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Hydration of *p*-Nitrobenzaldehyde[1a]

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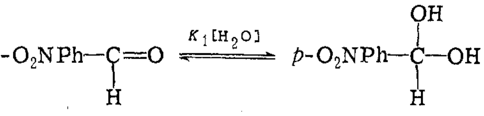
Although measurable hydration in neutral solution has been observed by Laviron, Troncin, and Tirouflet[2] for *o*-nitrobenzaldehyde and by Greenzaid[3] for 4-trimethylammoniobenzaldehyde iodide, it has been assumed[3,4] that the equilibrium constant, K_1, for this hydration reaction (eq 1)



$$p\text{-}O_2NPh{-}\underset{\displaystyle H}{C}{=}O \xrightleftharpoons{K_1[H_2O]} p\text{-}O_2NPh{-}\overset{\displaystyle OH}{\underset{\displaystyle H}{C}}{-}OH \qquad (1)$$

of *p*-nitrobenzaldehyde is negligibly small, and to the author's knowledge no experimental evidence supporting a significant extent of hydration of this aldehyde in neutral or weakly acidic aqueous solution has previously been reported. Several recent observations in this laboratory indicate that the value of $K_1[H_2O]$, although small, is measurable and has an approximate value of 0.25 ± 0.1 at 25°, corresponding to approximately 20% hydration of the aldehyde. This finding means that a small but significant correction of observed rate and equilibrium constants for reactions of *p*-nitrobenzaldehyde is required in kinetic studies, especially when this aldehyde is compared with other, less significantly hydrated, substituted benzaldehydes in structure–reactivity correlations.

The following three experimental observations provide strong qualitative evidence that *p*-nitrobenzaldehyde is significantly hydrated in neutral aqueous solution, and are consistent with an approximate value for $K_1[H_2O]$ of 0.25 ± 0.1.

(1) Upon addition of a sample of *p*-nitrobenzaldehyde in acetonitrile solution to 0.1 *M* aqueous potassium acetate–acetic acid buffer, pH 4.6, a time-dependent absorbance change at 268 nm with a pseudo-first-order rate constant of approximately 5×10^{-2} sec^{-1} is observed (curve A, Figure 1). This result is most easily accounted for by the establishment of an equilibrium between the unhydrated and hydrated forms of the aldehyde. If an estimate is made for the absorbance of the hydrate at 268 nm, based on the absorbance of the corresponding bisulfite addition product, the magnitude of the observed absorbance change corresponds to 17 ± 1% hydration of the aldehyde at equilibrium.

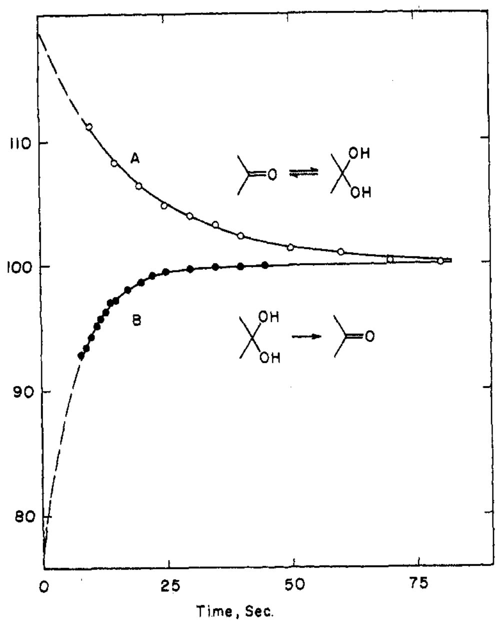
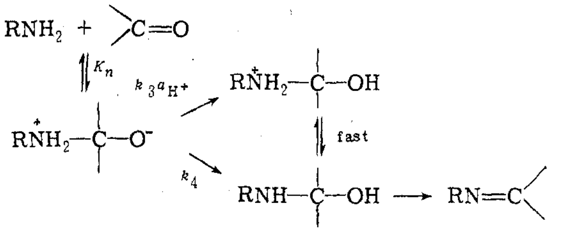


Figure 1. Time-dependent absorbance changes observed upon addition of *p*-nitrobenzaldehyde in acetonitrile solution to 0.1 *M* aqueous acetic acid–potassium acetate buffer, pH 4.6 (curve A), and *p*-nitrobenzaldehyde in aqueous solution to 0.5 *M* aqueous semicarbazide buffer, pH 2.8 (curve B). The spectral changes of curves A and B were followed at 268 and 320 nm, respectively, and corresponded to absolute absorbance changes of 0.080 (curve A) and 0.38 (curve B) for a total concentration of aldehyde in the reaction mixtures of 10^{-4} *M*. The broken portions of the curves represent extrapolated values determined from semilogarithmic plots of $(A_{obsd} - A_{final})$ or $(A_{final} - A_{obsd})$ against time.

(2) Addition of an *aqueous* solution of *p*-nitrobenzaldehyde to semicarbazide buffer, 88% acid, pH 2.8, causes an immediate burst of absorbance at 320 nm, followed by a measurably slow increase in absorbance to a final stable value (curve B, Figure 1). Under these conditions, the rate-determining step for semicarbazone formation is the proton transfer step, k_3 and k_4, in the formation of the cationic or neutral tetrahedral intermediate (eq 2),[5] and hence pre-



(2)

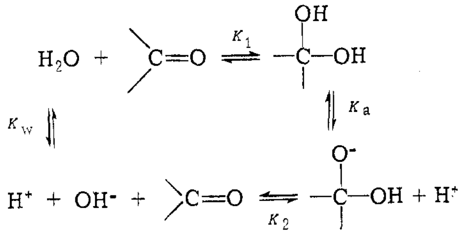
equilibrium accumulation of this intermediate is not responsible for the observed biphasic kinetics. The second phase that is observed in the reaction between *p*-nitrobenzaldehyde and 0.5 *M* (total) semicarbazide at pH 2.8 has a pseudo-first-order rate constant of 0.15 sec^{-1}, approximately 15 times slower than the pseudo-first-order rate constant, $K_n(k_3a_{H^+}+k_4)$ $[H_2NC(O)NHNH_2]$, of 2.3 sec^{-1} for buffer-independent semicarbazone formation under these conditions calculated from published rate constants.[5] The second phase of the reaction is less than first order in semicarbazide, as indicated by the fact that the pseudo-first-order rate constants for this process in the presence of

0.2 and 0.4 *M* total semicarbazide differ only by approximately 20%. This biphasic behavior is most easily explained[6] if the initial burst represents very rapid conversion of the free aldehyde to the semicarbazone, whereas the second phase of the reaction involves rate-limiting conversion of the fraction present as the hydrate to the free aldehyde. An extent of hydration of 23 ± 2% is calculated from the magnitude of the absorbance change corresponding to the second phase of the reaction.

(3) The 90-MHz Fourier transform NMR spectrum of a saturated solution of *p*-nitrobenzaldehyde in 25% CD_3CN–75% D_2O shows small peaks at δ 6.06 and 7.65 ppm that are assigned to the α proton of the hydrate and to the aromatic protons of the hydrate,[3] respectively. The ratio of the area of the peak at δ 6.06 to that of the peak corresponding to the aldehydic proton at 10.0 ppm is approximately 1.0:7.6 and the ratio of the areas of peaks for the aromatic protons in the hydrated (δ 7.65) and unhydrated (δ 8.2) aldehydes is approximately 1.0:8.2. This finding provides qualitative confirmatory evidence for the hydration of the aldehyde, and the value of approximately 11–12% hydration in D_2O containing 25% acetonitrile is consistent with the slightly greater extent of hydration observed in completely aqueous solutions.

These results for *p*-nitrobenzaldehyde are comparable with the observed value[2] of 0.43 for $K_1[H_2O]$ for *o*-nitrobenzaldehyde and with a calculated value of 0.08 for *m*-nitrobenzaldehyde.[3]

The value of 0.25 ± 0.1 for $K_1[H_2O]$ for *p*-nitrobenzaldehyde is consistent with the known equilibrium constant for formation of the anionic hydrate from *p*-nitrobenzaldehyde and hydroxide ion[3,4] and a value for the pK_a of the hydrate estimated from structure–reactivity correlations. From the interrelationship[3] of the equilibria shown in eq 3,



(3)

a pK_a value of 12.1 ± 0.2 for the hydrate may be calculated from $K_1[H_2O] = 0.25 \pm 0.10$ and $K_2 = 18 \pm 3\ M^{-1}$, obtained from $K_1[H_2O]$ and the observed[3,4,7] equilibrium constant of 14.8 ± 1.5 M^{-1} for the addition of hydroxide ion to hydrated plus unhydrated *p*-nitrobenzaldehyde in aqueous solution at 25°. A pK_a of 12.1 ± 0.2 is consistent with a value of pK_a = 12.3 estimated as follows. From the observed pK_a of 9.18 for 1,1-dihydroxy-1-(*m*-nitrophenyl)-2,2,2-trifluoroethane[8] and a ρ value of 1.11, the pK_a of the corresponding *p*-nitro compound is estimated to be 9.08. Substitution of the CF_3 group by CH_3 should give a ΔpK_a of 3.5 if ρ_I for ionization of the hydroxyl group[9] is taken as 8.4 and σ_I[10] for CF_3 is 0.42. This gives pK_a = 12.58 for 1,1-dihydroxy-1-(*p*-nitrophenyl)ethane, and substitution of H for CH_3 is expected to decrease the pK by ~0.3 unit,[9] giving pK = 12.28 for *p*-nitrobenzaldehyde hydrate.

The observed equilibrium constant of 0.25 ± 0.1 for hydration of *p*-nitrobenzaldehyde is also consistent with a predicted value of 0.18 ± 0.04 from the structure–reactivity correlation of Sander and Jencks[6] for addition of nucleophiles to aromatic aldehydes. Based on γ values of 1.13, 0.46, and −3.58 for methoxyamine,[11] semicarbazide, and water, respectively, and equilibrium constants of 40 and 125 M^{-1} for the addition of semicarbazide[13] and methoxyamine[12] to *p*-nitrobenzaldehyde, log $K_1 = -2.5 \pm 0.1$, corresponding to $K_1[H_2O] = 0.18 \pm 0.04$, was calculated from the relationship $\Delta \log K_{eq} = \Delta\gamma$.

Experimental Section

Semicarbazide hydrochloride was recrystallized and *p*-nitrobenzaldehyde was recrystallized or sublimed. Glass-distilled water was used in all reactions. Kinetics were followed at 25° and ionic strength 1.0, maintained with potassium chloride. Formation of the hydrated aldehyde was followed at 268 nm using a Cary 118 recording spectrophotometer, after addition of 50 μl of a $5 \times 10^{-3}\ M$ solution of *p*-nitrobenzaldehyde in acetonitrile to 2.5 ml of aqueous acetic acid–potassium acetate buffer solution. The reaction follows pseudo-first-order kinetics, and the absorbance change due to hydration of the aldehyde was determined from the intercept at time zero of a linear semilogarithmic plot of $(A_{final} - A_{obsd})$ against time. The absorbance expected for the fully hydrated aldehyde was estimated using the sulfite addition product as a model: after completion of the hydration reaction, 30 μl of Na_2SO_3–$NaHSO_3$ (1:1) solution, 1 *M* in SO_3^{2-} plus HSO_2^-, was added to the reaction mixture and the absorbance was measured. A correction of approximately 4% was applied for the absorbance of the sulfite–bisulfite solution alone. ΔA_{hyd} for complete hydration of the aldehyde was taken as $(A_0 - A_{SO_3^{2-}})$ where A_0 is the extrapolated value for the absorbance at zero time and $A_{SO_3^{2-}}$ is the absorbance of the sulfite addition product. The fraction of aldehyde converted to the hydrate, α, is then given by $\Delta A_{obsd}/\Delta A_{hyd}$, where ΔA_{obsd} is the observed time-dependent absorbance change. The equilibrium constant, $K_1[H_2O]$, for hydration is $\alpha/(1 - \alpha)$. For a typical experiment under these conditions using a concentration of approximately $10^{-4}\ M$ total aldehyde, observed values of A_0, A_{final}, and $A_{SO_3^{2-}}$ were 1.415, 1.335, and 0.903, respectively.

Time-dependent dehydration of the hydrated aldehyde was followed by measurement of the change in absorbance at 320 nm upon addition of 50 μl of a $(2.5\text{–}5) \times 10^{-3}\ M$ aqueous solution of *p*-nitrobenzaldehyde to 2.5 ml of semicarbazide buffer solution, 88% acid, ionic strength 1.0. The total absorbance change, ΔA_{tot}, for semicarbazone formation from hydrated plus unhydrated aldehyde was obtained by correction of the final absorbance value for the small (~11%) absorbance of *p*-nitrobenzaldehyde at 320 nm. The observed time-dependent absorbance change, ΔA_{obsd}, due to slow conversion of the hydrate to the aldehyde, was determined from the intercept at time zero of a semilogarithmic plot of $(A_{final} - A_{obsd})$ beginning 8–10 sec after mixing. The fraction, α, of aldehyde present as the hydrate in the initial solution is then given by $\Delta A_{obsd}/\Delta A_{tot}$. The *time-dependent* absorbance change observed upon mixing an acetonitrile solution of *p*-nitrobenzaldehyde with the semicarbazide buffer was negligible, the final absorbance value being reached too rapidly to measure under our conditions, as expected for a solution in which no hydrated aldehyde is present at time zero.

Analogous experiments using a Gilford Model 2000 spectrophotometer equipped with a rapid-mixing syringe,[14] and reaction mixtures containing 12% acetonitrile, gave results that were consistent with those described above.

The 90-MHz Fourier transform NMR spectrum of a saturated solution of *p*-nitrobenzaldehyde in 75% D_2O–25% acetonitrile (by weight) was determined using a Bruker WH90 Fourier transform NMR spectrometer. Chemical shifts relative to tetramethylsilane were determined from the observed chemical shifts relative to acetonitrile (δ 2.0 ppm).

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Registry No.—*p*-Nitrobenzaldehyde, 555-16-8; *p*-nitrotoluene-α,α-diol, 55649-04-2.

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Electrophilic Substitution in 1,8-Di-*tert*-butylnaphthalenes

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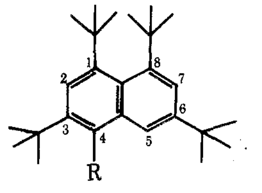
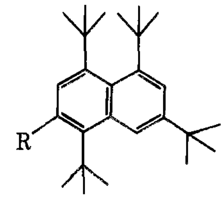
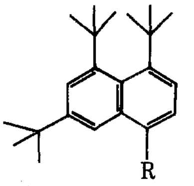


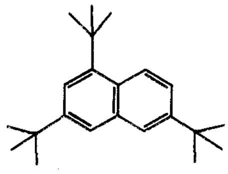
1, R = H
2, R = NO_2
3, R = Br



4, R = Br
9, R = H



5, R = H
6, R = Br
7, R = I



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In previous reports from our laboratories on 1,8-di-*tert*-butylnaphthalenes, the focus has been primarily on synthetic and spectroscopic studies.[2] This note describes our results with probing the strained system via electrophilic aromatic substitution.

Nitration of 1,3,6,8-tetra-*tert*-butylnaphthalene (**1**) was accomplished using acetyl nitrate at −40°, followed by warming to 25°, conditions used previously for substitution on azulene, (18)annulene, and 1,3,6,8-tetramethylnaphthalene.[3] NMR and TLC of the crude reaction mixture revealed the presence of a single product which after purification yielded 4-nitro-1,3,6,8-tetra-*tert*-butylnaphthalene (**2**) in 54% yield. The structural assignment was based on its NMR spectrum (Table I), particularly the shielded peri proton at δ 7.04. This value is shifted upfield by 0.17 ppm compared to the parent compound **1**, expected since the nitro group is rotated so that its shielding cone interacts strongly with the peri H. Similar results have been obtained with methylnitronaphthalenes by Wells.[4] Our reaction conditions and results may be compared to those for *o*-di-*tert*-butylbenzene which is nitrated using concentrated nitric acid in acetic acid to afford products with no nitro insertion ortho to *tert*-butyl.[5]

Bromination of **1** was effected in good yield with dioxane dibromide, a reagent normally used for bromination of phenols.[6] The NMR of the product (Table I) is consistent with both a rearranged structure **4** and the direct product **3**. In particular, the *tert*-butyl chemical shift of δ 1.64 is interpretable as an uncrowded peri-*tert*-butyl which is complementary to a neighboring peri H at δ 8.07. A reductive dehalogenation with butyllithium was performed on **3** to yield **1**, confirming lack of rearrangement in the bromination. Thus, the chemical shifts are due to the deshielding effects of the bromine. These bromination conditions were also applied to 1,3,8-tri-*tert*-butylnaphthalene (**5**) to afford 5-bromo-1,3,8-tri-*tert*-butylnaphthalene (**6**). The lesser deshielding of the peri proton by bromine compared to that in **3** can be explained by the lack of buttressing of the bromine by the *tert*-butyl.[7] The photochemical behavior of **6** has been reported.[2] These brominations also may be compared to those of *o*-di-*tert*-butylbenzene, which requires $FeBr_3$ catalysis for rapid reaction and which results in some dealkylation as well as substitution.[5] Lastly, 5-iodo-1,3,8-tri-*tert*-butylnaphthalene (**7**) was prepared by treating **5** with iodine and yellow mercuric oxide, a combination of reagents previously used for iodination of thiophene.[8]

These results, i.e., regiospecific attack at the 4 position, are consistent with our previous study of the acid sensitivity of peri *tert*-butylnaphthalenes which demonstrated greatest reactivity at the 4 position. From the NMR data accumulated in this series, we are now able to assign α and β protons in the entire series with more certainty. Using the data obtained in unstrained naphthalene **8** as a standard, we can conclude that there is, in fact, a decrease in ring current in the naphthalenes which are strained and thus distorted from planarity. This decrease in ring current appears to result in a shielding of approximately 0.3 ppm and is consistent with the distortion effects observed with other spectroscopic techniques applied to the naphthalenes and the similar NMR observation made with 1,2,3,5-tetra-*tert*-butylbenzene.[9]

Experimental Section[10]

4-Nitro-1,3,6,8-tetra-*tert*-butylnaphthalene (**2**). A solution of 30 mg (0.08 mmol) of naphthalene **1**[2] in 2 ml of acetic anhydride was placed in a Dry Ice–ethanol bath and allowed to stir until it reached −40°. To this solution was added acetyl nitrate (2 ml over a 10-min period) prepared as follows: 160 mg of $Cu(NO_3)_2$ was

Table I
NMR Data for *tert*-Butylnaphthalenes. Chemical Shift and *J* (Hertz), CCl_4

Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
9[a]	1.22	7.43 (2)	1.42	7.90 (2)	1.57	7.28 (8)	7.10 (8)	1.24
8[a]	1.65	7.78 (2)	1.43	7.57 (2)	7.57 (2)	1.43	7.48 (2, 9.2)	8.34 (9.2)
1[a]	1.30	7.48 (2)	1.40	7.22 (2)	7.22 (2)	1.40	7.48 (2)	1.30
2	1.33	7.62	1.48	NO_2	7.04 (2)	1.42	7.65 (2)	1.33
3	1.30	7.59	1.64	Br	8.07 (2)	1.45	7.59 (2)	1.28
6	1.30	7.63 (2.5)	1.47	7.79 (2.5)	Br	7.48 (8)	7.32 (8)	1.32
7	1.28	7.61 (2)	1.45	7.66 (2)	I	7.80 (8)	7.19 (8)	1.28

[a] Data taken from ref 2a.