Rapid Tautomeric Exchange in 4,7-Dihydroxyphenalenone

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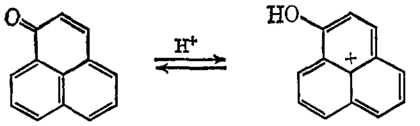
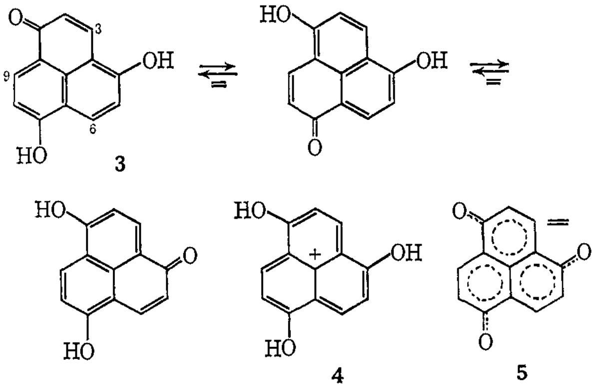
Abstract: A facile synthesis of 4,7-dihydroxyphenalenone (**3**) is described. This compound, **3**, was found to undergo rapid tautomeric exchange as evidenced by its nmr spectrum (DMSO), which consists of a simple AB system. The spectral properties of **3** and some of its derivatives are discussed.

Phenalenone (**1**) is a highly polarized ketone which dissolves reversibly in strong concentrated mineral acids to form its conjugate acid **2**.[1] Hydroxyphenalenones are amphoteric and tautomerism in suitably constituted systems often occurs; thus 7-hydroxyphenalenone yields a mixture of 7-methoxy- and 4-methoxyphenalenone when treated with methyl sulfate in alkali.[2]

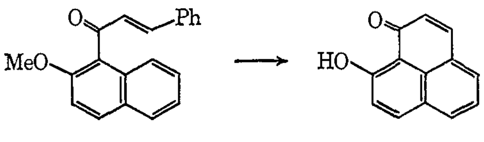


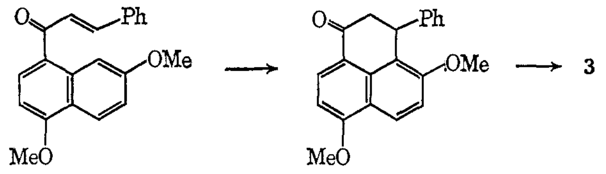
1 **2**

A key compound in the phenalenone series, and one not previously reported, is 4,7-dihydroxyphenalenone (**3**), which would be expected to form a highly stable symmetrical cation (**4**) and dianion (**5**), and would be capable of the high degree of tautomerism shown. In light of the interesting properties anticipated for **3** its synthesis was undertaken.



A facile synthesis of **3** was achieved through the utilization of a novel reaction previously described by Koelsch and Anthes.[3] These workers found that aluminum chloride catalyzed cyclization of 1-cinnamoyl-2-methoxynaphthalene was accompanied by elimination of a molecule of benzene and demethylation to produce 9-hydroxyphenalenone. In the present case, aluminum chloride catalyzed cinnamoylation of 1,6-dimethoxynaphthalene produced 1-cinnamoyl-4,7-dimethoxynaphthalene (**6**) in 80% yield. The assigned structure is consistent with the previous report that acetylation proceeds in a similar fashion.[4] Cyclization of **6** with polyphosphoric acid afforded 4,7-dimethoxy-3-phenyl-2,3-dihydrophenalenone (**7**) in 81% yield. When boiled in benzene in the presence of aluminum chloride, **7** reacted to produce **3** in 98.8% yield. Although **3** could also be obtained directly from **6**, low yields of highly impure product resulted.





6 **7**

On the nmr time scale, each of the three rings in **3**, although formally unique, are rendered identical with each other *via* tautomerism; the nmr spectrum (DMSO) of analytically pure **3** consists of a simple four-line AB system, τ_A 1.68, τ_B 3.02 (J = 9.2 Hz) (Figure 1). The protons at positions 3, 6, and 9 constitute the A component of the multiplet since they are deshielded respectively by the carbonyl conjugation, by the van der Waal's *peri* interaction of the hydroxyl group,[5] and by the anisotropy of the carbonyl. The hydroxyl protons appear as a broad peak at approximately τ −0.9.

Although the coincidence of the three AB systems formally expected for **3** may be fortuitous, it is unlikely; both its diacetate derivative and its dimethoxy derivative show three AB systems totaling 12 lines. The average of the coupling constants of the more electronically similar dimethoxy derivative (J = 8.4, 9.2, and 10.1 Hz) is also 9.2 Hz, and by comparing the nmr spectrum of **3** and its dimethoxy derivative (Figure 1) one can readily visualize the coalescence of the spectrum of the derivative into that of **3** *via* tautomerism.

Although one cannot preclude the possibility that trace amounts of acid or basic contaminants are catalyzing the tautomerism of **3**, it is to be noted that the peak widths of the AB system (0.7 cps *vs.* TMS 0.3) remain unchanged when trace amounts of triethylamine or methanesulfonic acid are added. Since **3** is amphoteric, its tautomerism might well be autocatalytic.

The ir spectrum of **3** further attests to the polarity of its carbonyl. Completely inert solvents could not

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[1] D. H. Reid, *Quart. Rev.* (London), **19**, 274 (1965).

[2] R. G. Cooke and W. Segal, *Austral. J. Chem.*, **8**, 413 (1955).

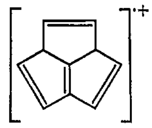
[3] C. F. Koelsch and J. A. Anthes, *J. Org. Chem.*, **6**, 558 (1941).

[4] Ng. Ph. Buu-Hoi and D. Lavit, *J. Chem. Soc.*, 1743 (1956).

[5] G. O. Dudek, *Spectrochim. Acta*, **19**, 691 (1963).

be used due to solubility factors but both a 5 and 1% solution of **3** in DMSO showed a carbonyl absorption at 1630 cm^{-1}. The OH absorption appeared as a broad peak extending between 2560 and 3300 cm^{-1}.

Mass spectral fragmentation of phenols characteristically involves loss of CO and CHO, which has been rationalized to proceed with generation of cyclopentadiene ions.[6] In the present case, three such losses take place successively to produce ultimately ions at *m/e* 128 (M − 3CO), 127 [M − (2CO + CHO)], and 126 [M − (CO + 2CHO)]. It is conceivable that the structures of this group of ions are of the triquinacene[7] type, as illustrated by the ion at *m/e* 128.



m/e 128

In ethanolic solutions, **3** is partially ionized, consequently its uv and visible spectrum was determined in acid-buffered ethanol. Save for its slightly different extinction coefficients and greater degree of fine structure, the uv and visible spectrum of **3** is quite similar to that of 4,7-dimethoxyphenalenone, thus the tautomerism of **3** is not apparent in its electronic spectrum.

The dihydroxyphenalenone **3** dissolves reversibly in dilute sodium carbonate to form a monoanion, in dilute sodium hydroxide to form the dianion **5**, and when stirred in dilute (5%) hydrochloric acid forms an insoluble hydrochloride, **4**, from which **3** can be recovered on further dilution. Spectral data for these ions are presented in the Experimental Section.

Experimental Section[8]

1-Cinnamoyl-4,5-dimethoxynaphthalene (6). Phosphorus pentachloride (80 g) was added with stirring to a cold solution of 1,6-dimethoxynaphthalene[9] (70 g) and cinnamic acid (55 g) in dry benzene (375 ml). After the reaction subsided the mixture was boiled for 5 min, cooled in ice, and aluminum chloride (52 g) was added in portions with stirring. The mixture was heated gently on a steam bath until the initial reaction subsided, and then boiled for 10 min. The mixture was hydrolyzed with iced hydrochloric acid, the benzene layer was separated, and the aqueous layer was extracted with additional benzene. The combined benzene extracts were washed successively with 10% hydrochloric acid, dilute sodium hydroxide, and water and dried ($MgSO_4$). Removal of the benzene and recrystallization from benzene–petroleum ether (bp 30–60°) afforded **6** (95 g, 80%), mp 94–97°. A highly purified sample melted at 96–98°: nmr ($CDCl_3$), τ 6.10 (s, 3), 6.03 (s, 3), 2.60 (m, 12); ir (Nujol) 1655 cm^{-1} ($\nu_{C=O}$).

Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 78.80; H, 5.73.

4,7-Dimethoxy-3-phenyl-2,3-dihydrophenalenone (7). Polyphosphoric acid (270 g) and **6** (95 g) were heated in a beaker on a steam bath with constant manual stirring until the reaction mixture became completely homogeneous (≈15 min). As much as possible of the hot viscous mass was poured over cold water (500 ml) in a beaker and additional water (300 ml) was added to the material remaining in the reaction beaker. Both beakers were heated on steam baths with stirring for 0.5 hr. The aqueous layers were decanted and extracted while still warm with benzene. Benzene was added to the beakers and boiled to dissolve some of the remaining solid. The benzene extracts were combined, and the process was repeated, beginning with the addition of water, until all of the solid dissolved. Approximately 2.5 l. of benzene was necessary. The benzene solution was filtered to remove a small amount of black tar, washed successively with water, dilute sodium hydroxide, and water and dried ($MgSO_4$). Evaporation of the benzene and recrystallization from benzene–petroleum ether afforded **7** (77.2 g, 81%), mp 171–173°; a highly purified sample melted at 173–174°; uv$_{max}$ (95% C_2H_5OH) 358 mμ (log ϵ 3.96), 323 (3.80), 311 sh (3.68), 261 sh (4.22), 237 (4.53); nmr ($CDCl_3$), τ 6.89 (m, 2), 6.18 (s, 3), 6.01 (s, 3), 4.94 (m, 1), 3.05 (m, 7), 1.80 (m, 2).

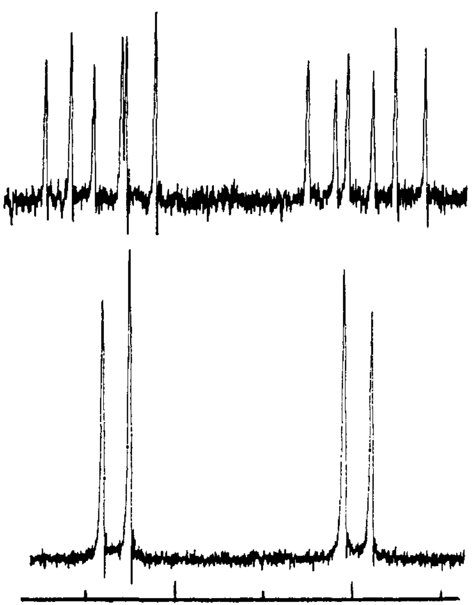


Figure 1. Nmr spectra of 4,7-dihydroxyphenalenone in DMSO (bottom) and 4,7-dimethoxyphenalenone in $CDCl_3$ (top).

Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.27; H, 5.81.

4,7-Dihydroxyphenalenone (3). Aluminum chloride (155 g) was added in portions with stirring to a solution of **7** (77.2 g) in benzene (1.10 l.) and the mixture was then boiled with stirring for 2 hr; the reaction should be monitored since a viscous mass which separates initially makes stirring difficult; on continued stirring and boiling the viscous material becomes granular and the mixture again becomes mobile. The reaction mixture was poured over iced hydrochloric acid and stirred to break up the larger pieces. The yellow-green solid was separated by filtration on a large Buchner funnel and washed thoroughly with 10% hydrochloric acid and benzene. The solid was then washed with water until the yellow-green color disappeared and the material became orange. The siltlike orange material was sucked partially dry and then dissolved in dilute sodium hydroxide and treated with charcoal. The filtered solution was washed with benzene and the product was precipitated with dilute acetic acid. The product was separated by filtration on a large Buchner funnel, washed thoroughly with water, and dried in a stream of air to constant weight. The yield of **3**, in the form of a dihydrate, was 59.5 g (98.8%). The purity of the unrecrystallized dihydrate, as determined by dehydration (100° (0.3 mm), 3 hr), was 99.2% (*Anal.* Calcd for $C_{13}H_8O_3 \cdot 2H_2O$: H_2O, 14.52. Found: H_2O, 14.40). In two other preparative runs, yields of 97.0 and 98.9% were obtained with purities of 99.8 and 99.0%, respectively. Both **3** and its dihydrate decompose without melting between 330 and 375°: mass spectrum (50 eV), *m/e* 212 (relative intensity 100) [M$^+$], 184 (79) [M − CO], 183 (8) [M − CHO], 156 (11) [M − 2CO], 155 (30) [M − (CO + CHO)], 128 (29) [M − 3CO], 127 (22) [M − (2CO + CHO)], 126 (15) [M − (CO + 2CHO)], 92 (22); visible and uv$_{max}$ (95% C_2H_5OH, 1.2 × 10^{-4} *N* $HClO_4$), 454

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(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, pp 115–118.

(7) R. B. Woodward, T. Fukunaga, and R. C. Kelly, *J. Amer. Chem. Soc.*, **86**, 3162 (1964).

(8) Visible and uv spectra were obtained on a Cary 11 spectrophotometer. Infrared spectra were obtained on a Perkin-Elmer 257 spectrophotometer and nmr spectra were obtained on a Varian Associates A-60 spectrometer. The mass spectrum was obtained on a Hitachi Perkin-Elmer RMU-6D spectrometer. Elemental analyses were performed by M-H-W Laboratories, Garden City, Mich. Melting points were determined on a calibrated hot stage.

(9) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

mμ (log ε 4.24), 446 sh (4.12), 429 (4.29), 406 (4.07), 366 (4.02), 270 (4.47).

Anal. Calcd for $C_{13}H_8O_3$: C, 73.58; H, 3.80. Found: C, 73.68; H, 3.62.

Compound **3** is insoluble in water and most organic solvents; it can be recrystallized from acetic acid but large volumes (4000/1) are needed. The hydrochloride of **3**, 1,4,7-trihydroxyphenalenium chloride, was obtained by stirring a mixture of **3** (0.686 g) and 5% hydrochloric acid (37 ml) for 1 day at room temperature, followed by filtration and drying (100° (0.3 mm), 12 hr). The resulting salt (0.798 g, 99%) decomposed without melting between 300 and 350° and regenerated **3** when stirred in water for 3 days at room temperature.

Visible and ultraviolet maxima for the various ions of **3** are as follows: monoanion (95% C_2H_5OH saturated with Na_2CO_3) 478 mμ (log ε 4.35), 452 (4.26), 380 (4.01), 368 sh (3.98), 280 (4.41), 236 (4.13); dianion **5** (95% C_2H_5OH, 0.02 *N* NaOH) 457 (4.41), 432 (4.43), 277 (4.41), 259 (4.39); cation **4** (95% C_2H_5OH containing 5% CH_3SO_3H) *424* (4.51), *412* sh (4.42), *245* (4.37).

4,7-Dimethoxyphenalenone (from **3** and methyl sulfate in aqueous alkali) showed the following characteristics: mp 176–178° (benzene–petroleum ether); visible and uv_{max} (95% C_2H_5OH) 455 mμ (log ε 4.06), 432 (4.23), 410 (4.10), 366 (4.00), 270 (4.51); nmr ($CDCl_3$) τ 5.95 (s, 3), 5.91 (s, 3), 3.37 (d, J = 10.1 Hz, 1), 3.08 (d, J = 8.4, 1), 2.86 (d, J = 9.2, 1), 1.86 (d, J = 10.1, 1), 1.68 (d, J = 9.2, 1), 1.41 (d, J = 8.4, 1); ir ($CDCl_3$) 1635 cm^{-1} ($\nu_{C=O}$).

Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.05; H, 5.07.

4,7-Diacetoxyphenalenone (from **3** and acetic anhydride containing a catalytic amount of sulfuric acid) showed the following characteristics: mp 180–182° (benzene); uv_{max} (95% C_2H_5OH) 380 mμ (log ε 4.07), 323 (3.71), 257 (4.45); nmr ($CDCl_3$), τ 7.55 (s, 3), 7.52 (s, 3), 3.37 (d, J = 9.9 Hz, 1), 2.72 (d, J = 9.1, 1), 2.55 (d, J = 8.1, 1), 2.22 (d, J = 9.9, 1), 2.00 (d, J = 9.1, 1), 1.47 (d, J = 8.1, 1); ir ($CHCl_3$) 1646 and 1777 cm^{-1} ($\nu_{C=O}$).

Anal. Calcd for $C_{17}H_{12}O_5$: C, 68.91; H, 4.08. Found: C, 69.30; H, 4.30.

Acknowledgment. The author is indebted to Professor Charles F. Koelsch for useful discussions related to this research and to the Esso Education Foundation for financial support.

Formation of Azo Radical Anions and Their Vinylogs[1]

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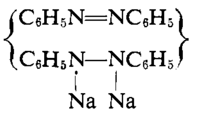
Abstract: Several types of reactions leading to azo-type radical anions have been investigated. Disproportion between RN=NR and RNHNHR can be readily observed in basic solutions for R = C_6H_5 or $CO_2C_2H_5$ and for the phenazine–dihydrophenazine, 2,3-diphenylquinoxaline–dihydro-2,3-diphenylquinoxaline, and diphenyltetrazine–dihydrodiphenyltetrazine systems. Oxidation–reduction of the type, $2\pi\text{-}CH_3 + 2\pi\text{-}CH_2^- \rightarrow 2\pi\text{-}CH_3\cdot^- + \pi\text{-}CH_2CH_2\text{-}\pi$, can be observed for 3,6-dimethyltetrazine, 3-benzyllumiflavin, and 1,4,5,8-bis(trimethylene)pyridazino[4,5-*d*]pyridazine (**3**) but not for the simple methylpyrazines. A wide variety of unsaturated compounds can be reduced to the radical anions by the propiophenone enolate anion. These compounds include azobenzene and ring-substituted derivatives, benzo[*c*]cinnaline, tetrazines, phenazine, 2,3-diphenylquinoxaline, and benzoxadiazole. Reaction with traces of oxygen in basic dimethyl sulfoxide solutions forms the radical anions from hydrazobenzene, dihydrophenazine, dihydro-2,3-diphenylquinoxaline, *o*- and *p*-phenylenediamines, benzidine, and N,N′-diphenylbenzidine.

Schlenk in his classical studies of the addition of sodium to unsaturated compounds recognized the existence of a 1:1 adduct with azobenzene.[3] However, he formulated this adduct as **1** rather than the "ketyl-type" radical anion **2**. The intermediacy of



$$\left\{\begin{matrix} C_6H_5N{=}NC_6H_5 \\ C_6H_5\underset{\displaystyle Na}{\underset{|}{N}}{-}\underset{\displaystyle Na}{\underset{|}{N}}C_6H_5 \end{matrix}\right\}$$

1

$$[C_6H_5N \doteq NC_6H_5]^-Na^+$$

2

radical anions could be inferred from later work that showed that the "di-Grignard" reagent of hydrazobenzene readily reduced benzil to benzoin[4] and that azobenzene oxidized many organometallic compounds.[5] For example, azobenzene converts phenyllithium or phenylmagnesium bromide to biphenyl in good yield.[5] The later process is consistent with reaction 1. Wittig

$$C_6H_5M + C_6H_5N{=}NC_6H_5 \longrightarrow C_6H_5\cdot + \mathbf{2} \qquad (1)$$

described a crystalline salt of a radical anion prepared by the reaction of azobenzene with the dilithium salt of hydrazobenzene,[6] although it is now known that in solution and in the presence of lithium cations that the equilibruim of eq 2 lies far to the left.[7] Wittig also

$$C_6H_5N{=}NC_6H_5 + [C_6H_5\underset{-}{\overset{-}{N}}{-}\underset{-}{\overset{-}{N}}C_6H_5]^{2-} \rightleftarrows 2[C_6H_5N{=}NC_6H_5]\cdot^- \qquad (2)$$

showed that the solid reaction product from benzo[*c*]cinnoline and its disodium salt was extensively paramagnetic (eq 3).[8]

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(1) Electron-Transfer Reactions. Part IX. This work was supported by grants from the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society.

(2) National Institutes of Health Predoctoral Fellow, 1965–1966.

(3) W. Schlenk, J. Appenrodt, A. Michael, and A. Thal, *Ber.*, **47**, 473 (1914).

(4) W. E. Bachman, *J. Am. Chem. Soc.*, **53**, 2758 (1931).

(5) H. Gilman and J. C. Bailie, *J. Org. Chem.*, **2**, 84 (1937), and references cited therein.

(6) G. Wittig, *Angew. Chem.*, **53**, 241 (1940).

(7) G. N. Aylward, J. L. Garnett, and J. H. Sharp, *Chem. Commun.*, 173 (1966).

(8) G. Wittig and A. Schumacher, *Ber.*, **88**, 234 (1955).