Notes

A Novel Method for Direct Measurement of the pK_a's of Weakly Acidic Hydrocarbons

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In the construction of thermodynamic acidity scales for hydrocarbons, several important approaches have been used.[1-5] One of these approaches involves using kinetic acidities, a thermodynamic pK_a of a standard compound, and the Brønsted relationship.[1,3] These pK_a's are often measured in different solvents at different temperatures or under conditions where the ionic strengths or types of bases are vastly different. The importance of these differences is emphasized by comparing the ΔpK_a of picric acid vs. benzoic acid as a function of solvent. In water the pK_a difference is 3.5; in methanol, 5.3; in DMF, 9.0; and in Me_2SO, 11.9. Extreme or even subtle changes in solution conditions can greatly affect the pK_a's calculated for weakly acidic hydrocarbons (p$K_a \sim$ 18–30). Other methods for the determination of carbon acidities have been reported recently by Jones,[6] Breslow,[7] and Bordwell.[8]

We wish to report here a relatively easy method for determining thermodynamic pK_a's of weakly acidic hydrocarbons. Our method involves the establishment of equilibrium 1.

$$\mathrm{RH} + \mathrm{MeO}^- \rightleftarrows \mathrm{R}^- + \mathrm{MeOH} \qquad (1)$$

After equilibrium is attained, the anions (MeO^- and R^-) are converted to their conjugate acids (MeOH and RH) by addition of a known volume of the equilibrated solution to a quench solution with a relative high total concentration of protons and tritons of known isotopic ratio.[9,10]

$$\mathrm{R}^- + \mathrm{MeO}^- + \text{excess } \mathrm{H}^+/\mathrm{T}^+ \rightarrow \mathrm{RH(T)} + \mathrm{MeOH(T)} \qquad (2)$$

After mixing, the hydrocarbon is quantitatively removed by extraction with toluene and washed with water to remove any remaining radioactive impurities. The hydrocarbon is then analyzed for tritium concentration by scintillation counting. This permits calculation of the concentration of RT. By knowing the initial and final isotopic ratios of H/T and the concentration of RT, the concentration of the conjugate base of RH(R^-) at equilibrium can be accurately calculated.

The isotope effect, $(K_H/K_T)^{RH(t)}$, for the hydrocarbon–methoxide reaction was calculated from K_H/K_D using the Streitweiser modification[11] of the Swain–Schaad equation.[12] The values of K_H/K_D for phenylacetylene in methanol were calculated by the method of Margolin and Long.[13] Next, the total isotope effect ratio (IER) for all of the exchangeable hydrogens was determined by permitting a mixture of phenylacetylene, methoxide, and tritiated methanol to come to dynamic equilibrium.[14] This was quenched with acidic methanol. By knowing the concentration of all species present including the ratio of protons to tritons in the solvent system, a ratio of the expected statistical incorporation to be experimentally determined quantity of tritium can be found, i.e., IER.

$$\mathrm{IER} = \frac{[\mathrm{RT}]\ (\text{theor eq})}{[\mathrm{RT}]\ (\text{exptl eq})} \frac{(K_H/K_T)^{\mathrm{MeOH(t)}}}{(K_H/K_T)^{\mathrm{RH(t)}}} = \frac{\text{Methanol–carbanion isotope effect}}{\text{hydrocarbon–methoxide isotope effect}}$$

By this method, the solvent isotope effect for this system was determined. The data are given in Table I.

Since the concentration of R^- is known and since the concentrations of the other species of eq 1 are known or can be calculated, the equilibrium constant can be determined for the reaction by the equation

$$K_{eq}{}^{\mathrm{I}} = \frac{[\mathrm{R}^-][\mathrm{MeOH}]}{[\mathrm{RH}][\mathrm{MeO}^-]} \qquad (3)$$

After $K_{eq}{}^{\mathrm{I}}$ is calculated and since the K_a of methanol (in pure methanol) is known, the K_a of RH can be determined from the equation

$$K_{eq}{}^{\mathrm{I}} = \frac{K_a{}^{\mathrm{(RH)}}}{K_a{}^{\mathrm{(MeOH)}}} \qquad (4)$$

$$\mathrm{PhC{\equiv}CH} + \mathrm{MeO}^- \rightleftarrows \mathrm{PhC{\equiv}C}^- + \mathrm{MeOH}$$

The data for the determination of the pK_a of phenylacetylene at 0, 10, and 25 °C are given in Table II. These compare with a value of 23.2 in cyclohexylamine[17,18] and 28.8 in Me_2SO.[8]

Even though sodium methoxide is known to form ion pairs,[19] the activity of methoxide in the concentration used has been shown to be unity.[20] This is supported by the observation that the pK_a of phenylacetylene obtained did not vary as a function of the concentration of NaOMe used. Ion pairing for sodium phenylacetylide does not appear to be important since quenching of the ion pair vs. the free acetylide ion would give the same results.

To test this method further, we have determined the pK_a of several substituted phenylacetylenes. By this method, the pK_a of the *p*-methylphenylacetylene was determined to be 18.24 and the *p*-bromophenylacetylene to be 17.74 at 25 °C. This reflects the electron-withdrawing effects of the *p*-bromo substituent and the electron donating effects of the *p*-methyl

Table I. Rate and Equilibrium Data for Phenylacetylene in Methanol

Compound	Registry no.	Temp, °C	Slope[a]	K_H/K_D	$(K_H/K_T)^{RH(t)}$	IER	$(K_H/K_T)^{MeOH(t)}$
PhC≡CH (RH)	536-74-3	−20	687 ± 10	0.81 ± 0.02	0.74 ± 0.03	2.56	1.89
PhC≡CD (RD)	3240-11-7	−20	844 ± 9				
RH		0	9 670 ± 260	0.92 ± 0.04	0.89 ± 0.06	2.38	2.12
RD		0	10 500 ± 270				
RH		10					2.20[b]
RH		25					2.31[b]

[a] An average of 5–7 points per run. [b] Calculated by extrapolation of the K_H/K_T vs. $1/T$ plot.

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Table II. Phenylacetylene Quench Equilibrium Data[a]

Run	Temp, °C	10^2[RH], M	$10^2[OMe^-]$, M	$10^5[R^-]$, M	$10^{18}K_i$(MeOH), M[b]	pK_a (PhC≡CH)
50	0.0	5.30	7.63	42.0	3.09	18.50
56	0.0	3.78	7.63	29.2	3.09	18.51
102	10.0	3.91	10.2	25.3	6.76	18.37
103	10.0	5.21	10.2	35.4	6.76	18.35
91	25.0	3.67	5.09	7.43	18.7	18.13
92	25.0	3.81	10.2	14.8	18.7	18.15

[a] Average of 5–7 points per run. [b] Reference 16.

substituent as they affect the stability of the resulting anion. The pK_a values of other substituted phenylacetylenes are being determined by this procedure.

This method for the determination of pK_a's of compounds is not limited to systems that have different spectral properties for compounds and their conjugate bases. It can be used for any compound whose pK_a in methanol is between 17 and 21. The limiting factors appear to be the concentration of the anion and the activity of the quench media so that one can obtain sufficient activity above background to give meaningful data.

Experimental Section

Phenylacetylene. This was obtained from Eastman Kodak Co. The IR and NMR spectra were consistent with published Sadtler spectra. The GC analysis showed only a one-component system. High resolution mass spectrographic analysis on a JEOL JMS D100 GC-MS gave a molecular weight of 102.02.

Phenylacetylene-*d*. A procedure used by Johnson[15] was modified for the preparation of this compound. The preparation of phenylacetylene-*d* was initiated by first preparing the ethylmagnesium bromide in ether. The phenylacetylene Grignard was obtained by change of the ethyl Grignard with phenylacetylene in ether. The resulting phenylacetylene Grignard was hydrolyzed by dropping into its ether solution deuterated water (99.82% D). The newly prepared phenylacetylene-*d* was extracted with pentane and purified by distilling twice under aspirator vacuum at a temperature of 48–49 °C. The IR spectrum of phenylacetylene-*d* was similar to that of phenylacetylene except for the difference in the C–H vs. C–D bonds. The NMR showed aromatic protons at δ 7.45 ppm with no noticeable acetylenic protons at δ 3.08 ppm. High resolution mass spectrographic analysis gave a molecular weight of 103.07.

Kinetic Runs. The kinetic rate data were obtained as described previously.[1a,13]

Equilibrium Quench Runs. The phenylacetylene solution was prepared by weighing, to 0.00001 g, phenylacetylene, sodium methoxide, and methanol in a 25-mL volumetric flask. The tritiated benzenesulfonic acid was prepared by the same procedure.

The equilibrium quench runs were made by mixing phenylacetylene and base and allowing the equilibrium to establish in methanol at the desired temperature. Once this equilibrium had been established, it was quenched by dropping the solution into tritiated benzenesulfonic acid in methanol. Since the proton to tritium ratio in the BSA solution is known, the concentration of the phenylacetylene anion at equilibrium can be calculated by scintillation counting.

A pro-pipet bulb equipped with a screw clamp was affixed to a graduated 10-mL pipet. The screw clamp was used on the pipet bulb so that the flow rate from the pipet could be controlled. The pipet was jacketed so that bath water (at the desired temperature) could be circulated around the pipet. Once the bath water was circulating through the jacket, the equilibrated phenylacetylene–base solution was drawn into the pipet.

Weighing vials containing the tritiated acid were placed in a bath to bring them to the same temperature as the phenylacetylene solution. After equilibration, they were placed on a magnetic stirrer and by adjustment of the flow rate with the screw clamp, the phenylacetylene solution was slowly dropped into the weighing vials, drop-by-drop, until approximately 1 mL of solution had been transferred into the vials. After the quench, the vials and their contents were weighed. The samples were then transferred to the separatory funnels, washed, and dried. A 2-mL sample of the dried toluene solution was placed in a glass scintillation vial and counted in the liquid scintillation counter.

Blanks for the quench runs were obtained, so that any radioactivity which might be due to exchange occurring after quench could be subtracted from the dpm's for each quench point. These were always very small.

Isotope Effect Ratio. In order to experimentally determine the values which a kinetic point would obtain at infinity time, selected kinetic point solutions[1a] were allowed to run for at least 20 half-lives. Some points were prepared by adding 50 μL of base and 1 mol of stock solution to a 5-mL ampule. The ampules were sealed and placed in a small jar which was submerged in the desired bath. After several days, the ampules were broken open, quenched, washed, and worked up as before.

Tritium Analysis Procedure. Scintillation vials containing 15 mL of scintillation solution (PPO and POPOP in toluene) were prepared and monitored in a nuclear Chicago Model 2 liquid scintillation spectrometer.[1a] Aliquots of samples to be counted were transferred to these vials. Tritium quench standards were used with each analysis with the appropriate standard quench correction curve being used to determine the counting efficiency. The absolute disintegration rate and thus the actual number of tritium atoms could be determined. The other calculations followed the usual analytical procedures.

References and Notes

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(9) No further T/H exchange occurs in excess acidic media as shown by separate experiments.

(10) (a) A comment from a reviewer suggested the possibility of an error in this measurement. When the phenylacetylene–phenylacetylide mixture is quenched with a mixture of H_2O–T_2O, it is assumed that the phenylacetylide ion will give RH/RT in the same ratio as H/T of the quench solution. This assumes little or no kinetic isotope effect on this step. It was suggested that experiments be done using a high enough concentration of base to convert all of the phenylacetylene to the acetylide ion and then quenching this. The observed H/T ratio would then give the isotope effect for that one step of the process. Several attempts to obtain these data failed due to the large heat of reaction involved with the reaction of the strong base with the strong acid. The isotope effect may be small[10b] or large[10c] which may change the pK_a values by as much as one unit, but in any case, the relative values are still correct. (b) Y. Pocker and J. H. Exner, *J. Am. Chem. Soc.*, **90,** 6764 (1968); (c) S. K. Hsu, C. K. Ingold, and C. L. Wilson, *J. Chem. Soc.*, 78 (1938).

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