Tetrahedron Letters No. 28, pp. 1993-1997, 1963. Pergamon Press Ltd.
Printed in Great Britain.

NUCLEAR MAGNETIC RESONANCE STUDIES OF TAUTOMERISM: LOSS OF AROMATICITY IN "LEUCO"-HYDROXY AND AMINO ANTHRAQUINONES

Stanley M. Bloom

Research Division, Polaroid Corporation, Cambridge 39, Massachusetts

Robert F. Hutton

Graduate Dept. of Biochemistry, Brandeis University

Waltham, Massachusetts

(Received 21 August 1963; in revised form 24 September 1963)

We should like to describe the results of our proton magnetic resonance study of keto-enol and enol-imine equilibria[1] occurring in the dye intermediates, leuco-quinizarin and leuco-1,4-dibenzylamino-anthraquinone. Our results show that, in solution, leuco-quinizarin (I or II or III) exists entirely as the non-aromatic tautomer (I), and leuco-1,4-dibenzylamino-anthraquinone (VII or VIII or IX) exists entirely as the non-aromatic tautomer (VII). In contrast, the reduction product of 1,4-dimethoxy-anthraquinone exists entirely as the fully aromatic tautomer, 1,4-dimethoxy-9,10-dihydroxy-anthracene (IV). The structures of these compounds have been in dispute for years.[2]

Leuco-quinizarin, obtained from quinizarin (1,4-dihydroxy-anthraquinone) by reduction with sodium dithionite or zinc and acetic acid, was first assigned structure (I) by Zahn and Ochwat[3] who were able to obtain the leuco compound from the condensation of 1,4-dihydroxynaphthalene with succinic anhydride. H. C. St. Flett[4], more recently, however, in a detailed infrared spectral

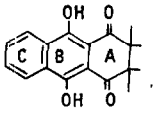
1. G. O. Dudek and R. H. Holm, J. Amer. Chem. Soc., 83, 2099 (1961) and G. O. Dudek and R. H. Holm, ibid 83, 3914 (1961) described earlier their work on the keto-enol equilibria in the 2:1 condensation products of acetyl acetone and various diamines and on the Schiff bases of ortho-hydroxy-naphthones.

2. See H. A. Lubs, "The Chemistry of Synthetic Dyes and Pigments", Reinhold Publishing Corp., N. Y. (1955), p. 373.

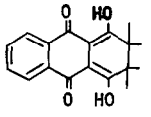
3. K. Zahn and P. Ochwat, Ann. 462, 72 (1928).

4. H. C. St. Flett, J. Chem. Soc. (1948), 1441.

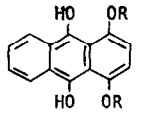
study could not differentiate between the tautomers (I) and (II) although a band at 2950cm^{-1} was presented as evidence for the existence of methylene groups. In Table I we have summarized data sufficient to demonstrate unequivocally the loss of aromaticity in one ring and to allow a definite choice between (I) and (II). Leuco-quinizarin lacks the singlet aromatic resonance



(I)



(II)



(III) (R = H)
(IV) (R = CH_3)

V (R = OH)
VI (R = H)

(7.27 p.p.m.) of the "A" ring of quinizarin. Present, however, is a new sharp singlet resonance at 3.03 p.p.m. (methylene), which is absent in quinizarin and which lies at the same frequency as that of the methylene groups of 1,4-dioxo-5,8-dihydroxy-2,3-dihydro-naphthalene (leuco-naphthazarin) (V) and 1,4-dioxo-2,3-dihydro-naphthalene (VI).[5] Under our conditions (5% w/v solution in $CDCl_3$) the methyl group of acetylacetone adjacent to the enolized carbonyl is found about 0.20 p.p.m. removed from the methyl group adjacent to the non-enolized carbonyl[6]; and, similarly, the two methylene resonances of dimedone (5,5-dimethyl-1,3-cyclohexanedione) differ by 0.26 p.p.m. Accordingly, the chemical shift of the methylene group of (I) would be expected to differ from the methylene group of (II) by a comparable and easily distinguished amount.[7] Comparison of the chemical shifts of the methylene groups of (V) and (VI) with that of leuco-quinizarin permits the assignment of leuco-quinizarin to (I).[8]

5. R. H. Thomson, J. Chem. Soc. (1950) 1737 reinvestigated the work of A. Madinaveitia and E. Olay, Anal. Fis Quim, 31, 134 (1931) and first proposed structure (VI) for the isomer obtained from 1,4-dihydroxynaphthalen on heating in vacuo. The data in Table I confirms Thomson's assignment.

6. H. S. Jarrett, M. S. Sadler, and J. N. Shoolery, J. Chem. Phys., 21 2092 (1953), L. W. Reeves, Can. J. Chem., 35, 1351 (1957), and L. W. Reeves and W. G. Schneider, ibid., 36, 793 (1958), found ca. 0.17 p.p.m. separation in neat acetylacetone.

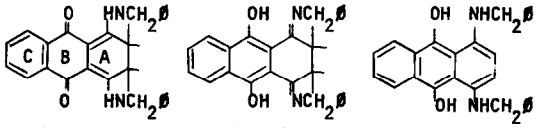
7. In dilute chloroform solution the methyl protons of acetophenone and those of ortho-hydroxy-acetophenone lie within 0.02 p.p.m.

8. The peak areas have been accurately determined and are in precise agreement with the assignments of structure.

Table 1[a]

Compound[b]	Aromatic (Ring "A")	Aromatic (Ring "B" or "C")	Methylene	Methylene of Benzyl	Phenyl of Benzyl	Hydrogen Bonded Protons
Quinizarin	7.27[s]	8.05[c] ("C")	-	-	-	12.9[s]
Leuco-Quinizarin	-	8.03[c] ("C")	3.03[s]	-	-	13.5[s]
1,4-Dioxo-5,8-dihydroxy-2,3-dihydronaphthalene (V)	-	7.23[c] ("B")	3.05[s]	-	-	12.0[s]
1,4-Dioxo-2,3-dihydronaphthalene (VI)	-	7.90[c] ("B")	3.08[s]	-	-	-
1,4-Dibenzylaminoanthraquinone	7.00[s]	7.98[c]	-	4.57(J=5.9±0.1c/s)[d]	7.30[s]	11.0(J=6.0±0.3c/s)[t]
Leuco-1,4-dibenzylaminoanthraquinone	-	8.02[c]	2.68[s]	4.61(J=5.8±0.1c/s)[d]	7.30[s]	14.4(J=6.0±0.3c/s)[t]
1,4-dimethoxy-anthraquinone	7.33[s]	7.93[c]	-[e]	-	-	-
Leuco-1,4-dimethoxyanthraquinone (IV)	6.33[s]	7.93[c]	-[f]	-	-	9.83[s]

a. Proton resonance data are reported in p.p.m. as displacements to lower field from internal tetramethylsilane. A 60 Mcs radio frequency spectrometer was used.
b. The compounds were examined at a concentration of 5% by weight or saturation in $CDCl_3$ containing ~1% dissolved tetramethylsilane. All solutions were sealed at ca. 0.1 mm Hg pressure and examined at ca. 27°. Essentially the same data were obtained at higher concentrations and in dimethyl sulfoxide-d_6 as solvent.
c. The geometric center of symmetrical multiplet is reported.
d. A doublet
e. The methoxyl resonance appears at 3.97 p.p.m.
f. The methoxyl resonance appears at 4.00 p.p.m.
t. A triplet
s. A singlet



(VII) (VIII) (IX)

Leuco-1,4-dibenzylamino-anthraquinone (VII or VIII or IX) served as a model for the leuco-1,4-dialkylamino-anthraquinones which are intermediates in the manufacture of dyes of industrial importance.[9] The data for the dye, 1,4-dibenzylamino-anthraquinone, and the leuco-compound derived from it by reduction, appear in Table I. Leuco-1,4-dibenzylamino-anthraquinone lacks the singlet aromatic resonance (7.00 p.p.m.) of the "A" ring of 1,4-dibenzylamino-anthraquinone. It possesses, however, a new sharp singlet resonance at 2.68 p.p.m. (methylene), which is absent in 1,4-dibenzylamino-anthraquinone. This establishes the loss of aromaticity in the "A" ring and excludes the tautomer, 1,4-dibenzylamino-9,10-dihydroxy-anthracene (IX). The spectra of both the dye and the leuco compound are marked by a splitting of the resonance of the methylene protons of the benzyl groups into a doublet ($J = \sim 5.8$ c/s) and the splitting of the resonance of the hydrogen-bonded proton (low field) into a triplet ($J = 6.0 \pm 0.3$ c/s) due to the adjacent CH_2. Substitution of a deuteron for the hydrogen-bonded proton, by precipitation of these compounds from acetone with D_2O, resulted in elimination of the resonance of the hydrogen-bonded proton, and the splitting of the benzyl methylene resonance. These observations establish the position of the hydrogen-bonded proton on nitrogen.[10]

9. See J. Houben, "Das Anthracene und die Anthrachinone", Georg Thieme, Leipzig (1929) and reference 2.

10. G. C. Dudek and R. H. Holm, J. Amer. Chem. Soc., 84, 2691 (1962).

The novelty of our findings centers on the absence of the aromatic isomers, 1,4,9,10-tetrahydroxyanthracene (III) in solutions of leuco-quinizarin and 1,4-dibenzylamino-9,10-dihydroxy-anthracene (IX) in solutions of leuco-1,4-dibenzylamino-anthraquinone. We attribute the stability of the non-aromatic isomers to the strong hydrogen bond between carbonyl and hydroxyl in (I), and the similarly strong hydrogen bond between imino NH and carbonyl oxygen in (VII). The importance of this hydrogen bonding is evidenced by our demonstration (Table I) that the stable product resulting from reduction of 1,4-dimethoxyanthraquinone with zinc and acetic acid is the fully aromatic 1,4-dimethoxy-9,10-dihydroxyanthracene (IV), not the incorrectly assigned[3], dearomatized tautomer, 1,4-dimethoxy-2,3-dihydro-anthraquinone. The absence of any detectable quantities of (II) in solution may be attributed to the stability of the naphthalene nucleus in (I). The lack of C=N in compounds offering alternative structure has been discussed by Dudek and Holm[10] and provides an explanation for the absence of tautomer (VIII). The compounds examined by Dudek and Holm, however, precluded tautomerization to totally aromatic isomers.

These and other points relating to the stability of the non-aromatic tautomers related to (I) and (VII) will be treated in detail at a later date.[11,12]

11. We have enjoyed thoughtful discussions with Dr. M. S. Simon of Polaroid Corporation, and Dr. G. O. Dudek of Harvard University.

12. R. F. H. supported by grant CY-3611 from the National Institutes of Health, Present Address: Department of Chemistry, Brandeis University. This is publication No. 236 of the Graduate Department of Biochemistry.