

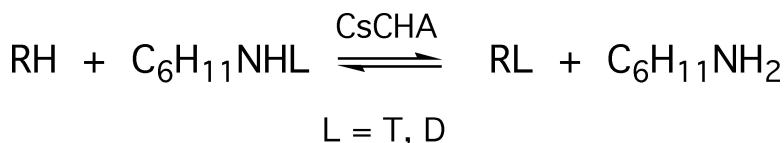
Article

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R = Me, Et, nPr, iBu, neoPe, cycloPr and others

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## Kinetic Acidity of Aliphatic Hydrocarbons. Hydrogen Isotope Exchange with Cesium Cyclohexylamide in Cyclohexylamine<sup>1</sup>

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**Abstract:** Kinetic acidities are reported for methane, ethane, propane, cyclopropane, isobutane, neopentane, tetramethylbutane, norbornane, nortricyclene, and adamantane by tritideprotonation or deuterideprotonation in cyclohexylamine catalyzed by cesium cyclohexylamide.

Little is known quantitatively about the acidity of alkanes in solution. Equilibria between alkylolithiums and iodobenzene in ether were used to determine relative acidities of several alkanes.<sup>2</sup> Similarly, equilibria between organomagnesium and organomercury compounds have been used, taking advantage of the difference in electronegativity of the two metals.<sup>3,4</sup> These methods were cited by Cram as part of his "MSAD" scale of carbon acidities in his book on carbanions in 1965,<sup>5</sup> and little has been added since then. Breslow deduced a  $pK_a$  for the tertiary position of isobutane by electrochemical studies on *tert*-butyl iodide,<sup>6,7</sup> but the method involves irreversible potentials and has not been applied to other alkanes. The most extensive data over the past several decades have come from our studies of hydrogen isotope exchange rates of a number of compounds with cesium cyclohexylamide (CsCHA; a list of acronyms used is given in Chart S1, Supporting Information) in cyclohexylamine (CHA). Some of the earlier results have been published, in particular the reactivities of cyclohexane<sup>8</sup> and other cycloalkanes,<sup>9,10</sup> methane,<sup>11</sup> and the bridgehead positions of trypticene compounds.<sup>12</sup> These early experiments were done by measuring deuterium incorporation from cyclohexylamine-*N,N*- $d_2$  (CHA-*d*) by mass spectrometry or tritium incorporation from cyclohexylamine-*N-t* (CHA-*t*) with liquid scintillation counting. More recently, these exchange reactions were studied with tritium NMR.<sup>13,14</sup> Recent publications concerned the kinetic acidities

of cubane<sup>15</sup> and 1,1,1-triphenylethane.<sup>16</sup> In the latter study the primary isotope effect was found to be similar to that of cyclohexane despite a  $10^4$  difference in rate and implying a similar transition structure.

Some of the work of the past several decades has not yet been published, particularly the relative reactivities of ethane, propane, and other aliphatic hydrocarbons. Such reactivities have become important recently as carbanion models for transition-metal hydrocarbon activation reactions.<sup>17</sup> Moreover, it is now possible to model the exchange reactions with *ab initio* calculations.<sup>18</sup> The resulting comparison of experimental and theoretical results should make a more useful contribution to chemistry, and such studies are now in progress. Some of the unpublished experiments involved deuterium exchanges in which the deuterium content was a significant fraction of the total hydrogen pool and complex kinetic analyses. We showed recently in studies with methane how such complex kinetics can be readily treated with modern spreadsheet approaches on a personal computer.<sup>19</sup>

In this paper we present kinetic results for deuterium and/or tritium exchange of ethane (EtH), propane (PrH), isobutane (<sup>i</sup>BuH), neopentane (neoPeH), and 2,2,3,3-tetramethylbutane (TMB) with CsCHA in CHA, and for reference include methane (MeH), cyclohexane (CHX), norbornane (Nor), adamantane (Ada), cyclopropane (cPrH), and nortricyclene (NTC). These compounds range from gases to solids, and several techniques were required, but in general, most reactions were run in stainless steel reaction vessels<sup>19</sup> in which materials could be introduced or removed under an inert atmosphere. Solids and solutions were added in a glovebox; liquids were distilled in, and gases were admitted on a vacuum line. The kinetics

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**Table 1.** Values Used for Solubilities of Hydrocarbons in CHA at 50 °C and 1.00 atm<sup>20</sup>

compd	mole fraction $x_2^a$	compd	mole fraction $x_2^a$
methane	0.00180	isobutane	0.0702
ethane	0.0112	neopentane	0.0970
propane	0.0362	cyclopropane	0.0521

<sup>a</sup> Henry's law constant  $K_{\text{Henry}} = 1/x_2$  at 1 atm.

**Table 2.** Relative Rates for Reactions of Alkanes with CsCHA at 50.3 °C

compd	relative rate CHX = 1	relative rate EtH = 1	relative rate MeH = 1	run
cyclopropane			30	DRT8
methane		240 ± 10		DRT7
propane- <i>I-d</i>		0.80 ± 0.03		K8, K5
isobutane- <i>I-d</i>		0.49 ± 0.03		K8, K5
neopentane	8.7 ± 0.4 <sup>a</sup>	0.22 ± 0.01		K6, DRT9, DRT7
tetramethylbutane	3.0 ± 0.1 <sup>b</sup>			K6
adamantane	0.28 ± 0.3			K7
norbornane	4.5 ± 0.4			K7
norbornane- <i>I-d</i>	7.7 ± 0.6 <sup>c</sup>			ECD6
nortricyclene- <i>3-d</i>	28 ± 2 <sup>c</sup>			ECD7

<sup>a</sup> 4.2 ± 0.1 at 101 °C (DRT5). <sup>b</sup> 2.0 ± 0.1 at 100 °C (ECD6, DRT5). <sup>c</sup> At 101 °C.

solutions were kept under nitrogen pressure so that aliquots could be ejected from the delivery tube as required.

For some of these compounds that are gases at the reaction temperature, corrections must be made for the amount of compound actually in solution. We had measured the solubilities of several hydrocarbons in CHA<sup>20</sup> and showed that they give normal correlations with the energy of vaporization at the boiling point.<sup>21</sup> These results were used to derive the solubilities in CHA at 50 °C summarized in Table 1. The moles of gas in solution,  $X_s$ , and the moles in the gas phase,  $X_g$ , were derived from the gas law,  $P$  (pressure of  $X_g$ ) =  $(X_gRT)/V$  (volume of free space in the reactor), and Henry's law,  $P/K_{\text{Henry}} = X_s/(X_s + S)$ , where  $S$  = moles of CHA.

In principle, the pseudo-first-order rates could be converted to second-order rate constants by correcting for the catalyst concentration. In practice, although this approach does work at times, we found more frequently that partial quenching of the base made the calculation of such rate constants unreliable especially over the long reaction times frequently required (months). As a result, we usually ran exchange reactions on mixtures containing at least two substrates to determine relative rates directly. The kinetic aliquots were generally quenched and separated by gas chromatography. Deuterium content was determined by low-voltage mass spectrometry; tritium content was determined by liquid scintillation or proportional flow counting. Because these compounds are relatively unreactive, most kinetics runs involved incorporation of deuterium or tritium from cyclohexylamine-*N,N-d\_2* or -*N-t*, respectively. Where appropriate, the kinetic analyses were done using the Excel spreadsheet method described previously. A summary of the relative rates obtained is given in Table 2. Rates relative to cyclohexane are summarized in Table 3. Complete results for each kinetic run are given in the Supporting Information.

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**Table 3.** Exchange Rates of Alkane Hydrogens Relative to Cyclohexane at 50 °C

compd	relative rate	log $K(\text{RLi} + \text{Ph})^e$	log $K(\text{RMg} + \text{PhHg})^f$
methane	9500 ± 750		1.8
ethane	40 ± 3	3.50	4.0
propane	32 ± 4 <sup>a</sup>	3.88	
cyclopropane	2.3 × 10 <sup>5</sup>	0.98	0.7
isobutane	20 ± 4 <sup>a</sup>	4.59	4.3
neopentane	8.7 ± 0.4	5.46	
tetramethylbutane	3.0 ± 0.1		
norbornane	4.5 ± 0.4		
adamantane	0.28 ± 0.03 <sup>b</sup>		
benzene	9.1 × 10 <sup>7</sup> <sup>c</sup>	0	0
ethylene	7.1 × 10 <sup>6</sup> <sup>d</sup>	−2.41	0.3
cyclobutane	28 ± 10 <sup>e</sup>	6.14	
cyclopentane	5.7 ± 0.3 <sup>e</sup>	6.90	
cyclohexane	(1)		> 6 <sup>g</sup>

<sup>a</sup> Primary hydrogens. <sup>b</sup> Secondary hydrogens. <sup>c</sup> Reference 8. <sup>d</sup> Reference 33. <sup>e</sup> Reference 2. <sup>f</sup> Reference 4. <sup>g</sup> Assumed to be the same as isopropyl.

## Experimental Section

**Propane-*I-d*.** To a 500 mL three-neck flask containing 0.50 g (0.021 mol) of dry magnesium turnings and a stir bar on the vacuum line and fitted with a reflux condenser and a dropping funnel was added 50 mL of diethylene glycol dimethyl ether which had been dried over lithium aluminum hydride. The system was evacuated to 10 μm, and the solvent was degassed by cooling to 0 °C and pumping for 30 min. A crystal of iodine and 1 mL (0.012 mol) of 1-bromopropane were added, and the mixture was heated to reflux. When the iodine color was gone, 2.0 mL (0.024 mol) of 1-bromopropane was slowly added, and the reaction mixture was heated at reflux for 3 h. The mixture was then cooled and degassed, and 2.0 mL (0.034 mol) of acetic acid-*d* (98% D) was added with vigorous stirring. After being stirred for 30 min, the mixture was cooled to 0 °C, and the propane was transferred to a flask cooled in liquid nitrogen. The flask was then warmed to 0 °C, and the propane was transferred to a gas bulb cooled to −196 °C. The low-voltage mass spectrum (10 eV) of the product showed it to be 87% deuterated, and free of diglyme.

A similar procedure was used to prepare propane-*2-d*. Mass spectral analysis of the product at 10 eV showed a purity of 98% C<sub>3</sub>H<sub>7</sub>D. There was no evidence of either ether or acetic acid.

**Isobutane-*I-d*.** A flask containing 1.01 g (0.042 mol) of dry magnesium turnings and fitted with a dropping funnel and a reflux condenser was evacuated to 1 μm, and 50 mL of dry diethyl ether and 15 drops of 1,2-dibromoethane were added. When the reaction had begun, 3.89 g (0.042 mol) of 1-chloro-2-methylpropane was added over a period of 10 min. The reaction was stirred for an additional 20 min, and refluxed for 45 min. The reaction mixture was allowed to sit overnight at room temperature, and the ether and other volatile components were vacuum transferred, leaving behind the solid Grignard reagent. This solid was pumped down to 30 μm, and 5.00 mL (0.086 mol) of acetic acid-*d* (98% D) was slowly added. The gas produced was collected in a gas bulb cooled in liquid nitrogen. The gas was then passed through a series of traps containing sulfuric acid and sodium hydroxide pellets, followed by two traps cooled in liquid nitrogen. This served to remove residual traces of ether in the gas sample. The product was found to contain 97% isobutane-*I-d*, and was without traces of ether or acetic acid in the low-voltage (10 eV) mass spectrum.

A similar procedure was used to prepare isobutane-*2-d*. Mass spectral analysis showed no contamination by ether in the gas sample, and that it had a purity of 95% C<sub>4</sub>H<sub>9</sub>D.

**Norbornane-*I-d*.**<sup>22</sup> (This procedure is a modification of the procedure of Nickon.) A mixture of 6.5 g of 1-chloronorbornane,<sup>23</sup> 4.6 g of lithium (as strips), 20 mL of <sup>t</sup>BuOD, and 232 mL of THF was heated

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under reflux for several hours. Unreacted lithium was decomposed with methanol. Pentane and aqueous NaCl were added, and the dried pentane solution was distilled to yield 20% norbornane-1-*d*: IR 2200, 721  $\text{cm}^{-1}$ ; 87.5% deuterium by low-voltage MS.

**Nortricyclene.** To a suspension of 4.0 g (0.1 mol) of lithium aluminum hydride in 70 mL of ether was added a solution of 10 g (0.058 mol) of 3-nortricyclyl bromide (Aldrich) in 30 mL of ether. After being stirred under reflux for 4 d, the mixture was worked up, and the nortricyclene was collected by GC (20% SE 30 column) at 75 °C to give 1.2 g (22% yield), mp 57–58 °C (lit.<sup>22</sup> mp 57–58 °C). Nortricyclene-3-*d* was prepared similarly using lithium aluminum deuteride.

**Cyclohexane.** Spectroquality cyclohexane was used without further purification.

**Cyclohexylamine.** Cyclohexylamine was fractionally distilled, bp 133–134 °C. Before use, it was dried over lithium cyclohexylamide. Cyclohexylamine-*N,N*-*d*<sub>2</sub> was prepared from several exchanges of cyclohexylamine, benzene, and D<sub>2</sub>O.<sup>24</sup> After each charge with D<sub>2</sub>O the water was removed by azeotropic distillation with benzene; the benzene was then removed by distillation followed by distillation of CHA-*d*<sub>2</sub>. The deuterium content was measured by NMR using mixtures with known amounts of H<sub>2</sub>O and D<sub>2</sub>O or with methanol-*d*; both methods showed >99% D. Cyclohexylamine-*N-t* was prepared from cyclohexylamine by addition of 50 mCi of tritiated water (1 Ci/mL) to 50 mL of cyclohexylamine. The mixture was dried over LiCHA and typically vacuum transferred into the reaction vessel.

Lithium cyclohexylamide was prepared in a manner similar to that described previously<sup>25</sup> except for the use of butyllithium. Cesium cyclohexylamide was prepared by allowing cesium metal (prepared by pyrolysis of cesium azide) to react with cyclohexylamine as described previously.<sup>26</sup> Note that, in the preparation of cesium cyclohexylamide-*N-d*, the reaction of cesium metal with CHA-*d*<sub>2</sub> is much slower than with undeuterated CHA.

**Kinetic Procedures.** Two different types of procedures were used. For most runs, kinetic reactors<sup>19</sup> were constructed of stainless steel with a threaded opening at the top for introduction of solid samples and fitted with two stainless steel Nupro valves for introduction of gaseous and liquid compounds while attached to the vacuum line and for sampling of liquid aliquots during a kinetic run. For gaseous or volatile substrates, a sample of vapor was bled from the reactor at intervals and analyzed. For others, the reactor was pressured with nitrogen or argon and a sample of the solution was ejected and quenched. For the runs at 101 °C, the reaction solutions were transferred on the vacuum line to tubes that were then sealed off and thermostated in a manner described previously.<sup>27</sup>

**Run K3 (neoPeH, TMB).** To a reactor containing a sealed glass vial (containing 6 mL of a CsCHA-*d* solution in CHA-*d*<sub>2</sub>) and a stainless steel ball were added 1.508 g (0.013 mol) of tetramethylbutane, cyclohexylamine-*N-d*<sub>2</sub> (42.32 g, 0.418 mol, dried over LiCHA), 1.56 g (0.0186 mol) of cyclohexane, 1.15 g (0.016 mol) of neopentane, and 1.75 g (0.016 mol) of *p*-xylene (to serve as infinity standard). The reactor was equilibrated at 50.0 °C in a constant-temperature bath, vigorously shaken until the base vial was broken, and replaced in the temperature bath. At intervals, 4.0 mL aliquots were ejected into 1.0 mL of water. These quenched aliquots were sealed into ampules and stored at 0 °C until all of the points had been taken. The aliquots were then all worked up simultaneously by adding the contents to 10 mL of water, 2.0 mL of hexane, and about 10 g of ice. The hexane extracts were washed with cold water and dried over magnesium sulfate. The hexane solutions were pipetted from the centrifuged drying mixture,

and stored in sealed vials at 0 °C. Precaution was taken not to allow the solutions to reach room temperature to reduce the chance of loss of neopentane. The extracts were separated by chromatography, collecting the *p*-xylene, tetramethylbutane, and cyclohexane in capillaries cooled to liquid nitrogen temperature and the neopentane in an evacuated gas bulb.

In the mass spectral analysis, even at 10 eV neoPeH and TMB gave no parent peak and D incorporation was estimated from the dominant *tert*-butyl cation peak assuming no isotope effect on fragmentation. Even after almost 2000 h of reaction, the amount of deuterium incorporation was small, 8% into neoPeH, 3% into TMB, and an amount into CHX too small to measure. The data are summarized in Table S1 (Supporting Information).

**Run K5 (EtH, PrH, <sup>i</sup>BuH).** CsCHA-*d* in CHA-*d*<sub>2</sub> (5.0 mL) was syringed into the reactor in a glovebox, and 75 mL (0.644 mol) of cyclohexylamine-*N,N*-*d*<sub>2</sub> (dried over LiCHA-*d*) was vacuum transferred in, followed, at –196 °C, by 0.0267 mol of ethane, 0.0413 mol of propane, and 0.0642 mol of isobutane. From the solubility data (Table 1) the following amounts of the hydrocarbons are calculated to be in solution at 50 °C: ethane, 79.0%, 0.267 M; propane, 92.7%, 0.485 M; isobutane, 96.2%, 0.780 M. Kinetic aliquots were obtained by removing the reactor from a 50.3 °C bath, placing it in a Dewar flask containing 50 °C water, and attaching the flask to a vacuum line. Approximately 2–5 cm of gas was admitted to the vacuum line, the reactor valve was closed, the pressure was read from the manometer, and the hydrocarbons were condensed in a gas sample holder with liquid nitrogen. The entire procedure generally took less than 5 min. The kinetic samples were stored at 0 °C and analyzed together by separation with gas–solid chromatography and low-voltage mass spectrometry. Results are summarized in Table S2 (Supporting Information).

**Run K6 (CHX, neoPeH, TMB).** The reactor contained 5.0 mL of CsCHA/CHA, 1.495 g (0.013 mol) of TMB, 2.0 mL (0.019 mol) of cyclohexane, 1.5 mL (0.012 mol) of *p*-xylene, 0.062 mol of neopentane, and 75 mL (0.643 mol) of cyclohexylamine-*t* (containing 50 mCi of tritiated water and dried over LiCHA). Kinetic points from a 50.3 °C bath were ejected as in run K3, separated by GC with each compound collected in a capillary, and counted by the scintillation counter. The quantity dpm/area was used as the measure of tritium activity. At the final point, the *p*-xylene was collected in a tared capillary, weighed, and counted in the scintillation counter. The activity of the *p*-xylene was found to be  $3.9 \times 10^7$  dpm/mmol, assuming a 10-proton infinity. The kinetic results are summarized in Table S3 (Supporting Information).

**Run K7 (CHA, Ada, Nor).** This run contained a mixture of 5.0 mL of CsCHA/CHA, 1.531 g (0.016 mol) of freshly sublimed norbornane, 1.410 g (0.010 mol) of freshly sublimed adamantane, 75 mL (0.643 mol) of dry degassed CHA-*t* (containing approximately 50 mCi of tritium), 2.00 mL (0.019 mol) of cyclohexane, and 1.5 mL (0.012 mol) of *p*-xylene at 50.3 °C. The points were handled as in run K6, and the data are summarized in Table S4 (Supporting Information).

**Run K8 (EtH, PrH, <sup>i</sup>BuH).** A reactor of 140 mL capacity contained 30 mL of CsCHA-*d*/CHA-*d*<sub>2</sub>, 0.0332 mol of ethane (79.2% in solution), 0.0534 mol of propane (92.8% in solution), and 0.0562 mol of isobutane (96.1% in solution) in 50 mL (0.428 mol) of CHA-*d*<sub>2</sub>. The kinetic aliquots from a 50.3 °C bath were analyzed as in run K5, and the data are summarized in Table S5 (Supporting Information).

A further analysis was made of the reaction products at the end of run K8 to determine the amount of exchange at the secondary and tertiary positions. We found using known deuterated isomers that we could not analyze for deuterium positions in propane and isobutane with infrared or mass spectrometry. The analysis was accomplished, however, by microwave spectroscopy following the reported analysis of deuterated propanes.<sup>28</sup> The microwave spectra of deuterated propanes

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and isobutanes have been reported.<sup>29</sup> Run K8 was kept in the 50 °C thermostat for several months after removal of the final aliquot. Propane and isobutane were isolated from the reactor and analyzed by Dr. LeRoy H. Scharpen of the Scientific Instruments Division of Hewlett-Packard Co. We are indebted to Dr. Scharpen for the analysis summarized in Table S6 (Supporting Information). Accurate values for the amount of undeuterated components were obtained, but values for the deuterated components were more difficult to calculate. For analysis of the monodeuterio components, the low dipole moments presented a major problem. The maximum available field strength (4000 V/cm) for Stark modulation was insufficient for complete modulation of the absorption lines. Consequently, differences in the Stark coefficients could affect the intensity of the lines. A major feature of the analysis was the inability to detect any signal for either propane-2-*d* or isobutane-2-*d*. Only an upper limit could be placed upon the amounts of these two species present. The lower limits for the ratio of deuterium incorporated into the methyl groups to deuterium incorporated into the secondary or tertiary position are 76 for propane and 39 for isobutane. Thus, the assumption that the measured rates of deuterium incorporation are measures of the incorporation into the primary positions is shown to be valid. Although the upper limit of detection for isobutane-2-*d* is higher than that for propane-2-*d*, it can be safely assumed that it is actually present in a smaller quantity than 0.4%. Since secondary protons are at least 76 times less reactive than the primary positions, it would certainly be unexpected to find the tertiary position to be more reactive than the secondary position.

**Run DRT2 (CHX, neoPeH, TMB).** This run was similar to run K3 except for the use of cyclohexylamine-*N-t* at 50 °C. Insufficient activity was introduced during the first points, and only the last few kinetics points gave useful data. Moreover, the neopentane was lost on storage. Tritium content was determined by proportional flow counting<sup>30</sup> using GC integration correction factors determined using a freshly prepared standard mixture. The useful data are given in Table S7 (Supporting Information).

**Run DRT5 (CHX, neoPeH, TMB at 100 °C).** A mixture of 1.50 g of cyclohexane, 1.58 g of neopentane, 0.98 g of tetramethylbutane, and 1.55 g of *p*-xylene (infinity standard) was transferred into a liquid nitrogen cooled reactor containing a glass vial of CsCHA and 65 mL of cyclohexylamine-*t*. Argon was added to 10 psi at -80 °C, and the reactor was equilibrated at 100 °C and shaken vigorously to break the CsCHA vial. A small sample was ejected into 4,5-methylenephenthrane whose color verified the release of base. Aliquots of 4 mL were ejected periodically into water over a 3-month period, acidified with HCl and ice, and extracted into hexane. At point 4 a white copious precipitate of dicyclohexylamine hydrochloride required repeated draining and extraction into hexane. The components were separated by GC and counted in a liquid scintillation counter. Relative GC/mmol factors were determined by calibration with known samples. The kinetic data are summarized in Table S8 (Supporting Information).

**Runs DRT7 (MeH, EtH, neoPeH) and DRT8 (MeH, cPrH).** These runs were presented previously in terms of methane kinetics in CHA-*d*<sub>2</sub>.<sup>19</sup> The data for ethane and neopentane in DRT7 are summarized in Table S9 and for cyclopropane in Table S10 (Supporting Information). Gas samples were removed at intervals and measured by low-voltage MS (10 V). Neopentane gave no parent peak; the highest *m/z* fragmentation peak was used, C<sub>4</sub>H<sub>9</sub><sup>+</sup>.

**Run DRT9 (CHX, neoPeH).**<sup>31</sup> This run contained 54.7 g of cyclohexylamine-*t*, 8.7 g of CsCHA solution, 0.849 g of toluene (as infinity standard), 0.551 g of neopentane, and 0.770 g of cyclohexane at 50 °C. It also contained 0.673 g of tetramethylsilane that decomposed during the course of the run and gave no useful information. The kinetic samples were quenched with water, extracted into hexane, and counted

with proportional flow counting as in run DRT2. The results are summarized in Table S11 (Supporting Information).

**Run ECD6 (CHX, Nor, TMB).** Using a method similar to that described previously,<sup>32</sup> a solution of norbornane-1-*d*, cyclohexane, tetramethylbutane, *p*-xylene (infinity standard), and CsCHA in cyclohexylamine-*t* was distributed among a number of sealed tubes which were kept in a 101 ± 0.3 °C thermostat and removed at intervals over a period of 2 months, and the contents were quenched, separated by GC, and counted by liquid scintillation counting. The deuterium content in norbornane-1-*d* was determined by low-voltage MS. The data are summarized in Table S12 (Supporting Information).

**Run ECD7 (CHA, NTC).** This run contained CHX and nortricyclene-3-*d* in CsCHA/cyclohexylamine-*t* and was similar to run ECD6. It also contained *exo*-tricyclo[3.2.1.0<sup>4,6</sup>]oct-1-ene-5,5-*d*<sub>2</sub>, which will be discussed in another paper. The CHX and NTC data are summarized in Table S13 (Supporting Information).

## Results

Previous results showed that isotope exchange with alkanes and cycloalkanes is exceedingly slow at 50 °C even with CsCHA. Thus, we first tried reactions at 100 °C but ran into two problems. With amounts of CsCHA of 0.15 M or more a precipitate was observed that redissolved on cooling. This precipitate was thought to be solid CsCHA, which would reduce the amount of active catalyst in solution. At long reaction times (weeks) another precipitate formed that was found to be dicyclohexylamine. This product is probably produced by a chain reaction initiated by loss of CsH from CsCHA. The resulting imine then reacts with CsCHA to form 1-cyclohexylamino-1-aminocyclohexane that readily loses ammonia to give another imine. Hydride transfer from CsCHA in a Meerwein-Ponndorf-type reaction then gives dicyclohexylamine and cyclohexylimine to start the cycle again.

Because of these side reactions, it was not possible to know the amount of base catalyst in solution at 100 °C. Accordingly, tritium incorporation into cyclohexane was used as the time scale to determine relative rates directly. For example, Figure 1 shows the tritium activity of TMB in run ECD6 compared to that of cyclohexane. Because the extents of reaction are so small, these activities are equivalent to the natural logarithms of reaction. The observed slope needs only to be modified by the different infinities—12 H for CHX, 18 H for TMB—to give a relative rate,  $k_T(\text{TMB})/k_T(\text{CHX}) = 1.83 \pm 0.08$  at 101 °C. The similar run DRT5 at 100 °C contained neopentane and tetramethylbutane with cyclohexane. That run gives after correction for relative GC response  $k_T(\text{TMB})/k_T(\text{CHX}) = 2.08 \pm 0.08$ , in good agreement with run ECD6, and  $k_T(\text{NeoPeH})/k_T(\text{CHX}) = 4.24 \pm 0.14$  (Figure S1, Supporting Information).

For Nor-1-*d* an infinity for CHX is required in run ECD6. This was obtained from the *p*-xylene present whose 10 hydrogens exchange rapidly under these conditions and reached equilibrium even at early kinetic points. For Nor-1-*d* itself, an infinity of 0% D is assumed and the slope in Figure 1 then gives  $k_D(\text{Nor})/k_T(\text{CHX}) = 13.8 \pm 1.0$ . Using the isotope effect determined previously for the exchange with CsCHA of 1,1,1-triphenylethane-2-*d*(*t*),  $k_D/k_T = 1.8$ ,<sup>16</sup> a relative rate of  $k_T(\text{Nor})/k_T(\text{CHX}) = 7.7 \pm 0.6$  is obtained.

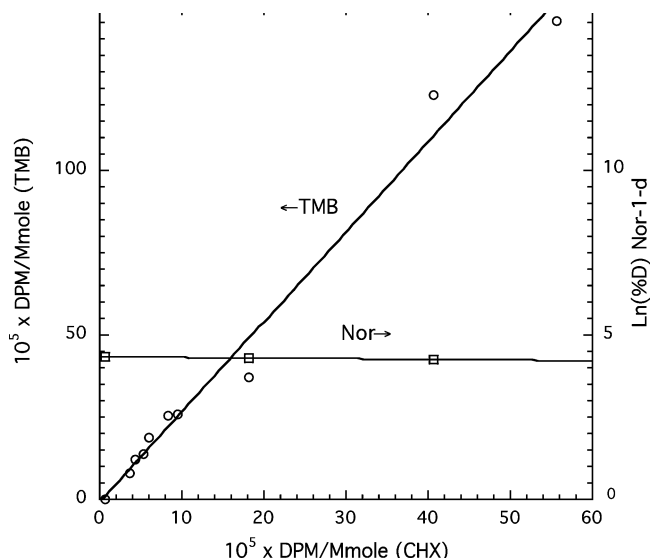
A similar approach is applied to nortricyclene-3-*d* in run ECD7. The data are in Table S13 (Supporting Information) and

(29) Lide, D. R., Jr. *J. Chem. Phys.* **1960**, *33*, 1514.

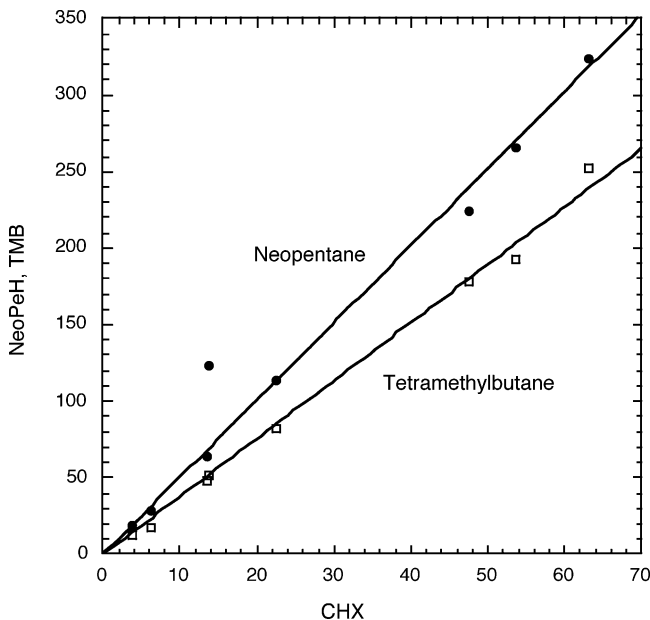
(30) Streitwieser, A., Jr.; Koch, H. F. *J. Am. Chem. Soc.* **1964**, *86*, 404–409.

(31) This run was initiated by Frank Mares.

(32) Streitwieser, A.; Lawler, R. G.; Perrin, C. *J. Am. Chem. Soc.* **1965**, *87*, 5383–5388.



**Figure 1.** Tritium incorporation into TMB (circles) and  $\ln(\% \text{ D})$  of Nor-1-d (squares) compared to tritium incorporation into CHX: circles,  $-0.80 \pm 2.83 + (2.74 \pm 0.12)x$  ( $R^2 = 0.984$ ); squares,  $4.34 \pm 0.003 - ((1.96 \pm 0.14) \times 10^{-8})x$  ( $R^2 = 0.995$ ). The CHX infinity value is calculated as  $7.044 \times 10^8$  dpm/mmol from the *p*-xylene present.



**Figure 2.** Run K6 (NeoPeH and TMB vs CHX at 50.3 °C). Units are dpm/area. Slopes shown are  $5.04 \pm 0.21$  ( $R^2 = 0.965$ ) and  $3.79 \pm 0.07$  ( $R^2 = 0.991$ ).

plotted in Figure S2 (Supporting Information); the resulting  $k_{\text{D}}(\text{NTC})/k_{\text{T}}(\text{CHX})$  of  $50.6 \pm 4.3$  when corrected for the primary isotope effect becomes  $k_{\text{T}}(\text{NTC})/k_{\text{T}}(\text{CHX}) = 28.1 \pm 2.4$ .

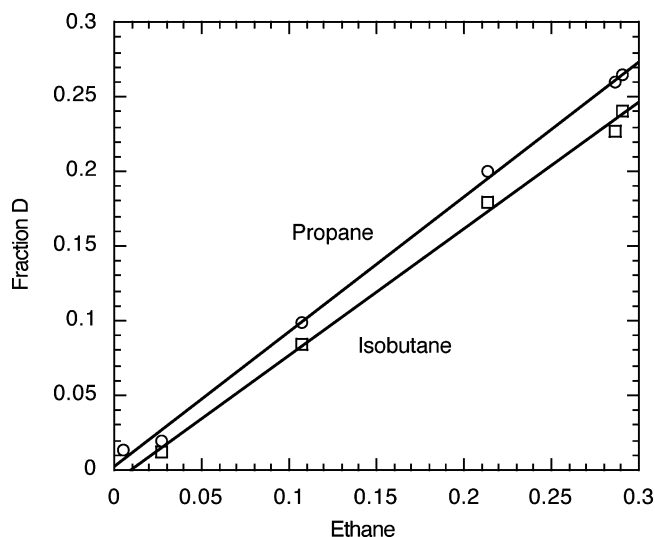
At 50 °C we observed none of the precipitation problems at 100 °C, even at very long reaction times (months). Accordingly, most of the kinetic studies were thereafter run at the lower temperature. Run K6 provides relative rates of neopentane and tetramethylbutane with CsCHA in tritiated CHA at 50.3 °C again by direct plots of their radioactivities since the extents of reaction were so small (Figure 2). The relative rates in this figure need to be corrected for differing numbers of reactive hydrogens and the relative GC response factors to give  $k_{\text{T}}(\text{NeoPeH})/k_{\text{T}}(\text{CHX}) = 8.54 \pm 0.36$  and  $k_{\text{T}}(\text{TMB})/k_{\text{T}}(\text{CHX}) = 3.04 \pm 0.06$ . Confirmation of these values comes from run DRT9, tri-

tiodeprotonation of NeoPeH and CHX at 50 °C. This run, in which the activities were determined by proportional flow counting instead of liquid scintillation counting, shows more scatter (Figure S3, Supporting Information), but the slope of  $10.2 \pm 1.0$  when corrected for the relative GC response of 0.889 gives  $k_{\text{T}}(\text{NeoPeH})/k_{\text{T}}(\text{CHX}) = 9.07 \pm 0.90$ , in good agreement with K6. We note, however, that the rates relative to cyclohexane are 1.5–2 times those at 101 °C; the differences indicate lower activation energies for the primary hydrogens of neopentane and tetramethylbutane of 3.3 and 2.1 kcal mol<sup>-1</sup>, respectively, compared to the secondary hydrogens of cyclohexane.

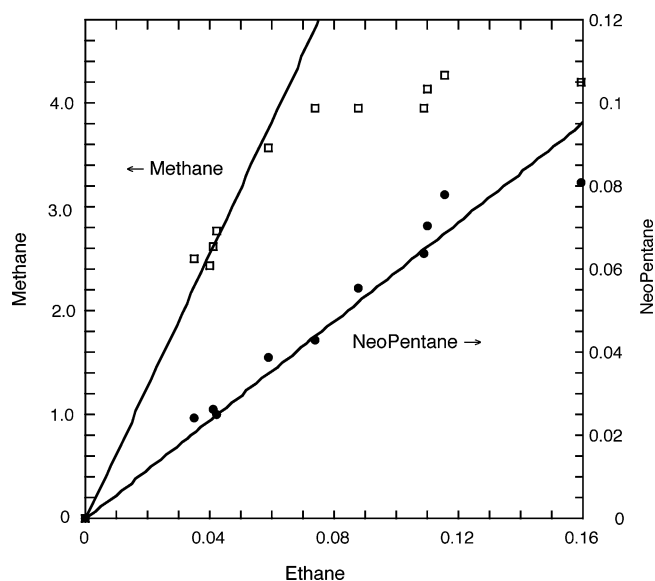
An alternative approach to exchange rates is deuteriodeprotonation in cyclohexylamine-*N,N*-*d*<sub>2</sub>. This approach measures  $k_{\text{H}}$  in the deuterated solvent compared to  $k_{\text{T}}$  in the tritiated solvent, but the solvent isotope effect is probably small when relative rates are compared. Measuring the deuterium content of branched hydrocarbons such as neopentane by mass spectrometry even at low voltage is made more difficult by the absence of parent peaks. Using fragment peaks in the absence of standards requires assuming that fragmentation is not seriously affected by isotope effects. A second problem is that as exchange dilutes the deuterium content of the solvent the rate of exchange slows accordingly. That is, the intermediate carbanion can react with the protonated solvent instead of deuterium; this effect is exacerbated by the primary isotope effect. Nevertheless, the effect of this complication is reduced by a direct measurement of relative rates. Figure S4 shows the percent undeuterated TMB vs NeoPeH in an  $\ln$ – $\ln$  plot for the data in run K3 (the infinity value is 0% for both); this figure shows respectable scatter, but the relative rate found,  $k_{\text{H}}(\text{TMB})/k_{\text{H}}(\text{NeoPeH}) = 0.22 \pm 0.05$ , is only approximate because the total amount of deuterium incorporated into TMB is only 3%.

A better and more important example is provided by run K8 in which ethane, propane, and isobutane are partially in the CsCHA/CHA-*d*<sub>2</sub> solution and partly in the vapor phase. Samples of the gas phase were withdrawn at intervals and examined by low-voltage mass spectrometry. Figure S5 (Supporting Information) shows the data plotted as first-order reactions; the acceptable straight lines take no account of the effect of the growing H content in the solvent. Since the rates are all of comparable magnitude, all three components are affected to approximately equal amounts by this effect, and more accurate results are obtained by comparing each component to each other. In Figure 3 relative rates compared to ethane are obtained by direct comparison of  $\ln(\text{extent of reaction defined as loss of undeuterated alkane})$ . These relative rates need to be corrected for relative numbers of reactive hydrogens taken as ethane, six, propane, six, and isobutane, nine, and for the amount of alkane actually in solution to give  $k_{\text{H}}(\text{PrH})/k_{\text{H}}(\text{EtH}) = 0.77 \pm 0.02$  and  $k_{\text{H}}(\text{<sup>i</sup>BuH})/k_{\text{H}}(\text{EtH}) = 0.46 \pm 0.02$ . Microwave analysis of a sample late in this run showed deuterium only in the primary positions; that is, the secondary position in propane and the tertiary position in isobutane were too slow to measure.

The earlier run K5 was similar, but the extent of incorporation of deuterium was much less than in run K8; thus, the data plotted in Figure S6 (Supporting Information) to give  $k_{\text{H}}(\text{PrH})/k_{\text{H}}(\text{EtH}) = 0.98 \pm 0.10$  and  $k_{\text{H}}(\text{<sup>i</sup>BuH})/k_{\text{H}}(\text{EtH}) = 0.64 \pm 0.06$  are considered to be less accurate than the precision indicates and serve only to confirm the approximate magnitudes found in K8.



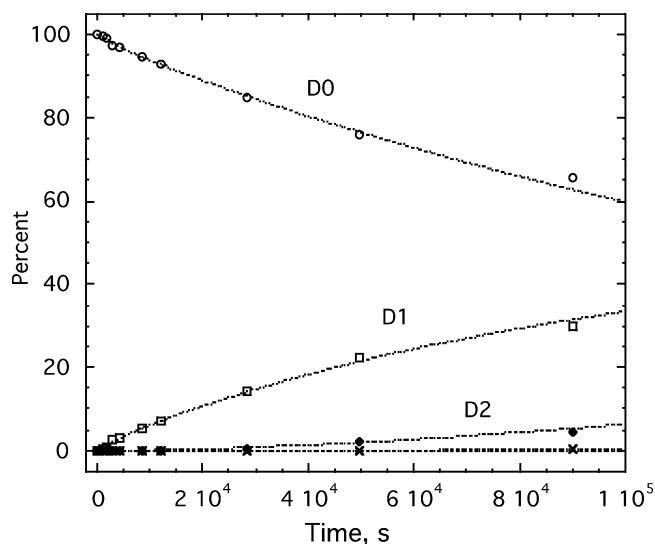
**Figure 3.** The lines shown are (propane (circles))  $0.0023 \pm 0.0038 + (0.905 \pm 0.020)x$  ( $R^2 = 0.998$ ) and (isobutane (squares))  $-0.0066 \pm 0.0036 + (0.842 \pm 0.019)x$  ( $R^2 = 0.998$ ).



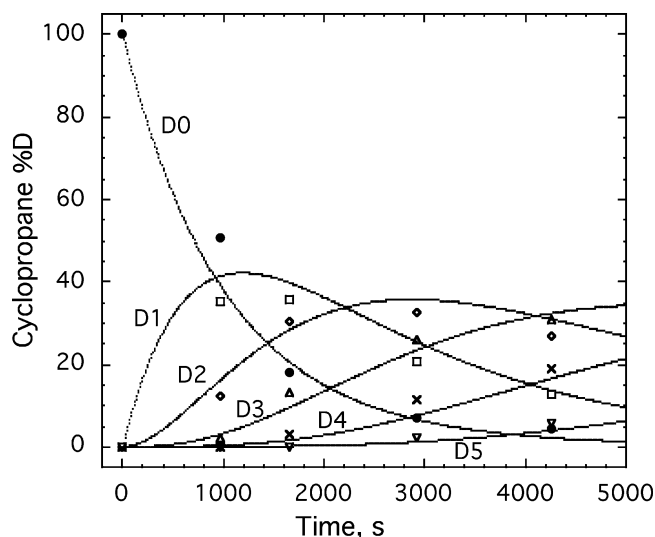
**Figure 4.** Relative rates of methane and neopentane in run DRT7 at 50 °C. The slopes shown are (neopentane (circles))  $0.60 \pm 0.02$  ( $R^2 = 0.950$ ) and (methane (squares, first five points only))  $64.0 \pm 1.6$  ( $R^2 = 0.980$ ).

In run DRT7 ethane is compared to methane and neopentane. The neopentane was used in relatively high concentration (0.6 M) so that enough was present (2% of the total) in the gas for analysis. The simulation of the results using a spreadsheet kinetic analysis was presented previously<sup>19</sup> to give  $k_{\text{H}}(\text{EtH}) = 1.05\text{E}-08 \text{ s}^{-1}$ ,  $k_{\text{H}}(\text{neoPeH}) = 3.3\text{E}-09 \text{ s}^{-1}$ ,  $k_{\text{H}}(\text{MeH}) = 1.1\text{E}-06 \text{ s}^{-1}$ ,  $k_{\text{H}}(\text{neoPeH})/k_{\text{H}}(\text{EtH}) = 0.24$ , and  $k_{\text{H}}(\text{MeH})/k_{\text{H}}(\text{EtH}) = 250$  when corrected for the amounts in solution.

The simulation only applies for the first  $10^6$  s; at later times progressive quenching of the base slows the reaction.<sup>19</sup> Direct comparison of relative rates again utilizes all of the data. Figure 4 shows the loss of undeuterated methane and neopentane compared to ethane over the entire 2-month course of reaction as  $\ln$ - $\ln$  plots of the extent of reaction. At long reaction times, the amount of undeuterated methane left is only on the order of 1–2% and the points deviate widely. The first five points shown, however, give a relative rate corrected for numbers of hydrogens and amounts in solution of  $k_{\text{H}}(\text{MeH})/k_{\text{H}}(\text{EtH}) = 229$



**Figure 5.** Simulation of the deuterium content of methane in run DRT8 with  $k_{\text{obs}} = 1.92\text{E}-6 \text{ s}^{-1}$ , using a primary isotope effect  $k_{\text{H}}/k_{\text{D}} = 4$  and secondary isotope effect  $k_{\text{H}}/k_{\text{D}} = 1.1$ , and corrected for the fraction of methane in solution (0.332),  $k_1 = 5.8\text{E}-6 \text{ s}^{-1}$ .



**Figure 6.** Simulation of the deuterium content of cyclopropane in run DRT8 with  $k_{\text{obs}} = 1.65\text{E}-4 \text{ s}^{-1}$ , using a primary isotope effect  $k_{\text{H}}/k_{\text{D}} = 4$  and secondary isotope effect  $k_{\text{H}}/k_{\text{D}} = 1.1$ , and corrected for the fraction of cyclopropane in solution (0.965),  $k_1 = 1.71\text{E}-6 \text{ s}^{-1}$ .

$\pm 6$ , in excellent agreement with the simulation; the latter uses the polydeuteration data of methane as well. The neopentane data give a corrected  $k_{\text{H}}(\text{neoPeH})/k_{\text{H}}(\text{EtH}) = 0.21 \pm 0.01$ , also in good agreement with the simulation.

Run DRT8 compared cyclopropane and methane. Cyclopropane is much more reactive, and when methane had incorporated only a few percent deuterium, only a few percent undeuterated cyclopropane remained. Four kinetic points were analyzed for cyclopropane over 70 min, but methane measurements were obtained over more than a day. The data, including multideuterations, were subjected to spreadsheet simulation with results shown in Figures 5 and 6. The analysis used 5 s time increments for cyclopropane and 250 s increments for methane. Figure 5 was inadvertently omitted from our previous paper on methane.<sup>19</sup> The spreadsheet codes are given as Chart S2 (Supporting Information). The results give  $k(\text{cPrH})/k(\text{MeH}) = 29.6$

The remaining run is straightforward to determine relative rates with CHX. Run K7 included Nor and Ada. The plots shown as Figure S7 (Supporting Information) give, after correction for relative GC response and numbers of hydrogens (taken as 12 for norbornane and adamantane, including the bridgehead hydrogens of Nor but not of Ada),  $k_{\text{Nor}}/k_{\text{CHX}} = 4.5 \pm 0.4$  and  $k_{\text{Ada}}/k_{\text{CHX}} = 0.28 \pm 0.03$ . The bridgehead position of Nor was found in ECD6 to be more reactive than CHX, but the unstrained tertiary position in Ada is assumed to be much less reactive than the secondary hydrogens.

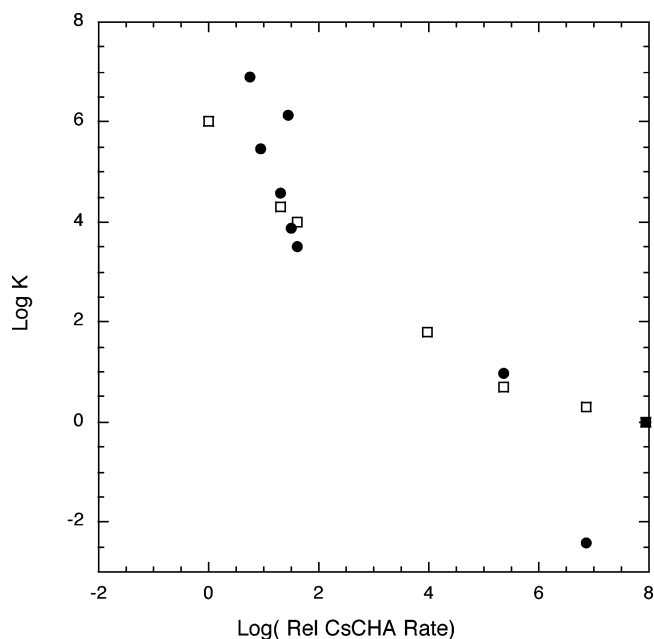
## Discussion

Since neopentane was measured relative to both CHX and EtH, it provides a bridge for relating all of the rates to cyclohexane (Table 2). For example, the relative rate of methane is given by the series  $[k(\text{NeoPeH})/k(\text{CHX})][k(\text{EtH})/k(\text{NeoPeH})] - [k(\text{MeH})/k(\text{EtH})] = 9500$ , assuming only that primary isotope effects are constant along the series. This number is somewhat greater than  $k(\text{MeH})/k(\text{CHX})$  estimated previously on the basis of second-order rate constants.<sup>19</sup> The new number is considered to be more reliable because of the problem of determining the effective base concentration in these runs. Similarly, the relative rate of cyclopropane is substantially greater than that given earlier on the basis of a single preliminary run.<sup>10</sup>

The complete relative rates summarized in Table 3 are themselves averages. For symmetrical compounds such as methane, ethane, cyclopropane, neopentane, and tetramethylbutane, the hydrogens are all equivalent. In adamantane, the secondary hydrogens are probably more reactive than the bridgeheads and all of the methylene protons are equivalent. Such is not the case for propane in which the methyl protons are of two types, anti and syn to the other methyl group, and probably have different reactivities. Even for cyclohexane, the axial and equatorial protons undoubtedly react at different rates.

The situation is more complex in the case of norbornane. Here there are three different proton types: eight secondary positions on the C2 bridges, two secondary positions on the C1 bridge, and two tertiary positions at the bridgeheads. A further complication is present as a result of the strained character of the bicyclo(2.2.1)heptane system, which increases the s-character in the bridgehead protons. Carbon-13 coupling constants predict the bridgehead proton to be bonded to a carbon orbital containing 28.4% s-character. The relative rate of the bridgehead positions of 7.7 at 101 °C is therefore not unexpected. If this relative rate also holds at 50 °C, the methylene hydrogens then have an average rate of about 4, about half that of the bridgehead hydrogens or slightly less than the average rate of cyclopentane.<sup>10</sup>

Early work on the kinetics and mechanism of CsCHA exchanges showed that the reactions are first-order in CsCHA ion pairs<sup>26</sup> and that the deprotonation rates parallel those with other bases.<sup>34</sup> The reactions appear to involve the corresponding organocesium compound as an intermediate. The normal primary isotope effect shows that the reprotonation of the RCs intermediate, although rapid, is not diffusion controlled. On the basis of Hammond's postulate,<sup>35</sup> the relative CsCHA rates are



**Figure 7.** Comparison of equilibrium constants for equilibria of RLi with  $\text{PhI}_2$  (filled circles) and of organomagnesiums with phenylmercury<sup>3</sup> (squares) with relative CsCHA rates.

expected to be similar to the relative energies of the corresponding organocesium compounds. Alternatively, since the relative RCs energies constitute a set of ion pair acidities, we expect the relative reactivities to form a Brønsted correlation, and they are thus measures of the ion pair acidity. Such a Brønsted correlation has been established previously for some related deprotonations by LiCHA.<sup>36</sup> What is then striking is how different these values are from gas-phase acidities. For example, gas-phase acidities of primary hydrogens are neopentane > isobutane > propane > ethane<sup>37</sup>—exactly the reverse order from the kinetic acidities in Table 3. Similarly the gas-phase acidity of the tertiary position in isobutane is greater than that of the secondary position in propane. It is now well understood that polarization plays an important role in the stabilization of anions in the gas phase.<sup>38–40</sup> Such polarization is inhibited by the cesium cation, which tends to strongly localize the charge. Thus, the kinetic acidities should be a much better guide to the stabilities of polar organometallics than the gas acidities.

It is also of interest to compare the present kinetic acidities to two historically important early measures of polar organometallic equilibria cited in the Introduction, the equilibrium constants for the reactions of alkyllithiums with iodobenzene<sup>2</sup> and of magnesium compounds with phenylmercury.<sup>3</sup> These equilibrium constants are summarized in Table 3 together with additional CsCHA relative rates from our earlier work. Plots of the log  $K$  values vs log(relative CsCHA rates) are shown in Figure 7. The general agreement is remarkably good considering the crudity of some of the equilibrium measurements and the known aggregation of alkyllithiums in ether, the mixture of divalent magnesium and mercury compounds, etc. A straight

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line plotted through all of the points has a slope of about  $-0.8$ , indicating that the organolithium, -magnesium, and -mercury equilibria are less sensitive to structure than the CsCHA rates.

We conclude that the relative CsCHA rates are valid measures of alkyl carbanion stability within polar organometallics and, indeed, are probably the best experimental measures currently available.

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**Supporting Information Available:** Tables of kinetic runs and additional figures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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