The measurements of the pyridinium hydration equilibria were made in ~4 Torr of methane containing water vapor in the 0.2-1 Torr range. The water used contained ~1×10^{-2} mol % pyridine such that a pressure of less than 10^{-4} Torr of pyridine resulted in the ion source. Under these conditions, protonation of water by the methane ions, CH_5^+ and $C_2H_5^+$, is fast. Rapid clustering reactions lead to $H^+(H_2O)_n$. Protonation and hydration of the pyridines occurs by the reaction

$$H^+(H_2O)_n + Xpy = XpyH^+(H_2O)_k + (H_2O)_{(n-k)}$$

By suitable choice of temperature, the equilibria

$$XpyHH_2O^+ = XpyH^+ + H_2O \qquad (5)$$

can be made to occur appreciably faster than the dimerization reaction

$$XpyH^+ + Xpy = XpyHpyX^+$$

This reaction is slow since the Xpy concentration is very low. The equilibrium constants K_5 were found to be constant in the range between 0.2 and 0.8 Torr water pressure.

The higher hydration equilibria (7) and (8) were measured similarly but at correspondingly lower temperatures. The water pressure range over which they could be observed was narrower than was the case for the monohydrates.

The STO-3G calculations of the phenols, phenoxides and monohydrates were made with the GAUSSIAN 70 program.[18] In general the standard geometries outlined by Pople and Gordon[19] were used except for the following: phenol, the carbon-oxygen bond distance and the COH angle were optimized; phenoxide ion, the carbon-oxygen bond was optimized; cyanophenol, carbon-oxygen distance and COH angle were optimized; cyanophenoxide, C-C_{arom}, C≡N, and C—O bonds were optimized, but optimum distances were essentially the same as in cyanophenol; hydrates, O · · · H—O distance and O · · · H—O angle was optimized.

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Remote Secondary Deuterium Kinetic Isotope Effects as a Probe of Steric Strain in the Solvolysis of Tertiary Alkyl Carbinyl Systems[1]

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Abstract: The kinetic isotope effects associated with the solvolysis of 9-*tert*-butyl-9-bicyclo[3.3.1]nonyl (**3**), 2-*tert*-butyl-2-adamantyl (**4**), and 2-*tert*-butyl-*endo*-camphenilyl (**5**) *p*-nitrobenzoates, completely deuterated at the *tert*-butyl groups, were found in 95.6% aqueous ethanol at 25 °C to be (k_H/k_D =) 1.030, 1.107, and 1.076, respectively. Compound **3** gave primarily unrearranged alcohol (7.7%) and the methyl-shifted alkene 9-(2′-propenyl)-9-methylbicyclo[3.3.1]nonane (88.4%) as solvolysis products. A preference for CH_3 migration over CD_3 migration by a factor of 1.35 was observed. Compound **4** similarly yielded unrearranged alcohol (6.9%) and the methyl-shifted alkene 2-(2-′propenyl)-2-methyladamantane (90.2%) and showed a preference for CH_3 over CD_3 migration in product formation by a factor of 1.25. The kinetic isotope effects are interpreted in terms of relief of constraints on vibrational freedom at the positions of isotopic substitution during the activation process. The kinetic isotope effects did not correlate well with the *t*-Bu/CH_3 substituent effects.

The problem of understanding the origins of chemical reactivity is a vexing one. Steric effects, together with effects of electronic origin, are important in governing chemical reactivity. It is now a generally accepted principle that relief of initial state steric strain can result in enhanced rates of solvolysis for sterically congested tetragonal molecules (**1**) which decompose in a unimolecular rate-controlling step to a trigonal, planar carbocation (**2**).[2] There is less agreement, however, on

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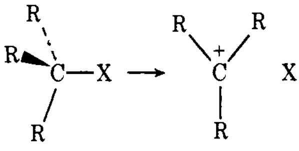

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how these steric effects may be measured and just how important they may be for a given reacting system when balanced against the cumulative magnitude of inductive, hyperconjugative, resonance, electrostatic, and solvation effects.

The kinetic probes commonly used to estimate steric strain effects in solvolysis reactions (such as **1** → **2**) are of a substitutive-comparative rate nature. A reference compound is chosen and its rate of reaction is measured. A structural modification is then made, such as the replacement of a methyl group by a *tert*-butyl group, and the rate of reaction of the structurally altered compound is determined and compared with that of the reference compound. In order to draw meaningful conclusions from such an experiment, the implicit assumption is then frequently made that the two compounds being compared react over potential energy surfaces which are identical except for the "steric" perturbation introduced by the structural modification. In truth, such a coincidence of reaction pathways traversed by two structurally discrete species would indeed be fortuitous! In recognition of this, adjustments due to other effects (e.g., inductive, etc.) are usually introduced into the comparison, provided that they may be estimated.

Even when such other effects can be estimated in a reasonable fashion, there may still be ambiguities in assigning a specific origin to a given steric effect as measured by rate comparisons made between different compounds. In reactions involving the transformations of sterically congested molecules of type **1** to cations of type **2**, there must be a blend of "steric" factors contributing to the activation energies which is likely not the same for each reactant. It seems certain that there are cases in which relief of nonbonded repulsions incurred among the R groups ("B" strain) and between the leaving group X and each of the R groups ("F" strain) are of differing importance in the different compounds compared.[3,4] Molecular structure determinations of such sterically hindered compounds as tri-*tert*-butylcarbinyl *p*-nitrobenzoate make it clear that strains of both kinds are present.[5] Unfortunately, such structural knowledge is not at present easily transferred to a quantitative dissection of steric effects in kinetic phenomena (or vice versa).

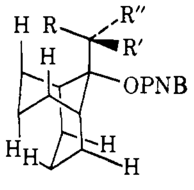
A good tool with which to study steric effects in solvolysis reactions of sterically congested systems which pass to less congested transition states would be the introduction of a substituent which does not alter the electronic potential energy surface traversed by the reference and substituted compounds as they proceed through the activation process. Secondary deuterium kinetic isotope effects, whose theoretical basis is well established within the context of transition state theory, potentially fulfill that criterion.[6] To a very close approximation, molecules which differ only in isotopic substitution must exist on the the same electronic potential energy surface and, hence, must undergo a given reaction by the same "mechanism". A difference in the rates of reaction between protium- and deuterium-substituted reactants is expected if bonds to the light and heavy isotopes experience changes in their vibrational force constants upon passage to the respective transition states. The greater part of the rate difference is seen as resulting from the inequality in zero-point energy differences between the initial and transition states of the protium and deuterium compounds, but *not* to differences in the potential energy surface experienced along the reaction coordinate.[7]

Provided that this distinction from normal "substituent" effects is kept in mind, the question of the origin of vibrational changes and, hence, of the isotope effect may be discussed in terms of the relative importance of inductive, hyperconjugative, and steric modes of intramolecular interactions.[8,9] These intramolecular interaction mechanisms will generally all be operative simultaneously during the course of a given activation process and will not necessarily affect the force constant changes in either the same direction or to the same extent.

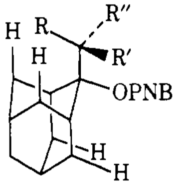
There is ample evidence from the literature that in certain cases steric interactions may be the predominant factor in causing the force constant changes which result in secondary deuterium isotope effects. In studies involving conformational changes and related reactions which occur without changes in electric charge, deuterium clearly behaves as though it is smaller than protium when severe nonbonded constraints are placed on its vibrational freedom.[11] These effects are seen as a consequence of the greater vibrational amplitude and mean bond length of C-H bonds compared with analogous C-D bonds.[12] In most experimental studies of "steric" isotope effects,[13] the constraints on vibrational freedom have been more severe at the transition state than in the initial state and, in accord with theory,[10,14] the resulting kinetic isotope effects have been inverse ($k_H/k_D < 1$).[15] A much smaller number of cases are known where a sterically congested initial state leads to normal isotope effects ($k_H/k_D > 1$).[1,16,17] A few other cases involving the observation of a normal secondary deuterium kinetic isotope effect are known, but with less confidence that steric rather than inductive or hyperconjugative interactions play the dominant role in causing force-constant decreases.[18]

It was our intention to experimentally explore the use of secondary deuterium kinetic isotope effects as probes of steric strain in solvolysis reactions of the type **1** → **2**. Our plan was to select several substrates for study whose reactivity was due predominantly to relief of nonbonded repulsions at sites remote from the reaction center. The magnitude of the kinetic isotope effect resulting from substitution of deuterium for protium at the points of maximum steric congestion should thus provide a quantitative estimate of site-specific interactions within the reactant.[14]

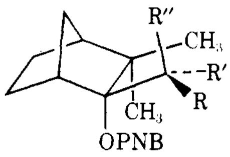
We chose as our systems for investigation the solvolysis of 9-*tert*-butyl-9-bicyclo[3.3.1]nonyl (**3**), 2-*tert*-butyl-2-adamantyl (**4**),[20] and 2-*tert*-butyl-2-*endo*-camphenilyl (**5**)[19] *p*-nitrobenzoates labeled with deuterium at the *tert*-butyl groups. These compounds were judged by several criteria to undergo solvolysis with considerable relief of nonbonded repulsions. First, they are among the most reactive tertiary alkyl substrates known. This is evident from their rates of solvolysis relative to that of *tert*-butyl *p*-nitrobenzoate (Table I). Second, they



3h, R = R' = R'' = CH_3
3d, R = R' = R'' = CD_3
6, R = R' = R'' = H



4h, R = R' = R'' = CH_3
4d, R = R' = R'' = CD_3
7, R = R' = R'' = H



5h, R = R' = R'' = CH_3
5d, R = R' = R'' = CD_3
8, R = R' = R'' = H

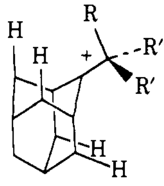


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Table I. Rates of Solvolysis of Tertiary *p*-Nitrobenzoates in 80% Aqueous Acetone at 25 °C

p-nitrobenzoate	k, s^{-1}	k_{rel}	$k(t\text{-Bu})/k(CH_3)$	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
tert-butyl[a]	7.45×10^{-11}	1.0		29.2	−7.1
9-methyl-9-bicyclo[3.3.1]nonyl (**6**)[b]	3.34×10^{-10}	4.5		28.4	−6.5
			104 000		
9-*tert*-butyl-9-bicyclo[3.3.1]nonyl (**3**)[b]	3.48×10^{-5}	467 000			
2-methyl-2-adamantyl (**7**)[c]	1.43×10^{-10}	1.9		30.2	−2.2
			239 000		
2-*tert*-butyl-2-adamantyl (**4**)[c]	3.42×10^{-5}	459 000		21.6	−6.5
2-methyl-*endo*-camphenilyl (**8**)[b]	2.31×10^{-11}	0.31		30.4	−5.1
			1 200 000		
2-*tert*-butyl-*endo*-camphenilyl (**5**)[b]	2.77×10^{-5}	372 000			

[a] H. C. Brown and W. C. Dickason, *J. Am. Chem. Soc.*, **91**, 1226 (1969). [b] Reference 19. [c] Reference 20.

Table II. Rates and Isotope Effects for 95.6% Aqueous Ethanol Solvolysis of *p*-Nitrobenzoate Esters Perdeuterated at the *tert*-Butyl Group

system	t, °C	$k \times 10^5$, s^{-1}	k_H/k_D	$\Delta\Delta G^{\ddagger}$, cal/mol
9-bicyclononyl, **3h**	25.00	3.7250 ± 0.0080[a]		
3d		3.6165 ± 0.0099[b]	1.0300 ± 0.0035	17.5 ± 2.0
2-adamantyl, **4h**	25.10	2.9165 ± 0.0013[b]		
4d		2.6342 ± 0.0209[b]	1.1072 ± 0.0088	60.4 ± 4.7
2-camphenilyl, **5h**	25.00	3.1698 ± 0.0010[c]		
5d		2.9456 ± 0.0035[c]	1.0761 ± 0.0014	43.5 ± 0.8

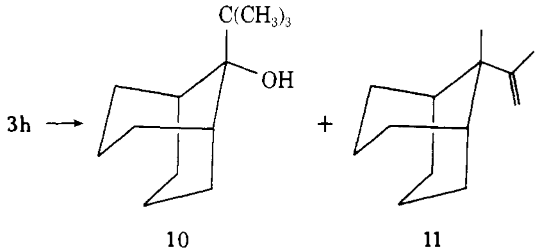
[a] Standard deviation of five runs. [b] Three runs. [c] Two runs.

exhibit the three largest t-Bu/CH$_3$ rate ratios which have yet been reported. If this measurement is indeed a valid probe of steric inflexibility and relief of nonbonded strains in the solvolysis of aliphatic tertiary carbinyl systems, as has been suggested,[19] then it would be expected that there should be considerable constraints placed on the vibrational motions of the C–H (C–D) bonds in the *tert*-butyl groups of compounds **3–5**. This should result in the observation of substantial normal kinetic isotope effects associated with the solvolysis of each. Finally, the 2-adamantyl system has been previously studied in some detail.[20] Molecular mechanical strain calculations, although not treating F strain, strongly suggest that the extreme reactivity of **4h** is due primarily to the nonbonded repulsions between methyl group R on the axially disposed *tert*-butyl group and the axial hydrogens on the same face of the inflexible chair-form cyclohexane ring. These repulsive interactions are largely diminished in a transition state which resembles cation **9**.

Results

The parent alcohols of compounds **3**, **4**, and **5** were prepared by addition of the appropriate ketone to either *tert*-butyllithium or *tert*-butyllithium-d_9.[19,20] Because of the high inherent reactivity of these systems, the *p*-nitrobenzoate esters were prepared and subjected to solvolysis in the rather poorly ionizing medium of 95.6% aqueous ethanol which was 0.01 M in triethylamine. The rates of solvolysis were determined by the conductometric method on solutions $\leq 10^{-4}$ M in substrate.[21,22] The rates and derived kinetic isotope effects are given in Table II.

In addition to the rate determinations, a study was made of the solvolysis products from compounds **3–5**. A large number of unidentified products were detected from the solvolysis of the camphenilyl ester **5h**. These were not investigated further.



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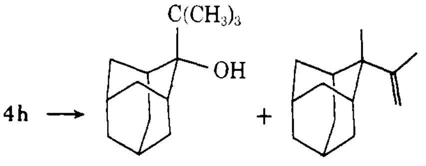
In contrast, systems **3** and **4** both gave rather simple product mixtures consisting primarily of the unrearranged parent alcohol and methyl-shifted alkene. VPC analysis of the solvolysis products obtained from the bicyclononyl compound **3h** revealed alcohol **10** and the alkene 9-(2′-propenyl)-9-methylbicyclo[3.3.1]nonane (**11**) in relative amounts of 7.72 and 88.4%, respectively. Deuterated ester **3d** gave the alcohol and olefin in 28.3 and 65.3% relative yields, respectively. Consideration of these data reveals an apparent preference for CH$_3$ migration from **3h** over CD$_3$ migration from **3d** by a factor of $k_{CH_3}/k_{CD_3} = 1.35$.

Similarly, the adamantyl ester **4h** gave unrearranged parent alcohol **12** and the methyl-shifted alkene 2-(2′-propenyl)-2-methyladamantane (**13**)[20] in relative amounts of 6.87 and 90.2%, respectively. Deuterated ester **4d** gave 24.1% alcohol and 72.1% alkene, indicating an apparent preference for CH$_3$ migration from **4h** over CD$_3$ migration from **4d** of $k_{CH_3}/k_{CD_3} = 1.25$.



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Discussion

Origin of the Isotope Effects Observed. The γ-deuterium kinetic isotope effects associated with the solvolyses of esters **3–5** are clearly of greater magnitude than those normally observed for other substrates undergoing limiting solvolysis in which deuterium is similarly situated in "nonhyperconjugative" positions. Comparison of the data in Table II with those of Table III shows this striking difference.

In the case of substrates in which deuterium is situated in a steric environment which is relatively noncongested, the experimental kinetic isotope effects are all centered within a few percent of unity. This indicates that force-constant changes in the relatively remote γ position for similar reactions involving charge formation at the transition state are quite small in the absence of severe nonbonded interactions. This is in accord with the results of model calculations.[23] However, the experimental evidence which is available reveals also that

Table III. Comparison of γ-Deuterium Kinetic Isotope Effects

compd	solvent[a]	t, °C	k_H/k_D	ref
$CH_3CH{=}C(CD_3)CHClCH_3$	95% EtOH	25	0.965	*b*
$(CH_3)_2CClCH_2CD_3$	80% EtOH	25	0.975	*c*
$(CD_3)_3CCH_2OMes$	H_2O	90	1.017	*d*
$(CD_3)_3CCH(OBs)CH_3$	97.3% TFE	25	1.011	*e*
	50% EtOH	25	1.003	*e*
	43% EtOH	40	0.979	*f*
	95% TFA	10	0.986	*f*
$[(CD_3)_2CH]_3COPNB$	60% dioxane	50.4	1.00	*g*

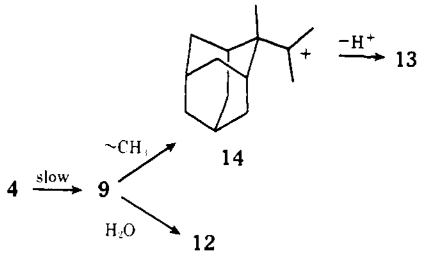
[a] TFE is 2,2,2-trifluoroethanol. TFA is trifluoroacetic acid. [b] R. H. Griffin and J. G. Jewett, *J. Am. Chem. Soc.*, **92**, 1104 (1970). [c] Reference 24. [d] M. J. Blandamer and R. E. Robertson, *Can. J. Chem.*, **42**, 2137 (1964). [e] V. J. Shiner, Jr., R. D. Fisher, and W. Dowd, *J. Am. Chem. Soc.*, **91**, 7748 (1969). [f] Reference 29. [g] Reference 25. Error limit ±0.05.

bonds to γ deuterium atoms located at noncongested sites within a substrate may actually undergo tightening during the activation process to produce an inverse isotope effect. This has led to the suggestion that the "normal" effect expected for γ-situated deuterium atoms in limiting solvolysis reactions is to produce an inverse kinetic isotope effect through an inductive mechanism which amounts to 2.5% per CD_3 group.[24] If this were to be the case in the solvolyses of the d_9 compounds **3–5**, they could each be expected to exhibit inverse isotope effects on the order of $k_H/k_D \simeq (0.975)^3 = 0.927$.

In contrast, the relatively large "normal" effects actually found for the solvolyses of **3–5** are consistent with the view that severe constraints placed upon the vibrational motions of one (or more) of the *tert*-butyl methyl C–H (C–D) bonds in these substrates result in a greater separation of the zero point energy levels between the protium and deuterium compounds in the initial states than at the transition states where nonbonded constraints on vibrational freedom are reduced. This is due to the greater vibrational amplitudes of C–H bonds compared with analogous C–D bonds.[14,26]

The Question of Methyl Participation. The possibility that the solvolytic reactivity of 2-*tert*-butyl-2-adamantyl *p*-nitrobenzoate might be enhanced through methyl migration concurrent with the rate-determining formation of a rearranged carbocation intermediate was considered earlier.[20] Although such methyl participation could not be completely ruled out, it was deemed unlikely on the basis that some alcohol of unrearranged structure was obtained in the products.[20]

The presently observed isotope effect on product distribution is best interpreted as a confirmation of this view of the discrete and sequential nature of the rate-determining and product-partitioning steps in the solvolysis of **4** (eq 1).[28] If the rate-determining and methyl-shift steps were one, then both the kinetic and methyl-migration isotope effects should have the same value.[29-31] The observation of a large disparity between the two isotope effects (1.11 vs. 1.25) precludes the coincidence of the two events. The even greater divergence of effects in the 9-bicyclo[3.3.1]nonyl system (1.03 vs. 1.35) demands a similar separation of rate- and product-determining steps.[32] It is unlikely that the camphenilyl system behaves in a substantially different fashion.



(1)

This apparent lack of methyl participation in the current study is consistent with the results of earlier studies involving other tertiary substrates whose high reactivity was attributed primarily to relief of initial state steric strain.[3,33]

Comparison of *t*-Bu-d_0/*t*-Bu-d_9 and *t*-Bu/CH_3 Rate Ratios as Probes of Steric Strain. If, for a given reaction series, one particular mode of intramolecular interaction mechanism similarly dominates the activation processes of both a kinetic isotope effect and another substituent effect, then it is reasonable to expect some form of linear free energy relationship to exist for the two effects within that series.[34] For example, a linear free energy relationship between the logarithms of the α-CH_3/H and α-CH_3/CD_3 rate ratios has been shown to exist by Shiner, Sunko, and co-workers for a number of solvolysis reactions.[35] This correlation is apparently a manifestation of the predominant importance of hyperconjugative interactions in both the methyl effect and the β-deuterium kinetic isotope effect. Establishment of correlations of this type is useful, because deviations then become mechanistically significant.[35]

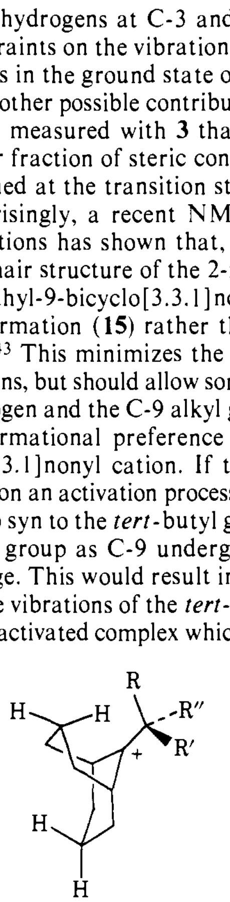
If reduction of steric constraints imposed on vibrational motions of the C–H (C–D) bonds of the *tert*-butyl groups is an important reason for the enhanced solvolytic reactivity of compounds **3–5** *and* if the corresponding methyl compounds **6–8** react all by similar mechanisms, then one might expect a linear relationship to exist between the logarithms of the *t*-Bu/CH_3 and *t*-Bu-d_0/*t*-Bu-d_9 rate ratios for this reaction series. In fact, such a correspondence is not found. Although the *t*-Bu/CH_3 ratios are in the order **3**/**6** < **4**/**7** < **5**/**8**, the *t*-Bu-*d*-$_0$/*t*-Bu-d_9 ratios are in the order **3** < **5** < **4**.

In order to understand this lack of correspondence, it is necessary to consider the individual components of the *t*-Bu/CH_3 rate ratios. The absolute solvolysis rates of the *tert*-butyl esters **3–5** are almost identical (within a factor of 1.3), both in 80% aqueous acetone (Table I) and in 95.6% aqueous ethanol (Table II). As a result, it is apparent that variations in the values of the *t*-Bu/CH_3 rate ratios for these systems must therefore depend upon the reactivities *not* of the *tert*-butyl esters **3–5**, but rather of the methyl esters **6–8**! Relative to the adamantyl system then, the 9-bicyclo[3.3.1]nonyl system is seen to have a lower *t*-Bu/CH_3 ratio primarily because the reactivity of its methyl ester **6** is slightly more than twice that of adamantyl ester **7**. The camphenilyl system exhibits the highest *t*-Bu/CH_3 rate ratio because the reactivity of its methyl ester **8** is only about one-sixth that of **7**.[36] The less than obvious reasons for this ordering of the *t*-Bu/CH_3 rate ratios warn against any untempered use of such ratios for quantitative comparisons of "strain" in these and similar systems.

The γ-deuterium kinetic isotope effect differences exhibited in the solvolyses of the *tert*-butyl esters **3–5**, although small on an absolute basis, are significantly outside experimental error and must thus be regarded as guides to the relative net reduction of vibrational force constants experienced during the progression from initial state to activated complex. It seems reasonable that the extent of charge development at the respective transition states is similar for **3**, **4**, and **5**. From this viewpoint it follows that the net decrease in steric strain which originates from nonbonded repulsions among the hydrogens of the *tert*-butyl group and the remainder of the molecule occurs in the order **3** < **5** < **4** during solvolysis. Although additional work is necessary in order to precisely define the origins of these differences, sufficient information is available to permit reasonable speculation on the qualitative ordering.

Superficially, the 2-adamantyl and the 9-bicyclo[3.3.1]nonyl systems appear quite similar. The ground-state conformation of 9-*tert*-butyl-9-bicyclo[3.3.1]nonyl *p*-nitrobenzoate is undoubtedly double-chair.[37-40] As in the case of the adamantyl ester, it is likely that considerable nonbonded and angle strains in **3** are caused by the repulsive interactions of the methyl group R with the cyclohexane-like ring over which it lies.[20] Unlike the more rigid adamantyl system, some of the strain in **3** is distributed into nonbonded interactions between the endo hydrogens at C-3 and C-7.[41] Thus the severity of the constraints on the vibrational freedom of the R group should be less in the ground state of **3** than in **4**.

Another possible contributing factor for the smaller isotope effect measured with **3** than with **4** is the likelihood that a larger fraction of steric congestion at the *tert*-butyl group is retained at the transition state for solvolysis of **3** than for **4**. Surprisingly, a recent NMR study made under stable ion conditions has shown that, in contrast to the enforced double-chair structure of the 2-methyl-2-adamantyl cation,[42] the 9-methyl-9-bicyclo[3.3.1]nonyl cation assumes a chair-boat conformation (**15**) rather than a double-chair arrangement (**16**).[43] This minimizes the C-3:C-7 endo:endo hydrogen repulsions, but should allow some repulsions between the exo-C-3 hydrogen and the C-9 alkyl group. It is possible that this same conformational preference holds for a 9-*tert*-butyl-9-bicyclo[3.3.1]nonyl cation. If this were the case, then one can envision an activation process for **3** in which the C-3 methylene group syn to the *tert*-butyl group moves up to follow the *tert*-butyl group as C-9 undergoes the $sp^3 \rightarrow sp^2$ hybridization change. This would result in less net reduction of constraints on the vibrations of the *tert*-butyl C–H (C–D) bonds in going to an activated complex which resembles **15** rather than **16** and would be expected to cause a diminution of the kinetic isotope effect for **3** as compared with **4**, as is observed.



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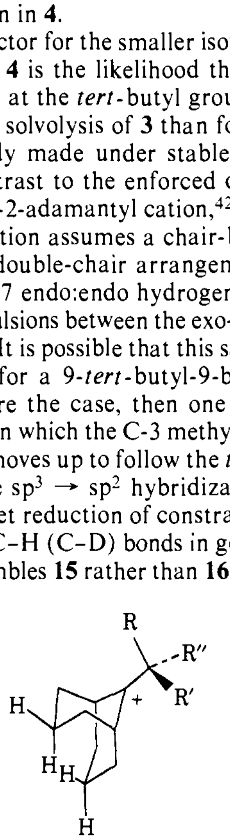

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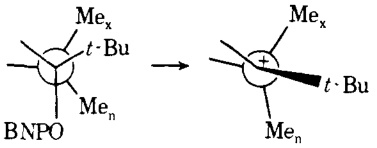
The t-Bu-d_0/t-Bu-d_9 value for the 2-*tert*-butyl-2-*endo*-camphenilyl system indicates appreciable relief of steric congestion at the *tert*-butyl group in going to the activated complex, although less so than in the 2-adamantyl system. Because of its lack of symmetry, the behavior of this system is more difficult to understand than systems **3** or **4**. In the ground state of **5**, the *tert*-butyl group is eclipsed with the exo methyl and the leaving group is eclipsed with the endo methyl of C-3. Molecular models suggest that both methyl groups R′ and R″ of the *tert*-butyl group of **5** probably suffer nonbonded repulsive interactions with the exo methyl of C-3 and that the R″ methyl is further compressed against the syn hydrogen of C-7. These interactions are all greatly diminished in a transition state which resembles a 2-*tert*-butyl-2-camphenilyl cation, but all strain is not relieved. As the *p*-nitrobenzoate group leaves and C-2 undergoes $sp^3 \rightarrow sp^2$ rehybridization, the *tert*-butyl group moves simultaneously further from the exo methyl, but closer to the endo methyl.[44] This reduces the net change in vibrational force constants during the activation process and causes the "steric" isotope effect to be less than it would otherwise be if all nonbonded strain were relieved at the transition state.[46] The Newman projections shown below along the C-2:C-3 bond illustrate this point.



Comments on the Importance of Leaving-Group Steric Effects. Dubois and co-workers have recently suggested that relief of leaving-group strain must be regarded as important in the solvolysis of 2-*tert*-butyl-2-adamantyl *p*-nitrobenzoate.[49] This conclusion was based upon the small t-Bu/CH_3 ratio for the "dehydration" of 2-alkyl-2-adamantanols in glacial acetic acid containing sulfuric acid (1820) compared with the larger ratio observed for the solvolysis of the respective *p*-nitrobenzoates in 80% acetone (239 000). It was argued that the exalted value of the latter must be due to relief of leaving-group steric strain. We are compelled to comment on this position.

There is no doubt that the *p*-nitrobenzoate group can potentially produce F strain effects. The effects of nonbonded repulsions between this group and other parts of a molecule may affect both the molecular structure[5] and the rate of solvolysis of certain tertiary carbinyl systems.[50,51] It is true that the kinetic isotope effects observed in the present work do not directly answer the question of whether or not F strain release is important in the solvolysis of *p*-nitrobenzoates **3–5**. Reduction in vibrational constraints at the positions of isotopic substitution of these esters for any reason, whether because of interactions between the *tert*-butyl group and the "backside" of the molecule or with the leaving group, will contribute cooperatively to produce an exalted "normal" isotope effect.

Molecular models suggest that one of the methyl groups (R) in the camphenilyl ester **5** experiences some direct nonbonded repulsive interactions with the carbonyl oxygen of the leaving group, but such *direct interactions* between the points of isotopic substitution and the leaving group are *not* apparent for either the 9-bicyclo[3.3.1]nonyl or 2-adamantyl systems. In addition, available experimental evidence clearly demonstrates that the introduction of a *p*-nitrobenzoate group at the C-2 position of a tertiary adamantyl moiety does *not* give rise to any special F strain effects. The relative rate ratio for solvolysis of 2-methyl-2-adamantyl and 2-methyl-2-propyl *p*-nitrobenzoates is 2:1 (Table I); for the corresponding bromides the ratio is 10:1.[52] Any special leaving-group effect associated with the *p*-nitrobenzoate group at a 2-adamantyl position would be expected to produce a larger ratio for the *p*-nitrobenzoate than for the bromide—an effect not seen. Other evidence in favor of such a viewpoint is the good correlation of chloride/*p*-nitrobenzoate solvolysis rates for the 2-methyl-2-adamantyl system with those of other systems which display "normal" behavior.[50]

In fact, we do not feel that the smaller t-Bu/CH_3 ratio observed for alcohol dehydration is inconsistent with the larger value observed for *p*-nitrobenzoate solvolysis; it is simply an expected manifestation of the mechanistic differences of the two reactions. The rate-determining step for alcohol dehydration is presumably the loss of water from the protonated alcohol:[53]

$$ROH + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R\overset{+}{O}H_2 \xrightarrow{k_2} R^+ + OH_2 \qquad (2)$$

The activation process for this step involves the separation of neutral water from the incipient carbocation, a much more facile process than the separation of oppositely charged ions required in *p*-nitrobenzoate (and related) solvolyses.[54] As the transition state for alcohol dehydration is of lower energy and is reached earlier along the reaction coordinate, it must resemble more the strained precursor and less the 2-alkyl-2-adamantyl cation than is the case for ester solvolysis.[55]

The "compression" of the *t*-Bu/CH_3 rate ratio for alcohol dehydration relative to ester solvolysis is therefore seen primarily as a natural consequence of the smaller amount of strain released during progression to the activated complex in the former reaction series. Relief of a certain amount of F strain during the solvolysis of 2-adamantyl *p*-nitrobenzoates very likely does occur, but we do not feel that it is of paramount importance in determining the reactivity of **4**. Additional insight into this problem will be gained when empirical force fields are developed which can treat different leaving groups.[56]

Conclusion

The present study supports the conclusion that remote secondary deuterium kinetic isotope effects may be used as site-specific probes of extreme intramolecular nonbonded interactions. When applied to solvolysis reactions in which the steric congestion at the point of isotopic substitution is reduced, the magnitude of the effect is reasonably understood as a measure of the net reduction of congestion during the activation process. Substituent effects such as *t*-Bu/CH_3 rate ratios are probably rough guides to "steric strain" in such systems, but should not be expected to form precise quantitative correlations with steric isotope effects.

Experimental Section

General. All nuclear magnetic resonance spectra were obtained on a Varian T-60A instrument using tetramethylsilane (Me_4Si) as an internal standard. Infrared spectra were obtained on either a Perkin-Elmer 137 or 621 spectrophotometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus in sealed capillaries and are uncorrected. Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz., and Spang Microanalytical Laboratory, Eagle Harbor, Mich. Preparative vapor phase chromatography was performed on a Varian 90-P instrument equipped with a thermal conductivity detector. Analytical vapor phase chromatography was performed on a Hewlett-Packard 5711A dual FID instrument equipped with a Linear Instruments Model 282 recorder with electronic integrator.

General Syntheses. The three alcohols, 9-*tert*-butyl-9-bicyclo[3.3.1]nonanol,[19] 2-*tert*-butyl-2-adamantanol,[20] and 2-*tert*-butyl-2-*endo*-camphenilol,[19] were synthesized by reaction of *tert*-butyllithium with either bicyclo[3.3.1]nonan-9-one (Aldrich), 2-adamantanone (Aldrich), or 2-camphenilone (ChemSampCo.). In a typical preparation, a 100-mL three-necked flask and a constant-pressure addition funnel were thoroughly oven dried at 200 °C and assembled while passing dry helium rapidly through the hot glassware. After cooling, a Teflon coated stir bar was placed in the flask with 0.44 g of lithium sand containing 4% sodium.[57] The lithium sand was rinsed with two 15-mL portions of anhydrous diethyl ether and suspended in 15 mL of diethyl ether. *tert*-Butyl chloride (2.00 g, 0.02 mol) was placed in the addition funnel and a few drops were added neat to the lithium suspension at room temperature. After the solution was stirred for a few minutes a precipitate began to form and the flask was immediately cooled to −35 °C. The alkyl chloride was diluted with 5 mL of ether and added dropwise to the reaction flask over a period of 2 h. The reaction mixture was stirred for an additional 1 h at −35 °C and cooled to −78 °C and the ketone (0.01 mol), dissolved in 30 mL of diethyl ether and dried over 3A molecular sieves, was added dropwise over a period of 1 h. The reaction mixture was allowed to warm slowly to room temperature and then quenched with water. The ether layer was extracted with saturated aqueous NaCl solution and dried over $CaSO_4$. Removal of the solvent produced the tertiary alcohol in 60–95% yield. Five to forty percent of the isolated material consisted of a mixture of unreacted ketone and secondary alcohol that resulted from reduction of the ketone. All of the alcohols were purified by preparative VPC (6.4 mm × 2 m column of 4.1% SE-30 on Anachrome ABS 80/90).

The spectral and physical properties of 2-*tert*-butyl-2-adamantanol[20] and 2-*tert*-butyl-2-*endo*-camphenilol[19] were the same as those reported in the literature. The NMR spectrum ($CDCl_3$) of 2-*tert*-butyl-9-bicyclo[3.3.1]nonanol showed signals at δ 1.07 (9 H, s) and 1.20–2.50, most prominent at 2.03 (15 H, m). The IR spectrum (CCl_4) showed bands (cm^{-1}) at 3630, 3000 (shoulder), 2920, 1481, 1390, 1360, 1041, 983, and 940. The solid melted at 67.8–68.8 °C.

The corresponding d_9 alcohols were prepared in a similar fashion using *tert*-butyllithium-d_9 which was prepared from *tert*-butyl chloride-d_9. The latter was prepared by four exchanges of *tert*-butyl chloride with 12 M DCl solution.[58,59] The atom percent deuterium of the *tert*-butyl chloride-d_9 was determined to be 99.2 by NMR using toluene as an internal standard.[60]

Preparation of *p*-Nitrobenzoate Esters.[61] The tertiary alcohols were converted to the corresponding *p*-nitrobenzoate esters by dissolving 100 mg of the purified alcohol in 5 mL of diethyl ether and adding a stoichiometric amount of *n*-butyllithium. After the mixture was stirred for 3–4 h, 10 mL of ether solution containing 10% less than the stoichiometric amount of *p*-nitrobenzoyl chloride was added over a period of 10 min. The reaction mixture was allowed to stir for 8–12 h and was then extracted with 5 mL of water, 5 mL of 10% aqueous NaOH, and 5 mL of distilled water. An equal volume of heptane was added to the remaining ether solution and the solution was boiled to half volume and cooled to −78 °C. The light yellow crystals were recrystallized in a similar fashion at least three more times. All esters were then stored in a vacuum desiccator until used. Usually 30–40 mg of purified material was obtained. The physical properties were as follows: **4h**, mp 150 °C (slow decomposition) (lit.[20] mp 150 °C dec); **5h**, mp 130 °C (slow decomposition) (lit.[19] mp 133 °C dec); **3h**, mp 120 °C (slow decomposition) (lit.[19] mp 123–124 °C dec).

Preparation of 9-(2′-Propenyl)-9-methylbicyclononane (11). A solution of 0.50 g of 9-*tert*-butyl-9-bicyclo[3.3.1]nonanol in 15 mL of diethyl ether was treated with 5 drops of concentrated hydrochloric acid and stirred for 4 h. The ether was removed and the olefin was isolated by preparative VPC (4.1% SE-30 on Anachrome ABS 80/90): mp 54.0–56.0 °C; NMR ($CDCl_3$) δ 1.07 (3 H, s), 1.72 (3 H, br s), 1.17–2.33, most prominent at 1.85 (14 H, multiplet), 4.88 (1 H, br s), 4.92 (1 H, br s); IR (CCl_4) 3090, 2990, 2920, 1634, 1490, 1467, 1454, 1447, 1371, 1359, 1266, 1120, 1100, 892, 878 cm^{-1}.

Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.66; H, 12.22.

Product Analysis. Approximately 1 mg of the ester was placed in a Kontes Microflex tube with a magnetic stirrer and ca. 0.6 mL of solvolysis solvent. Both protium and deuterium compounds were prepared simultaneously and placed in the constant-temperature bath at 25.00 °C. After 5 days the samples were analyzed directly by VPC using both 3 mm × 0.5 m 10% Carbowax 20M on Anachrome ABS 80/90 and 10% UCW-982 on 80/100 WAW columns. The individual components were identified by comparison of their retention times on the two different columns with authentic samples. The estimated error in the reported values of k_{CH_3}/k_{CD_3} for methyl migration in systems **3** and **4** is ±0.04.

Kinetic Procedure. The solvolytic decomposition of the *p*-nitrobenzoate esters was followed by the change in solution conductance.[62] Solvolysis solvent was prepared by first distilling "95%" ethanol (binary azeotrope) under nitrogen and then adding sufficient triethylamine, itself freshly distilled twice from KOH under nitrogen, to make the amine concentration 0.01 M. Conductance cells of ~10-mL capacity with bright platinum electrodes and nominal cell constants of 0.1–1[63] were filled under a dry nitrogen atmosphere with solutions $\leq 10^{-4}$ M in ester. The same initial concentration of ester was used for each set of kinetic runs.

The solution conductance was measured with a Wayne-Kerr B331 Mark II autobalance conductance bridge having a precision and accuracy rating of 0.01%. During a kinetic run the bridge was preset at a point into which the reacting system would drift. At the balance point, a trigger signal from the bridge's recorder output caused a 10-MHz crystal-driven digital clock to freeze its LED display.[63] The clock continued to count real time while holding its display at the reading at which the balance condition of the bridge was achieved. This permitted the operator to record conductance and time values from static displays and minimized error. The process was repeated for each of the 80–100 points taken over 2–3 half-lives during each kinetic run. First-order rate constants were determined by a leastsquares computer fit of the data. Adherence of the conductance data to a first-order line was within 0.1–0.01% even without conductance-concentration correction factors, *provided that* ester concentrations were kept below 10^{-4} M, the system was kept scrupulously clean, and the temperature was precisely controlled.

A Tamson TEV-40/150 constant-temperature bath filled with Sunelect transformer oil was used to maintain a constant-temperature environment for the conductance experiments. The controlled portion of the bath was quite well stirred and well insulated. Cooling was necessary to maintain the bath at any temperature below 40 °C and was provided by a second bath maintained at 15.0 ± 0.1 °C. Coolant was pumped into a constant-pressure reservoir and allowed to flow from the reservoir at a constant rate through the cooling coils of the Tamson bath. The 1100-W auxiliary heater installed in the bath was connected to a rheostat and was used to augment the control heater when necessary. The original mercury thermoregulator was replaced with a thermistor-based proportional temperature controller[64] and the 1300-W quartz control heater supplied with the bath was replaced with a 100-W Sargent-Welch S-40825 flexible immersion heater. This arrangement provided short- and long-term temperature control of ± 0.001 °C. The most critical components of this system appeared to be the maintenance of a fairly constant coolant temperature and flow rate and the use of a small-wattage control heater. Temperature was measured with a Hewlett-Packard 2801A quartz thermometer.

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(44) By analogy with the known structure of camphene-8-carboxylic acid,[45] a related compound with sp^2 hybridization at C-2, it is likely that the *tert*-butyl group is actually forced closer to the endo methyl than to the exo methyl in the 2-*tert*-butyl-2-camphenilyl cation.

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(46) The observation of very large steric substituent effects is probably predictive of observable remote steric kinetic isotope effects in solvolysis reactions, but the correspondence is by no means assured. For example, dimethylneopentylcarbinyl chloride is reported to undergo solvolysis in 80% ethanol about 13 times faster than does *tert*-amyl chloride,[47] and yet the deuterated compound $(CD_3)_3CCH_2C(CH_3)_2Cl$ exhibits an *inverse* δ-isotope effect, $k_H/k_D = 0.983$, a value inconsistent with the relief of severe nonbonded repulsions at the point of deuterium substitution in the initial state.[48] In contrast, Karabatsos and co-workers[16] observed a substantial normal remote steric isotope effect, $k_H/k_D = 1.17$ (−34 °C), for the aqueous acetone solvolysis of 8-(methyl-d_3)-1-naphthoyl chloride, a value in agreement with that calculated from Bartell's steric origin hypothesis.[14] It is interesting that 8-methyl-1-naphthoyl chloride reacts only 10 times faster than the parent 1-naphthoyl chloride.

(47) H. C. Brown and H. L. Berneis, *J. Am. Chem. Soc.*, **75**, 10 (1953).

(48) J. G. Jewett and R. P. Dunlap, *J. Am. Chem. Soc.*, **90**, 809 (1968).

(49) J. S. Lomas, P. K. Luong, and J.-E. Dubois, *J. Am. Chem. Soc.*, **99**, 5478 (1977).

(50) J. Slutsky, R. C. Bingham, P. v. R. Schleyer, W. C. Dickason, and H. C. Brown, *J. Am. Chem. Soc.*, **96**, 1969 (1974).

(51) Cf. T. T. Tidwell, *J. Org. Chem.*, **39**, 3533 (1974).

(52) J. L. Fry, J. M. Harris, R. C. Bingham, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **92**, 2540 (1970).

(53) Tidwell[2c] has, correctly, we believe, questioned the meaning of the rates obtained from such experiments. He has pointed out that, since a pre-rate-determining step equilibrium is established which determines the kinetically important concentration of protonated alcohol, the observed rate constant is a composite (equal to k_1k_2/k_{-1}) which incorporates into it the basicity of the alcohol. Comparing directly observed rates from such studies is thus equivalent to assuming that the basicities of all alcohols being

compared are either the same or exhibit proportional changes throughout the series. Such an assumption may not be justified.
(54) The low activation energies for alcohol dehydration are easily seen in the very large observed specific rates.[49]
(55) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).
(56) D. F. Detar and C. J. Tenpas, *J. Am. Chem. Soc.*, **98**, 7903 (1976).
(57) P. D. Bartlett and E. B. Lefferts, *J. Am. Chem. Soc.*, **77**, 2804 (1955).
(58) H. C. Brown and C. Groot, *J. Am. Chem. Soc.*, **64**, 2223 (1942).
(59) A. F. Thomas, "Deuterium Labeling in Organic Chemistry", Appleton-Century-Crofts, New York, 1971, p 115.
(60) F. Kasler, "Quantitative Analysis by NMR Spectroscopy", Academic Press, New York, 1973, p 103.
(61) J. D. Buhler, *J. Org. Chem.*, **38**, 904 (1973).
(62) Essentially the same values for the kinetic isotope effects were obtained, but with less precision, by spectrophotometrically following the decrease in ester absorbance at ca. 260 nm.
(63) R. C. Badger, Ph.D. Thesis, The University of Toledo, 1977.
(64) R. C. Badger, *J. Chem. Educ.*, **55**, 747 (1978).

Sources of Hydrogen in the Electrochemical Reduction of Iodobenzene in Dimethylformamide Solution

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Abstract: Iodobenzene has been reduced in dimethylformamide solution containing known amounts of H_2O and D_2O; both lithium chloride and tetraethylammonium bromide have been used as electrolytes. The deuterium content of the resulting benzene and the known isotope effect have been used to calculate the fraction of benzene protonated by water. The amount of tetraethylammonium ion losing a proton is given by the yields of triethylamine and ethylene. The results indicate that water is by far the best proton donor present. Tetraethylammonium ion is less effective but can furnish significant quantities of hydrogen ion. However, at least a part of this is done indirectly with water serving as the transfer medium. In the absence of adequate amounts of better proton donors dimethylformamide itself can be a hydrogen source, although benzene yields fall off because of side reactions.

Most work on the electroreduction of the carbon–halogen bond has been concerned primarily with the nature and yield of the products; only recently has there been interest in the source of the hydrogen appearing in the monomeric hydrocarbon that is usually the principal product:

$$\text{R-}\underset{\cdot\cdot}{\ddot{\text{X}}}\text{:} + 2e^- + \text{H-A} \rightarrow \text{R-H} + \text{:}\underset{\cdot\cdot}{\ddot{\text{X}}}\text{:}^- + \text{:A}^- \qquad (1)$$

Webb, Mann, and Walborsky[1] were among the first to address this problem and used CD_3CN to show that the solvent was the principal hydrogen source in the reduction of 1-bromo-1-methyl-2,2-diphenylcyclopropane in acetonitrile with tetraethylammonium bromide as electrolyte:

$$\text{R-X} \xrightarrow[-\text{X}^-]{1e^-} \xrightarrow{1e^-} \text{R:}^- \xrightarrow[{[\text{CD}_2\text{-CN}]^-}]{\text{CD}_3\text{-CN}} \text{R-D} \qquad (2)$$

Their results also indicated that, although some of the observed ethylene and triethylamine might have been formed by direct reaction of alkyl carbanion with tetraethylammonium ion

$$\text{R:}^- + [\text{H-CH}_2\text{-CH}_2\text{-NEt}_3]^+ \rightarrow \text{R-H} + \text{CH}_2\text{=CH}_2 + \text{NEt}_3 \qquad (3)$$

the bulk of these products must have been formed by attack of the solvent anion on tetraethylammonium ion:

$$[\text{CD}_2\text{-CN}]^- + [\text{H-CH}_2\text{-CH}_2\text{-NEt}_3]^+ \rightarrow \text{HCD}_2\text{-CN} + \text{CH}_2\text{=CH}_2 + \text{NEt}_3 \qquad (4)$$

Cockrell and Murray[2] found that reductions of aryl iodides in deuterium oxide–acetonitrile mixtures with lithium perchlorate electrolyte gave efficient deuterium labeling of the resulting aromatic hydrocarbons. The addition of tetraethylammonium perchlorate led to lowered percentages of deuterated product, indicating that tetraethylammonium ion could compete to some extent with deuterium oxide as a hydrogen donor under their experimental conditions. In similar experiments Semmelhack and co-workers[3] prepared labeled spiro compounds by reducing the corresponding chloro compounds in electrolyte containing deuterium oxide. More recently Grimshaw and Trocha-Grimshaw[4] showed that addition of 1% deuterium oxide to a dimethylformamide–tetrapropylammonium perchlorate system led to deuterium uptake in the reduction of those aromatic halides which would be expected to form carbanion intermediates but not in the cases of those halides which were thought to form radical intermediates.

The dimethylformamide used by electrochemists, although nominally "dry", always contains water. The lowest "guaranteed" water analyses for commercial dimethylformamide are 0.05–0.15% (28–83 mM); the actual water content of freshly opened bottles can be as low as 10 mM and as high as 200 mM.[5] Once a bottle has been opened, the water content can rise rapidly unless effective precautions are taken to prevent moisture uptake during storage and solvent transfer operations.[5,6] With even the very best technique water concentrations of 1–10 mM will prevail during electrolysis. The work reported here was undertaken to study the role of water as a hydrogen source in such water–dimethylformamide mixtures. Although these water concentrations are low, they are comparable to those of the substrates being reduced and water can therefore be expected to play an important part in the chemistry of the system.

In our experiments iodobenzene was electrolyzed in dimethylformamide containing known amounts of H_2O and D_2O.[7] After electrolysis mass spectrometric determination of the deuterium content of the benzene product indicated the extent to which D_2O had been a hydrogen source. The contribution of H_2O was then calculated from the H_2O/D_2O ratio and the relative rates of reaction of the water isotopes. Some experiments were run with lithium chloride electrolyte instead of tetraethylammonium bromide so that water and solvent would be the only possible hydrogen sources. Iodobenzene was selected as substrate, since it reduces sufficiently readily to permit the use of lithium chloride electrolyte instead of tetraethylammonium bromide and since olefin formation by E2 elimination from the substrate is excluded.

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