Participation of the β Phosphonate Group in Carbocation Formation

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Participation of the β Phosphonate Group in Carbocation Formation

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Diethyl (2-(tosyloxy)cyclohexyl)phosphonates have been prepared to test the hypothesis that the strongly electron-withdrawing phosphonate group can stabilize the formation of a β carbocation through hyperconjugation. Systems were constructed with the 180° dihedral angle between phosphonate and tosylate that is optimal for such participation and with the 60° dihedral angle that minimizes it. Reactions were carried out in aqueous mixtures of ethanol, trifluoroethanol, and hexafluoro-2-propanol. The 60° case had the standard profile for bimolecular reaction with solvent (kₚ), with a slower rate that is sensitive to solvent nucleophilicity. The 180° case had the standard profile for a carbocation pathway (kᵢ), with a faster rate that is independent of solvent nucleophilicity and with products that are possible only with a carbocation intermediate. These results suggest that the phosphonate group is capable of stabilizing a carbocation, presumably through hyperconjugation, relative to the expectation based solely on its polar effect.

In recent years there have been numerous studies of the effect of electron-withdrawing groups attached directly to carbocations (α effects). Such groups, including trifluoromethyl, sulfonyl, and nitro, in general have a profound destabilizing influence through their polar effects on the already electron deficient positive charge center. In some cases, however, the destabilization is less than expected from polar effects as measured for example by σ constants. For cyano, the destabilization is partially offset by positive charge delocalization, >C=C=N, reminiscent of the more standard cases of methoxyl and halogen.

Whereas such α effects of substituents on carbocations are almost always a tradeoff between a destabilizing polar effect and a stabilizing π resonance effect, the situation is quite different for a β substituent. The polar effect is much diluted and may become secondary. The major β effect for electron-donating substituents such as silicon and tin is their ability to delocalize σ electrons through hyperconjugation (vertical stabilization). 1 The desirable property of the substituent here is very high polarizability. In addition, there is a large group of β substituents capable of classical anchimeric assistance (nonvertical stabilization), including hydroxyl, alkoxyl, halogen, amino, phenyl, and alkenyl, e.g., 2. The desirable property here is strong nucleophilicity derived from the presence of either a lone pair or a π pair.

All the existing examples of β stabilization involve net electron donors. Is it possible, as with α cyano, for a net electron-withdrawing β substituent to stabilize positive charge? Such a possibility is unprecedented and as yet unstudied except in a single case of β carbonyl, in which the dihedral dependence expected of vertical participation was not explored. We have sought to determine whether there are β groups for which hyperconjugation might compensate to some extent for high electronegativity and provide some stabilization of carbocations. To avoid the mechanism involving anchimeric assistance (2), we excluded groups with lone pairs or strong π bonds. This exclusion applies to most unsaturated carbon-containing groups, to Group VII (halogens), to divalent Group VI (ethers, sulfides, etc.), and to trivalent Group V (amines, phosphines, etc.). Consequently, we directed our attention to high valent examples from Groups V and VI, as represented, respectively, for example, by phosphonates and sulfonates. Although there is the possibility of anchimeric assistance from the oxygen atoms, the main group element has no lone pairs and only weak π bonds. Of these groups, the phosphonate is less electron withdrawing than the sulfone or sulfonate (respective σ constants about 0.51 for (EtO)₂P=O and 0.64 for MeSO₂).

Consequently, we have chosen to explore the question of whether the phosphonate group is capable of providing β stabilization, whereby the polarizability of high valent phosphorus in part compensates for polar destabilization. The work of Mastalerz and co-workers has provided some precedent for such a phenomenon. They found that NH₂-CH₂O(OH)(Ph)PO₂H₂ when diazotized rearranged fully to (Ph(C=O)CH₂PO₂H₂ in which the phosphonate has undergone a Wagner-Meerwein shift intact. In particular, there was no involvement of the oxygen atoms. In this case the driving force for phosphonate migration was formation of the oxonium ion. The work of Warren et
al. also found that phosphine oxides undergo Wagner-Meerwein rearrangements, again with the C–P bond intact (no P to O rearrangement). In both cases the observation of a phosphorus 1,2 shift implies some ability of high valent phosphorus to stabilize positive charge on a β carbon. We have undertaken the evaluation of the ability of the phosphonate group to provide this stabilization, which can be represented by the hyperconjugative interaction 3.

For such an interaction to be significant, the polarizability of the C–P bond must to some extent compensate for the destabilizing inductive effect. An interaction such as that shown in 3 is subject to a dihedral angle dependence in the starting material. The largest effect will be exerted when the P–C–C–X dihedral angle is 180° (parallel orbitals) (P represents the phosphonate group, X is a leaving group) and the smallest at 90° (orthogonal orbitals), with a cosine-squared gradation in between.

To test for the existence of this novel β effect, we have prepared three stereoisomers based on the cyclohexyl framework, 4–6. In the cis isomer 4 the dihedral angle is about 60°, and the phosphonate group should provide little hyperconjugation. The trans isomer 5 is in equilibrium with the diaxial form, in which the optimal antiperiplanar (180°) stereochemistry is present. The biased trans isomer 6 has been frozen into the diaxial form. As with silicon, it is expected that the unbiased trans form readily interconverts between the diequatorial and diaxial forms but the biased form provides the better model for a β effect. We report herein the preparation of 4–6 and the subjection of suitable derivatives to conditions conducive to carbocation formation. By kinetics, solvent variation, and product structures, we assess the ability of the phosphonate group to exert a stabilizing β effect.

**Results**

Diethyl (cis-2-hydroxy-1-cyclohexyl)phosphonate (4-OH) was prepared by the procedure given in Scheme 1. The phosphonate group was introduced by treatment of 3-bromocyclohexene with triethyl phosphate in the absence of solvent. The resulting diethyl (2-cyclohexen-1-yl)phosphonate was oxymercured to give either the alcohol (4-OH) or the methyl ether (4-OMe), depending on conditions. Of the four possible regio- and stereo-isomers, the desired cis-1,2 isomer was formed in predominance. The intermediate mercurinium ion for steric reasons apparently is formed preferentially trans to the existing phosphonate group, so that the incoming hydroxy or methoxy group then enters cis to phosphonate. In six-membered rings, the opening of fused threemembered rings such as epoxides occurs preferentially in a diaxial fashion, the microscopic reverse of the ring formation. Axial attack by solvent at the 3 position would result in an axial phosphonate group, whereas axial attack at the 2 position results in an equatorial phosphonate group. After mercury is removed by reduction, the resulting product is the cis-1,2 isomer. These steric considerations are summarized by structure 7.

The reaction actually produced three of the four possible 1,2 and 1,3 isomers. The 1,2 isomers were easily distinguished from the 1,3 isomers by 3J(CCP), which connects the oxygen-substituted carbon with the phosphorus. The 1,3 isomers do not have such a coupling. Our assignments follow those of Buchanan and Bower, who studied 13C–31P couplings in phosphonates. Most of the structural work was carried out on the methoxy derivatives, which were more soluble and gave easily recognized methoxy resonances. Once 4-OMe had been identified, 4-OH was proved analogously and by conversion to 4-OMe. The stereochemistry of the alcohol also was proved by comparison with the trans-1,2 isomer (below).

Diethyl (trans-2-hydroxy-1-cyclohexyl)phosphonate (5-OH) was prepared straightforwardly by the treatment of cyclohexene oxide with diethyl phosphonate (Scheme 2). This previously unknown procedure was patterned after a low yield reaction of aldehydes with diethyl phosphonate. The use of a stoichiometric amount of ethoxide as base greatly improved the reported yield. The isomeric nature of the cis and trans alcohols was evident from the 1H NMR spectra. The expected trans stereochemistry from the epoxide ring opening (5) confirmed...
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Scheme 2

\[
\begin{align*}
\text{D} & \rightarrow \text{H}^{+} (\text{OE})_{2} \rightarrow \text{PO}_{2} \text{E}_{2} \text{OH} \\
& \text{Key: (a) NaOEt/ETOH/Δ.}
\end{align*}
\]

Table 1. Rate Constants

<table>
<thead>
<tr>
<th>solvent</th>
<th>temp, °C</th>
<th>rate, s⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-OTs (cis)</td>
<td>97% TFE</td>
<td>80.0</td>
</tr>
<tr>
<td></td>
<td>70.0</td>
<td>1.04 × 10⁻⁴</td>
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<td>60.0</td>
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<td>25.0</td>
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<tr>
<td>80% TFE</td>
<td>70.0</td>
<td>2.31 × 10⁻⁵</td>
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<tr>
<td>60% TFE</td>
<td>70.0</td>
<td>8.88 × 10⁻⁵</td>
</tr>
<tr>
<td>80% EtOH</td>
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<td>2.05 × 10⁻⁵</td>
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<tr>
<td>70% EtOH</td>
<td>70.0</td>
<td>3.03 × 10⁻⁵</td>
</tr>
<tr>
<td>60% EtOH</td>
<td>70.0</td>
<td>5.22 × 10⁻⁵</td>
</tr>
<tr>
<td>97% HFIP</td>
<td>70.0</td>
<td>1.37 × 10⁻⁵</td>
</tr>
<tr>
<td>5-OTs (trans)</td>
<td>97% TFE</td>
<td>80.0</td>
</tr>
<tr>
<td></td>
<td>70.0</td>
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<td>3.46 × 10⁻⁵</td>
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<td>80% EtOH</td>
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<td>70.0</td>
<td>1.14 × 10⁻⁵</td>
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<td>60% EtOH</td>
<td>70.0</td>
<td>2.79 × 10⁻⁵</td>
</tr>
<tr>
<td>97% HFIP</td>
<td>70.0</td>
<td>6.65 × 10⁻⁵</td>
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<tr>
<td>6-OTs (biased trans)</td>
<td>97% TFE</td>
<td>86.0</td>
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<td></td>
<td>80.0</td>
<td>1.04 × 10⁻⁴</td>
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<td></td>
<td>70.7</td>
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<tr>
<td>60% EtOH</td>
<td>80.0</td>
<td>6.61 × 10⁻⁵</td>
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<tr>
<td>97% HFIP</td>
<td>70.0</td>
<td>2.66 × 10⁻⁴</td>
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Table 2. Activation Parameters in 97% Trifluoroethanol (25 °C)

<table>
<thead>
<tr>
<th></th>
<th>4-OTs (cis)</th>
<th>5-OTs (trans)</th>
<th>6-OTs (biased trans)</th>
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<tbody>
<tr>
<td>E_a, kcal/mol</td>
<td>32.5</td>
<td>29.0</td>
<td>26.1</td>
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<tr>
<td>log A</td>
<td>15.77</td>
<td>13.73</td>
<td>12.16</td>
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<tr>
<td>ΔF^*, kcal/mol</td>
<td>31.9</td>
<td>28.5</td>
<td>26.5</td>
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<tr>
<td>ΔS^*, cal/deg mol</td>
<td>11.6</td>
<td>2.3</td>
<td>-5.2</td>
</tr>
<tr>
<td>ΔG^*, kcal/mol</td>
<td>28.4</td>
<td>27.7</td>
<td>26.9</td>
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</table>

Table 3. Product Studies at 70 °C

<table>
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<tr>
<th>substrate</th>
<th>product</th>
<th>97% TFE</th>
<th>80% EtOH</th>
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<tbody>
<tr>
<td>4-OTs (cis)</td>
<td>8-H</td>
<td>73</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>5-OEt</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-OCH₂CF₃</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-OH</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>5-OTs (trans)</td>
<td>8-H</td>
<td>12</td>
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<td></td>
<td>9-H</td>
<td>45</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>4-OEt</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4-OCH₂CF₃</td>
<td>20</td>
<td></td>
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<tr>
<td></td>
<td>4-OH</td>
<td>23</td>
<td>8</td>
</tr>
<tr>
<td>6-OTs (biased trans)</td>
<td>8-tert-butyl</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>9-tert-butyl</td>
<td>52</td>
<td>55</td>
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<tr>
<td></td>
<td>10-OEt</td>
<td>9</td>
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<tr>
<td></td>
<td>10-OCH₂CF₃</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-OH</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Discussion

The three substrates include a material in which phosphonate is stereoelectronically available for hyperconjugation in an intermediate carbocation (the biased trans form, 6-OTs), a second material with minimal hyperconjugation that would react directly with solvent (the cis isomer, 4-OTs), and a third material that is a mixture of conformations and might react by a mixture of mechanisms (the trans isomer, 5-OTs). The carbocation pathway is referred to as kₗ, and the direct reaction with solvent as kₗ. The latter reaction encompasses solvent displacement at carbon, elimination by reaction of solvent with a hydrogen β to tosylate, and solvent attack on other atoms of the nucleofuge (more common for hydrolysis of carboxylate leaving groups). If all three substrates reacted by the kₗ mechanism, and if the phosphonate provides the common function of slowing down departure of the nucleofuge through σ electron withdrawal, they should all have the same reactivity profile. Consequently, our objective was to see if there are mechanistic differences between the cis and the biased trans molecules, with the unbiased trans molecule serving as an intermediate case. We have used three lines of evidence to characterize the systems: (1) relative rates, (2) response to changes in solvent nucleophilicity and ionizing power, and (3) product structures.

The β effect of silicon is the classic example of hyperconjugative stabilization of an adjacent carbocation. Whereas cyclohexyl tosylate reacts in aqueous medium by a standard kₗ pathway, introduction of a β silyl group changes the mechanism to kₗ. The presence of a trans β silyl group imparts an enormous rate acceleration to the system. For this reason, we examined the present phosphonates for kinetic evidence of hyperconjugation. The appropriate point of comparison again is cyclohexyl tosylate (k(25 °C) = 1.70 × 10⁻⁶ s⁻¹ and k(70 °C) = 2.77 × 10⁻⁴ s⁻¹ by our own measurements in 97% TFE). At 25 °C in 97% TFE, the cis tosylate reacts 0.0054 times as fast as cyclohexyl, because of the very large rate depressing effect of phosphonate through its polar effect (positive charge is developed in the transition state). The biased trans form reacts 0.069 times as fast as cyclohexyl and the unbiased trans form 0.0174 times as fast.

Table 2) or a 6.5 kcal mol\(^{-1}\) enthalpic difference, as the cis form has a more favorable entropy of activation. We also examined the three systems in 97% HFIP at 70 °C and found a biased trans/cis ratio of 19.4 and an unbiased trans/cis ratio of 4.9. These accelerations are suggestive of but not compelling for a mechanistic change.

If the change in the rate acceleration from 3.2 for the unbiased trans tosylate to 12.7 for the biased form is due entirely to a freezing in of the diaxial conformation, the small increase implies that there already is a substantial amount of diaxial form present in the unbiased case. Although the \(A\) values of phosphonate at about 2.5 and of tosylate at about 1.0 imply a large diequatorial proportion, the interaction between the two groups militates against this form. Thus, introduction of the biasing tert-butyl group has a smaller effect on the rate than expected from the \(A\) values. Consistent with this observation, the line width for the proton \(\alpha\) to phosphonate changes only from 16.1 Hz for the unbiased 5-OTs to 13.2 Hz for the biased 6-OTs. These observations may even imply anomic-effect-like ground-state stabilization of the antiperiplanar form, as found for \(\beta\)-silyl esters.\(^{14}\)

In order to explore differences in molecularity, we utilized the Raber-Harris\(^{15-17}\) approach, which exploits the differences in nucleophilicity and ionizing power of aqueous ethanol and of aqueous TFE. Whereas variation of the proportion of ethanol with water changes the ionizing power but not the nucleophilicity, variation of the proportion of TFE with water changes the nucleophilicity but not the ionizing power. Raber, Harris, and their co-workers plotted the logarithm of the rate of a given substrate versus that of 1-adamantyl bromide, which must react by a carbocation mechanism (\(k_c\)). If the substrate also reacts by a \(k_s\) mechanism, the plot yields a straight line (the TFE points cluster in the upper righthand corner, as there are no rate changes with nucleophilicity along either axis). On the other hand, if the substituent reacts by a solvent participation (\(k_s\)) mechanism, the two solvents give different lines: the ethanol points stretch out along the \(x\) axis as the adamantyl rate varies with ionizing power, whereas the trifluoroethanol rates stretch out along the \(y\) axis as the substrate rate varies with nucleophilicity.

The Raber-Harris plot for the cis substrate (Figure 1) contains the two lines (\(r = 0.989\) and \(0.9999\)) that are diagnostic for solvent participation (\(k_s\)), similar to cyclohexyl tosylate. In particular, the rate in the TFE mixtures varies about 1 order of magnitude in response to changes in solvent nucleophilicity. On the other hand, the plot for the biased trans substrate (Figure 2) has the classic form for a carbocation pathway (\(k_c\)), a single line (\(r = 0.995\)) with the TFE points bunched because the rate is not sensitive to solvent nucleophilicity, similar to the plots for \(\beta\)-silyl esters.\(^{10}\) It is clear that there has been a mechanistic change between the two structures. It is interesting that the unbiased trans case exhibits an intermediate form (Figure 3). The TFE points here are bunched for 5-OTs, suggesting that in this solvent the mechanism is \(k_c\), but the ethanol points are not on the same line. By themselves, the ethanol points of 5-OTs give a linear plot with \(r = 0.9997\), but with the TFE

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**Figure 1.** Raber-Harris plot for diethyl (cis-2-(tosyloxy)-cyclohex-1-yl)phosphonate (4-OTs).

**Figure 2.** Raber-Harris plot for diethyl (r-4-tert-butyl-t-(tosyloxy)-c-1-yl)phosphonate (6-OTs).
The expected result for ion pairs. The product-forming
reaction with solvent occurs after the rate-determining
step in a \( k_b \) reaction, so that these observations are
entirely in accord with the Raber–Harris plots.

The observation of the alkene 11 in the reaction of the
biased trans substrate is extremely significant, as it is
the expected product from the fragmentation that is
implied by the hyperconjugative resonance structure 3.
In the systems lacking tert-butyl, the analogous product
is cyclohexene, whose presence or absence could not be
confirmed, since its retention time was obscured by
solvent. The fragmentation product 11 cannot be ration-}

points \( r = 0.88 \) (the dotted line in Figure 3). Examination of the data indicates that linearization for the biased
trans tosylate occurs because the rate in TFE becomes
faster. The Raber–Harris plots therefore support a
change of mechanism, whereby an antiperiplanar geom-
etry between phosphonate and tosylate leads to a car-
ocation mechanism.

The products from the cis tosylate are straight-
forwardly explained in terms of a \( k_a \) process (Table 3). The vinyl phosphonate 8-H is formed by removal of the
proton that is geminal to phosphonate and trans to
tosylate. It is the only observed alkene product. The

remainder of the product is from substitution with
inversion. In the trans substrates there is no proton that
is geminal to phosphonate and trans to tosylate, as
phosphonate itself resides at the trans position. None-
theless, the same product, 8-H or 8-tert-butyl, is observed,
as well as 9. In the absence of a syn elimination, 8 can
only come from a carbocation intermediate. The remain-
ing products are unremarkable for a carbocation mecha-
nism, although it is noteworthy that the substitution
products (4 and 10) are all formed with inversion. It is
the expected result for ion pairs. The product-forming
reaction with solvent occurs after the rate-determining
step in a \( k_b \) reaction, so that these observations are
entirely in accord with the Raber–Harris plots.

Conclusions

The Raber–Harris plots support a definite change in
mechanism between the cis substrate (4-OTs, 60° dihe-
dral angle between phosphonate and tosylate) (Figure 1)
and the biased trans substrate (6-OTs, 180° dihedral
angle) (Figure 2). The two-line plot for 4-OTs is the
standard appearance for a \( k_b \) pathway, which involves
direct solvent attack in the transition state, leading to
substitution and elimination. The one-line plot for 6-OTs
is the standard appearance for a \( k_c \) pathway, which
involves a carbocation intermediate prior to solvent
attack. The unbiased trans substrate 5-OTs exhibits a
Raber–Harris plot of intermediate form (Figure 3). The
clustering of the TFE points for both trans substrates,
however, indicates that in this solvent the rate has lost
its dependence on solvent nucleophilicity, as expected for
a \( k_c \) mechanism.

Although Figures 1–3 clearly demonstrate a change in
mechanism that is stereoelectronically based, it is not
possible to provide a definitive rationale. Hyperconju-
gative stabilization of the transition state leading to the
carbocation, as in 3, when the nucleofuge and electrophuge
are antiperiplanar to each other provides one possible
explanation. Product and kinetic studies support this
interpretation, but by themselves are not compelling. The
biased trans form reacts 12.7 times faster than the cis
form in 97% TFE at 25 °C or 3.5 times faster at 70 °C.
This modest rate acceleration is consistent with hyper-
conjugation that is not sufficiently strong to overcome
the large electron-withdrawing effect of the phosphonate

group that destabilizes the carbocation intermediate. The
ratio is outside the usual range of structurally similar
axial and equatorial systems, whereby the higher ground
state of the axial system increases the \( k_c \) rate by a factor
of 3–5 at 25 °C.\(^{19}\) Moreover, the biased trans/cis rate
ratio increases from 3.5 to 19.4 at 70 °C in the more
ionizing HFIP, an observation that supports a \( k_b \) mecha-
nism but is not expected for sterically based ground state
differences in a \( k_c \) mechanism.

Stabilization of an \( \alpha \)-CN carbocation with respect to a
\( \beta \)-CN carbocation originally was described in terms of

\(^{18}\) Satterthwait, A. C.; Westheimer, F. H. J. \textit{Am. Chem. Soc.} 1981,
103, 1177–1180.

\(^{19}\) Lambert, J. B.; Salvador, L.; So, J.-H. \textit{J. Org. Chem.} 1993, 58,
5489–5493.
resonance delocalization in the former case, \( \text{C}^=\text{C}=\text{N}^+ \). It also, may be explained by relief of geminal destabilization of the ROCCN grouping.\(^{23}\) Such electronically based ground state effects do not apply to the current situation. The dipoles (CO and CP) in fact are more repulsive in the gauche (60°) than in the anti (180°) form (compare the relative orientations of the dipoles or alternatively note that the negative end of the CP dipole in the anti form is closer to the positive end of the CO dipole and hence is stabilizing). The favorable interaction lowers the anti ground state with respect to the gauche form and hence serves to decrease the anti/gauche ratio. Moreover, such a ground state effect cannot explain the change in mechanism from \( k_1 \) to \( k_2 \) between cis and biased trans or the increase in the acceleration from 3.5 in 97% TFE to 19.4 in HFIP. Both observations require an explanation that stabilizes a carbocation transition state over one involving attack by solvent directly on the substrate.

Finally, the cis and trans systems have somewhat different product mixtures. Whereas the alkene product 8 from the cis tosylate is exclusively that expected for the E2 mechanism, the presence of the same vinylic dipole and hence is stabilizing. The favorable interaction lowers the anti ground state with respect to the gauche form and hence serves to decrease the anti/gauche ratio. Moreover, such a ground state effect cannot explain the change in mechanism from \( k_1 \) to \( k_2 \) between cis and biased trans or the increase in the acceleration from 3.5 in 97% TFE to 19.4 in HFIP. Both observations require an explanation that stabilizes a carbocation transition state over one involving attack by solvent directly on the substrate.

From these lines of reasoning but primarily from the change in mechanism documented by the Rabin–Harris plots, we believe that we have found evidence for \( \beta \) stabilization of carbocations by the very unlikely phosphonate group, in comparison with expectations from polar factors alone. These observations comprise only a beachhead on the problem, but they indicate that a search of second generation systems may document more fully \( \beta \) stabilization of carbocations by highly electron withdrawing groups.

**Experimental Section**

**Diethyl (2-Cyclohexen-1-yl)phosphonate.** A dried, 25-mL, three-necked flask containing a magnetic stirring bar and fitted with a N\(_2\) inlet adapter, a reflux condenser, and a rubber septum was charged with 3-bromocyclohexene (3.28 g, 20.0 mmol) and triethyl phosphate (7.04 mL, 60.0 mmol). The mixture was heated with stirring to 160 °C for 14 h. At that time, GC indicated no remaining starting material and the presence of only two major components. The crude mass balance was 7.51 g (83% of the combined mass of the phosphonate and the excess phosphite). Multiple chromatography on silica gel (70% of product as a colorless oil: \( 1^\text{H} \) NMR (CDCl\(_3\)) \( \delta \) 1.30 (t, 6H), 1.61 (m, 1H), 1.85 (m, 3H), 2.01 (m, 2H), 2.60 (m, 1H, \( J_{\text{CP}} = 30 \) Hz), 4.09 (m, 4H), 5.69 (m, 1H), 6.88 (m, 1H); \( 1^\text{C} \) NMR (CDCl\(_3\)) \( \delta \) 16.3 (d, \( J_{\text{CP}} = 5.8 \) Hz), 20.7 (d, \( J_{\text{CP}} = 9.2 \) Hz), 22.4 (d, \( J_{\text{CP}} = 4.7 \) Hz), 24.4 (d, \( J_{\text{CP}} = 3.2 \) Hz), 34.4 (d, \( J_{\text{CP}} = 142.9 \) Hz), 61.6 (d, \( J_{\text{CP}} = 6.5 \) Hz), 61.9 (d, \( J_{\text{CP}} = 6.7 \) Hz), 121.2 (d, \( J_{\text{CP}} = 8.6 \) Hz), 130.8 (d, \( J_{\text{CP}} = 12.4 \) Hz); \( ^{31} \)P NMR (CDCl\(_3\)) \( \delta \) 31.0; MS (EI) \( m/z \) 218 (92) (M\(^+\)), 190 (12), 162 (9), 139 (70), 138 (53), 111 (89), 93 (16), 83 (53), 82 (31), 61 (65), 81 (25), 80 (100).

**Diethyl (cis-2-Methoxy-cyclohexen-1-yl)phosphonate (4-OH).** A dried, N\(_2\)-flushed vial containing a magnetic stirring bar and fitted with a rubber septum was charged with mercuric acetate (0.38 g, 1.19 mmol) and CH\(_3\)OH (1.0 mL). To the rapidly stirring suspension was added diethyl (2-cyclohexen-1-yl)phosphonate (0.26 g, 1.19 mmol) as a solution in methanol (1.0 mL). The solid material gradually disappeared, and the solution became clear and nearly colorless. The deprotonation step was carried out by cooling the solution to 0 °C and adding 3 N aqueous NaOH (0.4 mL, 1.19 mmol) followed by 0.5 M NaBH\(_4\) (in 1 M aqueous NaOH, 1.19 mL, 2.38 mmol of hydride). The metallic Hg that was produced as a colloidal suspension was allowed to precipitate, and the solution was decanted off. The residue was rinsed with ether (5.0 mL), and the aqueous solution was extracted with ether (3 x 5 mL). The combined organic phases were dried with anhydrous MgSO\(_4\) and concentrated to yield 0.74 g of a yellow oil. Chromatography on silica gel (70 g) (60% hexane–acetone as eluent) gave 0.28 g (93%) of a colorless oil containing the product and its trans isomer in a 92:8 ratio by GC and a 94:6 ratio by \( ^{1} \)H NMR: \( ^{1} \)H NMR (CDCl\(_3\)) \( \delta \) 1.35–1.6 mm, 1.95 (br, 2H), 2.1 (m, 1H), 3.30 (3H, 3.55 (m, 1H), 4.1 (m, 4H); MS (EI) \( m/z \) 250 (7.6) (M\(^+\)), 235 (100), 219 (24), 165 (70), 139 (16), 198 (15), 113 (92), 111 (28), 109 (10).

**Diethyl (cis-2-Hydroxy-cyclohexen-1-yl)phosphonate (4-OH).** The same reaction conditions reported above for 4-OHMe were utilized, although the reaction was carried out at the 26.0 mmol scale and with H\(_2\)O instead of CH\(_3\)OH. The crude product (5.15 g, 84%) was pumped down overnight at 50 °C and then chromatographed three times on alumina (400 g) (slow CH\(_2\)Cl\(_2\) to CH\(_3\)OH gradient as eluent) to yield 3.49 g (57%) of a pale yellow oil, which was 94% pure by GC and 95.6% pure by \( ^{1} \)H NMR: \( ^{1} \)H NMR (CDCl\(_3\)) \( \delta \) 1.25 (m, 6H), 1.75 (m, 2H), 2.21 (dt, 1H, \( J_{\text{HP}} = 20 \) Hz), 2.6 (br, 1H), 4.04 (m, 4H), 4.10 (m, 1H); \( ^{13} \)C NMR (CDCl\(_3\)) \( \delta \) 16.4 (d, \( J_{\text{CP}} = 5.4 \) Hz), 19.5 (d, \( J_{\text{CP}} = 15.3 \) Hz), 25.2 (d, \( J_{\text{CP}} = 4.8 \) Hz), 29.2 (d, \( J_{\text{CP}} = 144.5 \) Hz), 30.2, 32.1 (d, \( J_{\text{CP}} = 3.8 \) Hz), 61.5 (d, \( J_{\text{CP}} = 6.8 \) Hz), 64.9, 65.0; \( ^{1} \)P NMR (CDCl\(_3\)) \( \delta \) 34.5; MS (EI) \( m/z \) 236 (20) (M\(^+\)), 218 (20), 208 (8), 193 (10), 179 (12), 165 (100), 158 (55), 111 (40), 109 (20). Anal. Caled for C\(_{10}\)H\(_{16}\)O\(_3\): C, 50.84; H, 6.9%; Found: C, 50.69; H, 6.8%.

**Diethyl (cis-2-(Tosyloxy) cyclohexen-1-yl)phosphonate (4-OTs).** A dried, 50 mL, round-bottomed flask containing 4-OH (1.69 g, 7.15 mmol) was flushed with N\(_2\) cooled to 0 °C and charged with pyridine (25 mL) and tosyl chloride (2.73 g, 14.3 mmol). The mixture was swirled at 0 °C until all had dissolved and was placed in the refrigerator until no additional pyridinium hydrochloride precipitated out. After 27 days the solution was poured onto ice (200 g) and ether (200 mL). The aqueous solution was extracted with ether (2 x 100 mL). The combined organic phases were washed with 2 N HCl (8 x 50 mL), dried with a 1:1 mixture of anhydrous Na\(_2\)SO\(_4\) and anhydrous K\(_2\)CO\(_3\), and concentrated to 7.94 g. From these lines of reasoning but primarily from the change in mechanism documented by the Rabin–Harris plots, we believe that we have found evidence for \( \beta \) stabilization of carbocations by the very unlikely phosphonate group, in comparison with expectations from polar factors alone. These observations comprise only a beachhead on the problem, but they indicate that a search of second generation systems may document more fully \( \beta \) stabilization of carbocations by highly electron withdrawing groups.
β Phosphonate Group in Carboxylation Formation

(slow CHCl₃ to CH₃OH gradient as eluent) yielded, after an additional overnight pumping, 2.58 g (44%) of a white solid, which was 96.9% pure by GC, mp 62–64 °C: [H] NMR (CDCl₃) δ 1.08–1.40 (m, 4H), 1.32 (dq, 6H), 1.65–1.80 (m, 3H), 1.91 (dm, 1H), 2.08 (m, 1H), 3.65 (m, 1H), 3.81 (br s, 1H), 4.09 (dp, 4H); [13C] NMR (CDCl₃) δ 16.2 (d, JCP = 5.4 Hz), 24.0, 24.9 (d, JCP = 10.3 Hz), 34.4 (d, JCP = 15.3 Hz), 43.1 (d, JCP = 137.2 Hz), 56.3 (s, 6H), 61.6 (d, JCP = 6.5 Hz), 61.9 (d, JCP = 7.0 Hz), 68.5, 68.6; [31P] NMR (CDCl₃) δ 32.4; MS (EI) m/z 236 (11) (M⁺), 208 (44), 207 (100), 206 (71), 205 (14). After an additional overnight pumping, (dm, slow CHCl₃ to CH₃OH gradient as eluent) yielded, after an additional overnight pumping.

A flask was fitted with a rubber septum and a magnetic stirring bar and was charged with 5 mmol of diethyl (trans-4-tert-butylcyclohex-1-yl)phosphonate before being stirred at room temperature in a NMR tube. The solution was removed by rotary evaporation, and the water layer was extracted with another organic solvent. The resulting solution was then analyzed with GC and GC-MS. In the systems lacking tert-butyl, assignments were made by comparing the mass spectra with those of authentic materials. For the tert-butyl-biased system, characterizations were made by analyzing the mass spectra and by comparing the [31P] chemical shifts with those of tert-butyl-free compounds. Quantitations were based on GC (FID detector) without correction.

**NMR Kinetic Experiments.** A series of 24 oven-dried 5-mm NMR tubes was charged with approximately 50 mg (0.12 mmol) of tosylate (4-OTs or 5-OTs) and 0.70 mL of the appropriate solvent. The resulting solutions were then stored at 78 °C. The solutions were prepared via the transmission of that data to the LOTUS package, and graphical presentations were prepared via the transmission of that data to the LOTUS FREELANCE PLUS program.

**Variable Temperature NMR Calibration.** The actual temperature in the NMR probe was determined and calibrated by means of the methanol calibration curve. The software of the XLA-400 includes a program, TEMCAL(M), that determines the temperature from the frequency difference between the two peaks of a neat sample of methanol. A calibration curve may be generated from several temperatures. In practice, however, it was simpler to use the curve only as a guide and to determine the actual temperature each day with the methanol sample.

**Product Studies.** A 0.2–0.5 M solution of the substrate in 80% ethanol or 97% trifluoroethanol (0.7 mL) was prepared in a NMR tube. The solution was sealed and put into a constant temperature bath at 70 °C. After at least 10 half-lives, the samples were cooled and checked by [31P] NMR spectroscopy to ensure that the reaction was complete. The mixtures were then analyzed with GC and GC–MS. In the systems lacking tert-butyl, assignments were made by comparing the mass spectra with those of authentic materials. For the tert-butyl-biased system, characterizations were made by analyzing the mass spectra and by comparing the [31P] chemical shifts with those of tert-butyl-free compounds. Quantitations were based on GC (FID detector) without correction.

**Diethyl (trans-2-Tosylxy)cyclohex-1-yl)phosphonate (6-OTs).** A dried, 25-mL, three-neck flask containing 5-OH (0.59 g, 2.50 mmol) was cooled to 0 °C with ice and chilled with pyridine (0.5 mL) and tosyl chloride (0.97 g, 5.00 mmol). After 1 day at 0 °C, the mixture was allowed to react at room temperature for 14 days and then was returned to 0 °C for an additional 7 days to complete the precipitation of the pyridinium hydrochloride. The crude product was isolated in the same manner as for 4-OTs. After trituration with pentane, the solubility was pumped down to yield pure 4-OTs as a pale yellow, extremely viscous oil: [H] NMR (CDCl₃) δ 1.26 (m, 6H), 1.2–1.75 (m, 4H), 1.98–2.23 (m, 3H), 2.43 (s, 3H), 4.03 (m, 4H), 4.79 (m, 1H), 7.32 (d, 2H), 7.81 (d, 2H); [13C] NMR (CDCl₃) δ 16.3 (d, JCP = 5.6 Hz), 21.6, 21.9, 23.1 (d, JCP = 8.5 Hz), 25.4 (d, JCP = 4.5 Hz), 31.1 (d, JCP = 6.5 Hz), 39.1 (d, JCP = 139 Hz), 61.7 (d, JCP = 7.5 Hz), 82.0 (d, JCP = 6.5 Hz), 79.2, 127.0, 127.9, 129.6, 130.2; [31P] NMR (CDCl₃) δ 28.0. MS (EI) m/z 290 (4) (M⁺), 345 (3), 377 (2), 386 (35), 399 (17), 298 (67), 284 (10), 283 (27), 256 (12), 255 (33), 242 (18), 235 (46), 220 (18), 219 (100), 218 (71), 207 (4), 206 (71), 205 (14). **Diethyl (4-4-Tert-Butyl-4-hydroxy-c-1-yl)phosphonate (6-OH).** An oven-dried, N₂-flushed, 50 mL round-bottomed flask was fitted with a rubber septum and a magnetic stirring bar and was charged with 1.93 mL (15 mmol) of diethyl phosphate in 15 mL of anhydrous THF. The solution was cooled to −75 °C, and 6 mL (15 mmol) of 2.5 M BuLi in hexane was introduced dropwise to the stirred solution through a syringe. The solution was stirred for 15 min, and 0.77 g (5 mmol) of trans-4-tert-butylocyclohexene oxide in 3 mL of anhydrous THF was added dropwise. The solution was stirred another 15 min, and 2.5 mL (20 mmol) of BF₃·Et2O was introduced slowly. After being stirred at −75 °C for 2 h, the reaction was quenched with 10 mL of saturated aqueous NH₄Cl. The mixture was warmed to room temperature, the organic solvent was removed by rotary evaporation, and the water layer was extracted with 3 × 30 mL of ether. The combined organic layers were washed with brine, dried (MgSO₄), and concentrated by rotary evaporation. The residue was purified by column chromatography over silica gel with hexane/ethyl acetate (1/1) and pure ethyl acetate as eluents. The product was a very viscous, pale green oil: 1.19 g (82%); [H] NMR (CDCl₃) δ 0.84 (s, 9H, tert-butyl), 1.30–1.40 (m, 6H), 1.40–2.18 (m, 9H), 4.02–4.22 (m, 5H), 4.40 (m, 1H); [13C] NMR (CDCl₃) δ 16.5 (d, JCP = 6.6 Hz), 20.5, 22.8, 27.4, 31.9 (d, JCP = 79.6), 38.2, 40.0, 40.1, 61.5, 66.2 (d, JCP = 5.2 Hz); [31P] NMR (CDCl₃) δ 32.0; MS (EI) m/z 292 (M⁺, weak), 269 (11), 236 (28), 235 (100), 218 (50), 217 (12), 207 (24); HRMS (M⁺) calcd 292.1503, obsd 292.1506.