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BASE-CATALYZED HYDROGEN ISOTOPE EXCHANGE AND THE AQUEOUS ACIDITY OF TOLUENE[1]

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Abstract: Measurements of hydrogen isotope exchange of toluene-α-*d* and -α-*t* in aqueous sodium hydroxide are reported for temperatures of 150-200 °C. The reaction shows essentially no primary isotope effect. The rate extrapolated to 24 °C is combined with the rate constant for reaction of benzyl anion with water obtained earlier by Bockrath and Dorfman[8] to derive the aqueous pK_a of toluene as 39.6 (per hydrogen basis).

Toluene has long been one of the key reference compounds on scales of carbon acidities; a *pK* value of 35.5 was assigned on Cram's MSAD scale.[2] This value is apparently too low based on more recent values of 41.2 on the cesium cyclohexylamide (pK_{CsCHA}) ion pair scale,[3] and an estimate of 42 in dimethyl sulfoxide.[4] In this paper we derive a value for the pK_a of toluene in aqueous solution.

Toluene is slightly soluble in water and we used solutions that were 0.02-.05M in toluene at room temperature. In order to obtain more accurate values for tritium content of kinetic aliquots by liquid scintillation counting, the toluene-α-*t* used was mixed with toluene labeled with ^{14}C; the kinetics was followed from the decrease in the $^{3}H/^{14}C$ ratio with time. In this way, kinetic aliquots could be extracted with ordinary toluene for counting. Determination of the amount of substrate in the liquid scintillation system is often the principal source of error. The infinity value was obtained by oxidation of a sample to benzoic acid using potassium permanganate. In those runs that also included toluene-α-*d*, deuterium content was determined by low voltage mass spectrometry of an aliquot.

The kinetic measurements were carried out in Monel reactors from which aliquots were removed at intervals and cooled. Only a fraction of the kinetic solutions were used; solutions of toluene in water are far from ideal[5] and we found it important to keep the vapor space as small as possible relative to the solution volume in order to obtain good pseudo-first order kinetics. The results are summarized in Table I. Measurements were made in the temperature range 150-200 °C. Only for run 5 at 150 °C was the reaction followed for less than one half-life. Runs 1 and 2 at 190 °C with [NaOH] = 0.9 and 1.8M, respectively, show that the reaction is first order in sodium hydroxide even at these high base concentrations. At these high temperatures no "salt effect" correction[6] needs to be made and no enhanced basicity is involved. The absence of a significant primary isotope effect shows that internal return is important;[7] the reaction product of toluene and hydroxide ion is most probably a benzyl anion hydrogen bonded to water. The rate-determining step is then the replacement of this water by another. This mechanism is consistent with the near-zero entropy of activation. We note also that significant amounts of internal return were found for exchange reactions of di- and triarylmethanes in methanol at temperatures of 100 °C.[7] The above results also suggest that the benzyl anion intermediate involved is essentially a free anion rather than ion-paired.

The results in Table I permit extrapolation to room temperature. The Eyring versus the Arrhenius equations give rate constants at room temperature differing by only 10%. Taking this value as the forward step in the equilibrium between toluene and hydroxide ion involves the more important approximation that the exchange mechanism has not changed importantly over this long temperature extrapolation despite the differences in water structure involved. Nevertheless, if hydrogen-bonded benzyl anion is involved at elevated temperatures, such hydrogen bonding is certainly not less important at room temperature.

For the reverse step of reaction of benzyl anion with water we turn to rate data of Bockrath and Dorfman[8] who studied this reaction in tetrahydrofuran solution. We assume that their rate constant of $5.3\times10^{7}\ M^{-1}s^{-1}$ at 24 °C applies as well to an aqueous solution. This necessary assumption is probably not too bad an approximation. This rate is somewhat below the diffusion-controlled limit and all of their rate constants for reactions of benzyl anion with alcohols differ by no more than an order of magnitude. We note also that the isotope effect that they report for reaction of benzyl anion with ethanol or ethanol-O-*d*, $k_H/k_D = 1.2$, is consistent with our result above.

Combining both sets of results and using our Eyring extrapolated rate constant at 24 °C of $7.4\times10^{-17}\ M^{-1}s^{-1}$ gives the following equilibrium constant:

$$K_{eq} = \frac{[R^-][H_2O]}{[RH][OH^-]} = \frac{7.4 \times 10^{-7}}{5.3 \times 10^{7}} = 1.4 \times 10^{-24} \qquad (1)$$

This value is converted to the equilibrium acidity by:

$$K_a = \frac{[R^-][H^+]}{[RH]} = \frac{K_{eq}K_w}{[H_2O]} = 2.6 \times 10^{-40}\ M \qquad (2)$$

or pK_a (toluene) = 39.6 per hydrogen. This derivation assumes that $k_H = k_T$, but the isotope effect has been shown to be small. The derived net pK_a is 39.1. The derivation requires a number of assumptions but the result is probably reliable to about ±1 p*K* unit. This result indicates that toluene is slightly more acidic in water than suggested by the pK_{CsCHA} or pK_{DMSO}, probably because of hydrogen-bonding solvation of benzyl anion; that is, benzyl anion, despite delocalization of charge to the benzene ring still has a relatively large charge at the α-carbon.

Finally, the value derived here is clearly higher than the MSAD[2] value of 35.5 and this now out-dated MSAD value should no longer be used.[9]

Table I. Hydrogen isotope exchange kinetics for toluene in aqueous NaOH.

Run	Isotope	Temp °C	[NaOH] M^b	$10^6 k_{exp}{}^c$ s^{-1}	$10^6 k_2{}^d$ $s^{-1} M^{-1}$	$10^6 k_{calc}{}^e$ $s^{-1} M^{-1}$	$k_D/k_T{}^f$
12	T	200	1.348	6.22	4.61	4.62	
1	T	190	0.916	1.72	1.88		
2	T	190	1.801	3.34	1.85	1.86	
7	T	175	1.767	0.789	0.446	0.440	1.03 ± 0.04
	D			.789	.446		
9	T	175	1.642	0.661	0.403		1.07 ± 0.01
	D			.703	.428		
3	T	160	1.881	0.178	0.095	0.094	
5	T	150	1.889	0.060	0.032	0.032	1.01 ± 0.07
	D			.056	.030		
6	T	25				9.3×10^{-11} g	

(a) Uncertainty ±0.1 °C.

(b) Corrected for solvent expansion. No difference in concentration was found before and after a run. Toluene concentrations were 0.02-.05*M*.

(c) Pseudo-first order rate constant; estimated uncertainties are about 5%.

(d) $k_{exp}/[NaOH]$

(e) From the Eyring correlation: $\Delta H^{\ddagger} = 38.724 \pm 0.5$ Kcal mol^{-1}, $\Delta S^{\ddagger} = -2.048 \pm 1.1$ e.u. The corresponding Arrhenius correlation gives $E = 39.615 \pm 0.5$ Kcal mol^{-1}, $A = (9.065 \pm 5) \times 10^{12}$.

(f) From a direct comparison of D and T data with time eliminated.

(g) Arrhenius extrapolation gives $k_{calc} = 8.5 \times 10^{-17}\ s^{-1}\ M^{-1}$.

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9. The MSAD value derived by Cram over two decades ago is still to be found in some current textbooks.

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