1 mol of reactive base, X^-, per mole of bromide produced. The base is lost because the unreactive heteroconjugate, lutidinium hydro X, is stable in acetone.[22–26] Thus, rates of the concurrent S_N2 and E2 reactions followed a single second-order rate expression (9). This expression is useful for *recording* rates, but we do not

$$\frac{d[Br^-]}{dt} = k_2(a - x)(b - x) \tag{9}$$

give it much mechanistic significance (*cf.* eq 4). The combined rate constant, k_2 in eq 9, can be split into its elimination and substitution components through the fraction of elimination $F_E = [H^+]/[Br^-]$, *i.e.*, $k^E = F_E k_2$. Rate expression 9 was used also for the S_N2 reactions of *n*-butyl bromide (Table II).

For reactions in acetone of Cl^-, OAc^-, CN^-, and NO_2^-, if 2,6-lutidine was absent, stable homoconjugates, *e.g.*, HCl_2^-, etc., are formed and these remove 2 mol of reactive base per mole of bromide ion produced by dehydrobromination.[4, 22–26] Rate expression 10 must be used to record rates as k_2, if acid production is followed.

$$k_2 = \frac{2.303}{(b - (1 + F_E)a)} \times \Delta t \Delta \log \frac{b - [H^+](1 + F_E)}{[H^+]_\infty - [H^+]} \tag{10}$$

In eq 10, F_E is the fraction of dehydrobromination to total bromide ion produced, b is the initial stoichiometric concentration of NBu_4Cl, and a is the initial concentration of *tert*-butyl bromide.

The dehydrobromination in dimethylformamide by chloride ion fitted rate expression 11 when bromide ion and acid were followed.[9] Solvent DMF is more basic than acetone, so that HCl_2^- and lutidinium hydrochloride are less stable in DMF. Thus, reactive chloride ion is not removed by both elimination and substitution, as in acetone, but only disappears according to the fraction of substitution, represented by F_S in eq 11.

$$\frac{d[Br^-]}{dt} = k_2(a - [Br^-])(b - F_S[Br^-]) \tag{11}$$

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The E2C Mechanism in Elimination Reactions. IV.[1] Primary Hydrogen Isotope Effects

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Abstract: Primary hydrogen isotope effects (k^H/k^D) on the rate of some halide-induced dehydrotosylations of alkyl tosylates in acetone (E2C-like reactions) are 2.3–3.2. This is considerably less than for many E2 reactions promoted by strong hydrogen bases (E2H-like reactions). The dehydrotosylation of 3-methyl-2-butyl tosylate by sodium ethoxide in ethanol gives $k^H/k^D = 2.6$ for formation of the Saytzeff olefin, 2-methyl-2-butene, but k^H/k^D is 6 for formation of the Hofmann olefin, 3-methyl-1-butene. These observations confirm the need for a spectrum of E2 transition states, positions in the spectrum depending on the nature of the base and of the substrate. The β-hydrogen isotope effect on the rate of substitution reactions accompanying E2C-like reactions is negligible, *i.e.*, $k^H/k^D = 1$, but there is a small isotope effect on the combined substitution and elimination reactions. This confirms that C_B–H bonding is different in the transition states leading to substitution and elimination products. The small kinetic isotope effects in E2C-like reactions do not distinguish between a nonlinear configuration, or an asymmetric linear configuration, of C_β, H_β, and base in the transition state but they are in accord with a paene olefin E2C-like transition state.

The hydrogen isotope effect on rates of elimination and substitution reactions enables us to focus attention on the behavior of the C_β–H bond in the respective transition states.[3–10] We will discuss the isotope effect on eliminations in terms of structures I and III, *i.e.*, the E2H–E2C spectrum of transition states. The spectrum has been described elsewhere[11–14] and will be further justified in this series of papers.

The kinetic hydrogen isotope effect for reactions proceeding through E2H-like transition states I, *i.e.*, those with a linear configuration of C_β, H, and base, B, has been observed on numerous occasions in the reactions of strong hydrogen bases, such as alkoxides, with alkyl and aralkyl halides.[5–7, 10] At 25°, k^H/k^D is most often between 6 and 7,[5] but lower values are

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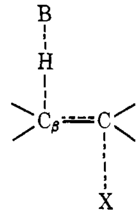
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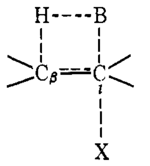
E2H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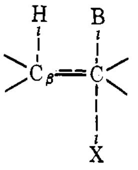
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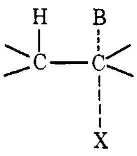
E2C


S_N2

observed in reactions in which the C_β– –H partial bond is thought to be considerably more or less developed than the B– –H partial bond in the transition state.[6] The qualitative explanation has been thoroughly documented[3–10] following Westheimer,[4] and need not be repeated here, except to say that for reactant or product-like (asymmetric) linear transition states, smaller isotope effects are expected, but for "central"[7] or symmetric linear transition states, normal isotope effects[6] are expected.

A few results for reactions which we would classify as E2C-like have been published. Bunnett, Davis, and Tanida[15] reported $k^H/k^D = 2.4–2.6$ for the dehydrochlorination of benzyldimethylcarbinyl chloride ($C_6H_5CH_2(CH_3)_2CCl$) by sodium methoxide and sodium thioethoxide in methanol. Kevill, Coppens, and Cromwell[16] observed $k^H/k^D = 2.5–3.3$ in the dehydrobromination of bromo ketones with bromide ion and Kevill and Dorsey[17] observed k^H/k^D of 3.81 in the E2 dehydrochlorination of *tert*-butyl chloride by chloride ion. Dehydrotosylation of cyclohexyl tosylate has $k^H/k^D = 4.5$, when sodium ethoxide is the base, but the more E2H-like dehydrotosylation by *tert*-butoxide has the "normal" value of 7.5.[10]

The kinetic hydrogen isotope effect to be expected from a cyclic transition state, II like III, *i.e.*, from an E2C-like reaction, has been estimated by More O'Ferrall.[18] He has reported calculations for transition states with nonlinear configurations about a reacting hydrogen.[19] He gives as examples 1,2 hydride shifts,[20,21] borane hydrolyses,[22] E2C-like eliminations, and miscellaneous hydrogen transfers through cyclic transition states. Both bending and stretching vibrations must be taken into account, whereas only a stretching mode is important for linear transition states.[23] He concluded[18] that there would be a significant reduction (to 2–4) of k^H/k^D in the E2C-like mechanism, *i.e.*, below the "usual" k^H/k^D value of 6–7. The ratio would remain low, even if there were considerable variation in the extent of C_β–H and B–H partial bond formation. The isotope effect is only mildly dependent on the degree of asymmetry in the bent transition state. Since small isotope effects may be observed for linear as well as bent transition states, a minimum requirement for inferring a nonlinear E2C-like geometry is that the small values persist over wide changes of substrate and base reactivity, within the reaction type. This requirement is being tested.

Hydrogen isotope effects on the rate of bimolecular substitution reactions will be very small when the isotopic variation is at a carbon atom β to the reaction center, provided that the S_N2 reaction proceeds through the generally accepted transition state structure, IV.[3] However, if there is any close similarity between E2 and S_N2 transition states, this may be reflected in similar values of k^H/k^D for the S_N2 and E2 reactions. If they proceed through a common intermediate,[24] with no C_β–H breaking, which subsequently partitions into substitution and elimination products in a fast step, then the isotope effect on the total reaction could be unity, but the isotope effect on the elimination rate could be >1 and on the substitution rate could be <1.

Results and Discussion

Rate constants for the combined substitution and elimination reactions of NBu_4Cl with alkyl and cycloalkyl tosylates in acetone, together with fractions of elimination, estimated from acid produced and halide ion consumed, are in Table I. The same reactions of the undeuterated alkyl tosylates have been discussed in earlier papers;[11,25] identical procedures have been followed here for the new reactions of both deuterated and undeuterated compounds. The new reactions were performed concurrently in each set. At least two separate rate determinations were made.

Hydrogen isotope rate ratios for the combined eliminations and substitution k^H/k^D, the substitution k_S^H/k_S^D; and the elimination k_E^H/k_E^D, are also in Table I.

S_N2 Reactions in Acetone. The isotope effect on the substitution reaction is very close to 1. This is less than the isotope effect on the rate of the combined reactions and on the elimination reaction. The transition state leading to substitution products must be different from that for elimination products, at least as regards the behavior of the C_β–H bond. We cannot exclude rigorously the possibility of an intermediate common to S_N2 and E2 reactions. This intermediate must have some breaking of the C_β–H bond to explain $k^H/k^D > 1$ in Table I. It could rapidly partition to S_N2 and E2 products.[24] The chances of k_S^H/k_S^D being exactly unity in this situation are not high and a common intermediate is unlikely on other grounds.[11] The most likely explanation is that C_β remains sp^3 hybridized in the S_N2 reaction, but sp^2 hybridization and C_β–H breaking are well advanced at C_β in the E2C-like transition state. In S_N1 reactions with a 1:2 hydride shift, k^H/k^D is at least 2,[20,21] so that the S_N2 reactions in Table I do *not* involve hydrogen participation, perhaps in a preformed ion pair.

E2C-Like Reactions in Acetone. We would classify the elimination reactions in Table I as E2C-like.[11–14] The hydrogen isotope effects on the elimination rates are low, ranging from $k_E^H/k_E^D = 2.3$, for the reaction of NBu_4Cl with 3-methyl-2-butyl tosylate, to 3.2 for NBu_4Cl with *trans*-4-*tert*-butylcyclohexyl tosylate. They are close to the isotope effects observed for E2C-like re-

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Table I. Hydrogen Isotope Effects on E2 and SN2 Reactions[a]

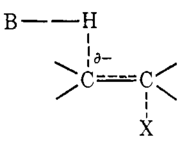
Substrate R in ROTS	$10^2 F_E$[b]	$10^3 k$, M^{-1} sec^{-1}	k^H/k^D SN2 + E2	$k_S{}^H/k_S{}^D$ SN2	$k_E{}^H/k_S{}^D$ E2
3-Methyl-2-butyl	48.9 ± 0.5^{e}	28.5 ± 0.7	1.5	1.1	2.3^{e}
3-Methyl-2-butyl-3-*d*	30.4 ± 0.4^{e}	19.2 ± 0.3			
trans-2-Methylcyclohex	24.0 ± 0.8^{f}	2.38 ± 0.08	1.2	1.0	2.7^{f}
trans-2-Methylcyclohex-2,6,6-d_3	12.2 ± 1.0^{f}	1.90 ± 0.10			
cis-2-Methylcyclohex[c]	93.5 ± 1.1^{g}	6.99 ± 0.18^{c}	2.7	1.0	3.0^{g}
cis-2-Methylcyclohex-2,6,6-d_3[c]	82.9 ± 2.0^{6}	2.48 ± 0.15^{c}			
trans-4-*t*-Butylcyclohex[d]	28.8 ± 0.3	2.75 ± 0.07	1.65	1.4	3.2
trans-4-*t*-Butylcyclohex-2,2,6,6-d_4[d]	15.2 ± 0.2	1.66 ± 0.05			

[a] Reactions of 0.035–0.040 *M* NBu_4Cl with 0.015–0.020 *M* alkyl tosylates in acetone at 75.0°. [b] F_E is the fraction of total reaction which is elimination, estimated from acid produced $[H^+]_t$ at time *t* and chloride ion consumed by substitution, *i.e.*, $F_E = [H^+]_t/([H^+]_t + [Cl^-]_0 - [Cl^-]_t)$. Mean value is for at least ten estimations at all stages of reaction in each of two runs. [c] Temperature is 50.0°. [d] Acetone contained 0.030 *M* 2,6-lutidine. [e] The olefin is the Saytzeff product, 2-methyl-2-butene; the reaction is discussed in ref 25. [f] The olefin is the product of anti elimination, 3-methylcyclohexene. [g] The olefin is the Saytzeff product of anti elimination, 1-methylcyclohexene.

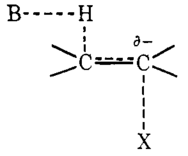
actions of benzyldimethylcarbinyl chloride,[15] of *tert*-butyl chloride,[17] and of α-bromo ketones,[16] but are much less than the values of *ca.* 6, usually observed in E2H-like dehydrohalogenations induced by alkoxide ions.[3–10] This variation between 2 and 7 in the kinetic primary hydrogen isotope effect on E2 reactions confirms the need for a spectrum of transition states[6,7,11–14] for E2 reactions of different bases in different solvents with substrates of different acidity and with different leaving groups.

The low isotope effect which we observe for E2C-like reactions imposes some limitations on the structures which can be proposed for the E2C-like transition states. We can exclude a symmetrical linear configuration of C_β, H, and base in the E2C-like transition state because this requires k^H/k^D of *ca.* 7 at 25°. Our structure, II, like III, had been considered by More O'Ferrall,[18] before he had access to the data reported in this paper. The low isotope effect which we observe in E2C-like reactions is almost quantitatively as predicted by him for a nonlinear configuration of C_β, H, and base, as in II. The C_β–H–B angle in II will depend on the bond order of C_β- - -H, C_α- - -B, and H- - -B. For an angle of 90°, More O'Ferrall calculates k^H/k^D as 1.7–2.3, at 25°. Thus a cyclic E2C-like transition state (II, like III) is not inconsistent with the observed isotope effect.

The variation in isotope effect in different E2 reactions has been interpreted by Bunnett in terms of another spectrum[6,7] of E2 transition states. He also follows the Westheimer[4] analysis. To explain low values of k^H/k^D a highly asymmetric, linear configuration of partial bonds between C_β, H, and base is suggested. Bunnett's spectrum is bounded by structures V and VI and is based on variations of structure I. Both V and VI would give low isotope effects on rate. A paenecarbanion transition state V, with a well-broken C_β- - -H bond, and well-developed B- - -H bond, seems unlikely for E2C-like reactions, in view of the low basicity of chloride ions toward hydrogen, but a paenecarbonium ion transition state, VI, with a slightly broken C_β- - -H bond might be utilized by weak bases and readily ionized secondary tosylates. This would explain the low isotope effect observed in E2C-like reactions. However, a paenecarbonium ion transition state does not explain other observations on E2C-like reactions,[12–14] particularly the requirement of a well-developed double bond in the transition state[11,25] and the negligible effect of electron-withdrawing and electron-donating substituents at C_α on rates of E2C-like reactions.[26]


V

paenecarbanion


VI

paenecarbonium

If E2C-like eliminations proceeded through paene olefin transition states I, *i.e.*, having a very well-developed C_α- - -C_β double bond and H- - -B bond, and with C_β- - -H and C_α- - -X bonds well broken, then the reactions would exhibit the low-isotope effects observed.[4] A paene olefin transition state for E2C-like reactions has been suggested on other grounds.[1,11,25,26] There remains the question of whether or not there is interaction between base and C_α[13] but β-hydrogen isotope effects give us no answer.

Reaction of 3-Methyl-2-butyl Tosylate with NaOEt in Ethanol. Table II gives the rates (as kM^{-1} sec^{-1}) of the reaction of 3-methyl-2-butyl *p*-toluenesulfonate and some deuterated derivatives, with sodium ethoxide in ethanol at 50.0°. In order to minimize solvolysis,[20] 0.7–1.0 *M* sodium ethoxide was used.

Isotope effects on the total rate k^H/k^D, the elimination $k_E{}^H/k_E{}^D$, and the substitution $k_S{}^H/k_S{}^D$ are shown in Table II. Knowledge of the olefin composition and the fraction of elimination allows calculation of the isotope effect for formation of 3-methyl-1-butene (Hofmann product) and 2-methyl-2-butene (Saytzeff product). Allowance was made for the fact that our "1,1,1-trideuterio-3-methyl-2-butyl tosylate" contained 2.49, rather than 3.0, atoms of deuterium per molecule.[20] Rates

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Table II. Hydrogen Isotope Effects on Reactions of 3-Methyl-2-butyl Tosylate in Ethanol at 50.0°

Substrate R in ROTS	[ROTS], *M*	[NaOEt], *M*	10^2F_E	10^4k, M^{-1} sec^{-1}	k^H/k^D E2 + SN2	k_S^H/k_S^D SN2	k_E^H/k_E^D Sayt[e]	k_E^H/k_E^D Hof[f]
$(CH_3)_2CHCHCH_3$[a]	0.180	0.587[b]		1.30				
$(CH_3)_2CHCHCH_3$[a]	0.180	0.587		1.35				
$(CH_3)_2CHCHCH_3$	0.240	0.910	82	1.47	1.7[c]	1.06[c]	2.35[c]	1.12[c]
$(CH_3)_2CDCHCH_3$	0.198	0.910	70	0.90	1.7[b]	1.12[d]	2.57[d]	1.12[d]
$(CH_3)_2CHCHCH_3$	0.150	0.770	81.5	1.45	1.22[c]	1.1[c]	1.09[c]	3.10[c]
$(CH_3)_2CHCHCD_3$[g]	0.150	0.770	80.5	1.20				6.31[d]

[a] Ethanolysis rates are 6.97×10^{-6} sec^{-1} in pure ethanol and 1.33×10^{-5} sec^{-1} in 0.14 *M* sodium perchlorate.[20] [b] This solution contained 0.28 *M* sodium perchlorate. [c] Observed isotope effects for reaction of partially deuterated substrate accompanied by ethanolysis (see text). [d] Observed values corrected for incomplete deuteration and ethanolysis as described in text. [e] For production of 2-methyl-2-butene (Saytzeff olefin). [f] For production of 3-methyl-1-butene (Hofmann olefin); *cf.* Table III. [g] Contains 2.49 atoms of deuterium per molecule (*cf.* ref 20).

Table III. Products of Bimolecular Elimination Reactions of 3-Methyl-2-butyl *p*-Toluenesulfonate and Deuterium Analogs with Sodium Ethoxide in Ethanol, 50.0°

R in ROTS	$[ROTS]_0$, 10 *M*	$[NaOEt]_0$, 10 *M*	3-Methyl-1-butene	2-Methyl-2-butene	2-Methyl-1-butene
$(CH_3)_2CHCHCH_3$[a]	1.83	8.42	17.4 ± 0.4	82.5 ± 0.5	0.61 ± 0.04
$(CH_3)_2CHCHCH_3$[a]	1.80	9.61	18.8 ± 1	80.5 ± 0.7	0.8 ± 0.1
$(CH_3)_2CDCHCH_3$	2.47	10.6	31.5 ± 0.3	67.7 ± 0.2	0.86 ± 0.06
$(CH_3)_2CHCHCD_3$	1.16	7.63	7.2 ± 0.1	92.3 ± 0.1	0.8
$(CH_3)_2CHCHCD_3$	1.53	10.17	6.5 ± 0.2	92.6 ± 0.2	0.8

[a] Results previously reported in ref 25.

of ethanolysis of 3-methyl-2-butyl tosylate show that *ca.* 18% of the observed reaction with sodium ethoxide in ethanol may be due to solvolysis.[20] The isotope effects observed on the total rate of ethanolysis[20] of 3-deuterio-3-methyl-2-butyl tosylate and on the total rate of the reaction with sodium ethoxide in ethanol are 1.92 and 1.79, respectively. The acetolysis of 1,1,1-trideuterio-3-methyl-2-butyl tosylate has an isotope effect of 1.15 and the reaction with sodium ethoxide in ethanol has an isotope effect on the total rate of 1.22.[20] Thus solvolysis would interfere roughly to the same extent with the rates of bimolecular elimination from the deuterated and undeuterated species, so that the same correction can be made to each pair of deuterated and undeuterated tosylates.

The actual F_E for the bimolecular reaction is higher than the F_E recorded in Table II, which includes olefin produced by solvolysis, since only 54% of the ethanolysis of 3-methyl-2-butyl tosylate produces olefin,[20] whereas the bimolecular elimination produces *ca.* 80% olefin. The actual rates for bimolecular elimination from deuterated and undeuterated material would be lower than observed. If 18% of the reaction is solvolytic, this contributes 11% 2-methyl-2-butene and 0.1% 3-methyl-1-butene[20] to the olefinic products recorded in Table III.

Both corrected and observed isotope effects on rate are recorded in Table II. The corrections for deviations from the pure bimolecular dehydrotosylations of deuterated and undeuterated analogs lead to $k_E^H/k_E^D = 2.6$ for the *Saytzeff elimination* to give 2-methyl-2-butene, from 3-deuterio-3-methyl-2-butyl tosylate, and $k_E^H/k_E^D = 6$ for *Hofmann elimination* to give 3-methyl-1-butene from 1,1,1-trideuterio-3-methyl-2-butyl tosylate. The isotope effect for rate of formation of the Saytzeff olefin by ethoxide ion in ethanol is very close to that observed for the same dehydrotosylation induced by halide ions in acetone, *i.e.*, in an E2C-like reaction (*cf.* Table I). In contrast, the isotope effect for rate of formation of the Hofmann olefin is high, like that most often observed for other E2H-like reactions of ethoxide ion in ethanol.[5,6,8] The C_β- - -H- - -OEt bonding must be different in the transition states for formation of these Hofmann and Saytzeff olefins by ethoxide ion. Saytzeff olefin is thought to be produced through a transition state which is considerably more E2C-like than is the transition state leading to Hofmann olefin. Reasons may be that the Hofmann transition state has a more acidic β-hydrogen so that transition states like I and V are favored. The partial double bond in a Hofmann transition state is less stable than that in a Saytzeff transition state at the same stage of development, so there is less advantage in the former case of utilizing a transition state with a very well developed double bond (*e.g.*, the E2C transition state).

Experimental Section

Rate measurements, product analyses, and preparation of reagents were as described in the papers dealing with the reactions of the undeuterated compounds.[1,11,25]

Preparation of Materials. ***trans*-4-*tert*-Butylcyclohexyl-*2,2,6,6-d*$_4$ Tosylate.** 4-*tert*-Butylcyclohexanone (15.4 g, Dow Chemical Co. sample purified by distillation, mp 47.2–47.8°) was added to a solution of deuterium oxide (100 g, 99.8% pure) in dioxane (250 ml, distilled from calcium hydride) in which sodium metal (0.9 g) had been dissolved. This mixture was allowed to reflux for 6 hr. It was extracted with pentane and the combined extracts were dried over magnesium sulfate. The solvent was distilled off through a Vigreux column and the residue was distilled at reduced pressure to give 12.5 g of ketone, bp 93° (6 mm).

The extent of deuteration of the equilibrated 4-*tert*-butylcyclohexanone was estimated by comparing the intensity of the infrared spectral bands at 1325 and 1222 cm^{-1}, exhibited only by the hydrogen compound, respectively, with those at 1310 and 1246 cm^{-1}, exhibited only by the deuterium isomer, and by comparing the band at 1422 cm^{-1}, shown only by the hydrogen compound, with that at 1475 cm^{-1} which is present in the spectra of the two isomers. Control mixtures showed that 2% of the hydrogen isomer could just be detected.

The infrared spectrum of the deuterated ketone showed that the bands at 1222, 1325, and 1422 cm^{-1} had disappeared and new bands at 1246 and 1310 cm^{-1} were present. This ketone was exchanged with more deuterium oxide (100 g) exactly as above. Extraction and distillation gave 4-*tert*-butylcyclohexanone-*2,2,6,6-d*$_4$ (10 g), bp 94° (6 mm). The infrared spectrum was identical with the previous one, indicating that the ketone contained less than 2% of the protium isomer.

This material was dissolved in 50 ml of anhydrous ether and the solution was slowly added to 1.5 g of lithium aluminum hydride in 50 ml of anhydrous ether at −78° with stirring over a period of 45 min. Stirring in the cold was continued for about 1.5 hr and then the solution was allowed to warm up to room temperature. After 3 hr, 6 ml of 10% sodium hydroxide was added and cooling was necessary. The ether solution was decanted and the solid in the flask was washed twice with more ether. The combined ether solutions were dried and distilled. The product was analyzed by vpc on a 0.25-in. column, 2 m, 25% Carbowax 4000. The ratio of trans–cis alcohol was 94:6. Separation of the two isomers was performed by chromatography on Silica gel (1 lb). With 10% ether–pentane as the eluent solvent the cis alcohol, contaminated with some trans alcohol, was collected. A solution of 30% ether–pentane gave the pure trans isomer. The product was recrystallized from pentane, mp 81.5–81.8°. Analysis by vpc indicated the presence of only *trans*-4-*tert*-butylcyclohexanol-*2,2,6,6*-d_4, with no contamination by the other isomer. Deuterium analysis by combustion gave 19.45 atom % excess deuterium. This corresponds to 3.89 deuterium atoms per molecule of alcohol.

Pure *trans*-4-*tert*-butylcyclohexanol-*2,2,6,6*-d_4 (2 g; 0.0125 mol) was treated with 4.7 g (0.0250 mol) of tosyl chloride in 10 ml of dry pyridine and kept in the cold room overnight. The tosylate was worked up in the usual way.[25] Three grams of product was obtained (77% yield); mp 89.0–89.5°.[24] It analyzed for $C_{17}H_{22}D_4SO_3$.

2-Methylcyclohexanone-*2,6,6*-d_3. 2-Methylcyclohexanone (22.75 g) was added to a solution of deuterium oxide (100 g) in tetrahydrofuran (250 ml) in which sodium (*ca.* 1 g) had been dissolved. This was left overnight at room temperature and then refluxed for 1 hr. The mixture was allowed to cool and extracted with pentane. The extract was dried ($MgSO_4$), the pentane was distilled out through a column packed with raschig rings, and the residue was distilled at reduced pressure to give ketone (20.8 g; 89%); bp 58° (7.5 mm); *ca.* 93% d_3 by infrared analysis. This ketone (20.8 g) was exchanged with deuterium oxide (100 g) exactly as above. After working up this gave 2-methylcyclohexanone-*2,6,6*-d_3 (19.65 g; 94%); bp 63° (22.5 mm), >98% d_3 by infrared analysis.

2-Methylcyclohexanols-*2,6,6*-d_3. 2-Methylcyclohexanone-*2,6,6*-d_3 (19.65 g) in anhydrous ether (100 ml) was added over a period of 2 hr to a solution of lithium aluminum hydride (6.5 g) in ether (150 ml) at −78°. After addition was complete the mixture was stirred for 3 hr at −78° and a further 2 hr at room temperature. The reaction was worked up by adding 10% sodium hydroxide (10.4 ml) and water (15 ml) dropwise and stirring for 2 hr. The aluminum hydroxide was filtered off and washed with ether. The ether solution was dried ($MgSO_4$) and distilled to give 2-methylcyclohexanol-*2,6,6*-d_3 (17.9 g; 89%); bp 74° (20 mm).

The alcohol was converted to the acid phthalate by adding it to a solution of phthalic anhydride (23.0 g) in pyridine (25 ml) and heating for 3 hr. The reaction mixture was cooled and ice and water were added. The acid phthalate was extracted with ether; the extract was washed with dilute hydrochloric acid and water and dried ($MgSO_4$), and the ether distilled off to give crude 2-methylcyclohexyl acid phthalate (38 g; 92%). This was fractionally crystallized from ethyl acetate–Skelly B to give pure *trans*-2-methylcyclohexyl-*2,6,6*-d_3 acid phthalate (15.4 g); mp 125.5–127.0° (lit.[27] mp 125.2–125.8° (corr)).

This trans acid phthalate was hydrolyzed with aqueous ethanolic potassium hydroxide and the alcohol was steam distilled out. After extraction of the steam distillate with pentane (five 100-ml portions), the extract was dried ($MgSO_4$) and distilled to give *trans*-2-methylcyclohexanol-*2,6,6*-d_3 (5.7 g; 85%); bp 74° (20 mm).[1]

The tail fraction from the crystallization (2.2 g), mp 106–108° (mixed with trans, mp 93–102°), was hydrolyzed with aqueous ethanolic potassium hydroxide. The hydrolysate was poured into water (50 ml) and extracted with pentane (five 100-ml portions). The extract was dried ($MgSO_4$) and solvent distilled off to give an oil (*ca.* 1 g) which was tosylated in the usual manner. The solid tosylate was recrystallized from pentane to give *cis*-2-methylcyclohexyl-*2,6,6*-d_3 *p*-toluenesulfonate (0.67 g) as white platelets; mp 53.6–54.8°.[1]

3-Methyl-2-butyl *p*-Toluenesulfonate-*3*-*d*. The synthesis was *via* 2-deuterio-2-propanol, as described for the synthesis of 3-methyl-2-butyl *p*-toluene sulfonate from 2-propanol.[25] 2-Deuterio-2-propanol was prepared from 10 g of dry acetone in 60 cm^3 of diethylcarbitol, which had been directly distilled from lithium aluminum hydride. This was added to a slurry of 2.5 g of 98% lithium aluminum deuteride in 140 ml of diethylcarbitol.

The 3-deuterio-3-methyl-2-butyl alcohol was analyzed through the courtesy of Dr. N. R. Trenner of Merck and Co., Rahway, N. J., and contained 0.93–0.94 atom of deuterium per molecule. The tosylate was not analyzed for deuterium.

3-Methyl-2-butyl *p*-Toluenesulfonate-*1,1*-d_3. The synthesis was *via* 1,1,1-trideuteriomethanol. Carbon dioxide was generated by the action of 30% perchloric acid on barium carbonate in diethyleneglycol diethyl ether and reduced by an excess of lithium aluminum deuteride. The 1,1,1-trideuteriomethanol, bp 64°, gave only one peak on vpc analysis; no methyl formate was present.

1,1,1-Trideuteriomethyl iodide was prepared from the alcohol and 36.2 g (0.25 mol) in 100 cm^3 of ether was added dropwise to magnesium (7.57 g; 0.312 mol) in ether (150 cm^3) while the reaction solution was stirred. The time of addition was 1 hr and the solution was then refluxed for 20 min. The mixture was cooled to −17°. Isobutyraldehyde (16.2 g; 0.225 mol) in 100 cm^3 of ether was added dropwise at −5 to −12° over 1 hr. The solution was poured onto ice and the excess magnesium was picked out. The basic magnesium halide was dissolved out with 15% sulfuric acid. The ether layer was separated and the aqueous layer extracted with four portions of fresh ether. Removal of ether gave 1,1,1-trideuterio-3-methyl-2-butanol, bp 111°. The product was 99% pure by vpc. The deuterium analysis (courtesy of Dr. N. R. Trenner) was 2.49 deuterium atoms per molecule. The alcohol was converted to the *p*-toluenesulfonate in the usual way.[25]

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