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Note

Kinetic acidities of some hydrocarbons by tritium NMR†‡

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ABSTRACT: Exchange rates in cyclohexylamine-*N*-^{3}H catalyzed by cesium cyclohexylamide were determined by ^{3}H NMR for the vinyl positions of 3,3-dimethyl-l-butene (1-*trans* > 1-*cis* > 2-) and the cyclopropyl methylene positions of norcarane (*exo* > *endo*) relative to the ring position of *p*-xylene. The kinetic acidity of cubane was confirmed. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{3}H NMR; exchange rates; cesium cyclohexylamide; kinetic acidity; hydrocarbon

INTRODUCTION

Several years ago we reported on the use of ^{3}H NMR spectroscopy for measuring hydrogen isotope exchange kinetics.[1] In the present work, we applied this method to measuring the exchange kinetics of several hydrocarbons with cesium cyclohexylamide (CsCHA) in cyclohexylamine (CHA). Our objective was to establish the method further and to determine its limitations. We also wanted to confirm the kinetic acidity of cubane reported previously,[2] particularly since that measurement differed so much from one reported earlier with lithium cyclohexylamide (LiCHA).[3] We included a compound containing a cyclopropyl ring, norcarane, because an early correlation with $J(^{13}\mathrm{C,H})$ coupling constants depended greatly on a single measurement of cyclopropane itself.[4] Finally, we included an alkene for comparison. Few alkenes could be studied by this technique because most alkenes with allylic hydrogens would undergo rapid allylic rearrangements under these conditions. *tert*-Butylethylene has no allylic hydrogens and is particularly suitable for the present study.

EXPERIMENTAL

Materials

Cyclohexylamine (CHA). Cyclohexylamine (99%, Aldrich) was dried over CaH_2 and distilled through a 6 ft column immediately before use.

Lithium cyclohexylamide (LiCHA). Into a Schlenk flask containing a known amount of dry cyclohexylamine at 0 °C was added slowly 0.8 equiv. of a 2.0 M solution of *n*-butyllithium in hexane in a nitrogen atmosphere. The solution was stirred vigorously during the addition and was then further stirred for 30 min. A white, cloudy solution was obtained. The excess cyclohexylamine and butane were removed in vacuum and lithium cyclohexylamide was obtained as a white powder. The solid was degassed and stored in a freezer within a glove-box filled with argon.

Cesium cyclohexylamide (CsCHA). Cyclohexylamine was dried over CaH_2 and distilled into a Schlenk flask. The flask was degassed by 3–4 freeze–pump–thaw cycles and placed in the glove-box. A small amount (0.1–0.2 mg) of biphenylyldiphenylmethane (BDPM) was added as an indicator. The previously prepared solid LiCHA was then added to the solution until the characteristic blue color of biphenylyldiphenylmethyllithium (BDPMLi) persisted. BDPMLi has a large extinction coefficient and is well suited as the indicator. The Schlenk flask was taken out of the glove-box, attached to a vacuum line and degassed. The dry cyclohexylamine was then vacuum transferred into an oven-dried Schlenk flask, degassed and placed in the glove-box for the preparation of cesium cyclohexylamide.

Cesium cyclohexylamide was prepared by treating an appropriate amount of cesium metal with dried cyclohexylamine at 50 °C in the glove-box. The reaction typically takes 3–4 days to complete. A clear, lemon-colored solution of cesium cyclohexylamide in cyclohexylamine was obtained. It was found that cyclohexylamine with traces of water yields cloudy solutions, presumably owing to the formation of cesium hydroxide. Accordingly, any cloudy solution of cesium cyclohexylamide was discarded and a new one was prepared.

Cyclohexylamine-*N*-^{3}H (CHA-^{3}H). Cyclohexylamine-*N*-^{3}H with the desired radioactivity was synthesized by the following procedure. A Schlenk flask equipped with a Teflon plunger and a No. 9 O-ring joint was charged with 15 ml of a 0.5 M solution of cesium cyclohexylamide in cyclohexylamine. The flask was attached to a metal vacuum line in the fume hood and degassed via three freeze–pump–thaw cycles at 18 μmHg. Approximately 30 ml of 10% T_2–H_2 gas was generated by heating UT_3 in a metal container, and introduced into the Schlenk flask containing CsCHA–CHA. The manometer showed a pressure of 580 mmHg. The solution was stirred for 1.5–2 h, and most unreacted T_2–H_2 gas was absorbed by activated charcoal at liquid N_2 temperature. The remaining T_2–H_2 was pumped out until the vacuum reached 50 μmHg or better. The CHA-^{3}H–CHA was then vacuum transferred into a dry Schlenk flask for future use, and a small amount of CHA-^{3}H–CHA (*ca.* 0.2 ml) was used to measure the activity by liquid scintillation counting. The entire operation was carried out on the vacuum system of the National Tritium Labelling Facility and Physical Biosciences Division, E. O. Lawrence Berkeley National Laboratory.

***p*-1,4-Di-*tert*-butylbenzene.** *p*-1,4-Di-*tert*-butylbenzene (98%, Aldrich) was sublimed under vacuum before use. Its purity was confirmed by m.p. determination and ^{1}H NMR. ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.30 (s, 18H), 7.31 (s, 4H).

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† Dedicated to Professor John D. Roberts on the occasion of his 80th birthday.

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p-Xylene. p-xylene (99+ + %, Aldrich) was dried over sodium and benzophenone. The solution was stirred in a Schlenk flask until a blue–purple color persisted. p-Xylene was then vacuum transferred into a dry Schlenk flask, degassed and stored in the glove-box for use.

3,3-Dimethyl-1-butene (*tert*-Butylethylene). 3,3-Dimethyl-1-butene (95%, Aldrich) was fractionally distilled into an ampoule with a small spinning band column; b.p. 41 °C. The purity was further confirmed by ^{1}H NMR. The ampoule was degassed on a vacuum line and flame-sealed. The ampoule was stored in a glove-box and broken immediately before use. ^{1}H NMR ($CDCl_3$). δ (ppm) 1.00 (s, 9H), 4.82 (d, 1H, $J = 10.7$ Hz), 4.91 (d, 1H, $J = 17.5$ Hz), 5.85 (dd, 1H, $J = 10.7$ 17.5 Hz).

Bicyclo[4.1.0]heptane (norcarane). The compound was synthesized following Kawabata *et al.*[5] and the product was distilled through a small spinning band column; b.p. 116–116.5 °C (lit.[5] b.p., 116–117 °C). ^{1}H NMR showed trace contamination by benzene, which was separated by preparative GC to give pure product. ^{1}H NMR ($CDCl_3$): δ (ppm), −0.03 to 0.01 (1H, m), 0.48–0.54 (1H, m), 0.80–0.84 (2H, m), 1.13–1.25 (4H, m), 1.57–1.63 (2H, m), 1.83–1.90 (2H, m).

Pentacyclo[4.2.0.02,5.03,8.04,7)octane (cubane). The sample of cubane was generously provided by Professor P. E. Eaton (University of Chicago) and used in our previous study;[2] ^{1}H NMR ($CDCl_3$): δ 4.00 ppm (s, 8H).

General procedure for kinetic acidity studies

It was found that very dry CHA-^{3}H–CHA is essential for reproducible tritium kinetic studies. Therefore, the same procedure as used to dry cyclohexylamine was followed for CsCHA. Into an NMR sample tube with a Teflon plunger and a No. 9 O-ring joint was added *ca.* 0.4 ml of the desired concentration of CsCHA–CHA solution, depending on the expected rate of proton–tritium exchange. An appropriate amount of the compounds to be studied (usually two competing compounds with 10–20 mg each) was added to the tube. The tube was attached to a vacuum line and degassed; 0.2 ml of CHA-^{3}H–CHA was then vacuum transferred into the NMR sample tube at liquid N_2 temperature. The system was again degassed and the tube was flame-sealed. The tube can be left in liquid N_2 indefinitely without H–T exchange. The transfers were facilitated by a specially built Schlenk bridge consisting of a NMR sample tube sealed to a manifold containing three No. 9 O-ring joints for attaching to flasks containing the CHA-^{3}H–CHA and the substrates to be measured and to a vacuum line. The H–T exchange was initiated by thawing the contents of the sealed NMR sample tube. The tube was placed in the NMR probe as soon as possible and data acquisition was started. The concentration of CsCHA solution was chosen so as to give an exchange half-life of about 10–20 h.

The ^{3}H NMR spectra for all titration–deprotonation experiments were acquired on an IBM/Bruker AF 300 MHz spectrometer (consequently the observing frequency for ^{3}H is 320 MHz) equipped with a 10 mm ^{3}H–^{1}H dual probe. The growing ^{3}H signals were monitored for as long as necessary until the signals reached their equilibrium values. The acquisition parameters were kept as constant as possible and all FIDs were processed with the same parameters. The intensity of each ^{3}H signal was expressed as a function of time and imported into a non-linear curve-fitting program for the calculations of the pseudo-first-order tritiation rate constants.

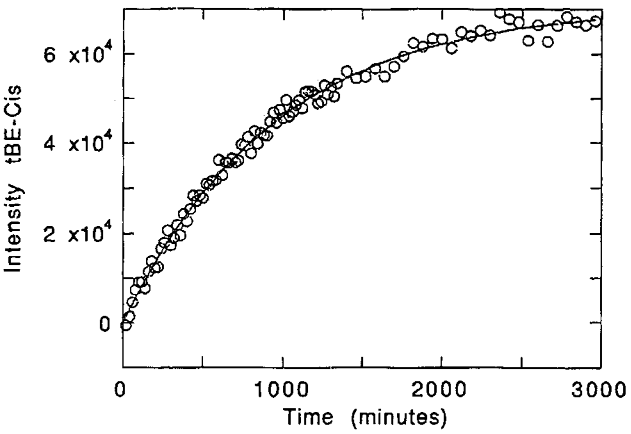

Figure 1. Plot of non-linear least-squares curve fit for *tert*-butylethylene-H_{cis}. The solid line is the theoretical fitted curve for $k = 105\ (\pm 3) \times 10^{-5}\ \text{min}^{-1}$.

Several control experiments were carried out to compare the intensity to the peak integration of each signal. The rate constants obtained were virtually identical, with negligible differences. A typical plot of a non-linear least-squares curve fit is shown in Fig. 1.

In applying this method, the reactivities of competing protons should not differ too greatly to avoid having one position essentially at equilibrium while another is still reacting. Similarly, very slow reactions are not suitable for this technique because of changes in NMR settings over a prolonged period.

RESULTS AND DISCUSSION

The results of the six runs of competitive tritiodeprotonations are given in Table 1 and the average relative rates are compared with benzene and cyclohexane in Table 2.

One of the goals of this study was to confirm the reactivity of cubane. The rate relative to the ring of p-xylene, 0.0060, found in the present work compares well with the values of 0.0052 and 0.0066 reported previously.[2] Hence the deviation of cubane from the previously established correlation[6] of reactivities with CsCHA and $J(^{13}C,H)$ values seems to be confirmed. We note, however, a temperature difference; the correlation with $J(^{13}C,H)$ was established from relative rates of tritium exchange at 50 °C rather than the 25 °C in the present work. The $J(^{13}C,H)$ values of the methylene hydrogens in the cyclopropyl ring of norcarane (158 Hz)[7] are similar to that in cyclopropane (160.45 Hz).[8] The calculated reactivity relative to cyclohexane based on $J(^{13}C,H)$[6] is log(relative rate) = 4.50. The experimental value for the *exo*-hydrogen [assuming k(benzene)/k(cyclohexane) = 10^8][9] is log(relative rate) = 4.57, in close agreement, and suggests that the temperature

Table 1. Tritium NMR kinetic results with CsCHA at 25 °C

Compound[a]	Pseudo-first order rate constants (10^{-5} s^{-1}) Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Av. (rel. rates)
p-Di-*t*BuB	4.73 ± 0.10	2.28 ± 0.03					0.23 ± 0.01
p-Xylene	100 ± 17		18.9 ± 0.6				4.8 ± 0.3
*t*BuE-H_t	26.3 ± 3.3	9.03 ± 0.35	3.67 ± 0.15	23.8 ± 1.9	18.7 ± 0.9	14.8 ± 0.5	(1)
*t*BuE-H_c	2.58 ± 0.18	1.11 ± 0.05	0.42 ± 0.02	2.28 ± 0.05	1.75 ± 0.05	1.73 ± 0.03	0.107 ± 0.003
*t*BuE-H_g		0.26 ± 0.09		0.62 ± 0.03	0.42 ± 0.07	0.48 ± 0.01	0.030 ± 0.001
Nor-H_x				0.40 ± 0.03			0.017 ± 0.002
Nor-H_n				0.053 ± 0.005			0.0022 ± 0.0003
Cubane						0.43 ± 0.02	0.029 ± 0.002

[a] *p*-di-*t*BuB, *p*-di-*tert*-butylbenzene; *t*BuE, *tert*-butylethylene; *trans* (H_t), *cis* (H_c) and geminal (H_g); Nor, norcarane, *exo* (H_x) and *endo* (H_n).

effect on relative rates is small. The lower reactivity of the *endo*-hydrogen obviously results from steric hindrance by the six-membered ring.

The *trans*-hydrogen of *tert*-butylethylene, H_t, has a reactivity relative to benzene of 0.023 in the present work. This value can be compared with that estimated for dedeuteration of ethylene-*d*, 0.078. The lower rate for the substituted ethylene can clearly be ascribed to the inductive effect of the *tert*-butyl group. For comparison, the *meta*- and *para*-ring positions in toluene are 0.54 and 0.50, respectively, as reactive as benzene towards LiCHA at 49.9 °C.[10] The *cis*-hydrogen (H_c) is much less reactive, as expected from steric hindrance effects of the *tert*-butyl group. In fact, this position is only a factor of two different in reactivity from that of a ring position in *p*-di-*tert*-butylbenzene (Table 1). The two hydrogens are structurally similar but there are some significant differences: the shorter C—C bond in the ethylene would be expected to enhance steric effects and the inductive effect of the second *tert*-butyl group should reduce the reactivity of the aromatic proton. The geminal proton (H_g) of *tert*-butylethylene is the least reactive, both because it is secondary rather than primary and because of the steric effects of the adjacent *tert*-butyl group. Finally, the reactivity of *p*-di-*tert*-butylbenzene reported in this work, 0.0053, differs from that reported previously at 50 °C, 0.0091.[9]

Table 2. Average relative rates for tritium exchange with CsCHA at 25 °C

Compound	Relative rate	Log(relative rate)
Benzene	(100)	0
Di-*tert*-Butylbenzene	0.53	-2.28
p-Xylene	11[a]	-0.96
tert-Butylethylene-H_t	2.3	-1.64
tert-Butylethylene-H_c	0.25	-2.60
tert-Butylethylene-H_g	0.069	-3.16
Norcarane-H_{exo}	0.039	-3.41
Norcarane-H_{endo}	0.0050	-4.30
Cubane	0.066	-3.18
Cyclohexane[b]	1.05×10^{-6}	-7.98

[a] Ref. 1.
[b] at 50 °C; Ref. 9.

CONCLUSIONS

The kinetic acidity of cubane reported earlier is confirmed. The reactivities of the cyclopropyl protons in norcarane, the vinyl protons in *tert*-butylethylene and the ring protons in *p*-xylene and *p*-di-*tert*-butylbenzene show the expected qualitative effects of hybridization as measured by $J(^{13}C,H)$, inductive effects and steric effects.

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