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Deuterium Isotope Exchange between Molecular Hydrogen and Cyclohexylamine[1a,c]

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Abstract: Deuterium isotope exchange between molecular hydrogen and cyclohexylamine (CHA) has been studied by using the LiCHA, NaCHA, KCHA, and CsCHA salts as catalysts in a stirred reactor over the temperature range -15 to $+15$ °C. The reaction in solution is very fast (comparable to the amide/ammonia and methylamide/methylamine systems), and even at -15 °C (CHA fp -17.8 °C) rate constants independent of mass transfer could be obtained only for the Li and Na salts in the present apparatus. For these, the kinetic isotope effect (k.i.e., 1.7–2.0) and activation parameter (E_a, 11–17 kJ·mol^{-1}) data have been compared with literature values for base-catalyzed exchange with other protic solvents. Reasons for the observed relative catalyst reactivity LiCHA ≪ NaCHA < KCHA < CsCHA are considered. It has been found that, under some experimental conditions, mass transfer effects can lead to an incorrect k.i.e. value when this is derived from data for a single kinetic run $D_2 \rightarrow HD \rightarrow H_2$. The solubility of H_2 in CHA has been measured over the temperature range -15 to $+15$ °C.

Introduction

Isotope exchange between molecular hydrogen and simple liquid amines under base catalysis has been the subject of considerable study since Wilmarth and co-workers first reported, in the early 1950's, deuterium exchange in the ammonia–D_2 system with potassium amide as catalyst.[2] Since then, much effort has been applied to determining the mechanism of this reaction in liquid ammonia,[3-7] by using various isotopes and alkali metal amide catalysts. The reaction was shown to be first order in dissolved hydrogen, but the question of the relative roles of the free amide ions and ion pairs present in this solvent (dielectric constant $\epsilon = 22.4$ at -33.4 °C) was more difficult to resolve. From the dependence of the rate constant on free amide ion concentration, which was derived from electrical conductivity data for the catalyst solutions, Delmas et al.[7] finally concluded that only the free $^{-}NH_2$ ion is active in liquid ammonia.

Some work has been done with alkylamines like methylamine,[8-10] dimethylamine,[8,9] ethylamine,[8] and isopropylamine,[9] and aniline,[11] with the anion of each solvent as catalyst. Here the dielectric constants are lower than for ammonia, and the relative importance of free alkylamide ions and their corresponding ion pairs as catalysts is less certain; Rochard and Ravoire[9] state that ion pairs "appear to be the main catalytic species", although electrical conductivity data for these solutions were lacking. We have recently reported conductivity data for potassium methylamide in methylamine.[12] However, it is practically impossible to apply such data, valid only for *ion pairing* in such a low dielectric constant solvent ($\epsilon = 10.8$ at

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0 °C) and only at concentrations below about 5×10^{-4} mol·L^{-1},[12] to higher concentrations of catalyst where the effect of triple ion formation cannot be adequately allowed for.

Streitwieser and co-workers have been reporting regularly from 1962 through 1978, in their Acidity of Hydrocarbons series,[13,14] on studies of isotope exchange of hydrocarbon acids in cyclohexylamine (CHA), the catalyst being lithium or cesium cyclohexylamide. As a result, there is a large body of data available for this solvent system (ϵ only 4.5 at 20 °C[15]), including some conductivity and spectrophotometric results. The types and relative reactivities of ion pairs in solution have been considered. The cesium salt of CHA, CsCHA, was found to be up to 35 000 times more effective for exchange than the lithium salt.[16] Experiments with the corresponding sodium and potassium salts have not been mentioned, presumably because of catalyst synthesis problems (see Experimental Section). With this background, and because the handling of liquid CHA is much easier than, e.g., liquid ammonia and methylamine, it was decided to study the exchange reactivity of molecular hydrogen in CHA; the goal was to identify the catalytic species. High reactivity was expected, since the CsCHA/CHA system is reported to be comparable in activity to the KNH_2/NH_3 system for hydrocarbon acid proton exchange.[16]

Experimental Section

Reagents. Cyclohexylamine (CHA) (Eastman, 97%) was purified by fractional distillation onto activated 4A molecular sieves. Gas chromatography of samples indicated less than 0.02% by weight impurities (TC, Pennwalt 223 + 4% KOH on Gas Chrom R). Freezing point was −17.8 ± 0.1 °C. Final drying was done over molten potassium.

The correct density of CHA is 0.8684^{20} g·mL^{-1}.[17]

Methylamine (Matheson of Canada Ltd.) was purified as described previously.[12]

H_2 (extra dry, 99.9%) and D_2 (CP grade, 99.5%) were used as obtained from Matheson of Canada Ltd. HD (nominally 98%) was purchased from Merck Sharp & Dohme Canada Ltd.

The alkali metals were used as received: Li (0.45 kg ingot, 99.98%), Koch-Light Laboratories; 5-g ampules of Na (99.95%), K (99.95%), and Cs (99.98%) from Alfa Division, Ventron Corp. The hydrides LiH (dry, 98%), NaH (dry, 99%), and KH (in oil) were also obtained from Ventron Corp. All metals and hydrides were handled in a drybox under He atmosphere.

Hydrogen Solubility in CHA. The solubility of H_2 was determined by a gas chromatographic method as before;[19] a gas sampling valve was used for calibration of the stripping cell. Temperature control of the gas/liquid equilibration flask was maintained at ±0.05 °C in the range −15.0 to +15.0 °C. Liquid samples withdrawn from the flask by syringe were recorded by weight.

Catalyst Preparation. Dried CHA was handled by vacuum line transfer. All Pyrex vessels were constructed with greaseless valves (J. Young (Scientific Glassware) Ltd., England); in some cases, the Teflon/Pyrex valve stems were replaced with chemically more resistant polyethylene stems.

None of the alkali metals dissolve in CHA, and only Cs reacts at 30 °C with the *dry* solvent. There is no blue color, indicating that few solvated electrons and metal anions are produced.[20] The CsCHA solution is a clear greenish-yellow color. Li, Na, and K metals do not react with CHA, even at 80 °C.[21] Thus molten K spheres were employed as the final drying agent. Both 18-crown-6 and 2.2.2 cryptate, often found valuable in solubilizing alkali metals in low dielectric constant solvents like ethers[20,23] and amines[20] (ϵ 3–10), proved ineffective in CHA. Dye et al.[20] reported that K would not dissolve in triethylamine (ϵ 2.4) even with cryptate present. Of the LiH, NaH, and KH hydrides, only the latter reacts, slowly, with CHA even above 80 °C.

The *methylamide* salts of Li, Na, and K were fairly readily made from dried, purified methylamine by direct reaction with the metal, although Na dissolved much more slowly than the other two. The corresponding CHA salts were prepared by vacuum distilling CHA into a flask containing some of the appropriate methylamide/methylamine solution, and distilling out the methylamine. Any residual methylamine in the CHA solution could be determined by gas chromatography. Whenever the methylamine was removed *before* CHA addition, the dry methylamide salt reacted only very slowly with the CHA. The resulting MCHA solutions are clear and yellow for K^+, very pale yellow for Na^+, and colorless for Li^+; the change in color intensity with cation suggests a shift in equilibria involving the types of ions and aggregates present.

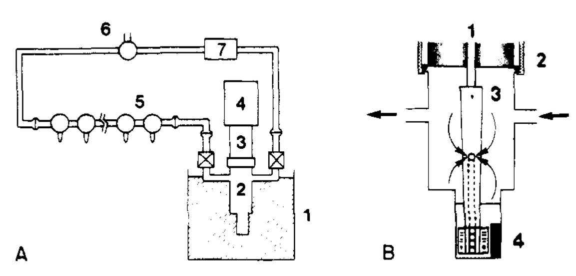


Figure 1. (A) Schematic of apparatus for D_2 exchange runs. (1) Constant temperature bath; (2) stainless steel stirred reactor; (3) ferrofluid rotary feedthrough; (4) high speed motor; (5) sample tube unit; (6) to vacuum, hydrogen supply; (7) metal bellows gas circulation pump. (B) Stirred reactor detail, gas flow indicated. (1) Rotary feedthrough; (2) Edwards vacuum fitting with O-ring seal; (3) stirrer shaft, lower half hollow to four blades; (4) baffle.

These solutions must be protected from contact with air—exposure leads almost instantaneously to a color change and loss of catalytic reactivity. The cyclohexylamide broad, featureless absorption band in the 250–430-nm region of the ultraviolet-visible spectrum disappears.

Catalyst concentrations were determined by a gas chromatographic method.[24] Solubility limits (±5%) measured for the salts at 25 °C were as follows: LiCHA, >0.16; NaCHA, 0.090; KCHA, 0.045; CsCHA, >0.20 mol·L^{-1}.

Solutions were stored at ambient temperature; isotope exchange kinetic runs were carried out at lower temperatures. Above about 40 °C, these solutions are subject to slow thermal decomposition. Tests done with a 0.1 mol·L^{-1} CsCHA solution at 60 °C indicated a gradual loss of color over 300 h, formation of unidentified, prismatic, white crystals, and changes in the ultraviolet-visible spectrum. There is evidence that a polymerization reaction is occurring.[25]

Isotope Exchange Kinetic Runs. A schematic of the apparatus and details of the stirred reactor (designed by W. J. Holtslander and R. E. Johnson at CRNL) are given in Figure 1. The system was later modified by (a) adding small scoops at the gas inlet ports of the hollow shaft and more, smaller holes in the blades, and (b) admitting the circulating gas through a stainless steel frit at the bottom of the solution compartment, to improve efficiency of gas–liquid mixing. Top speed of the original motor was 12 500 r·min^{-1}, as measured by a stroboscope; for higher speeds up to 22 000 r·min^{-1}, a wood-working router was modified to mate with the brass housing holding the ferrofluid rotary feedthrough (Ferrofluidics Corp., Burlington, Mass.).

The dried reactor was loaded under vacuum with about 20 mL of weighed catalyst solution. After equilibration in the low temperature bath (±0.05 °C), D_2 or 1.3 mol % HD in H_2 was admitted to 101 kPa (760 mm), the bellows pump (nominal 11 L·min^{-1}) and the stirrer were started, and up to eight 2-mL gas samples were taken in the Pyrex sample tube unit over a suitable period of time. Very often, several runs were carried out with the same solution by changing sample tube sets, pumping out the old hydrogen mixture from the cell, and reloading with D_2. The ratio of exchangeable H to D was always greater than 20, so that D_2 concentration at infinite time was negligible. For the kinetic plots for HD runs, a correction for HD remaining at equilibrium (calculated by computer) was necessary, since its concentration does not fall to a negligible value.

D_2/HD/H_2 Analysis (Mass Spectrometer Calibration for D_2). Most analyses were done on a CEC 21-614 residual gas analyzer. Response (relative sensitivity) factor calibration curves proved difficult to obtain accurately for D_2 concentrations above 90 mol %, because of H_2 desorption effects (and to a lesser extent exchange effects) in the analyzer head. As a result, response factors were much greater than one, rising rapidly with increasing D_2 concentration. This problem was compounded because it was necessary to know the relative HD/H_2 composition at high D_2 so that the correct response factor curves could be

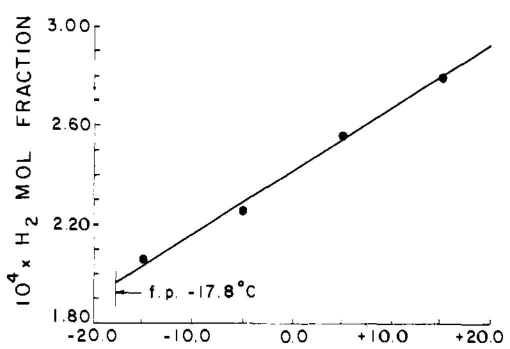


Figure 2. Temperature dependence of H_2 solubility in cyclohexylamine.

used. For reaction rate-limited kinetic runs (LiCHA) at high D_2, the HD/H_2 concentration ratio is greater than one and therefore equilibrium $D_2/HD/H_2$ standards are valid. These were prepared by equilibrating D_2 and H_2 over a Pt filament at 925 °C in Pyrex flasks.[26] However, for mass transfer limited runs, the corresponding HD/H_2 ratio is generally less than one, and "nonequilibrium" standards of similar ratios are necessary; these were made from D_2, HD, and H_2 stocks, with back diffusion from the Pyrex preparatory flasks being minimized by the use of a glass capillary inlet. The response factor behavior was less extreme for these standards.

The above conditions were found to exist in several different models of mass spectrometer tested, although the severity was a function of ultimate background pressure and analyzer head design.

Results

H_2 Solubility in CHA. The data are shown in Figure 2; values taken from the least-squares line are believed to be accurate to within ±2%. In this temperature range the H_2 solubility (2 to 3 $\times 10^{-4}$ mol fraction at 101 kPa (1 atm)) is similar to that for other amines like ethylamine and *n*-propylamine, and slightly greater than for ammonia and methylamine.[27] From standard plots of ln (mol fraction solubility) vs. reciprocal absolute temperature and ln (absolute temperature), the partial molal enthalpy and entropy of solution, respectively, were found to be 6.6 ± 0.4 $kJ \cdot mol^{-1}$ and 24.4 ± 2.0 $J \cdot mol^{-1} \cdot K^{-1}$ (standard state 101 kPa H_2).

The solubility of HD at 25 °C was taken as 3% greater, and of D_2 6% greater, than that of H_2, factors which are reasonable for a protic solvent—the D_2/H_2 solubility ratio in water is reported to vary from 1.065 at 30.0 °C to 1.086 at 5.0 °C.[28] For nonpolar solvents this ratio is smaller, tending to fall between 1.02 and 1.03.[29] It has been assumed that the fairly low concentrations of catalyst salts used in the isotope exchange runs will have only a small effect on these hydrogen solubilities.

D_2 Exchange Kinetics. The data from mass spectrometric analysis of the samples were treated kinetically as pseudo-first-order plots of ln % D_2 vs. time. Such plots were linear for the time periods studied (up to 6 half-lives). Least-squares treatment yielded the observed rate constants, k'_{obsd}, for gas phase composition change; reproducibility was generally ±5%. The measured value of k'_{obsd} depends on the volume of solution used, for fixed total gas-plus-solution volume, and inversely on the total volume for fixed solution volume. The in-solution first-order constants, k_{obsd}, were obtained where appropriate by first correcting to a constant 20.0 mL of solution and constant total volume, and then multiplying these k'_{obsd} by the ratio (total deuterium circulated/deuterium dissolved in solution).[7] This ratio ranged between 140 and 200.

The dependence of k'_{obsd} on stirring rate for each of the catalyst systems studied is shown in Figures 3 and 4.

The dependence of k'_{obsd} on D_2 starting pressure was examined in a set of runs with NaCHA solution at −15 °C, at four pressures from 40 to 160 kPa (300 to 1200 mm). There was a small but gradual increase in k'_{obsd} of about ten percent for the quadrupling of pressure.

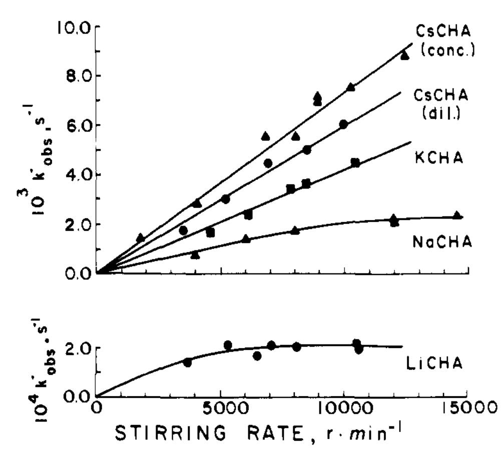


Figure 3. Stirring rate dependence of k'_{obsd} for D_2 exchange with 20.0 mL of 0.16 $mol \cdot L^{-1}$ LiCHA at −12.0 °C, 0.072 $mol \cdot L^{-1}$ NaCHA at −15.1 °C, 0.050 $mol \cdot L^{-1}$ KCHA at −18.0 °C, 0.13 and 0.023 $mol \cdot L^{-1}$ CsCHA at −12.0 °C; gas volume, 205 mL.

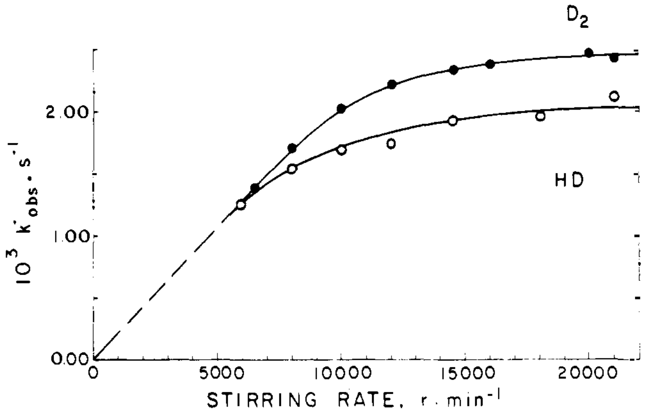


Figure 4. Stirring rate dependence of k'_{obsd} for independent D_2 and HD exchange kinetic runs with 0.072 $mol \cdot L^{-1}$ NaCHA at −15.1 °C.

Because k'_{obsd} data independent of stirring rate could not be obtained for the Cs and K salts (Figure 3), reliable Arrhenius activation parameters based on in-solution rate constants could be calculated only for LiCHA and NaCHA under the present experimental conditions. These are recorded in Table I. Even for a 0.0024 $mol \cdot L^{-1}$ CsCHA solution, k'_{obsd} was linearly dependent on the stirring rate beyond 10 000 $r \cdot min^{-1}$.

Kinetic Isotope Effect $2k_{HD}/k_{D_2}$. Although k_{D_2} is measured directly from kinetic runs with D_2, k_{HD} can be obtained either directly from runs started with HD or indirectly by monitoring the HD concentration as a function of time for the D_2 runs. The latter method is to be preferred since k_{D_2} and k_{HD} are then determined under identical experimental conditions. A computer program was set up to obtain, by adjusting k_{HD}, a best fit between the experimental values of mole percent HD for a D_2 kinetic run and theoretical values calculated assuming a simple set of two consecutive pseudo-first-order reactions (eq 1).[30]

$$D_2 \xrightarrow{k_{D_2}} HD \xrightarrow{k_{HD}} H_2 \qquad (1)$$

For cases where mass transfer limitation did not interfere (LiCHA runs) this approach worked well and gave reasonable values[31] for the kinetic isotope effect (k.i.e.), $2k_{HD}/k_{D_2}$, for molecular hydrogen (Table I). However, for the CsCHA and KCHA runs, and even for NaCHA runs in the region where k'_{obsd} was independent of stirring rate (plateau in Figure 4),

Table I. Activation Parameters[a] and Kinetic Isotope Effects for D_2 Isotope Exchange in LiCHA and NaCHA Solutions, Obtained over the Temperature Range −15.0 to +15.0 °C

catalyst	$2k_{HD}/k_{D_2}$	$E_a(D_2)$,[b] kJ·mol^{-1}	$\Delta H^{\ddagger}(D_2)$,[b] kJ·mol^{-1}	$\Delta S^{\ddagger}(D_2)$,[b,c] J·mol^{-1}·K^{-1}
LiCHA	1.9 ± 0.1[d]	16.5 ± 2.5	14.2 ± 2.5	-202 ± 9
NaCHA	1.9–2.0[e] 1.7 ± 0.1[f]	11.3 ± 0.5	9.0 ± 0.5	-195 ± 4

[a] Calculated from in-solution pseudo-first-order rate constants, k_{obsd}: 0.084 mol·L^{-1} LiCHA, 0.072 mol·L^{-1} NaCHA. 1 kcal·mol^{-1} = 4.1868 kJ·mol^{-1}. [b] Values given are averages for two independent sets of experiments in different reaction vessels. [c] Calculated at 0 °C via equation $\Delta S^{\ddagger} = R(\ln k_2 - 24.764 - \ln T + E_a/RT)$, with k_2 from k_{obsd} divided by stoichiometric catalyst concentration. [d] Computer fit from D_2 runs. [e] Independent k_{HD} and k_{D_2}; a slight increase with decreasing temperature. [f] Limiting value above 12 000 r·min^{-1} at −15.0 °C, separate set of measurements from *e*.

the fit was found to be very poor, as shown in Figure 5A. The addition of reversible steps in eq 1 did not produce a significant improvement, but allowance for an alternate step whereby some D_2 was *apparently* converted directly to H_2 (eq 2)

$$D_2 \xrightarrow{k^*_{D_2}} H_2 \qquad (2)$$

led to very good fits with the observed data (Figure 5A). Nevertheless, the resultant k.i.e.'s were still abnormally high (10–25 range). For $k'_{obsd} = k_{D_2} + k^*_{D_2}$, the direct route fraction $k^*_{D_2}/k'_{obsd}$ necessary for optimum fit depended on the stirring rate, but dropped only from ca. 0.7 to 0.5 as the stirring rate was increased to the apparent plateau level for the NaCHA runs at −15 °C. For LiCHA runs on the comparable plateau, no direct route correction was necessary. For KCHA runs (all dependent on stirring rate), fractions up to 0.8 were required.

The above results suggest that, rather than having an actual chemical step $D_2 \rightarrow H_2$ under mass-transfer-limited conditions, a large fraction of the HD formed in the first step from D_2 just does not escape the solution to be "counted" before reacting to form H_2. Indications of this effect were: (a) the percent H_2 value rose faster than the percent HD during such a run; (b) the maximum percent HD observed during the run was smaller than expected, values as low as 5 mol % being found for some KCHA runs at the slowest speeds, whereas reaction rate-limited values fall in the range 30–50% for k.i.e.'s of about 1.5–2.0; (c) the maximum HD for the NaCHA runs was dependent on the stirring rate; (d) at −15 °C and 12 000 r·min^{-1}, when the NaCHA concentration was reduced from 0.072 to 0.014 mol·L^{-1}, k'_{obsd} decreased by only a factor of two, the HD maximum rose from 16 to 29 mol %, and the factor $k^*_{D_2}/k'_{obsd}$ needed for best fit dropped from 0.55 to 0.35. These observations show that the greater the actual *chemical* rate constant in solution (higher active catalyst concentration), the stronger the mass-transfer-masking effect on the *isotope effect* for the NaCHA solutions.

The magnitude of the HD maximum can also be used to determine k_{D_2} and k_{HD}.[32,33] However, the above discussion indicates that this maximum must first be shown to be independent of mass transfer effects before reliable k.i.e. values can be obtained.

To avoid these complications, some kinetic runs were carried out with HD so that k_{HD} could be measured directly for the NaCHA and LiCHA systems (included in Figure 4 for NaCHA). The k.i.e. values based on these independently measured k_{HD} and k_{D_2} data are recorded in Table I; they were found to be constant and reasonable, but only when both rate constants were independent of stirring rate. At slower speeds, the ratio $2k_{HD}/k_{D_2}$ rose with decreasing speed. This indicates that the k'_{obsd} measured for HD and D_2 on the plateaus in Figure 4 are true chemical values.

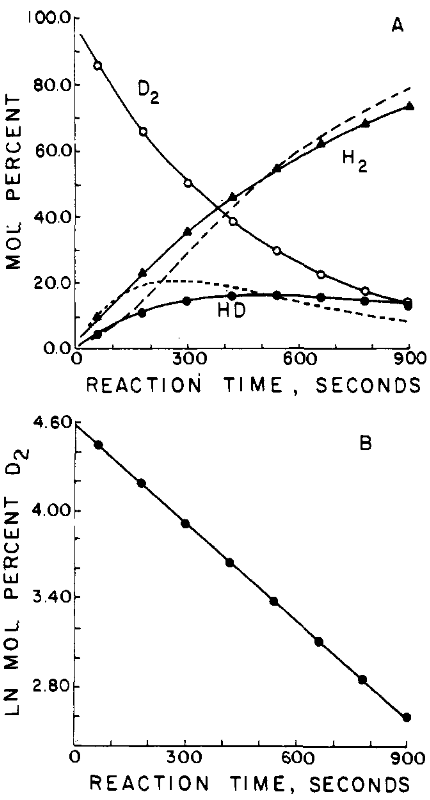


Figure 5. Kinetic run CHAD2-83 with 0.072 mol·L^{-1} NaCHA at −15.1 °C and 12 000 r·min^{-1}. (A) Points are experimental data. Solid lines for HD and H_2 calculated for $k^*_{D_2}/k'_{obsd} = 0.55$, dashed lines for no contribution from $k^*_{D_2}$ (see text). Percent H_2 by difference, 100.0 − (D_2 + HD). (B) Pseudo-first-order plot of percent D_2 for same run, period of 3 half-lives.

Discussion

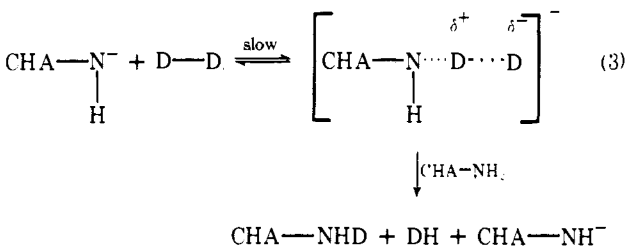
Relative Reactivities of the Cyclohexylamide Salts. In spite of mass-transfer limitations with the KCHA and CsCHA solutions, some conclusions can still be drawn concerning the relative reactivity of the alkali metal salts for catalyzing isotope exchange between D_2 and CHA. The observed order is CsCHA ≳ KCHA > NaCHA ≫ LiCHA, with the Cs salt being at least a factor of 10^3 more effective than the Li salt. However, the actual state of the catalyst ions may vary over this series. Streitwieser et al. have concluded from several studies with hydrocarbon acids that: (a) very few *free* cyclohexylamide ions are present for CsCHA and LiCHA;[16,34] conductivity data for LiCHA suggest the dissociation constant for ion pairs to free ions is $\simeq 10^{-10}$ mol·L^{-1};[34] (b) CsCHA exists mainly as catalytically active monomeric ion pairs, whereas LiCHA ion pairs are strongly aggregated.[16,35] The relative reactivities of these two salts have been compared directly for tritium exchange in several hydrocarbon systems.[35] CsCHA was generally about 10^4 more effective than LiCHA, and comparable to the KNH_2/NH_3 system. Both LiCHA and CsCHA "monomers" are believed to be contact rather than solvent-separated ion pairs;[36] therefore, the observed order for catalysis of D_2 exchange with CHA must reflect the cation-dependent degree of aggregation of these monomers to less reactive or unreactive dimers, triple ions, etc.

The D_2-CHA Exchange Mechanism. Of several possible paths for reaction between molecular hydrogen and a proton donor (amine, alcohol, water) catalyzed by the solvent anion, the associative mechanism (eq 3 for CHA) generally gives the best match between the experimental data[4,7,31,37] and theory.[38]

Table II. A Comparison of Some Kinetic Data for Base-Catalyzed Isotope Exchange of D_2 and/or HD in Various Protic Media

dielectric[a] constant	solvent	anion salt	pK_a[b] (NH → N^-) (OH → O^-)	rel D_2 exchange rates	E_a:[c] kJ·mol^{-1}	temp range, °C	$\Delta S^{\ddagger}$,[c] J·mol^{-1}·K^{-1}	isotope effect $2k_{HD}/k_{D_2}$	ref
6.6 (70 °C)	CH_3CO_2H	Na^+	4.8	extremely slow	≥150	60 to 100			46
56 (100 °C)	H_2O	Na^+	15.7	very slow	~101	60 to 100			46
		K^+			~101	80 to 110	+29[k]	1.24	47
i	H_2O/Me_2SO	$(CH_3)_4N^+$	i	slow	70–105[i]	35 to 80	−30 to −90[i]	1.2–1.7[i]	31,39
25 (55 °C)	CH_3OH	K^+	16	very slow	~70[f]	75 to 125		1.1–2.0[g]	37
		Na^+			101	75 to 115			46
		K^+			101	47 to 65	+17		8
5.9 (70 °C)	$C_6H_5NH_2$	K^+	27	very slow	~100	85 to 100		1.1–1.9[g]	11
22.4 (−33 °C)	NH_3	K^+	~36	fast	~33	−40 to +20			3
		K^+			31	−69 to −46	−38	1.29[h]	4
		Na^+			33	−69 to −46	−38		4
15.5 (−62 °C)	CH_3NH_2	K^+	~37[j]	very fast	17	−30 to −10			10
		K^+			28	−90 to −62	−21		9
		Li^+			15	−56 to −10	−117	1.27[h]	8
		$NaNH_2$			22	−56 to −10			8
6.3 (0 °C)	$(CH_3)_2NH$	K^+	~38[j]	very fast	29	−60 to −90	−8		9
4.5 (20 °C)[d]	$C_6H_{11}NH_2$	Li^+	41.6[e]	very fast	17	−15 to +15	−202	1.9	present work
		Na^+			11	−15 to +15	−195	1.7–2.0[h]	

[a] Weast, R. C., Ed. "Handbook of Chemistry and Physics", 51st ed.; Chemical Rubber Co.: Cleveland, Ohio, 1970. [b] Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965. [c] 1 kcal = 4.1868 kJ. Activation parameter values are quite dependent on hydrogen solubility data used.[7] [d] Ref 15. [e] Ref 14. [f] From concentrated solution rate data extrapolated to infinite dilution.[37] [g] Values dependent on both temperature and catalyst concentration; determined by computer fit of $D_2 \rightarrow HD \rightarrow H_2$ runs data. [h] From independent D_2 and HD runs. [i] Values dependent on solvent composition. [j] An estimate relative to NH_3. [k] Calculated by Bar-Eli and Klein.[8]



$$\mathrm{CHA{-}\underset{\underset{H}{|}}{N^-}} + \mathrm{D{-}D} \underset{}{\overset{\text{slow}}{\rightleftharpoons}} \left[\mathrm{CHA{-}\underset{\underset{H}{|}}{N}\cdots \overset{\delta+}{D}\cdots \overset{\delta-}{D}}\right]^- \quad (3)$$

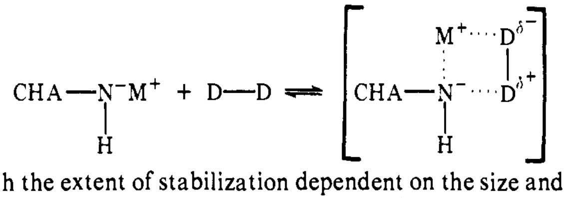
$$\xrightarrow{\mathrm{CHA{-}NH_2}} \mathrm{CHA{-}NHD + DH + CHA{-}NH^-}$$

Based on the results of Ritchie and King's theoretical calculations for the *gas* phase interactions $NH_3 + H^- \rightleftharpoons$ weak complex $NH_4^- \rightleftharpoons NH_2^- + H_2$,[38b] the formation of a weak complex of the type shown in eq 3 might be expected. Their calculations in fact predict complex formation and no classical barrier to proton transfer for both the $OH^- + H_2$ and $NH_2^- + H_2$ systems in the gas phase.[38]

It is obvious that the cation plays a key role in determining the observed rate of D_2 isotope exchange. But does the involvement extend beyond equilibria of the type in eq 4?

$$\mathrm{CHA{-}NH^- + M^+} \rightleftharpoons \mathrm{CHA{-}NH^-M^+} \rightleftharpoons \text{ion aggregates} \quad (4)$$

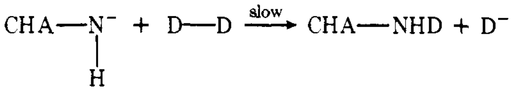
It is reasonable that the transition state/intermediate in eq 3 could be stabilized by a cation, e.g., eq 5,



$$\mathrm{CHA{-}\underset{\underset{H}{|}}{N^-}M^+} + \mathrm{D{-}D} \rightleftharpoons \left[\begin{array}{l} \quad\quad\quad\quad \mathrm{M^+\cdots D^{\delta-}} \\ \mathrm{CHA{-}\underset{\underset{H}{|}}{N^-}\cdots D^{\delta+}} \end{array}\right] \quad (5)$$

with the extent of stabilization dependent on the size and polarizability of the particular cation M^+, and the type of $CHA\text{-}NH^-M^+$ ion pair involved. For D_2 exchange catalyzed by hydroxide ion in water and aqueous dimethyl sulfoxide, where the dielectric constant ϵ is quite high, the enthalpy of activation data tended to rule out the presence of the large cation $(CH_3)_4N^+$ in the transition state.[39] In amines, where ϵ is much lower (especially for CHA), direct participation by a smaller cation seems more likely.

An alternate reaction path that first involves formation of free hydride ion (H^- or D^-), e.g., eq 6,



$$\mathrm{CHA{-}\underset{\underset{H}{|}}{N^-}} + \mathrm{D{-}D} \xrightarrow{\text{slow}} \mathrm{CHA{-}NHD + D^-} \quad (6)$$

has usually been regarded as less probable. However, it is interesting to note that a value of 41.6 was estimated for the pK_a of CHA in CsCHA/CHA solution,[14] while a value in the neighborhood of 37 has been estimated for H_2 under similar conditions,[40] subject to some uncertainty about the contribution of ion association and CsH solubility.[40] Both estimates were obtained from comparisons of the relative equilibrium acidities of weak hydrocarbon acids. If the above pK_as reflect the true *relative* acidity of H_2 and CHA, then one might expect a very significant conversion of the dissolved H_2 to H^- or Cs^+H^- in CsCHA solution.

It is known that the H^- ion and/or K^+H^- is definitely present at low concentration in potassium methylamide/methylamine solutions exposed to H_2 gas, since at H_2 pressures above about 1.4 MPa, KH precipitates from solution.[41] In contrast, although kinetic data show that H_2 is a stronger acid than NH_3 in the gas phase,[42] in amide/ammonia solution apparently only solvated electrons are generated at high H_2 pressure.[43]

Lithium hydride alone does not catalyze D_2 exchange in ammonia or methylamine,[8] which suggests that one or both of reactions 7 and 8 do not occur to any extent. For reaction 7,

$$D_2 + H^- \rightleftharpoons HD + D^- \quad (7)$$

$$RNH_2 + D^-(H^-) \rightleftharpoons RNH^- + HD(H_2) \quad (8)$$

Ritchie and King's theoretical calculations for the system $H_2 + H^- \rightleftharpoons H^- + H_2$ predict no complex formation and a 63 kJ·mol^{-1} (15 kcal·mol^{-1}) energy barrier for the *gas* phase reaction.[44] Commercial LiH is practically insoluble in amines and does not react with CHA; however, hydride generated in situ can be more reactive, at least in methylamide/methylamine solution.[45] In any case, reaction 8 would produce amide catalyst, but no D_2 exchange was observed in the absence of added amide catalyst.[8] Therefore, *if* D^- is present in CHA catalyst solutions, as some function of D_2 pressure, the only very slight dependence of k'_{obsd} on D_2 pressure for the NaCHA runs indicates that this $D^-(H^-)$ does not contribute significantly to catalysis of the D_2 exchange reaction via reactions 7 and 8.

A Comparison of Literature Data for Base-Catalyzed Exchange of D_2, HD. Some representative literature data for base-catalyzed D_2 exchange with protic media have been compiled in Table II. Because of differences in the methods used to determine the rate constants (stirred reactor, shaken reactor, laminar flow systems), only a qualitative comparison is made regarding relative reactivity in the range of solvents. Also, because the pK_as have been determined or estimated for different solvents, they are not directly comparable. However, the following general trends are seen: the stronger the base, as reflected in its relative pK_a value (as free anion?), the faster the reaction, the smaller the E_a, and the more negative the $\Delta S^{\ddagger}$. There seems to be no correlation with solvent dielectric constant; this suggests that electrostatic effects are much less important than, e.g., hydrogen bonding in controlling the extent of ion pair and ion aggregate formation,[48] which in turn should control the catalytic reactivity.

It is reasonable to assume a common general mechanism over this range of solvents. Ritchie and King argued that for reaction in water the major barrier to formation of the complex $HOHH^-$ was necessary partial desolvation of the base.[38a] In moving down through the solvents in Table II there is a progressive change to poorer anion solvating ability. At the same time E_a drops gradually, until for CHA it is close to the 8-12 kJ·mol^{-1} (2-3 kcal·mol^{-1}) range predicted by Ritchie and King for the proton transfer step itself.[38a] Judging by the corresponding change to more negative $\Delta S^{\ddagger}$, the transition state structure must become *relatively* better solvated than the base (whatever the active form—free ion or ion pair). This is consistent with a fairly complex transition state, perhaps one in which the cation participates.

The kinetic isotope effect values, where available, all fall in the range 1.1-2.0. These are small by hydrocarbon acid standards, but still large enough at 1.5-2.0 to be consistent with rate-determining hydrogen transfer from molecular hydrogen.[31] The unusual dependence of k.i.e. on temperature and catalyst concentration seen for some systems is not well understood;[37] for the present system, CHA, mass transfer effects in the apparatus often led to incorrect, high values (see Results section). The variation of k.i.e. with solvent system in Table II is not great, but the values measured for CHA are comparable to the maximum observed in the Me_2SO-water system.[31] Cox and Gibson[49] have considered the problem of understanding the solvent dependence of kinetic hydrogen isotope effects for carbon acids. In the systems examined, they found no correlation between the magnitude of the k.i.e. values and the nature of the solvent, the reaction rate, or the ΔpK between substrate and base.

Cyclopentylamine. This study is being extended to cyclopentylamine (fp −85.7 °C[50]), to permit kinetic measurements at much lower temperatures where mass transfer effects are expected to be reduced. The effect of cation-complexing agents (crown ethers, cryptates) will be examined, although it is unlikely they will be chemically stable in these solutions.[45]

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