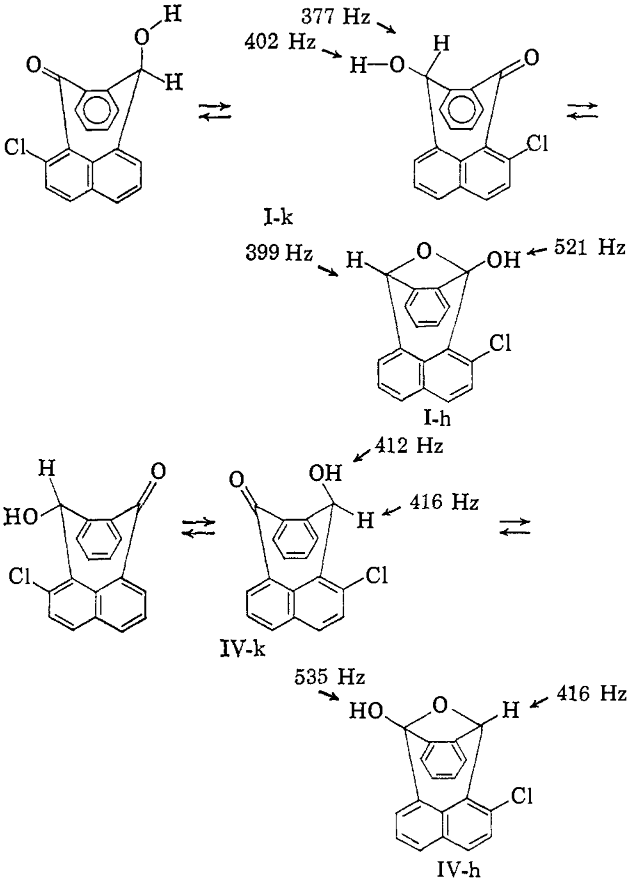

Table II. Kinetics of Rearrangement of IIc to IIIc in Dimethyl Sulfoxide Containing 5 Mole % *t*-Butyl Alcohol

| Temp,$^a$ °K | $k_1$, sec$^{-1}$ |
|---|---|
| 311 | $8.2 \times 10^{-5}$<br>$9.2 \times 10^{-5}$ |
| 321 | $2.6 \times 10^{-4}$<br>$2.3 \times 10^{-4}$ |
| 330 | $7.2 \times 10^{-4}$<br>$6.7 \times 10^{-4}$ |
| 342 | $2.9 \times 10^{-3}$<br>$2.8 \times 10^{-3}$ |

[a] Probable accuracy ±1°.

Since benzoins normally rearrange by an enediol mechanism(13) and I can be considered as a "transan-

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(11) The keto alkoxide formulation for II and III, rather than the isomeric hemiketal salt structures, are supported by strong carbonyl absorption at 6.02 and 6.10 $\mu$, respectively, in their infrared spectra (DMSO solution). These results do not exclude the possible existence of substantial amounts of the hemiketal salts, however. Even if some of the latter species exist in equilibrium with II, the keto alkoxide is certainly the most plausible intermediate for the subsequent rearrangement.

(12) Estimated errors are *ca.* ±1 kcal/mole in $E_a$ (and $\Delta H^*$) and *ca.* ±3.0 eu in $\Delta S^*$. For a discussion of errors in determination of entropies of activation, see L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, 1, 1 (1963).

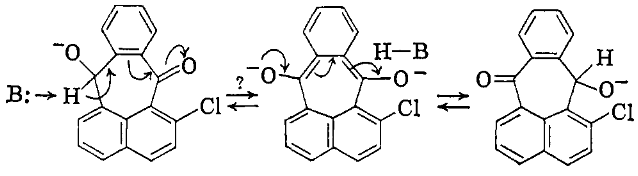
(13) C. J. Collins and J. F. Eastham in "The Chemistry of the Car-

Table III. Metal Ion Effects in Rearrangement of II to III at 321 °K in Dimethyl Sulfoxide Containing 5 Mole % *t*-Butyl Alcohol

| Metal ion | $\delta_{C_7\text{-}H}$,[a] Hz | $\delta_{C_{12}\text{-}H}$,[a] Hz | $k_1$, sec$^{-1}$ | $\Delta F^*_{321°}$, kcal/mole | $k_{rel}$ |
|---|---|---|---|---|---|
| Li | 364 | 393 | $4.5 \times 10^{-5}$<br>$4.0 \times 10^{-5}$ | 25.3 | 1 |
| Na | 372 | 398 | $1.4 \times 10^{-4}$<br>$1.5 \times 10^{-4}$ | 24.4 | 3.4 |
| K | 375 | 401 | $2.6 \times 10^{-4}$<br>$2.3 \times 10^{-4}$ | 24.1 | 5.8 |
| Cs | 380 | 404 | $4.9 \times 10^{-4}$<br>$5.0 \times 10^{-4}$ | 23.6 | 12 |

[a] Chemical shifts in hertz at 60 MHz for external tetramethylsilane.

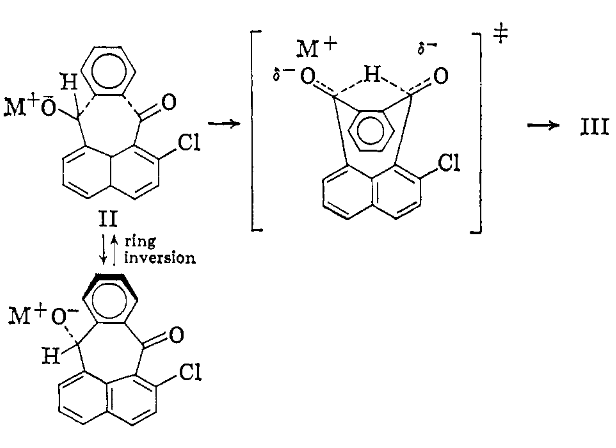
nular benzoin," it was necessary to consider such a mechanism for the isomerization II → III, in spite of the reported difficulty in generating pleiadene intermediates.[7] This possibility was ruled out by the finding that I-7-$d_1$ rearranged in DMSO with potassium *t*-butoxide to give IV with no observable loss of deuterium, as indicated by the absence of the $C_{12}$-proton signal in the nmr spectrum of product IV (obtained as the hemiketal by recrystallization from benzene). In fact, partial rearrangement of a mixture of IIc and IIIc deuterated at $C_7$ and deuterium analysis of the recovered starting material provided an estimate of the primary deuterium isotope effect, $k_H/k_D \sim 3$.

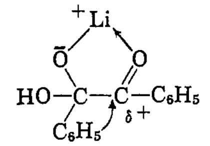


II

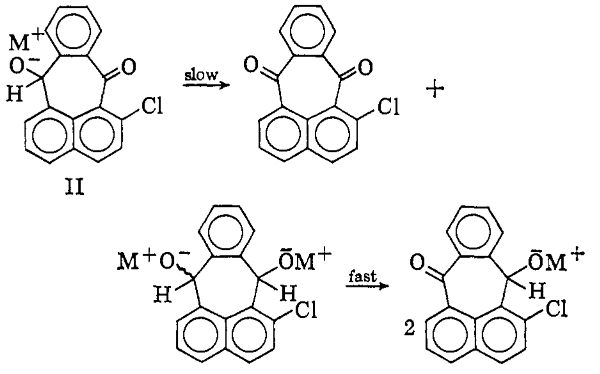
III

All of the above data on metal ion effects, deuterium retention, and the kinetic and isotope effect data are consistent with rate-determining transannular hydride transfer, in which the transition state has less rotational freedom than the ground state (note $+\Delta S$ for hemiketal ⇄ ketol equilibria, Table I). However, since $\Delta S^*$ is within experimental error of 0 eu, it would appear that restricted conformational mobility in the transition state is compensated for by simultaneous loosening of solvent structure due to charge diffusion. The increasing rate of rearrangement with increasing metal–oxygen ionic character in II (Cs > K > Na > Li) is consistent with the postulation of intimate ion pairs in DMSO solution (*ca.* 0.7 *M*), wherein the metal ion is not able to complex intramolecularly with the transannular carbonyl group to provide electrophilic catalysis. Such chelation is, however, possible in the related benzilic acid rearrangement,[13] and in fact the alkali metal ion effect was in that case[14] reversed from the present work (Li$^+$ > other metal ions).





The possibility of a bimolecular mechanism leading from II to III by two consecutive intermolecular hydride transfers is not eliminated by the deuterium tracer results. However, $\Delta S^*$ should be highly negative for the slow step, not to mention the second-order kinetics expected. Neither of these expectations was realized, in spite of the demonstrated base-catalyzed disproportionation of diol and diketone to III (the fast step depicted above).



III

Finally, some comment on the driving force for the one-way transannular rearrangement of I to IV is in order. Perhaps relief of electrostatic repulsion between the parallel $C_{12}$-carbonyl and $C_1$–Cl dipoles in II is an important factor[15] as well as chlorine–metal ion bonding in one conformation of III, in which case other groups like a $C_1$–$CH_3$ should effect the reverse rearrangement[16] (*i.e.*, III → II). A second possibility is that the $C_{12}$-carbonyl group is sterically prevented from maximum conjugation with the aryl rings by *any* sufficiently large $C_1$ substituent, regardless of its electronic effect. We have previously shown that a variety of 1-substituted 7,12-pleiadiones show two carbonyl stretching frequencies in the infrared spectrum,[3] the high frequency one supposedly corresponding to the $C_{12}$-carbonyl group, owing to steric compression.[3] That the second factor is at least of major importance is shown by the facile rearrangement of 1-methyl-7-hydroxy-12(7H)-

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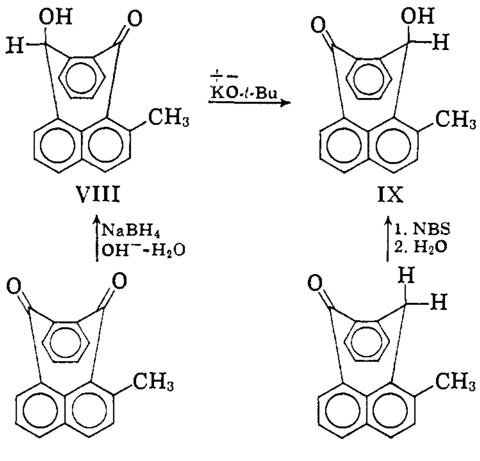
bonyl Groups," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1966, pp 778–787.

[14] W. H. Puterbaugh and W. S. Gaugh, *J. Org. Chem.*, **26**, 3513 (1961).

[15] For conformational preferences in α-halocyclohexanones, see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, p 460.

[16] This possibility could result from *attractive* methyl–carbonyl interaction, as evidenced from the preferred eclipsed conformation of propionaldehyde: G. J. Karabatsos and N. Hsi, *J. Am. Chem. Soc.*, **87**, 2864 (1965).

pleiadenone (VIII) to 1-methyl-12-hydroxy-7(12H)-pleiadenone (IX), when treated with potassium *t*-butoxide in DMSO, as in I → IV. Further studies now underway will provide information on the equilibrium ratios of isomeric hydroxy ketones as a function of $C_1$ substitution,[17] as well as the rates of transannular rearrangement. We hope to report on these points in the near future.



## Experimental Section[18]

**Preparation of 1-Chloro-7-hydroxy-12(7H)-pleiadenone (I).** Sodium hydroxide (50 mmoles) was added to a solution of 1.5 g (5.1 mmoles) of 1-chloropleiadione[7] in a 2:1 methanol–THF (or water–THF) solvent mixture and stirred for 15 min at room temperature. The solution was then treated with 10.2 mmoles of sodium borohydride and stirred for 3 hr, prior to hydrolysis with 10% hydrochloric acid. The resulting crystalline product was removed by filtration and recrystallized from benzene to give I-h in 75% yield, mp 203–204°. The cyclic hemiketal I-h showed strong infrared absorption at 3340, 1340, 1268, 975, 830, and 682 $cm^{-1}$ and was transparent in the carbonyl stretching region.

*Anal.* Calcd for $C_{18}H_{11}O_2Cl$: C, 73.33; H, 3.76. Found: C, 73.49; H, 3.78.

When a sample of I-h was dissolved in ether and the solvent removed by flash evaporation, the ketol I-k was obtained, mp 170–172°, which showed infrared carbonyl absorption at 1670 $cm^{-1}$ and other bands at 3340, 832, and 768 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{11}O_2Cl$: C, 73.33; H, 3.76. Found: C, 73.37; H, 3.73.

Recrystallization of ketal I-k from benzene regenerated hemiketal I-h.

**Preparation of 1-Chloro-7(12H)-pleiadenone (VII).** 1-Chloro-7,12-dihydropleiadene[7] (4.79 g, 18 mmoles) was oxidized by refluxing for 3 hr in a solution of 2.4 g (24 mmoles) of chromium trioxide in 350 cc of 90% aqueous acetic acid. The reaction mixture was then poured onto 500 g of ice and, after melting, the solid was removed by suction filtration. Recrystallization afforded 3.76 g (75%) of ketone VII, mp 163–164° (white needles from benzene–petroleum ether). VII showed a carbonyl band at 1660 $cm^{-1}$ and other strong bands at 833 and 745 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{11}OCl$: C, 77.55; H, 3.98. Found: C, 77.51; H, 3.94.

Mixed hydride reduction[2] (lithium aluminum hydride or deuteride plus aluminum chloride in ether) of VII led back to 1-chloro-7,12-dihydropleiadene or the 7,7-$d_2$ isomer, which were characterized by nmr and mixture melting point determinations.

**Preparation of 1-Chloro-12-hydroxy-7(12H)-pleiadenone (IV).** Benzylic bromination of VII (1.02 g, 3.67 mmoles) was effected by refluxing for 10 hr with 0.653 g (3.67 mmoles) of N-bromosuccinimide in 100 ml of carbon tetrachloride. The cooled solution was filtered to remove succinimide and solvent evaporated to produce a solid residue, which was recrystallized from benzene–hexane to provide 0.733 g (56% yield) of 1-chloro-12-bromo-7(12H)-pleiadenone, mp 204–206°, $\nu_{max}$ 1668, 1300, 761, and 714 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{11}OBrCl$: C, 60.43; H, 2.82. Found: C, 60.57; H, 3.00.

The above bromo ketone (0.493 g) was refluxed for 15 min in 25 ml of 95% aqueous dioxane, then diluted with water to provide 0.39 g (96% yield) of hemiketal IV-h, mp 211–212° (from benzene), $\nu_{max}$ 3330, 1275, 992, 828, 760, and 750 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{11}O_2Cl$: Cl, 73.33; H, 3.76. Found: C, 73.21; H, 3.85.

**Preparation of 12-Hydroxy-7(12H)-pleiadenone.** As in the preparation of I, 0.47 mmole of 7,12-pleiadione[2] and 50 mmoles sodium hydroxide were dissolved 1:2 THF–methanol and reduced sodium borohydride (0.20 mmole) for 1 hr at room temperature. Hydrolysis with 10% hydrochloric acid and recrystallization of the crude product gave 100 mg (83% yield) of ketol, mp 215–216°, $\nu_{max}$ 3330, 1650, and 1020 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{12}O_2$: C, 83.04; H, 4.65. Found: C, 82.94; H, 4.81.

**Preparation of 1-Methyl-7-hydroxy-12(7H)-pleiadenone (VIII).** Using the same procedure as for synthesis of I, 0.138 g (0.51 mmole) of 1-methylpleiadione,[19] 10 mmoles of sodium hydroxide, and 1 mmole of sodium borohydride in 25 ml of 2:1 tetrahydrofuran–methanol were treated at room temperature for 1.5 hr. Hydrolysis and work-up as above afforded 0.12 g (80% yield) of ketol VIII-k, mp 204–206°, $\nu_{max}$ 3400 (O–H stretch), 1650 (carbonyl stretch), 1130 (C–O stretch), and 767 $cm^{-1}$.

*Anal.* Calcd for $C_{19}H_{14}O_2$: C, 83.18; H, 5.15. Found: C, 83.31; H, 5.38.

**Preparation of 1-Methyl-12-hydroxy-7(12H)-pleiadenone (IX).** As in the synthesis of IV, equimolar amounts of 1-methyl-7(12H)-pleiadenone[20] and N-bromosuccinimide in carbon tetrachloride were refluxed in carbon tetrachloride to produce the crude bromo ketone, after filtration to remove succinimide and solvent evaporation. The oily product was hydrolyzed with refluxing aqueous dioxane and the product purified by alumina chromatography (ether eluent) and recrystallization from benzene, giving 0.405 g (76%) of ketol IX-k, mp 175° dec. The infrared spectrum showed O–H stretching at 3470 $cm^{-1}$ and the carbonyl band at 1660 $cm^{-1}$.

*Anal.* Calcd for $C_{19}H_{14}O_2$: C, 83.18; H, 5.15. Found: C, 83.36; H, 5.32.

**Preparative Scale Rearrangement of I to IV.** Equivalent quantities of I (1.21 g, 4.1 mmoles) and potassium *t*-butoxide (0.46 g, 4.1 mmoles) in 50 ml of DMSO were heated at 60° for 30 min. The reaction mixture was then poured over ice and the aqueous solution extracted with ether. The latter extract was washed with water, dried over magnesium sulfate, and evaporated. Recrystallization of the residue from benzene yielded 1.15 g (96%) of IV-h, mp 204–206°, identical by infrared and mixture melting point determination with authentic IV prepared independently (above).

**Kinetic Measurements on Rearrangement of II to III.** Reagent grade dimethyl sulfoxide was distilled and stored over Linde 5-A Molecular Sieves prior to use. Lithium *t*-butoxide was provided by Lithium Corporation of America and sodium, potassium, and cesium *t*-butoxides were gifts from MSA Research Corp.

Kinetic runs were made on the Varian A-60 spectrometer equipped with a A-6040 variable-temperature controller, which was calibrated using ethylene glycol. To a dried sample tube were added (by hypodermic syringe from capped serum bottles) 0.3 ml each of 1.36 *M* solutions of I and potassium *t*-butoxide (or another alkoxide) in DMSO. The resulting 0.68 *M* solution of IIc (or IIa, -b, or -d) in DMSO containing *ca.* 5 mole % *t*-butyl alcohol was placed in the nmr probe which had previously been set at the desired temperature. The reaction was followed by periodic integration of the diminishing $C_7$-proton signal, at 373 Hz[21] for IIc,

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[17] With a small $C_1$ group, such as fluorine, substantial amounts of both compounds should be present at equilibrium if polar factors are not too critical. If the latter effects are important also, then solvent effects on $K_{eq}$ will be evident.

[18] Melting points were recorded on a "Mel-Temp" capillary tube apparatus and are uncorrected. Infrared spectra were taken as Nujol mulls on a Beckman IR-5A spectrometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60 instrument, using chloroform-*d*, dioxane, and DMSO as solvents with TMS as internal standard in all cases except the kinetic runs in DMSO. Elemental analyses were by Dr. A. Bernhardt, Mulheim, Germany.

[19] W. S. Lee, Ph.D. Dissertation, The Ohio State University, 1964.

[20] L. F. Fieser and M. A. Peters, *J. Am. Chem. Soc.*, 54, 3742 1932).

[21] From external tetramethylsilane (neat, in sealed capillary within sample tube).

(giving $a - x$), and the developing $C_{12}$-proton signal, at 401 Hz[21] for IIIc, whose area was proportional to $x$. Plotting ln $[a/(a - x)]$ *vs.* time gave first-order rate constants by graphical analysis. The data gave a nonlinear plot $[1/(a - x)$ *vs.* $t]$ when tested for a second-order reaction involving two molecules of IIc in the rate-determining step.

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# Inhibition of Free Radical Reactions. III. Kinetic Study of the Reactions of Peroxy Radicals and Phenoxy Radicals in Hydrocarbon Systems

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**Abstract:** A systematic study has been made of the rates of oxygen absorption of solutions of 9,10-dihydroanthracene (DHA) and 2,2′,3,3′-tetraphenylbutane containing a number of nonhindered phenols and varying amounts of hydroperoxide. The phenolic compounds studied were phenol, 3-hydroxyphenol, 4-methoxyphenol, 4-phenylphenol, 2-hydroxynaphthalene, and 3-hydroxypyrene. An analysis of the oxidation data has been carried out by means of a derived general rate expression I. The numerical results obtained by means of this analysis have yielded previously unattainable information regarding the relative rates of formation, of hydrogen abstraction, and of termination reactions of the phenoxy radicals. This information was then interpreted in terms of the energies of the HOMO of the phenols and hydroquinones as calculated by the Hückel technique. Although the log of the relative rates of reaction of the parent phenolic compound with the peroxy radical may be correlated for the simple phenol series and for the dioxyhydroquinone series, a variation of the values for the Coulomb and bond integrals failed to yield a single correlation for both series. This result was attributed to the difference in $\sigma$-bond energies of the two series. A variation of approximately 1000 in the ratio of the rate constant for the peroxy radical–phenoxy radical termination reaction to the square root of the rate constant for the bimolecular termination reaction of the phenoxy radical is observed. This variation was accounted for as arising from a decrease in the value of the bimolecular phenoxy termination rate as the phenoxy radical becomes more resonance stabilized. The smaller variation in the rate of the peroxy–phenoxy termination reaction was discussed in terms of polar stabilization of the transition for the reaction and the energy difference of the HOMO of the peroxy and phenoxy radicals. The relative rates of hydrogen abstraction from the hydroperoxide and from the hydrocarbon by the phenoxy radical were found to be relatively insensitive to the phenolic structure, indicating that both reactions are affected to the same extent by the stability of the phenoxy radical. The experimental rate data of earlier workers who utilized the tetralin–AIBN system for the study of phenol and 4-methoxyphenol have been subjected to the same analysis. From the curve fit of their data by means of eq I, the reactivity ratios for hydrogen abstraction from 9,10-dihydroanthracene and from tetralin at 60° were calculated to be 24 for the peroxy radical, 70 for the unsubstituted phenoxy radical, and larger than 200 for the 4-methoxyphenoxy radical. The significance of the high selectivity of the phenoxy radical in other chemical systems was then discussed.

Much of the present knowledge of the ease of formation and chemical reactivity of free radicals and atoms has been obtained from kinetic studies of chain reactions in which these species occur as reactive intermediates. A free-radical species of considerable interest in many areas of chemistry is the phenoxy radical.[1] A potentially useful system for the study of phenoxy radicals is the free-radical-initiated, liquid-phase oxidation of hydrocarbons containing small amounts of phenolic compounds.

In earlier work from this laboratory[2] the ideality of the experimental system consisting of the hydrocarbon, 9,10-dihydroanthracene (DHA), and the initiator, 2,2′,3,3′-tetraphenylbutane (TPB), for the kinetic study of hydrocarbon inhibition by hydroquinones and hindered phenols was demonstrated. In the present study, the kinetically complex behavior of nonhindered phenols is examined by means of this system. The work has several goals. The first is an analysis of the oxidation data by means of a generalized rate expression, avoiding the use of limiting rate expressions. The second is to use the numerical results obtained from this analysis to yield previously unattainable information regarding the relative rates of formation, of hydrogen abstraction, and of modes of destruction of phenoxy radicals. The third goal is to analyze the data of earlier workers by means of the same generalized rate expression in order to derive estimates of the reactivity ratios for peroxy and phenoxy radicals in hydrogen abstraction reactions.

## Results

**A. The General Rate Equation.** The reactions of intermediate phenoxy radicals with hydroperoxides[3,4]

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[1] *Cf.* J. H. I. Joschek and S. I. Miller, *J. Am. Chem. Soc.*, **88**, 3273 (1966), for an extensive list of references.

[2] L. R. Mahoney, *ibid.*, **88**, 3035 (1966).

[3] J. R. Thomas, *ibid.*, **85**, 2166 (1963).

[4] J. R. Thomas, *ibid.*, **86**, 4807 (1964).