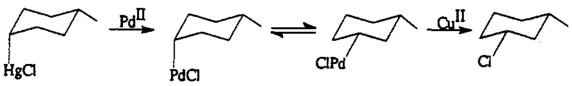
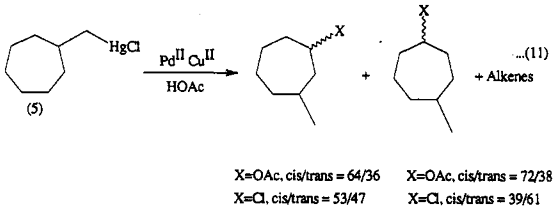


...(10)

Similar [HPdX]-mediated processes may operate with the cycloheptylmethyl system **5**, but a different blend of cleavage modes for the C–Pd bond is indicated by the increased acetate fraction (38% acetate, 38% chloride, 14% cycloalkenes) compared with the cyclohexyl case. No 2-methyl chlorides or acetates were detected[5,19] (eq 11).



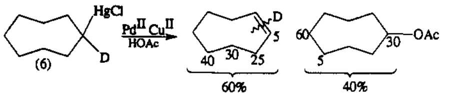
(5)

...(11)

Cycloheptylmercuric chloride,[18] under the same conditions, provides predominantly cycloheptyl acetate (66%) and chloride (28%) and cycloheptene (6%).[5,19]

Extension to cyclooctylmercurials reveals that the [HPdX] mediated processes are now supplanted by direct C–Pd heterolysis and carbocation formation.[2-4] For example, treatment of [1-$^2H_1$]cyclooctylmercuric chloride[18] (**6**) with Pd(II)–Cu(II) in the normal way provided cyclooctene and cyclooctyl acetate, with a barely detectable level of cyclooctyl chloride (eq 12). This contrasts markedly with the product patterns in eqs 3 and 10.

The ^2H distribution in the product acetate (eq 12), with 60% located at C-5, reflects predominating 1,5-transannular hydride shifts, along with direct replacement ($\sim$ 30%). This result is inconsistent with Pd-migration of the type outlined in Scheme I but is similar to that observed by us in tosylate solvolysis[20-22] (eq 13) or in carbocation-mediated demercuration[23] (eq 14). Cyclooctylmethylmercuric chloride[18] (**9**) provides largely methylcyclooctenes, some cyclononene, and *cis*-4-methylcyclooctyl acetate[24] (eq 15), such products being consistent with carbocation intermediacy. Cycloalkyl chlorides were present at very low levels.



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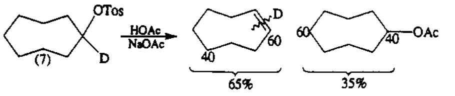

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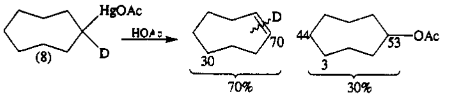

(8)

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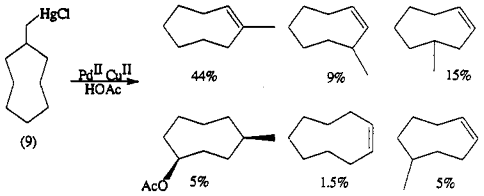

(9)

...(15)

Therefore, a range of mechanistic possibilities for Pd(II)-promoted demercuration in the presence of Cu(II) appears to exist, with [HPdX]-mediated processes in the cyclohexyl system competing favorably with other routes, whereas the easily reached cyclooctyl cation results from direct oxidation of the C–Pd bond. A full report of this and related work will appear at a later date.

Acknowledgment. The authors are grateful to the Australian Research Council for support and for a scholarship to A.P.W.

Supplementary Material Available: ^1H, ^2H, and ^{13}C NMR spectra of compounds 1 and 8, ^1H and ^2H NMR spectra of compound 2 from eq 4, ^{13}C NMR spectra of cyclooctyl acetate and cyclooctene from acetolysis of compound 7 in eq 13, detailed description of the Pd(II)–Cu(II)-mediated reaction of mercurial 1, and a listing of the assigned ^{13}C NMR chemical shifts for the *cis*- and *trans*-3- and -4-methylcycloheptyl alcohols, acetates, and chlorides (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[17] Reaction of [1-$^2H_1$]cyclohexylmercuric chloride leads cleanly to a mixture of cyclohexyl chloride (88%) and cyclohexyl acetate (12%). The chloride consists of the 1-$^2H_1$ (36%), trans 2-$^2H_1$ (31%), and trans 3-$^2H_1$ (21%) isomers. This pattern is consistent with stereospecific [HPdX] eliminations and readditions and retentive chloride displacement of palladium.[10,11]

[18] Characterized by high-quality NMR spectra (^1H, ^2H, ^{13}C as applicable), elemental analyses, and/or high-resolution mass spectra.

[19] For a discussion of the ^{13}C NMR spectra of the regioisomeric methylcycloheptanols, see: Christl, M.; Roberts, J. D. *J. Org. Chem.* **1972**, *37*, 3443. Authentic samples of the corresponding acetates and chlorides were prepared as part of the present study, and their ^{13}C NMR spectra were assigned.

[20] [1-$^2H_1$]Cyclooctyltosylate was solvolyzed in acetic acid in the present study and the location of ^2H in the products, cyclooctene and cyclooctyl acetate, was determined by careful ^{13}C NMR spectroscopy. In this connection, see: Penman, K. G.; Kitching, W.; Wells, A. P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2501–2507. See also: Cope, A. C.; Gale, D. M. *J. Am. Chem. Soc.* **1963**, *85*, 3747. Allinger, N. L.; Szbrybalo, N. *Tetrahedron* **1968**, *24*, 4699.

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[22] The ^2H distribution in the cyclooctene product is complicated by subsequent exchange and possible Pd(II)-induced double-bond migration. This latter effect may apply to eq 15 also.

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Ab Initio Investigation of Substituent Effects in 4-Substituted Bicyclo[2.2.2]oct-1-yl Cations. Computational Support for Through-Bond Stabilization via Double Hyperconjugation

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Summary: Ab initio calculations support the interpretation of experimental substituent and isotope effects in terms of double hyperconjugative stabilization of bicyclo[2.2.2]oct-1-yl cation.

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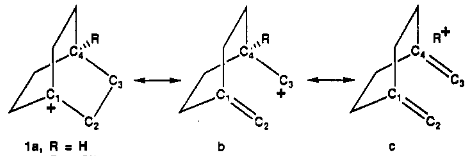
Recently, Adcock et al. reported the rates of solvolysis of 4-deuterio- and several 4-metalloidal($M(CH_3)_3$, M = Si, Ge, and Sn)bicyclo[2.2.2]-oct-1-yl sulfonate esters.[1] A significant δ-deuterium isotope effect was found (k_H/k_D = 1.05), and rate accelerations of 10^1–10^3 were observed for the metalloidal substituents ($k_{Sn} \gg k_{Ge} > k_{Si} > k_H$). These results were interpreted in terms of through-bond, double hyperconjugative stabilization of the carbocation **1** via a contribution from resonance structures of type **c**, as first proposed by Grob and Rich.[2] However, calculations at the RHF level by Wenke and Lenoir on 4-substituted bicyclo[2.2.2]oct-1-yl cations gave no indication of double hyperconjugation in **1**.[3] Instead Wenke and Lenoir proposed that the operative mechanism for stabilization of the cations by substituents at C_4 involved a through-space, field effect.



1a, R = H
2a, R = SiH_3
3a, R = SnH_3
b
c

Inclusion of electron correlation is important for describing molecules with delocalized structures,[4] and it has been shown to be particularly important in obtaining an adequate description of nonclassical cations.[5] We have recently found this to be the case for the cubyl cation,[6] and our continued interest in bridgehead carbocations led us to carry out calculations on **1**–**3** that included electron correlation at the MP2 level of theory. Our results support the operation of double hyperconjugation in these carbocations.

Geometries of cations **1**–**3** and of the corresponding hydrocarbons were optimized[7] at the RHF level, using the 3-21G basis set.[8] The RHF/3-21G geometries of bicyclo[2.2.2]octane (**1-H**) and **1** were reoptimized with 6-31G*[9] and with both basis sets at the MP2[10] level of theory. Important bond lengths in the optimized geometries are given in Tables I and II.[11] Vibrational analyses were performed at each RHF and MP2-optimized geometry.[12,13] Energies at the RHF geometries were recalculated at the MP2 level with the 3-21G(*)[14] and 6-31G* basis sets. The energies for all three basis sets are given in Table III. The δ-deuterium equilibrium isotope effect (k_H/k_D) for formation of **1** was computed from reduced isotope partition functions, which were obtained with the program QUIVER,[15] using the quadratic cartesian force constants from the vibrational analyses.

Table I. Optimized Bond Lengths (Å) in Hydrocarbon 1-H[a] and in Cation 1[b]

	3-21G				6-31G*			
	RHF		MP2[c]		RHF		MP2[c]	
	1-H	1	1-H[d]	1[e]	1-H[f]	1[g]	1-H[h]	1[i]
r_{12}	1.541	1.461	1.552	1.460	1.536	1.464	1.532	1.449
r_{23}	1.561	1.637	1.570	1.675	1.552	1.608	1.546	1.626
r_{34}	1.541	1.542	1.552	1.545	1.536	1.538	1.532	1.527
r_{14}	2.601	2.378	2.616	2.409	2.589	2.350	2.581	2.354
r_{4H}	1.084	1.083	1.097	1.100	1.086	1.083	1.097	1.097

[a] D_3 symmetry for 1-H. [b] C_{3v} symmetry for 1. [c] Full MP2. [d] E(MP2) = −310.1301 hartrees. [e] E(MP2) = −309.2553 hartrees. [f] E(RHF) = −311.1036 hartrees. [g] E(RHF) = −310.2465 hartrees. [h] E(MP2) = −312.1898 hartrees. [i] E(MP2) = −311.3062 hartrees.

Table II. RHF/3-21G and RHF/3-21G(*) Optimized Bond Lengths (Å) in Hydrocarbons 2-H[a] and 3-H[a] and in Cations 2[b] and 3[b]

	3-21G		3-21G(*)		3-21G	
	2-H	2	2-H[c]	2[d]	3-H	3
r_{12}	1.539	1.456	1.539	1.456	1.538	1.452
r_{23}	1.561	1.652	1.560	1.650	1.562	1.665
r_{34}	1.549	1.540	1.554	1.545	1.549	1.532
r_{14}	2.623	2.412	2.630	2.416	2.626	2.427
r_{4R}	1.922	1.957	1.889	1.927	2.170	2.215

[a] C_3 symmetry for 2-H and 3-H. [b] C_{3v} symmetry for 2 and 3. [c] E(RHF) = −598.0341 hartrees. [d] E(RHF) = −597.1781 hartrees.

As shown in Table I, at the RHF/3-21G and 6-31G* levels, on forming cation **1**, the optimized geometry of bicyclo[2.2.2]octane (**1-H**)[16] changes in the way expected for a contribution from resonance structure **1b** but not **1c**. The decrease in r_{12} and increase in r_{23} indicate substantial hyperconjugation of the cationic center with the C–C bonds β to it. If the cation were also stabilized by double hyperconjugation of the C_4–H bond, a decrease in r_{34} and an increase in r_{4H} would be expected. At the RHF level the changes in these two bond lengths are small but in exactly the opposite direction expected for a contribution from **1c**. Additionally, the δ-deuterium isotope effects are calculated at the RHF/3-21G and 6-31G* levels to be, respectively, k_H/k_D = 1.005 and 1.010. These RHF values are considerably smaller than the value of k_H/k_D = 1.05 that was found experimentally.[1]

At the MP2/3-21G and 6-31G* levels the changes in r_{12} and in r_{23} on cation formation are even larger than at the RHF level. However, in contrast to the results obtained at the RHF level, the MP2-optimized structures reveal that formation of **1** from **1-H** leads to small changes in r_{34} and in r_{4H} that are opposite to those found at the RHF level and in the directions expected for a small contribution

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(11) Complete lists of optimized geometrical parameters are available as supplementary material.

(12) Vibrational analyses at the MP2/3-21G level using analytical second derivatives were carried out with CADPAC. Amos, R. D.; Rice, J. E. *CADPAC: The Cambridge Analytic Derivatives Package*; Issue 4.0, Cambridge, 1987. Vibrational analyses at the MP2/6-31G* level using numerical second derivatives were carried out with GAUSSIAN 90.[7]

(13) With one exception all optimized geometries proved to be minima. Although at the RHF/6-31G* level the C_{3v} geometry for **1** was a minimum, at the MP2/6-31G* level the vibrational analysis for the C_{3v} cation found one imaginary frequency (63i cm^{-1}) corresponding to torsion about the C_1–C_4 axis. MP2/6-31G* reoptimization of **1** in C_3 symmetry gave a geometry[11] (r_{12} = 1.449 Å, r_{23} = 1.623 Å, r_{34} = 1.528 Å, r_{14} = 2.354 Å, r_{4H} = 1.097 Å, ϕ_{2143} = 7.6°) which differed only slightly from that of the C_{3v} optimized structure and an energy that was only 0.1 kcal/mol lower.

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Table III. Energies[a] of Cations 1–3 and of the Corresponding Hydrocarbons (1-H–3-H) Calculated at RHF/3-21G Geometries with the 3-21G, 3-21G(*), and 6-31G* Basis Sets

	3-21G		3-21G(*)		6-31G*	
molecule	RHF	MP2[b]	RHF	MP2[b]	RHF	MP2[c]
1	−308.5347	−309.2524	−308.5347	−309.2524	−310.2453	−311.2642
1-H	−309.3926	−310.1278	−309.3926	−310.1278	−311.1032	−312.1477
2	−597.0840	−597.8716	−597.1776	−597.9931	−600.3155	−601.4217
2-H	−597.9398	−598.7421	−598.0335	−598.8647	−601.1727	−602.3021
3	−6306.3517		−6306.4284	−6307.2635		
3-H	−6307.2029		−6307.2795	−6308.1282		

[a] Energies in hartrees. [b] Full MP2. [c] Frozen core MP2.

from 1c.[17] Moreover, the isotope effects calculated at the MP2/3-21G level ($k_H/k_D = 1.063$) and the MP2/6-31G* level ($k_H/k_D = 1.040$) are much larger than at the RHF level and in much better agreement with experiment.[1] The increase in the calculated isotope effect cannot be attributed to an increase in through-space bonding between C_1 and C_4 at the MP2 level, since, on going from the RHF to the MP2 optimized structure for 1, r_{14} increases.[18]

If, as suggested by the results of our calculations on 1, there is some delocalization of the electrons in the C_4–H bond in the carbocation, weakening this bond should provide increased stabilization for the cation. This is what was observed experimentally by Adcock et al. on replacing H at C_4 by metalloidal substituents.[1] That the observed rate accelerations are, in fact, a result of enhanced double hyperconjugation can be seen from comparison of the optimized geometries (Table II) and calculated energies (Table III) for the 4-substituted, bridgehead cations 2 and 3 with those for the corresponding alkanes, 2-H and 3-H.

As in the case for formation of the unsubstituted cation (1), at the RHF level r_{12} decreases and r_{23} increases on formation of 2 and 3. However, when a weak bond to a metalloidal substituent (R = SiH_3 in 2 and R = SnH_3 in 3) replaces the C_4–H bond in 1, even at the RHF level r_{34} decreases and r_{4R} increases. As expected for a larger contribution from structure **c** in 3 than in 2, the sizes of the changes in these bond lengths are larger for R = SnH_3 than for R = SiH_3. The changes in r_{14} are nearly the same for formation of all three cations, and the small differences in Δr_{14} (1 > 2 > 3) are in the opposite order from those expected for through-space bonding between C_1 and C_4 in the cations. The data in Table II also show that, although the optimized bond lengths change on going from the 3-21G to the 3-21G(*) basis set, the differences between the bond lengths in 2 and 2-H remain essentially the same.

In agreement with experiment, the energy required for cation formation decreases in the order 1 > 2 > 3. At the RHF level with the 3-21G, 3-21G(*), and 6-31G* basis sets, substitution of R = H at C_4 by R = SiH_3 reduces the energy required for carbocation formation by, respectively, 1.3, 1.3, and 0.4 kcal/mol. Since inclusion of electron correlation increases the importance of the doubly hyperconjugated resonance structure **c**, it is not surprising that at the MP2 level of theory the magnitudes of these energy reductions increase to 3.1, 2.4, and 1.9 kcal/mol. For R = SnH_3 the RHF energy reductions are 4.2 and 4.3 kcal/mol with, respectively, the 3-21G and 3-21G(*) basis sets and 6.7 kcal/mol at the MP2/3-21G(*) level.

The relative rates of carbocation formation at 25 °C in the gas-phase that are computed from the MP2/3-21G(*)//RHF/3-21G energies are qualitatively similar to those found in the solvolysis studies.[1] The silyl substituent is calculated to afford a modest rate increase, $k_{Si}/k_H = 58$; and the stannyl substituent is predicted to yield a substantially larger acceleration, $k_{Sn}/k_H = 82\,000$. The experimental rate ratios in 97% trifluoroethanol at 25 °C are 1:49:2841.[1] Our calculations provide strong support for the interpretation of these rate ratios in terms of increasing stabilization of 1–3 via double hyperconjugation, as depicted by structure **c**.

Acknowledgment. We thank the National Science Foundation for its support of this research and for providing funds that enabled the purchase of the Convex C-2 computer, on which some of the calculations reported here were performed. We also thank the San Diego Supercomputer Center for a generous allocation of time on the Cray Y-MP8/864 computer at SDSC.

Supplementary Material Available: Optimized geometries of 1–3 and 1-H–3-H (15 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[17] The MP2/6-31G* optimized C_4–H bond length in 1 is 0.0005 Å longer than that in 1-H.

[18] Flattening of C_1 on carbocation formation results in the decrease in r_{14} that is calculated on going from 1-H to 1.

Ruthenium-Catalyzed Hydration of Nitriles and Transformation of δ-Keto Nitriles to Ene–Lactams

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Summary: Hydration of nitriles and transformation of δ-keto nitriles to ene–lactams can be performed efficiently by using $RuH_2(PPh_3)_4$ catalyst under mild conditions. The effectiveness of the reaction is illustrated by the short-step synthesis of (−)-pumiliotoxin C.

The hydration of nitriles under mild and neutral reaction conditions is of importance from both an enzymatic[1]