μ-Hydrido Bridging in Tricycloalkyl Carbocations

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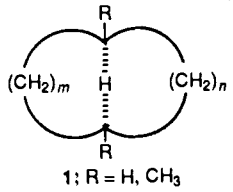
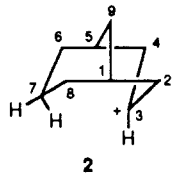
Abstract: From 2-adamantanone, a series of tricyclic alkenes **5** (n = 5–8) were synthesized in 10 steps. The analogous alkene **5** (n = 4) could not be prepared by the same route. These structures, in each case, were designed to have an inwardly pyramidalized bridgehead hydrogen, which is suitably positioned so that the formation of a cationic center on the opposite bridgehead could then potentially lead to a μ-hydrido-bridging interaction. The nature of the hydrido bridge was found to be very structure-dependent, and one can correlate this behavior with the distance d between the terminal bridge-supporting carbons (C--H–C$^+$) in the tricycloalkane framework. For the shortest distances, one develops a fully symmetric μ-H bridge, while larger d result in a gradation toward a normal tertiary carbocation structure. The cation **4** (n = 5) is quite stable in a pK_a sense (p$K_a \approx -1$), and the pK_a relationship between this cation and the n = 6 case was computed with semiempirical MO theory. The calculated pK_a was −5.3, in good agreement with an experimental bracketing of the pK_a between −3 and −8. One also predicts from the MO theory that the unknown cation **4** (n = 4) will have p$K_a \approx +10$, i.e., stable in neutral water.

NMR-observable μ-hydrido-bridged carbocations **1** were first reported in a ten-membered ring in 1978.[1] Subsequently, they were also found in eight-, nine-, and eleven-membered rings.[2] Previous to this, a number of solvolysis and acid catalysis reactions involving medium-ring organics were postulated to involve such structures as plausible reaction intermediates.[3] Mass spectrometric[4] and laser IR studies[5] of hydrogen-bridged gas-phase cations have also been reported.

Bicyclic systems, in particular the 3-position of the bicyclo[3.3.1]nonyl ring **2** have also been actively studied, although the solvolysis evidence for μ-hydrido bridging in a 3-yl cation intermediate is mostly negative.[6]



1; R = H, CH_3



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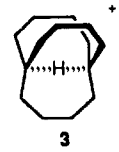
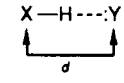


3

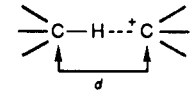
More recently, McMurry and Hodge[7] have prepared the 1-bicyclo[4.4.4]tetradecyl cation **3**, which is μ-hydrido-bridged and also very stable, both thermally and in terms of a pK_a value.

μ-Hydrido bridging has not been observed in open-chain systems,[8] and one appears to require a molecule in which the carbocation center and a remote C–H bond have a somewhat forced proximity, such as one finds for transannular positions in medium rings. From theoretical calculations[2,9] and various experimental determinations,[2] including IR spectroscopy,[7] it appears that most of the reported μ-hydrido-bridged cations probably have a symmetric μ-H bond, i.e., a single potential minimum is involved. The bonding in a symmetric μ-hydrido bridge involves a two-electron three-center bond (σ-conjugation). In contrast, the much better known hydrogen bonding involves a four-electron three-center bond. In hydrogen bonding, there are known to be many variations in the potential energy surface, with both symmetric and unsymmetric cases. As expected, symmetric hydrogen bonds involve shorter

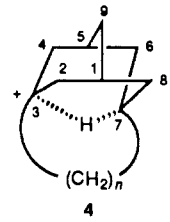


distances than do unsymmetric ones.

The intent of the present work was to examine μ-hydrido bridging under conditions where one could hope to fix the overall



distance in a systematic way, i.e., for various d values. The superstructure chosen for this study was based on the previously mentioned 3-bicyclo[3.3.1]nonyl ring, by adding a variable length "cinch" to the 3- and 7-positions, as shown in structure **4** (for ease of comparison, the bicyclo[3.3.1]nonane numbering system will be used to describe these cations).



4

As was anticipated from the previous solvolysis work[6] and X-ray parameters for bicyclo[3.3.1]nonan-3-ones,[10] the unconstrained bicyclo[3.3.1]nonane ring has a C3–C7 distance that is too long to accommodate a symmetric μ-hydrido-bridged cation. Thus,

(1) Kirchen, R. P.; Sorensen, T. S. *J. Chem. Soc., Chem. Commun.* **1978**, 769.

(2) (a) Kirchen, R. P.; Sorensen, T. S.; Wagstaff, K. *J. Am. Chem. Soc.* **1978**, *100*, 6761. (b) Kirchen, R. P.; Ranganayakulu, K.; Rauk, A.; Singh, B. P.; Sorensen, T. S. *J. Am. Chem. Soc.* **1981**, *103*, 588–96. (c) Kirchen, R. P.; Okazawa, N.; Ranganayakulu, K.; Rauk, A.; Sorensen, T. S. *J. Am. Chem. Soc.* **1981**, *103*, 597–604. (d) Kirchen, R. P.; Ranganayakulu, K.; Singh, B. P.; Sorensen, T. S. *Can. J. Chem.* **1981**, *59*, 2173. (e) Kirchen, R. P.; Sorensen, T. S.; Wagstaff, K.; Walker, A. M. *Tetrahedron* **1986**, *42*, 1063–1070.

(3) (a) Prelog, V.; Traynham, J. G. *Molecular Rearrangements*; de Mayo, P., Ed.; Interscience: New York, 1963; Vol. 1, p 593. (b) Cope, A. C.; Martin, M. M.; McKervey, M. A. *Q. Rev., Chem. Soc.* **1966**, *20*, 119. More recently, additional solvolysis and acid-catalysis studies have been published. (c) Schneider, H.-J.; Heiske, D. *J. Am. Chem. Soc.* **1981**, *103*, 3501. (d) Nordlander, J. E.; Owuor, P. O.; Cabral, D. J.; Haky, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 201. (e) Nordlander, J. E.; Kotian, K. D.; Raff, D. E., II.; Njoroge, F. G.; Winemiller, J. J. *J. Am. Chem. Soc.* **1984**, *106*, 1427–32.

(4) For a review of the extensive literature in this area, see: Hiraoka, P.; Kebarle, P. *Adv. Mass Spectrom.* **1978**, *7B*, 1408.

(5) Yeh, L. I.; Price, J. M.; Lee, Y. T. *J. Am. Chem. Soc.* **1989**, *111*, 5597–5604.

(6) (a) Eakin, M. A.; Martin, J.; Parker, W.; Egan, C.; Graham, S. H. *J. Chem. Soc., Chem. Commun.* **1968**, 337. (b) Moodie, W. T.; Parker, W.; Watt, I. *J. Chem. Soc., Perkin Trans. 2* **1979**, 664–72. (c) Stéhelin, L.; Kanellias, L.; Ourisson, G. *J. Org. Chem.* **1973**, *38*, 847. (d) Saito, S.; Yabuki, T.; Moriwake, T.; Okamoto, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 529.

(7) (a) McMurry, J. E.; Hodge, C. N. *J. Am. Chem. Soc.* **1984**, *106*, 6450. (b) McMurry, J. E.; Lectka, T.; Hodge, C. N. *J. Am. Chem. Soc.* **1989**, *111*, 8867–72.

(8) An open-chain aliphatic dication has been found to have μ-hydrido bridging: Buffam, D., University of Calgary. Unpublished work.

(9) (a) Hirao, K.; Yamabe, S. *Chem. Phys.* **1984**, *89*, 237. (b) Raghavachari, K.; Whiteside, R. A.; Pople, J. A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5649.

(10) Richardson, J. F.; Sorensen, T. S. *Can. J. Chem.* **1985**, *63*, 116–69.

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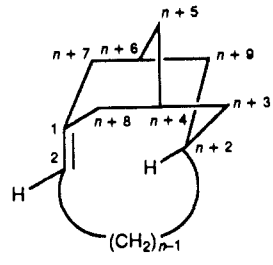
one should be starting in **4**, if n is large, with distances that are also too long for bridging. However, by decreasing n, one should be able to progressively shorten this distance.

It was anticipated that one would be able to prepare a number of these cations and that ^1H and ^{13}C NMR spectral parameters would offer a means of characterizing the details of the carbocation bonding.

The projected precursors of cations **4** were the alkenes **5**. It is obvious that as n in **5** becomes smaller, the inside-pyramidalized hydrogen (IPH) in these structures will eventually introduce large van der Waals repulsion energies. However, the expectation was that the cations **4** would be able to better use this hydrogen (i.e., in a bonding interaction) so that the alkenes should become increasingly more basic as n decreases.

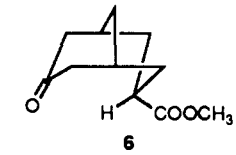


5

There is an added synthetic advantage in using a tricyclic alkene precursor such as **5**. In this case, one can *fix* the stereochemistry at C(n+2) in an inwardly pyramidalized manner while constructing the final ring from C1 to C(n+2). In a bicyclic case such as the alkene precursor to cation **3**, one has no control over the bridgehead stereochemistry when constructing the second ring. Fortunately, in the latter case the IPH alkene appears to be the most stable stereoisomer.[7]

Results and Discussion

Alkenes **5** could be efficiently prepared from 2-adamantanone. The latter has previously been converted to the keto acid ester **6** by a sequence of Baeyer–Villiger oxidation, epimerization of the carboxyl group, oxidation to the ketone, and esterification.[11] Ketone **6** was protected as the acetal, the ester functionality reduced to the alcohol, and the latter converted to tosylate **7**, which could then be elaborated to the individual precursors of **5**. For



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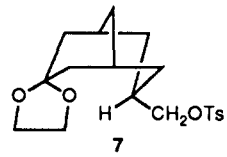

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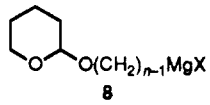

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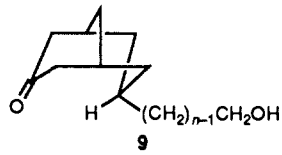

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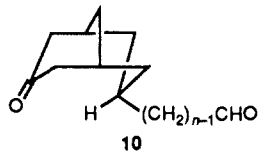

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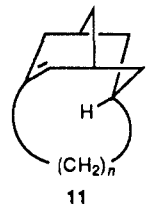

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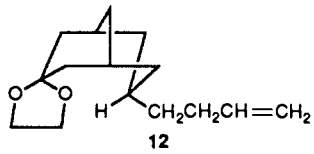


12

the cases where n = 5–8, tosylate **7** was coupled[12] with the protected Grignard reagent **8** to give, after hydrolysis of both protecting groups, the keto alcohols **9**. Swern oxidation[13] of **9** to the aldehydes **10** followed by McMurry cyclization[14] gave the alkenes **5**, either singly or as mixtures of alkenes where the double bond had moved into the bicyclic ring, i.e., **11**. Alkenes **11** are expected to be equally good precursors for the carbocations. For the case where n = 4, the corresponding Grignard reagent **8** (n = 4) proved to be thermally too labile to couple with **7**. Therefore, **7** was coupled with allyl Grignard to give **12** and then hydroborated to the alcohol **9** (n = 4). Unfortunately, the aldehyde **10** (n = 4) did not produce alkene **5** (n = 4) on attempted McMurry cyclization.

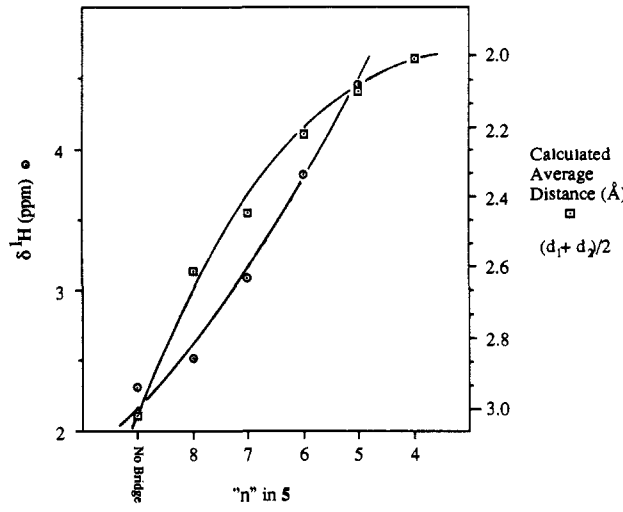
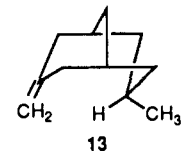


Figure 1. Empirical correlation between the ^1H chemical shifts of the IPH in alkenes **5** (⊙, left axis) and the calculated distance between this IPH and the alkene functionality in **5** (⊡, right axis), as a function of n in **5**. The distances d_1 and d_2 are measured from the IPH to C1 and C2 of the alkene.

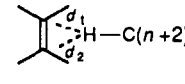
Unrelated to their utility as carbocation precursors, alkenes **5**, as a series, were found to have unusual ^1H NMR properties. The IPH shows a progressive downfield displacement as one goes from an open model system **13**, to the n = 8 bridge, and then progressively down to the n = 5 bridge. These data are plotted in



13

Figure 1. The NMR spectral parameters of other structurally related atoms in **5**, such as the alkene proton, the alkene carbons, or the C(n+2) carbon, show no discernible trends. Furthermore, alkenes like **11**, in which the double bond has moved into the [3.3.1]nonane ring, show no unusually low-field resonances for this same hydrogen.[15]

None of the alkenes **5** were obtained crystalline, so X-ray data are not available. However, MNDO semiempirical MO calculations,[16] with geometry optimization, have been carried out. For the n = 5 alkene, for example, these MO calculations show that the IPH sits almost equidistant between the alkene carbons and fully in the "face" of the alkene π-system. There is, in fact, a direct correlation between the calculated distance parameters



(11) Renzoni, G. E.; Borden, W. T. *J. Org. Chem.* **1983**, *48*, 5231–36.

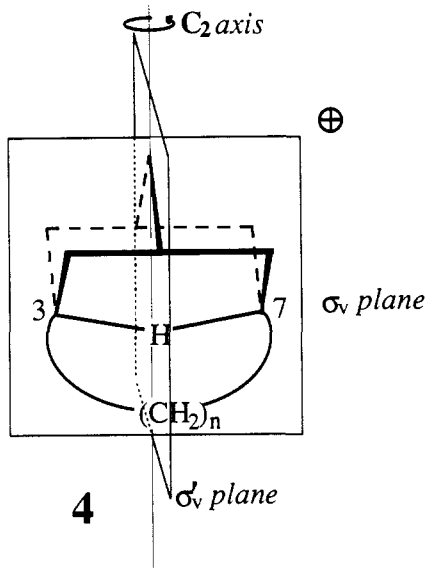
(12) Fouquet, G.; Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 82–83.

(13) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

(14) McMurry, J. E.; Kees, K. L. *J. Org. Chem.* **1977**, *42*, 2655.

(15) The IPH in alkenes **11** was not located because it occurs in a severely overlapped high-field region; however, one would have seen this hydrogen if it had been positioned >2.5 ppm.

(16) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4499.

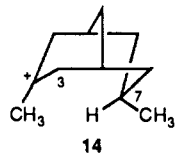


POSSIBLE SYMMETRY IN CATIONS 4	POINT GROUP
1. σ_v and σ_v' planes (includes C2 axis)	C_{2v}
2. σ_v plane only	C_s
3. σ_v' plane only	$C_{s'}$
4. C2 axis only	C_2
5. No symmetry elements	C_1

Figure 2. Possible point groups for cations **4**.

and the ^{1}H chemical shifts, as shown in Figure 1. The lower field shift, as n decreases, is consistent with an increasing polarization of the C–H bond by the alkene π-electron density; i.e., the hydrogen becomes more H^+-like.

Preparation and Characterization of Cations 4. The "open" 3,*exo*-7-dimethyl-3-bicyclo[3.3.1]nonyl cation **14** was first prepared, since this represents the behavior of an unconstrained system. At all accessible temperatures, one sees only five ^{13}C peaks and six resonances in the ^{1}H NMR spectrum, both results indicative of a species with effective C_{2v} symmetry (σ_v and σ_v' symmetry planes in Figure 2). The NMR data are listed in Tables I and II.



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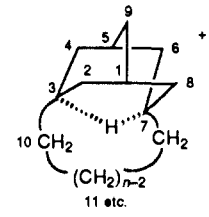
There are, however, two clear-cut pieces of evidence that rule out a static C_{2v}-symmetric μ-hydrido-bridged structure for **14**:

1. The H7 hydrogen is found at δ 0.30, far lower field than what one would expect for a μ-bridged structure.[2]

2. On cooling to −120 °C, one sees a progressive broadening of the C3–C7 peak in the ^{13}C NMR spectrum at 100 MHz. This indicates that one is slowing a degenerate hydride exchange from C7 to C3 (and vise versa), i.e., that **14** is not a static symmetrical structure. One would expect this particular peak to broaden selectively since the "frozen-out" positions for C3 and C7 are expected to be separated by ca. 30000 Hz, a far greater separation than that expected for any other exchanging pair of carbon peaks. Standard NMR line-broadening analysis leads to a calculated barrier for the hydride shift of $\Delta G^{\ddagger} = 3.5 \pm 0.5$ kcal/mol, an extremely small barrier for this double-well potential.

The H7 hydrogen is, nevertheless, at a somewhat high field, being shifted on protonation of the double bond in alkene **13** from δ 2.38 (the alkene) to δ 0.30 (the cation). This point will be discussed later.

Table I. ^{1}H NMR Data[a] (δ) for Cations **4** and **14**



4

	position[b]					
		H2,4,6,8		H7		
cation	H1,5	axial	equatorial	(μ-H)	H9	ring or other
4 (n = 5)	3.42[c]	2.43[d,e]	2.26[d,e]	−5.64[f]	1.99[h]	2.65[c] H10,14
						2.02[h] H11,13
						1.85[g] H12
4 (n = 6)	3.27[c]	2.44[e]	2.29[e]	−4.28[f]	1.96[c]	2.64[i] H10,15
						1.86[c] H11,14
						1.58[c] H12,13
4 (n = 7)	3.25[c]	2.47[e,j]	2.59[e,j]	−1.46[c]	2.09[c]	2.82[c] H10,16
						1.92[k] H11,15
						1.54[g] H12,14
						1.40[g] H13
4 (n = 8)	2.88[c,h]	2.64[e,h]	2.90[e,h]	0.07[c]	2.02[c]	2.61[c,h] H10,17
						1.90[k] H11,16
						1.52[k] H12,15
						1.40[c] H13,14
14	2.81[c,h]	2.56[e]	2.68[e,h]	0.3[c]	1.92[c]	2.34[c] (CH_3,s)

[a] Data at 25 °C for cation **4** (n = 5), −10 °C for **4** (n = 6), and −25 °C for **4** (n = 7 and 8). Cation **14** is insensitive to temperature changes in the ^{1}H spectrum over all accessible temperatures. The line broadening exhibited by **4** (n = 4–8) is described qualitatively in the text. [b] Relative to internal CH_2Cl_2 at δ 5.30. [c] Broadened singlet. [d] Assigned on the basis that it will be the axial H that exchanges with CD_3COOD. The assigned axial proton peaks are also broader than the equatorial ones, as expected for larger unresolved couplings. [e] AB pair, J = 15 Hz. [f] Characteristically broad. The COSY spectrum shows coupling to the axial hydrogens H2,4,6,8 and weakly to the H10,14 hydrogens. [g] Quintet, $J \approx 7$ Hz. [h] Peaks are overlapping with others. [i] Poorly resolved doublet. [j] Assigned on the basis that the high-field peaks are now broader. Note that the axial–equatorial assignments have switched back to "normal". [k] Poorly resolved quintet.

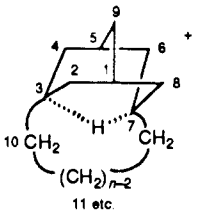
Before discussing the structure of cations **4**, we show in Figure 2 the possible symmetry elements that one might find in these cations and assign working definitions of the two possible symmetry planes and rotation axis. The unfunctionalized chair–chair bicyclo[3.3.1]nonane ring has inherent C_{2v} symmetry. In cations **4**, the $-(CH_2)_n-$ bridge conformation and the actual geometry of the C3---H–C7 carbocation bonding can reduce this symmetry. Case 2 in Figure 2 is highly unlikely as a static species, since symmetry in the σ_v plane will almost certainly result in a σ_v' plane as well (C_{2v}). However, dynamic conformational processes in the $-(CH_2)_n-$ bridge could result in time-averaged σ_v symmetry by itself.

Cation 4 (n = 8). An eight-carbon methylene bridge appears from molecular modeling to put very little added strain on a bicyclo[3.3.1]nonane framework, and this supposition is in good agreement with the properties of cation **4** (n = 8). The cation was prepared in situ at −80 °C with 1:1 FSO_3H–SbF_5 in SO_2ClF solvent. The cation is thermally fairly stable, decomposing to ill-defined material only at ca. −20 °C.

The ^{1}H NMR spectrum (Table I) at −20 °C shows peaks characteristic of a molecule with C_{2v} symmetry (see Figure 2). However, at lower temperatures beginning at ca. −50 °C, some of these peaks show the beginning of a dynamic line-broadening process, with only the bridgehead hydrogens H1 and H5, the H7 hydrogen and the hydrogens on C9 remaining relatively sharp. The ^{13}C NMR spectrum measured at ca. −30 °C shows only one sharp peak (assigned to C9) and a further number of broad to very broad lines.

On cooling the solution to ca. −100 °C, one eventually obtains a ^{13}C spectrum showing 13 distinct resonances, including several

Table II. ^{13}C NMR Data[a] (δ) for Cations **4** and **14**



4

cation	position[b] C1,5	C2,4,6,8	C3,7	C9	ring or other
4 (n = 5)[c]	51.8	42.6	166.8	31.5	45.2 C10,14 29.9 C11,13 32.5 C12
4 (n = 6)[c]	47.9	43.5	170.1	30.6	42.2 C10,15 24.3 C11,14 24.2 C12,13
4 (n = 7)	46.6[d] 46.4[d]	55.63 52.06 51.13 } C2,4,10	296.5 (C3) 63.5 (C7	31.4[d]	39.17, 35.68 35.50, 28.39 21.78, 20.64 17.75 } C6,8,12,14,15,16 21.61[d] C13
4 (n = 8)[e]			324.8 (C3)	29.1[d]	
14[f]	54.9	50.4	177.7[g]	28.7	31.6 (CH_3's)

[a] Data at 25 °C for cations **4** (n = 5, 6), −112 °C for **4** (n = 7), and ca. −120 °C for cation **4** (n = 8). Data for cation **14** are at ca. −100 °C. The line broadening exhibited by **4** (n = 4–8) and by **14** is described in the text. Cations **4** (n = 5, 6) and **14** list data for the averaged structures, while that for cations **4** (n = 7, 8) represent frozen-out structures. [b] Relative to internal CD_2Cl_2 at δ 53.6. [c] ^{13}C and ^1H assignments correlated via an INVERSE HETCOR measurement. Multiplicities of ^{13}C determined from DEPT 135 spectra. [d] These peaks remain sharp on warming and are, therefore, assigned to carbons on the σ_v' plane of Figure 2. [e] The large CD_2Cl_2 peak obscures the δ 53–55 region. Unassignable broad peaks at δ 64.7, 61.5, 37.7, 33.7, 32.4 (×3?), 30.0, 27.7, 24.2 (×2 broad), 21.4, 20.9, on 19.4. [f] ^{13}C and ^1H assignments correlated via a HETCOR measurement. [g] Peak is somewht broad, due to the hydrogen-exchange process.

that appear to be of multiple-carbon area. The significant feature of this latter spectrum, however, is the appearance of a peak at δ 324.8, a uniquely low-field position characteristic of the C^+ resonance of a "normal" tertiary carbocation. The H7 hydrogen is found at δ 0.07, slightly higher field than in **14** but still in a far lower field position than one would expect for a μ-hydrido species (and together with the δ 324.8 peak in the ^{13}C NMR spectrum, indicating a simple tertiary carbocation structure for **4** (n = 8)).

The major difference between **14** and **4** (n = 8) involves the dynamics of the reversible hydride shift from C7 to C3. In **4** (n = 8), the low-temperature spectra indicate a molecule with, at best, C_s symmetry (see Figure 2), the same symmetry as in **14**. However, in **4** (n = 8), an unsymmetrical $-(CH_2)_8-$ bridge conformation must "hold" the hydride at C7 and the C^+ at C3. The reversible hydride shift from C7 to C3 can only occur as a consequence of a conformational change in the $-(CH_2)_8-$ moiety. Since the latter has a reasonably high barrier, one is able to "freeze out" the reversible hydride shift, unlike in **14**. One cannot really comment much, however, on the detailed conformational processes in the $-(CH_2)_8-$ ring. On cooling, the high-temperature-averaged C_{2v} "structure" for **4** (n = 8) first loses the σ_v' plane shown in Figure 2. Thus, the bridgehead hydrogens, H1 and H5, and the H7 hydrogen are expected to be unaffected, as found. There is indeed some evidence that a second line-broadening process involving the σ_v plane may be taking place at the lowest temperatures, but the data are not definitive in this regard.

Cation 4 (n = 7). This cation is thermally stable to about −10 °C in 1:1 FSO_3H–SbF_5/SO_2ClF solution. At −112 °C, the cation shows no symmetry and all 16 ^{13}C peaks are observable, and assignments were made on the basis of a DEPT experiment and the observed "averaging" behavior at higher temperatures (Table II). The C^+ carbon is now found at δ 296.5 and the "opposite" carbon at δ 63.5. In the ^1H spectrum (Table I), the H7 hydrogen is found at δ −1.46.

At higher temperatures, both the ^{13}C and ^1H NMR spectra show line broadening and eventual coalescence to an averaged "structure" that has C_{2v} symmetry (Figure 2). At 400 MHz, the ^1H NMR spectrum of this C_{2v} "structure" is fully resolved and could be completely assigned with the help of a COSY spectrum.

There are very probably two distinct symmetrization processes that are involved (independent symmetrization operations for the σ_v and σ_v' planes), but they are not well separated kinetically. However, the spectra show qualitatively that the σ_v' symmetrization is slower than the σ_v process. The H7 hydrogen and C9 carbon are unaffected by either process and remain sharp over the whole temperature range.

As with the n = 8 case, the conformational aspects of the seven-carbon methylene bridge dictate the rate of the hydride shift and essentially "freeze" an unsymmetrical conformation at low temperatures so that one can directly observe the NMR parameters without the problems associated with a very rapid hydride transfer, such as occurs in **14**.

Cation 4 (n = 6). This cation could be prepared in several acidic solutions, including a mixture of 1 drop of fluorosulfonic acid in 0.5 mL of trifluoroacetic acid (TFA). However, the cation is not observable in pure TFA. The cation is stable at room temperature for at least several days.

The ^1H and ^{13}C NMR parameters are reported in Tables I and II. The position of H7 at δ −4.26 (−10 °C) is indicative of μ-hydrido bridging. At room temperature, one also sees both ^{13}C and ^1H NMR spectra indicative of a symmetrical C_{2v} molecule. Both COSY and HETCOR 2D spectra were used to make a complete assignment of the NMR peaks.

After the cation solution is cooled, it is apparent that the NMR spectra are not as simple as the room-temperature results would indicate. The μ-H chemical shift position is temperature-dependent, moving from δ −4.26 at −10 °C to δ −4.56 at −105 °C. At this latter temperature, one also sees marked line broadening of the peak. The ^{13}C NMR spectrum also shows selective line broadening when cooled and other ^1H peaks besides the μ-H are also broadened. The pattern in the dynamic NMR line broadening is different however from that seen in the n = 8 and 7 cases and can be interpreted in terms of two cationic species, a major and a minor population. At moderate temperature, the nondegenerate interchange between the two structures is fast and, thus, only chemical shift changes occur as one begins to lower the temperature. However, at even lower temperatures, one begins to

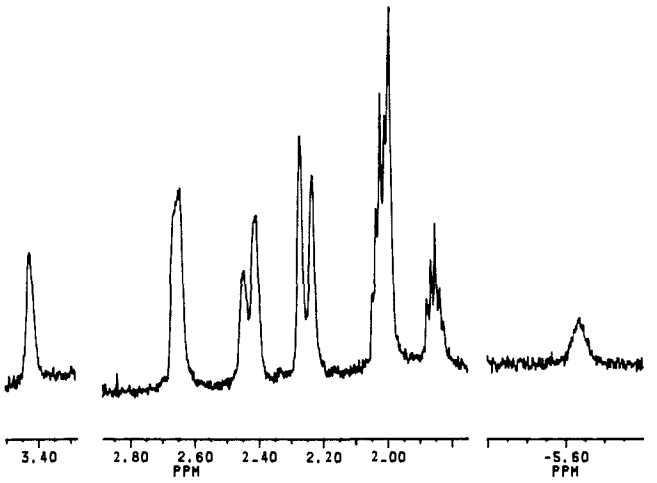


Figure 3. 400-MHz ^{1}H NMR spectrum of cation **4** (n = 5). The acid solvent and reference peaks, as well as several impurity peaks, fall outside the range shown (see Table I for peak identifications).

slow the interchange process itself, resulting in NMR line broadening. Since the μ-H ^{1}H position moves to higher field at lower temperatures, the major cationic species must have an even higher field value than δ −4.56 and, conversely, the minor species has a much lower field chemical shift for this hydrogen. This would be consistent with the major species being "symmetrically" bridged and the minor species something less so. This point will be discussed later.

Cation 4 (n = 5). This cation is completely stable at 25 °C in TFA. One can dilute the TFA with water to about a 50% solution before there is appreciable loss of cation signals.

The ^{1}H and ^{13}C NMR parameters for **4** (n = 5) are reported in Tables I and II. The position of H7 at δ −5.64 is completely consistent with μ-H bridging. The ^{13}C and ^{1}H NMR spectra at 25 °C indicate a C_{2v} symmetric averaged structure, and DEPT, COSY, and INVERSE HETCOR NMR experiments were used to make a complete NMR assignment. The ^{1}H NMR spectrum is shown in Figure 3.

Molecular model studies indicate that it is virtually impossible for **4** (n = 5) to form a static C_{2v} structure incorporating the $-(CH_2)_5-$ chain. Not surprisingly, therefore, on cooling the solution of **4** (n = 5), one sees again dynamic NMR line broadening. The two ^{13}C peaks that broaden are the bridgehead C1–C5 peak and the four-carbon C2, C4, C6, C8 peak. From model studies and MO calculations (see later), there are several reasonable conformations for the pentamethylene bridge, and the perfectly symmetrical versions of these are sketched in Figure 4. Conformations A and B have C_s' symmetry (Figure 2), while C has C_2 symmetry. One can rule out C on the basis of the observed ^{13}C line broadening since, in the structure, C2 and C6 are not equivalent with C4 and C8, but C1 = C5; i.e., only the one ^{13}C peak should broaden. In the C_s' symmetry case, both ^{13}C peaks would be expected to broaden since C1 and C5 are nonequivalent and C2–C8 are nonequivalent with C4–C6. The MO calculations, in fact, favor a structure closely related to conformer A. At very low temperatures (<−100 °C), there are indications that additional ^{13}C peaks are beginning to broaden, so that the actual structure probably does not have a strict mirror plane symmetry. This actually agrees well with the MO calculations, in which conformers A–C are somewhat distorted from these idealized cases. The ^{1}H NMR spectra also show low-temperature line broadening, and in this case the change from "average" C_{2v} symmetry to C_s' symmetry makes the individual methylene protons of the $-(CH_2)_5-$ chain nonequivalent, becoming pseudoaxial and pseudoequatorial. The μ-H hydrogen peak is unaffected over the whole temperature range, indicating that, unlike **4** (n = 6), a single molecular species is involved, i.e., that the NMR line-broadening processes are degenerate.

In TFA–D_2O mixtures, cation **4** (n = 5) undergoes very rapid H–D exchange (observed by ^{1}H NMR). The exchange involves

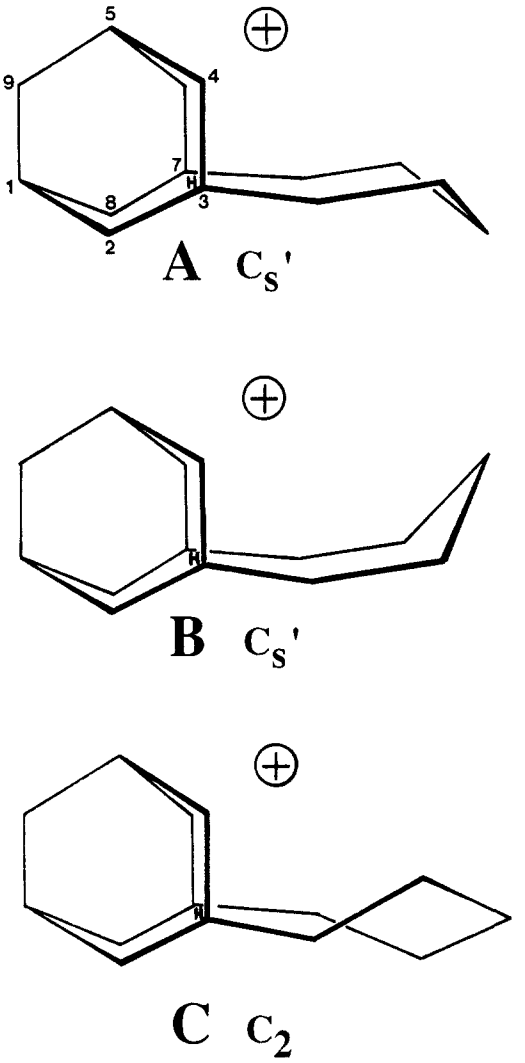


Figure 4. Three possible symmetric conformations of cation **4** (n = 5).

Table III. ^{1}H–^{13}C Coupling Constants for C3–C7 and H7

cation	δ(^{1}H) (H7)	δ(^{13}C) (C3–C7)	$J_{^{13}C-^1H}$ (±2 Hz) gated	INEPT
14	0.30	177.7	56	63
4 (n = 6)	−4.2[a]	170.1	40	48
4 (n = 5)	−5.64	166.8	37	46

[a] Temperature-dependent. The quoted value is at ca. 25 °C.

only the axial protons of the [3.3.1]nonane ring and the α-methylene protons of the C5 bridge. This exchange occurs with essentially equal rates in the two different positions.

^{13}C–^{1}H Coupling Constants Involving H7 and C3–C7. These data were obtained for the averaged ^{13}C peak for the "open" cation **14**, which we have shown to be an equilibrating system (fast 7,3-hydride shift but not μ-hydrido-bridged), and for cations **4** (n = 5, 6), which have ^{1}H chemical shifts for H7 indicative of μ-H bridging. The data are reported in Table III. For reasons that are not entirely clear, somewhat different values for **J** were obtained for INEPT and for gated (NOE-enhanced) coupled ^{13}C spectra, so both sets are separately reported.

In terms of ^{13}C NMR data alone, ^{1}H–^{13}C coupling constants provide a superior measure of μ-H bridging, compared to the ^{13}C chemical shift data. For example, the δ(^{13}C) value for **14** is about 4% larger than for **4** (n = 5 and 6), while the $J_{^{13}C-^1H}$ value is about 45% larger. There is, however, more experimental uncertainty in the latter values.

Molecular Orbital Calculations. In order to aid in evaluating both the structural aspects of the cations **4** and for considerations of hyperstability in these systems, we have performed semiempirical MINDO/3 computations[17] on **4** (n = 3–8).

Table IV. Computed Heat of Formation Data[a] for Cation 4, Alkenes 5, and Other Compounds

n	exocyclic alkene 5	endocyclic alkene 11	cations 4 (best conformn)	out-H cations 15	alcohols 16	tetracyclic hydrocarbon 17	pK_a or (calc.)[b]
3	84.07	80.30	204.98	179.65	2.34		
4	42.59	41.27	185.99	177.56	-22.55	-10.55	(+10)
5	15.29	15.31	175.50		-37.55	-7.07	-1
6	-1.25	4.16	167.25		-45.46		(-5.3)
7	-11.13		158.26		-55.26		(-6.0)
8	-9.62		156.77				

[a] In kilocalories per mole. MNDO used for the neutral compounds, MINDO/3 for the cations. The ΔH_f data for the two methods should not be directly compared; however, one can compare differences within each method to differences in the other. Within a given column, the ΔH_f values should "normally" decrease by about 5 kcal/mol per each increase in n (the ΔH_f change for the extra CH_2 unit involved). [b] Assuming $\Delta\Delta H = \Delta\Delta G$ for both cations and alkenes.

Structural Aspects: Comparison of Computation to Experiment. MINDO/3 optimation of the chair-chair cation **14** gives a classical cation structure. The C7-H7 bond length is 1.13 Å vs a 3.11 Å distance from H7 to C3. The only noteworthy feature is a slightly negative charge (-0.07) computed for the H7 hydrogen, perhaps rationalizing the high-field position (δ 0.30) of this hydrogen in the ^1H NMR spectrum. It is quite probable that this negative charge results from a long-range polarization of the C7-H7 bond by the C^+ center at C3.

For the cations **4** with n = 3-7, a search of various possible ring conformers was made since the structural optimization routines generally locate minima with geometries similar to the input geometry (and not necessarily the global minimum). For the n = 8 case, a single computation was carried out with use of a "best estimate" conformation based on molecular model studies.

In the **4** (n = 8) case, the computed result is clearly not a μ-H-bridged cation. The C7-H7 distance is 1.138 Å, and the C3-C7 distance is 2.582 Å. The H7 hydrogen is slightly more negatively charged than it is in **14**, -0.109, perhaps in agreement with the slightly higher field value for the ^1H shift (δ 0.07 vs δ 0.30 in **14**).

In the **4** (n = 7) case, the computed most stable cation conformation also does not have a "symmetric" μ-H-bridged structure. The computed distances are C3-H7 = 2.512 Å and C7-H7 = 1.137 Å. The charges on C3 and C7 are +0.369 and +0.084, respectively, while H7 is -0.111. The experimental data for **4** (n = 7) seem to indicate the onset of some weak partial μ-H bridge, since H7 is at δ -1.46, C3 has "moved" upfield to δ 296.5, and C7 is found at the somewhat low-field position of δ 63.5. The experimental results indicate a cation with no symmetry elements in the static structure, and this also agrees with the results of the MO calculations.

In the **4** (n = 6) case, the computed lowest energy structure is also not a "symmetrical" μ-H-bridged structure. The C3-H7 distance is 2.249 Å, and the C7-H7 distance is 1.145 Å. The computed charges are +0.373 on C3, +0.094 on C7, and -0.13 on H7. By imposing local symmetry on the C7-H7 and C3-H7 bond distances, we have calculated a "symmetric" μ-H-bridged structure, and this is found to be 5.1 kcal/mol higher in energy (bond distances are C3-H7 = C7-H7 = 1.376 Å). The experimental results are somewhat at odds with these computations, in that a μ-H-bridged structure appears to be the dominant population for **4** (n = 6), with a minor population of an unbridged (or, more likely, partially bridged) structure, i.e., opposite to the computations. However, given the uncertainty in these rather crude computations, the agreement between theory and experiment is reasonable.

In the **4** (n = 5) case, the computed lowest energy structure is a μ-H-bridged cation, with a structure closely related to conformer A in Figure 3. The C3-H7 = C7-H7 distance is 1.354 Å. An unsymmetrical μ-H-bridged structure is, however, only marginally higher in energy (0.45 kcal/mol), with C3-H7 and C7-H7 distances of 1.788 and 1.181 Å, respectively. The experimental data clearly suggest only a single μ-H-bridged structure. In both the n = 5 and n = 6 cases, therefore, the computations seem to be slightly underestimating the strength of the μ-H bridging, with use of the experimental data for comparison.

Cation Stabilities: Hyperstability. Cation "stability" can obviously mean one of two things: (1) a heat of formation comparison and (2) stability in the pK_a sense. It is in the latter form that we consider these cations, although one cannot totally ignore ΔH_f considerations.

As one goes from **4** (n = 8) to **4** (n = 5), the cations are experimentally becoming weaker acids. A difficulty associated with a quantitative treatment of these systems is the choice of the appropriate equilibrium:

$$\text{cation} \rightleftarrows \text{alkene} + [H^+] \quad (1)$$

$$\text{cation} + H_2O \rightleftarrows \text{alcohol} + [H^+] \quad (2)$$

For all cases that we have studied, there is no evidence that the second equilibrium is operative.[18]

For the cation **4** (n = 5), one can estimate a pK_a corresponding approximately to the acidity function for a 50% v/v aqueous TFA solution ($\chi_{TFA} \approx 0.2$), for which H_0 is given as -0.68[19] (the approximate pH value is calculated to be -1). For the following computational purposes, we will, thus, assume that cation **4** (n = 5) has a pK_a of -1, to one significant figure.

Although it may be attractive to attribute this weak acidity (cation stability) to the μ-hydrido-bridged structure, the evidence suggests that this factor contributes only in a minor way to the energetics. By far, the dominant factor relates to the energy difference [steric strain of the alkene precursors **5** or **11**] - [steric strain of the cations **4**]. In the alkenes **5**, the IPH causes significant van der Waals repulsions, which naturally become worse as n becomes smaller. In the cation, this hydrogen can be used in the μ-H bonding, and while steric factors do accumulate as n becomes smaller, this factor is relatively *less important*.

One can show this principle using the MO calculations for **4**, discussed in the previous section, together with computations for the alkenes **5**. The relevant ΔH_f data are listed in Table IV. If the pK_a of cation **4** (n = 5) is taken as -1, then one estimates a pK_a of -5.3 for the n = 6 compound. Experimentally, we have bracketed this pK_a between pure TFA (H_0 = -3.03)[19] and 1.4 M FSO_3H-TFA ($H_0 \approx -8$),[20] in good agreement. Going the other direction, one estimates a pK_a for **4** (n = 4) of +10, i.e., protonated in neutral water, and this cation would indeed be hyperstable in the pK_a sense. Although we were unsuccessful in preparing the alkene **5** (n = 4), other approaches to cation **4** (n = 4) are currently being explored. Aside from the basic veracity of the computations themselves, there are three other unknowns that might affect our conclusions regarding **4** (n = 4):

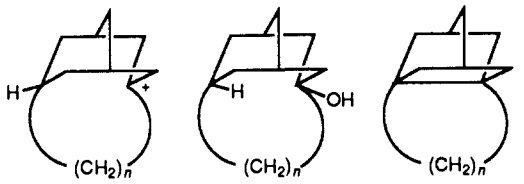
1. The outside-pyramidalized cation **15** (n = 4) is computed to be about 8.5 kcal/mol more stable than **4** (n = 4), so a rapid internal rearrangement is thermodynamically possible. However, an unstabilized and very strained secondary cation is the most obvious intermediate in such a rearrangement, so we have reason

(17) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

(18) Base-quenching studies on several of the cations **4** produced only alkene products. Also, alkene **5** (n = 5) in CD_3COOD instantly exchanges some of the protons (see Experimental Section), so there would be ample opportunity for the acetate to form if this was indeed stable.

(19) Randles, J. E. B.; Tedder, J. M. *J. Chem. Soc.* **1955**, 1218.

(20) No data exist for H_0 values of FSO_3H-TFA. We have used a measured value for H_2SO_4-TFA: Hyman, H. H.; Garber, R. A. *J. Am. Chem. Soc.* **1959**, *81*, 1847.



15 16 17

to believe that kinetically this transformation would be difficult.

2. The alcohol **16** (n = 4) is calculated to be relatively less strained than the alkenes **5** or **11** (n = 4), so it is possible that one could have a "switch over" in the equilibrium. Even if this were so, one would still expect **4** (n = 4) to have a pK_a in the hyperstable range.

3. One might "lose" the bridging hydride as a proton, forming a σ-bond between C3 and C7 and giving the tetracyclic hydrocarbon **17** (n = 4).[21] However, there is no evidence for this same reaction in **4** (n = 5), even though the computations in Table IV show that **17** (n = 5) is much more stable thermodynamically than **5** (n = 5) (22.4 kcal/mol). The situation is even more unbalanced with n = 4, but there is clearly a large kinetic barrier involved in the n = 5 case and no obvious reason why this would decrease for the n = 4 case. Overall, we consider that **4** (n = 4) is a reasonably viable synthetic target.

The same cannot be said for **4** (n = 3). This molecule is computed (Table IV) to be very strained relative to the isomeric structure **15** (n = 3).

Concluding Discussion

μ-Hydrido bridging in carbocations appears to require that the formal C^+ center and the potentially bridging remote H–C group have a fixed close proximity in space. The actual strength of this bond is apparently not sufficiently large that it will significantly distort the framework of a supporting hydrocarbon. Thus, the normal geometry of a chair–chair bicyclo[3.3.1]nonane structure has a C3–C7 distance that is well outside that needed for μ-H bridging, and the strength of a latent μ-hydrido-bonding interaction is simply not large enough to significantly alter this geometry.

However, one can "cinch" this bicyclic hydrocarbon with a variable-length methylene bridge such that the C3 and C7 centers are pulled closer. In the case of a pentamethylene-connecting link **4** (n = 5), one then develops a fully μ-hydrido-bridged structure, while for larger sizes **4** (n = 6–8) one sees a gradation of structures, leading in the case of the eight-carbon link back to a normal tertiary carbocation.

The μ-H-bridged cation **4** (n = 5) is also an abnormally weak acid, considering that the structure is formally an alkyl carbocation. We believe that this stability results mainly because the alkene equilibrium "partner" **5** (n = 5) is quite strained. For the same reason, we predict from semiempirical MO calculations that the next lower homologue, **4** (n = 4), will be an extremely weak acid (hyperstable in a pK_a sense).

Experimental Section

All reactions were performed in oven-dried glassware cooled under nitrogen or argon. Tetrahydrofuran (THF) was freshly distilled from the purple color of sodium benzophenone ketyl. Dimethoxyethane (DME) was freshly distilled from the purple color of potassium benzophenone ketyl under an inert argon atmosphere immediately before use. Pentane was washed with concentrated H_2SO_4 and water, dried over CaH_2, and distilled under N_2. It was degassed immediately before use by bubbling N_2 through it for at least 10 min. Methylene chloride was dried over anhydrous neutral alumina under N_2 before use. Dimethyl sulfoxide was dried over anhydrous neutral alumina. Dilithium tetrachlorocuprate (0.1 M in THF) and $TiCl_3$ were obtained from Aldrich Chemical Co., Inc. The zinc–copper couple was prepared according to the procedure of McMurry.[14] Titanium trichloride (ca. 2–4 g) from a freshly opened bottle was transferred to tared sample vials in a glovebox; the vials were sealed under vacuum and used as required. Flash chromatography was performed according to the procedure of Still.[22] Gas chromatography was performed on a Hewlett-Packard Model 5890A with a 10-m OV1 530-μm column. For preparative work, a 244 cm × 4 mm i.d., 3% OV-1 on Chromosorb W (80/100) column was used. NMR spectroscopy was carried out on a Bruker ACE-200 or AM-400 (δ values, J in hertz). In descriptions of the ^1H NMR spectra, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and b = broad; in most cases, small couplings are not reported. For the alkenes **5** and **11**, COSY and HETCOR (or INVERSE HETCOR) spectra were obtained as an aid in the assignments but the complete results are not described. For ^{13}C NMR, q = quaternary; multiplicities were determined from DEPT 90 and 135 spectra (δ values, J in hertz). Mass spectra were determined with a Kratos MS-80 (peak intensities in parentheses) and infrared spectra with a Nicolet 5-DX FT instrument. Peaks were reported as very strong (vs), strong (s), medium (m), or weak (w) (cm^{-1}).

Stable cations were prepared by the addition of a methylene-d_2 chloride solution (50 μL) of the appropriate alkene to a precooled (−78 °C) solution of 1:1 FSO_3H–SbF_5 in SO_2ClF. Several other acid solvent mixtures were used, and these are described in the text. Cation spectra were determined at 400 MHz (^1H) and 100 MHz (^{13}C), with use of DEPT spectra for multiplicities and COSY and HETCOR (or INVERSE HETCOR) for further characterization. Spectra were recorded locked (CD_2Cl_2) or unlocked. For determinations of the H_0 value for alkene **5** (n = 5), the cation was prepared in CF_3COOH and successive small additions of D_2O were made to this solution, spectra being recorded after each dilution.

7-*exo*-Carbomethoxybicyclo[3.3.1]nonan-3-one Diethylene Ketal. Keto ester **6**[11] (24.0 g, 0.13 mol), 10 g of ethylene glycol, 0.5 g of p-toluenesulfonic acid, and 300 mL of benzene were refluxed (Dean Stark trap). The reflux was continued for 10 days total, with two further 5.0-g additions of ethylene glycol added after 2 and 5 days (ethylene glycol is slowly lost in the Dean Stark trap). The course of the ketalization was monitored by GLC. After reaction, the solution was washed with dilute sodium carbonate and dried over $MgSO_4$. Removal of the solvent left 31.6 g of oil, which was directly reduced in the next step. ^{13}C NMR: 177.2 (C=O); 107.9 (q) C3; 64.1, 63.1 (both CH_2) ketal carbons; 50.9 (CH_3); 40.2 (CH_2) C2,4; 33.6 (CH) C7; 33.2 (CH_2) C6,8; 31.7 (CH_2) C9; 27.4 (CH) C1,5.

7-*exo*-Hydroxymethylbicyclo[3.3.1]nonan-3-one Diethylene Ketal. The above ketal ester (30.0 g, 0.125 mol) was dissolved in 100 mL of dry ether and the mixture added over a period of 0.5 h to a stirred suspension of $LiAlH_4$ (7.60 g, 0.2 mol) in 300 mL of ether under nitrogen. The resulting mixture was then refluxed for 24 h. The excess $LiAlH_4$ was carefully destroyed with ethanol–ether, and then 40 mL of water was added. The precipitated salts were filtered off and washed separately with ether. The combined ether layers were washed with water and dried over $MgSO_4$. Removal of the solvent left 20.1 g of an oil, mainly a single component by GLC. ^{13}C NMR: 108.6 (q) C3; 68.3 (CH_2) CH_2OH; 63.6, 62.9 (both CH_2) ketal carbons; 39.4 (CH_2) C2,4; 35.0 (CH_2) C6,8; 31.0 (CH_2) C9; 29.7 (CH) C7; 27.0 (CH) C1,5. The ^{13}C NMR spectrum also showed that a small amount of the deprotected ketone was also present. The crude product, on storage in a closed flask at room temperature, slowly formed increasing amounts of the deprotected ketone. The separation of these materials was more easily accomplished at the tosylate stage because some further hydrolysis probably occurs during the tosylate formation.

7-*exo*[(*p*-Toluenesulfonyl)oxymethylene]bicyclo[3.3.1]nonan-3-one Diethylene Ketal. The preceding alcohol, as a mixture with variable amounts of the unprotected keto alcohol (35% in this case), 1.0612 g total weight (3.25 mmol of ketal), was dissolved in 5 mL of pyridine, and 1.214 g (6.4 mmol) of p-toluenesulfonic acid was added. The resultant solution was allowed to stand overnight under N_2 (pyridinium hydrochloride precipitates), and then the solution was diluted with methylene chloride and water. The aqueous phase was washed with methylene chloride (2 × 20 mL), and the combined organic phase was washed with water, ice-cold 1 M HCl (2 × 20 mL), water, aqueous $NaHCO_3$, and water and then dried (K_2CO_3). After solvent removal, the resulting oil was flash chromatographed (3:1 hexane–ethyl acetate), the protected tosylate eluting ahead of the unprotected, yield 648.6 mg (55%), obtained as an oil after solvent removal. Mixed fractions and the keto tosylate account for most of the remaining material. ^1H NMR (400 MHz): 7.81 and 7.37 (both d, J = 8.3, 2 H each, aromatic H); ca. 3.94 and 3.87 (A_2B_2 m, 4 H acetal H); 2.99 (septet, J = 4.5, 1 H, H7); 2.48 (s, 3 H, CH_3); 2.13 (bs, 2 H, H1 and 5); 1.97 (d, J = 15, 7, 2 H, equatorial H2,4); 1.77 (d, J = 15, 2 H, axial H2,4); 1.68 (d, J = 12, 1 H, H9); 1.65 (d, J = 13, 2 H, equatorial H6,8); 1.36 (d, J = 12, 1 H, H9); 1.20 (t, d, J = 13, 4.5, 2 H, axial H6,8). ^{13}C NMR: 144.41 (q); 133.08 (q); 129.64 (CH); 127.75 (CH); 108.18 (q) C3; 74.41 (CH_2) C10; 64.21, 3.28 (both CH_2)

(21) If one cannot kinetically remove $[H^+]$ from **4** to give **17**, with a conjugate base, then the superacid protonation of **17** to give **4** should also be "forbidden", a conclusion similar to that made by us in the case of monocyclic μ-H-bridged cations.[2c]

(22) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

acetal C; 40.06 (CH_2) C2,4; 33.95 (CH_2) C6,8; 31.79 (CH_2) C9; 27.36 (CH) C1,5; 27.31 (CH_3); 21.48 CH (C7). MS: *m/z* 366 (M^+), 288, 234, 211, 172, 151, 91 (100), 65. IR: 1400 cm^{-1} ($\nu_{as}(SO_2)$).

***exo*-7-(5′-Hydroxy-1′-pentyl)bicyclo[3.3.1]nonan-3-one (9 (*n* = 5))**. The Grignard reagent from 4-bromo-1-[(tetrahydropyran-2′-yl)oxy]butane (**8** (*n* = 5))[23] was prepared in THF solution (1.2 M). This solution (27.5 mL, 3.3 mmol) was added under N_2 to a round-bottom flask and cooled to −5 °C. A THF solution of 0.1 M dilithium tetrachlorocuprate[12] (25 mL, 2.48 mmol) was added dropwise over a period of 5 min (−5 °C) and the mixture allowed to stir for an additional 2 min. The tosylate **7** (606.0 mg, 1.65 mmol) in 10 mL of THF was then added dropwise over 10 min. The solution was stirred for 10 min at −5 °C and for 3 h (GLC monitored) at 0 °C. During this time, the solution became very dark. After being warmed to 20 °C (occasionally overnight), the mixture was quenched into 30 mL of 3 M HCl and diluted with ether (50 mL). After separation of the organic phase, the aqueous phase was extracted with ether (3 × 25 mL), the organic phases were combined and dried (K_2CO_3), and the solvent was removed. The resultant liquid (ca. 2 mL) was dissolved in 25 mL of methanol containing 25 mg of *p*-toluenesulfonic acid and refluxed for 30 min. Most of the methanol was removed en vacuo, and the residue was taken up in 50 mL of ether and 50 mL of brine. The aqueous phase was extracted with ether (4 × 20 mL), and the combined organic phase was dried (K_2CO_3) and removed. Flash chromatography of the resulting oil (2.5:1 hexane–ethyl acetate) gave 248.1 mg (67%) of the title product, as an oil. In repeated runs, yields as high as 79% were obtained. In most cases, the crude reaction mixture contained some uncoupled keto tosylate, along with large amounts of 1,8-octanediol (or as the THP ether) from self-coupling of the Grignard reagent. Exact mass calcd for $C_{14}H_{24}O_2$: calcd, 224.1776; found, 224.1778. ^1H NMR (200 MHz): 3.60 (t, *J* = 7, 2 H, CH_2OH); 2.3–2.5 (m, 6 H); 1.1–2.0 (complex, 16 H). ^{13}C NMR: 213.26 (C=O); 62.80 (CH_2) C5′; 47.53 (CH_2) C2,4; 39.06 (CH_2) C6,8; 37.77 (CH_2); 32.75 (CH_2); 32.66 (CH_2); 30.65 (CH) C1,5; 28.79 (CH) C7; 26.31 (CH_2); 25.86 (CH_2). IR: 3523 (m), 2923 (vs), 2853 (s), 1698 (s), 1461 (m), 1440 (m), 1407 (m), 1227 (m), 1051 (m). MS: *m/z* 224 (M^+, 2), 194 (23), 137 (12), 109 (18), 95 (100), 81 (32), 67 (44), 55 (42), 41 (66).

***exo*-7-(1′-Hydroxy-6′-hexyl)bicyclo[3.3.1]nonan-3-one (9 (*n* = 6))**. From the Grignard reagent of 5-chloro-1-[(tetrahydropyran-2′-yl)oxy]-pentane (**8** (*n* = 5)) (ca. 20-fold excess) and tosylate **7** (129.3 mg, 0.35 mmol), with use of the procedure described for the preparation of **9** (*n* = 5), was obtained 52.3 mg (62%) of the title alcohol, as an oil. Exact mass for $C_{15}H_{26}O_2$: calcd, 238.1933; found, 238.1931. ^1H NMR (200 MHz): 3.64 (t, *J* = 7, 2 H, CH_2OH); 2.25–2.55 (6 H); 1.00–2.00 (complex, 18 H). ^{13}C NMR: 213.19 (C=O); 65.76 (CH_2) C1′; 47.55 (CH_2) C2,4; 39.10 (CH_2) C6,8; 37.71 (CH_2); 32.79 (CH_2); 32.66 (CH_2); 30.69 (CH) C1,5; 29.45 (CH_2); 28.75 (CH) C7; 26.38 (CH_2); 25.58 (CH_2). IR: 3397 (s), 2924 (vs), 2854 (m), 1700 (s), 1457 (w), 1227 (w). MS: *m/z* 238 (M^+, 18), 208 (62), 150 (54), 109 (62), 95 (100), 94 (78), 55 (90).

***exo*-7-(1′-Hydroxyhept-7′-yl)bicyclo[3.3.1]nonan-3-one (9 (*n* = 7))**. From the Grignard reagent of 6-chloro-1-[(tetrahydropyran-2′-yl)oxy]-hexane (**8**, (*n* = 6)) (ca. 20-fold excess) and tosylate **7** (555.6 mg, 1.52 mmol), with use of the procedure described for the preparation of **9** (*n* = 5), was obtained 247.0 mg (65%) of the title alcohol, as an oil. Exact mass for $C_{16}H_{28}O_2$: calcd, 252.2089; found, 252.2083. ^1H NMR (200 MHz): 3.61 (t, *J* = 7, 2 H, CH_2OH); 2.3–2.55 (6 H); 1.0–2.0 (complex, 20 H). ^{13}C NMR: 213.24 (C=O); 62.92 (CH_2) C1′; 47.55 (CH_2) C2,4; 39.11 (CH_2) C6,8; 37.89 (CH_2); 32.79 (CH_2); 32.71 (CH_2); 30.68 (CH) C1,5; 29.61 (CH_2); 29.23 (CH_2); 28.78 (CH) C7; 26.38 (CH_2); 25.59 (CH_2). IR: 3411 (s), 2924 (vs), 2853 (s), 1698 (s), 1462 (m), 1440 (m), 1407 (m), 1347 (m), 1227 (m). MS: *m/z* 252 (M^+, 8), 234 (10), 222 (41), 164 (18), 137 (31), 109 (38), 95 (100), 94 (76), 81 (62), 79 (63), 67 (78), 55 (87).

***exo*-7-(1′-Hydroxyoct-8′-yl)bicyclo[3.3.1]nonan-3-one (9 (*n* = 8))**. From the Grignard reagent of 7-bromo-1-[(tetrahydropyran-2′-yl)oxy]-heptane (**8** (*n* = 7))[24] (ca. 20-fold excess) and tosylate **7** (311.5 mg, 0.85 mmol), with use of the procedure described for the preparation of **9** (*n* = 5), was obtained 88.7 mg (39%) of the title alcohol, as an oil. In other runs, yields varied between 40 and 55%. Exact mass for $C_{17}H_{30}O_2$: calcd, 266.2246; found, 266.2244. ^1H NMR (200 MHz, 400 COSY): 3.60 (t, *J* = 7, 2 H, CH_2OH); 2.25–2.55 (6 H); 2.03 (s, 1 H, OH); 1.0–2.0 (complex, 21 H). ^{13}C NMR: 213.24 (C=O); 62.78 (CH_2) C1′; 47.48 (CH_2) C2,4; 39.06 (CH_2) C6,8; 37.74 (CH_2); 32.73 (CH_2); 32.69 (CH_2); 30.62 (CH) C1,5; 29.51 (CH_2); 29.36 (CH_2); 29.21 (CH_2); 28.70 (CH) C7; 26.39 (CH_2); 25.61 (CH_2). IR: 3401 (s), 2925 (vs), 2852 (s), 1695 (s), 1466 (m), 1443 (m), 1412 (m), 1350 (m). MS: *m/z* 266 (M^+, 4), 236 (17), 137 (22), 109 (25), 96 (22), 95 (100), 94 (51), 93 (32), 81 (41), 67 (56), 55 (69), 41 (78).

***exo*-7-(1′-Formylbut-4′-yl)bicyclo[3.3.1]nonan-3-one (10 (*n* = 5))**. To a solution of oxalyl chloride (95 μL, 133 mg, 1.05 mmol) in methylene chloride (5 mL) in a round-bottom flask, under N_2, and cooled to −60 °C was added dropwise a solution of DMSO (150 μL, 163 mg, 2.09 mmol) in 1 mL of methylene chloride.[13] The reaction mixture was stirred for 2 min at −60 °C, and then a solution of alcohol **9** (*n* = 5) (104.6 mg, 0.466 mmol), in 1 mL of methylene chloride was added dropwise. Stirring was continued for 15 min at −60 °C, and then the reaction mixture was quenched by the dropwise addition of 700 μL of triethylamine. After being stirred a further 5 min at −60 °C, the mixture was allowed to warm to 20 °C. Water (25 mL) and methylene chloride (25 mL) were added, the phases were separated, and the aqueous phase was extracted with 25 mL of methylene chloride. The organic phases were combined, washed with brine, 3 M HCl (2 × 20 mL), water, aqueous K_2CO_3, and water, and dried (K_2CO_3). After solvent removal, the residual oil was subjected to flash chromatography (5:1 hexane–ethyl acetate) to give 101.0 mg (97%) of the title aldehyde, as an oil. Exact mass for $C_{14}H_{22}O_2$: calcd, 222.1620; found, 222.1614. ^1H NMR (400 MHz): 9.75 (t, *J* = 2, 1 H); 2.48 (d, *J* = 17, 6, 2 H); 2.36–2.42 (m, 6 H); 1.88 (d, *J* = 13, 1 H); 1.72 (m, 3 H); 1.53–1.62 (m, 3 H); 1.40 (m, 1 H); 1.23–1.32 (m, 2 H); 1.22 (m, 1 H); 1.1–1.2 (m, 2 H). ^{13}C NMR: 213.0 (C=O); 202.6 (CHO); 47.5 (CH_2) C2,4; 43.7 (CH_2) C4′; 39.0 (CH_2) C6,8; 37.5 (CH_2); 32.7 (CH_2); 30.6 (CH) C1,5; 28.8 (CH) C7; 26.2 (CH_2); 22.2 (CH_2). IR: 2917 (vs), 2851 (m), 2720 (w), 1713 (vs), 1698 (vs), 1461 (m), 1441 (m), 1407 (m), 1347 (m), 1228 (m). MS: *m/z* 222 (1.5), 208 (0.7), 194 (21), 151 (8), 136 (18), 109 (13), 95 (100), 79 (33), 67 (50), 55 (47), 41 (95).

***exo*-7-(1′-Formylpent-5′-yl)bicyclo[3.3.1]nonan-3-one (10 (*n* = 6))**. With use of the Swern oxidation procedure[13] described for **10** (*n* = 5), 52.3 mg (0.219 mmol) of the alcohol **9** (*n* = 6) was converted to the title aldehyde (38.7 mg, 75%), isolated as an oil. ^1H NMR (200 MHz): 9.76 (t, *J* = 2, 1 H, CHO); 2.25–2.55 (8 H); 1.00–2.00 (complex, 15 H). ^{13}C NMR: 213.08 (C=O); 202.70 (CHO); 47.55 (CH_2) C2,4; 43.78 (CH_2) C2′; 39.08 (CH_2) C6,8; 37.61 (CH_2); 32.78 (CH_2); 30.67 (CH) C1,5; 29.28 (CH_2); 28.82 (CH) C7; 26.27 (CH_2); 21.95 (CH_2). IR: 2922 (vs), 2851 (s), 2719 (w), 1719 (s), 1701 (s), 1459 (m), 1439 (m), 1407 (m), 1346 (m), 1226 (m).

***exo*-7-(1′-Formyloct-8′-yl)bicyclo[3.3.1]nonan-3-one (10 (*n* = 7))**. With use of the Swern oxidation procedure[13] described for **10** (*n* = 5), 62.8 mg (0.249 mmol) of the alcohol **9** (*n* = 7) was converted to the title aldehyde (52.2 mg, 84%), isolated as an oil. ^1H NMR: 9.72 (t, *J* = 2, 1 H, CHO); 2.2–2.45 (8 H); 1.0–2.0 (complex, 17 H). ^{13}C NMR: 213.19 (C=O); 202.88 (CHO); 47.55 (CH_2) C2,4; 43.83 (CH_2) C2′; 39.06 (CH_2) C6,8; 37.76 (CH_2); 32.76 (CH_2); 30.64 (CH) C1,5; 29.46 (CH_2); 29.02 (CH_2); 28.81 (CH) C7; 26.31 (CH_2); 21.95 (CH_2).

***exo*-7-(1′-Formylhept-7′-yl)bicyclo[3.3.1]nonan-3-one (10 (*n* = 8))**. With use of the Swern oxidation procedure[13] described for **10** (*n* = 5), 80.8 mg (0.303 mmol) of the alcohol **9** (*n* = 8) was converted to the title aldehyde (47.7 mg, 60%), isolated as an oil. Exact mass for $C_{17}H_{28}O_2$: calcd, 264.2089; found, 264.2081. ^1H NMR (200 MHz): 9.72 (t, *J* = 2, H, CHO); 2.2–2.45 (8 H); 1.0–2.0 (19 H). ^{13}C NMR: 213.05 (C=O); 202.74 (CHO); 47.49 (CH_2) C2,4; 43.77 (CH_2) C2′; 39.05 (CH_2) C6,8; 37.78 (CH_2); 32.73 (CH_2); 30.62 (CH) C1,5; 29.47 (CH_2); 29.16 (CH_2); 28.97 (CH_2); 28.79 (CH) C7; 26.39 (CH_2); 21.96 (CH_2). IR: 2924 (vs), 2853 (s), 2717 (w), 1717 (s), 1699 (s), 1461 (m), 1440 (w), 1407 (m), 1346 (m), 1226 (m). MS: *m/z* 264 (M^+, 0.5), 236 (24), 178 (12), 137 (18), 95 (100), 94 (41).

***exo*-7-(1′-Hydroxybut-4′-yl)bicyclo[3.3.1]nonan-3-one (9 (*n* = 4))**. Tosylate **7** was coupled with use of a 20–40 M excess of allyl Grignard reagent, with the procedure described for **9** (*n* = 5). The reaction was quenched by pouring into NH_4Cl solution–ether at 0 °C. The aqueous phase was extracted with ether (2 × 20 mL), and the combined ether fractions were dried over K_2CO_3. From 293.2 mg (0.801 mmol) of **7** was obtained 253.1 mg of residual oil, containing the coupled alkene ketal, as determined by GLC–MS. Exact mass for $C_{15}H_{24}O_2$: calcd, 236.1776; found, 236.1756. MS: *m/z* 236 (M^+, 8.5), 195 (60), 179 (47), 139 (83), 112 (37), 95 (73), 86 (64), 67 (55), 55 (60), 41 (100). ^1H NMR (200 MHz, crude mixture): 5.2–5.9 (1 H); 4.9–5.1 (2 H); ca. 3.9 (m, 4 H); 1.0–2.5 (complex). Partial ^{13}C NMR (crude mixture): 139.46 (CH), 113.86 (CH_2); 109.20 (q); 64.07 and 63.48 (both CH_2).

The above residual liquid (205.1 mg) in 5 mL of THF was added dropwise to a solution of ca. 2.5 equiv of diisoamylborane in THF (prepared in situ) under N_2 at 20 °C, and the reaction progress was monitored by GLC. After disappearance of the alkene (several hours), the solution was quenched by the addition of water (gas evolution), followed by 1.5 equiv of 3 M NaOH (400 μL) and 3 equiv of 30% H_2O_2 (250 μL). The solution was stirred for 30 min, with intermittent heating to 60 °C, and then dissolved in 25 mL of methanol–0.5 g of *p*-toluene-

(23) Waelchli, P. C.; Eugster, C. H. *Helv. Chim. Acta* **1978**, *61*, 885–98.
(24) Chapman, O. L.; Mattes, K. C.; Sheridan, R. S.; Klun, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 4878.

sulfonic acid and heated to 60 °C for a few minutes. Workup, as for **9** (n = 5), and flash chromatography (5:1 hexane–ethyl acetate) gave 88.3 mg (64% from tosylate **7**) of the title alcohol, obtained as an oil. ^{1}H NMR (400 MHz): 3.57 (t, J = 7, 2 H, CH_2OH; 2.40–2.50 (6 H, H2,4 protons plus H1,5); 1.90 (d, J = 13, 1 H); ca. 1.75 (m, 3 H); 1.1–1.6 (complex, 10 H). ^{13}C NMR: 213.31 (C=O); 62.64 (CH_2) C1; 47.47 (CH_2) C2,4; 38.94 (CH_2) C6,8; 37.51 (CH_2); 32.81 (CH_2); 32.67 (CH_2); 30.58 (CH) C1,5; 28.78 (CH) C7; 22.71 (CH_2). IR: 3421 (s), 2916 (vs), 2854 (s), 1697 (s), 1459 (m), 1406 (m), 1346 (m). MS: m/z 210 (M^+, 7.5), 180 (13), 135 (17), 134 (16), 109 (24), 107 (15), 95 (100), 81 (41), 79 (39), 67 (64), 55 (53), 41 (73).

exo-7-(1′-Formylprop-3′-yl)bicyclo[3.3.1]nonan-3-one (10 (n = 4)). With use of the Swern oxidation procedure[13] described for **10** (n = 5), 79.7 mg (0.379 mmol) of the alcohol **9** (n = 4) was converted to the title aldehyde (54.4 mg, 69%), isolated as an oil. ^{1}H NMR (200 MHz): 9.76 (t, J = 2, 1 H, CHO); 2.3–2.5 (m, 8 H); 1.1–2.0 (complex, 11 H). ^{13}C NMR: 212.74 (C=O); 202.26 (CHO); 47.59 (CH_2) C2,4; 43.97 (CH_2) C2′; 38.96 (CH_2) C6,8; 37.31 (CH_2); 32.81 (CH_2); 30.70 (CH) C1,5; 28.80 (CH) C7; 19.18 (CH_2). IR: 2916 (s), 2848 (m), 2715 (w), 1718 (s), 1700 (s), 1407 (m), 1260 (m). MS: m/z 208 (M^+, 1.5%), 180 (34), 122 (42), 95 (100), 79 (49), 67 (57), 55 (66), 41 (85).

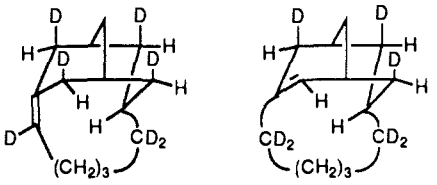
McMurry Cyclization Reactions. During the tenure of this project, a revised McMurry cyclization procedure was published,[25] so alkene **5** (n = 5) has been prepared by both the old and new methods. In our hands, the newer procedure does seem less capricious. For example, the alkene **5** (n = 5) preparation was undertaken six times with the older procedure and in two of these instances failed to yield much alkene product, in spite of reaction conditions ostensibly identical with those of the successful preparations. In three attempts with the newer procedure, alkene was produced in each case, although workup problems still plagued us (sensitive alkene).

Old Procedure.[14] A Zn–Cu couple was placed in the reaction flask, a condenser added, and the apparatus evacuated and released with Ar. Titanium trichloride (a large excess, usually about 1.5 g) was added with a miniglovebag and the flask again evacuated and released with Ar. Deoxygenated dimethoxyethane (DME) (50 mL) was then added and the mixture refluxed for 4 h (becomes green–black). The aldehyde **10** (usually 25–150 mg) in 20 mL of deoxygenated DME was added via syringe pump (ca. 0.8 mL/h) to the refluxing solution, and reflux was continued for several hours after the addition was complete. The mixture was cooled to 20 °C and transferred via cannula to 250 mL of dried, deoxygenated hexane. The hexane mixture was then passed through a pad of Celite–sand, and the solids were washed with 150 mL of hexane. The hexane was mostly removed under reduced pressure, the residue taken up in pentane and filtered again through a small pad of Celite–silica, and the solvent removed in vacuo. A GLC analysis at this point showed a major peak (or peaks if both **5** and **11** were present), together with a number of small impurity peaks. In most cases, the residual oil was distilled onto a cold finger to give material pure enough for use, while in other instances small-scale chromatography was carried out or preparative GLC collections were made.

New Procedure.[25] The complex $TiCl_3(DME)_{1.5}$ (2.30 g) was prepared, as described, and this was added to the Zn–Cu couple (Zn, 2.278 g; $CuSO_4$, 0.175 g). Degassed DME (80 mL) was added and the resultant slurry refluxed for 2.5 h, during which time a brown–black developed. To this was added the aldehyde **10**, as described in Old Procedure, with about 18 h for the addition and an additional 2-h reflux. The workup was the same as that described in Old Procedure.

***in*-Tricyclo[7.3.1.1^{7,11}]tetradec-1-ene (5 (n = 5)) and *in*-Tricyclo-[7.3.1.1^{7,11}]tetradec-11-ene (11 (n = 5)).** The above alkenes were obtained only as a mixture in ca. 20% yields, estimated by GLC techniques, using the new procedure. The equilibrium ratio of **5** (n = 5) to **11** (n = 5) is ca. 2:1, with **11** having the shorter GLC retention time. The workup leading to **5** (n = 5)–**11** (n = 5) is capricious, in that the first hexane extract cannot be taken to dryness. After silica gel chromatography, the pentane–hexane was removed, and the residue was distilled onto a cold finger and then dissolved in methylene-d_2 chloride for subsequent study. These alkenes were used as quickly as possible. Exact mass for **5** (n = 5) ($C_{14}H_{22}$): calcd, 190.1721; found, 190.1732. Partial ^{1}H NMR for alkene **5** (n = 5) (400 MHz): 5.12 (d, J = 12, 1 H); 4.46 (bq, J = 12, 1 H); 2.67 (d, q, J = 14, 2.5); 2.58 (d, J = 12); 2.42 (d, q, J = 12, 3). ^{13}C NMR: 146.30 (q) C1; 127.26 (CH) C2; 46.08 (CH_2); 40.05 (CH_2); 37.73 (CH_2); 37.43 (CH_2); 35.40 (CH_2); 35.25 (CH); 34.51 (CH_2); 32.68 (CH); 31.06 (CH_2); 30.47 (CH_2); 27.52 (CH) C7; 23.50 (CH_2). Both COSY and INVERSE HETCOR 2D NMR spectra were also obtained, principly to unequivocally locate the C(n+2) peak position. MS for **5** (n = 5): m/z = 190 (M^+, 26), 147 (54), 134 (72), 91 (100), 79 (79), 41 (88). For alkene **11** (n = 5), partial ^{1}H NMR (400 MHz): 5.27 (poorly resolved t, 1 H, H12). ^{13}C NMR: 143.08 (q) C1; 126.90 (CH) C12; 40.71; 39.86; 38.97; 35.90; 35.56; 33.52; 32.97; 31.55; 31.29; 31.01; 28.57; one uncertain. MS for **11** (n = 5): m/z 190 (M^+, 17), 147 (45), 134 (55), 91 (100), 79 (77), 41 (92).

^{1}H NMR Spectrum of 5 (n = 5) and 11 (n = 5) in CD_3COOD. In this solvent, one sees the "immediate" disappearance of alkene **5** (n = 5) peaks at δ 5.12 (the CH=C hydrogen) and 2.58 (an axial H). The exchanges of high-field hydrogens are not readily observable because of overlaps. The peaks at δ 2.67 and 2.42, which can be assigned to equatorial allylic protons, are now singlets. The proton on C(n+2) (μ-H) becomes a broadened singlet (loss of coupling to the vicinal axial hydrogens). In alkene **11** (n = 5), the alkene proton at δ 5.27 is now a clean doublet, J = 5 Hz). The other changes in **11** (n = 5) are less easily detected because of overlaps from **5** (n = 5). These results indicate that one now has the following deuterium-substituted alkenes:



5(n = 5) **11**(n = 5)

***in*-Tricyclo[8.3.1.1^{8,12}]pentadec-1-ene (5 (n = 6)) and *in*-tricyclo-[8.3.1.1^{8,12}]pentadec-13-ene (11 (n = 6))** were obtained as a colorless oil by microdistillation or by preparative GLC. Both old and new McMurry procedures were used. Exact mass for **5** (n = 6) ($C_{15}H_{24}$): calcd, 204.1852; found, 204.1858. ^{1}H NMR (400 MHz): 5.35 (bt, J = 6.5); 3.82 (m, μ-H); 2.76 (bd, J = 13); 2.5 (bd, J = 13); most of the remaining signals are overlapped, but COSY and HETCOR spectra allow one to make assignments for most of these. ^{13}C NMR (100 MHz): 146.28 (q); 119.47 (CH); 44.24 (CH_2); 41.29 (CH_2); 38.13 (CH_2); 37.01 (CH_2); 36.87 (CH_2); 34.48 (CH_2); 33.26 (CH_2); 31.83 (CH); 30.06 (CH); 25.67 (CH_2); 24.98 (CH_2); 24.76 (CH) C8; 24.22 (CH_2). MS: m/z 204 (M^+, 33), 163 (31), 148 (28), 105 (48), 93 (91), 91 (98), 79 (100), 41 (99). IR: 2959.5 (s), 2928.8 (s), 2873.2 (m), 2862.6 (m), 1459.7 (m).

Traces of acid isomerize **5** (n = 6) into **11** (n = 6). The equilibrium favors **11** (n = 6) by >5:1. ^{1}H NMR (400 MHz): 5.34 (b, 1 H); 2.46 (b, 1 H); 2.25 (d, J = 16, 1 H); remainder are unresolved. ^{13}C NMR (100 MHz): 139.32 (q); 127.32 (CH); 42.35 (CH_2); 37.46 (CH_2); 36.88 (CH_2); 35.40 (CH_2); 34.01 (CH_2); 32.50 (CH); 31.23 (CH_2); 31.05 (CH_2); 29.67 (CH_2); 25.52 (CH_2); 25.18 (CH); 24.63 (CH_2). One CH carbon was not located. Isomer **11** (n = 6) has the shorter retention time on GLC.

***in*-Tricyclo[9.3.1.1^{9,13}]hexadec-1-ene (5 (n = 7)) and *in*-tricyclo-[9.3.1.1^{9,13}]hexadec-1-ene (11 (n = 7))** were obtained in 60% crude yield as a colorless oil (83.7 mg from 159.0 mg of keto aldehyde), with the Old McMurry procedure. Exact mass for $C_{16}H_{26}$: calcd, 218.2034; found, 218.2019. ^{1}H NMR (200 MHz): 5.05 (d, J = 10.5, 1 H); 3.09 (q, J = 10–11, 1 H); 2.75 (d, J = 12); 2.50 and 2.30 (AB pair, $J \approx 13$); 2.4 (1 H); 2.2–0.8 (complex). ^{13}C NMR: several ^{13}C peaks are quite broad, indicating slow conformational interchanges at 20 °C; 142.4 (q); 121.25 (CH); 43.97 (CH_2); 40.11 (CH_2); 38.71 (CH_2); 36.53 (CH_2); 33.99 (CH_2); 33.26 (CH_2, b); 31.48 (CH); 30.79 (CH); 27.44; 25.86 (CH); 25.97 (CH_2, b); 24.66 (CH_2, b); 24.21 (CH_2, b); 21.25. MS: m/z 218 (M^+, 20), 105 (32), 89 (55), 90 (65), 91 (75), 79 (82), 41 (100).

Traces of acid will isomerize **5** (n = 7) into **11** (n = 7). The equilibrium constant **11** (n = 7):**5** (n = 7) $\approx$ 4 favors the rearrangement. These isomers are resolved on GLC with **11** (n = 7) having the shorter retention time. ^{1}H NMR: 5.42 (d, J = 5.5–6.0, 1 H); 0.8–2.4 (complex, overlapping). ^{13}C NMR: 139.3 (q); 127.77 (CH); 43.30 (CH_2); 37.13 (CH_2); 36.72 (CH_2); 35.03 (CH_2); 34.67 (CH_2); 31.36 (CH_2); 31.30 (CH); 29.23 (CH); 28.54 (CH_2); 26.31 (CH); 25.44 (CH_2); 25.05 (CH_2); 24.31 (CH_2); 22.74 (CH_2). MS: m/z 218 (M^+, 30), 162 (21), 105 (37), 89 (65), 90 (99), 91 (100), 79 (84), 41 (87).

***in*-Tricyclo[10.3.1.1^{10,14}]heptadec-1-ene (5 (n = 8)) and *in*-tricyclo-[10.3.1.1^{10,14}]heptadec-15-ene 11 (n = 8)** were obtained with the old McMurry procedure, and 8.9 mg of distilled alkene was produced from 40.2 mg (0.15 mmol) of the keto aldehyde (25%). Exact mass for **5** (n = 8) ($C_{17}H_{28}$): calcd, 232.2191; found, 232.2200. ^{1}H NMR: 4.94 (d, q, J = 11, 3, 1 H); 2.69 (d, J = 13, 1 H); 2.522 (m, the μ-H); 2.456 (d, J = 14, 1 H); 2.338 (m, 1 H); 2.27 (d, q, J = 14, 2, 1 H); 2.06 (m); 2.03; 1.985; 2.0–0.8 (complex). ^{13}C NMR: 139.95 (q); 122.34 (CH); 42.98 (CH_2); 40.79 (CH_2); 40.24 (CH_2); 39.65 (CH_2); 35.90 (CH_2); 34.22 (CH_2); 30.87 (CH); 30.76 (CH_2); 30.10 (CH); 28.66 (CH); 27.86 (CH_2); 26.89 (CH_2); 26.70 (CH_2); 24.96 (CH_2); 22.35 (CH_2). MS: m/z 232 (M^+, 60), 105 (42), 93 (64), 92 (100), 91 (82), 79 (81).

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Traces of acid isomerize **5** ($n = 8$) into an approximate 1:1 equilibrium mixture with **11** ($n = 8$). ^{1}H NMR: 5.44 (d, $J \approx 6$, 1 H); remainder are unresolved. ^{13}C NMR: 139.89 (q); 126.92 (CH); 41.99 (CH_2); 36.94 (CH_2); 36.53 (CH_2); 35.06 (CH_2); 33.45 (CH_2); 31.98 (CH_2); 30.59 (CH); 28.50 (CH); 27.30 (CH_2); 25.90 (CH_2); 25.25 (CH); 25.17 (CH_2); 24.70 (CH_2); 24.13 (CH_2); 22.61 (CH_2). MS: m/z = 232 (M^+, 35), 93 (58), 92 (100), 91 (75), 79 (51). On GLC isomer **11** ($n = 8$) has the shorter retention time.

***exo*-7-Methyl-3-methylenebicyclo[3.3.1]nonane (13).** This alkene has been reported[26] from the partial hydrogenation of the dimethylene analogue but is more easily prepared by methylenation of the ketone with Lombardo's reagent.[27] To a solution of the ketone (113.3 mg, 0.75 mmol) in methylene chloride (2 mL) and THF (0.5 mL) was added the methylenation reagent as a gray slurry. The starting material had disappeared in the GLC after 30 min. Standard workup and flash chromatography with pentane yielded **13** as a colorless oil (74.8 mg, 67%), pure by GLC and NMR.

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Electrochemical Oxidation of Enamines Related to the Key Intermediate on Thiamin Diphosphate Dependent Enzymatic Pathways: Evidence for One-Electron Oxidation via a Thiazolium Cation Radical

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Abstract: Electrochemical experiments were performed in Me_2SO on a number of 2-alkyl and 2-benzylthiazolium ions in the absence and presence of sodium bis(trimethylsilyl)amide ($pK = 26$). Under the latter conditions there is quantitative deprotonation at the C2α position leading to enamines that are structurally similar to the key enzyme-bound enamine intermediate present on all thiamin diphosphate dependent enzymes (Jordan, F.; Kudzin, Z. H.; Rios, C. B. *J. Am. Chem. Soc.* **1987**, *109*, 4415). For enamines derived from 2-alkylthiazolium salts in the presence of the strong base, but not in its absence, there was observed a cyclic voltammogram that is characteristic of irreversible processes. The relative peak potentials indicated that all enamines examined were easier to oxidize than ferrocene. The oxygen substituent at the C2α position facilitated oxidation compared to the hydrogen substituent by ca. 250 mV, and by ca. 120 mV compared to the methyl substituent. A series of para-substituted 2-(1-methoxy-1-phenylmethyl)thiazolium salts, when deprotonated at the C2α position, underwent reversible one-electron oxidation and gave a Hammett $\rho = -7.61$. The remarkably facile oxidation of all enamines was shown to proceed by a single-electron transfer according to controlled potential coulometry. The resulting cation radical undergoes dimerization according to spectroscopic analysis of the predominant product pursuant to electrolysis. Especially, the enamine derived from 2-(1-methoxyethyl)-3,4-dimethylthiazolium ion is a close analogue of the thiamin-bound intermediate. The results suggest that those enzymes responsible for oxidation at the C2α position may proceed by a stepwise redox mechanism via a thiazolium cation radical. These results constitute the first electrochemical determination of the redox properties of this key enamine intermediate and appear to have direct relevance to at least one enzymatic oxidative decarboxylation of pyruvic acid,pyruvate-ferrodoxin oxidoreductase, reported to proceed by a radical mechanism (Docampo, R.; Moreno, S. J.; Mason, R. P. *J. Biol. Chem.* **1987**, *262*, 12417).

There are a number of distinct thiamin diphosphate (TDP) dependent enzymes known to catalyze the oxidative decarboxylation of α-keto acids: (1) the α-keto acid dehydrogenases that utilize lipoamide as the immediate oxidizing agent and yield acetyl-coenzyme A;[1] (2) pyruvate oxidase utilizes flavin adenine dinucleotide as the oxidizing agent and yields acetate;[2] and (3) pyruvate-ferredoxin oxidoreductase[3a] and pyruvate-NADP oxidoreductase,[3b] also yielding acetyl-coenzyme A. All of these enzymes probably follow a common pathway through the decarboxylation step, forming an enamine or 2α-carbanion intermediate, similar in structure to **2**. We reported recently the generation of models for this key enamine intermediate,[4a,b] as well as pK_a's in Me_2SO for the precursor 2-(1-hydroxyethyl)thiazolium salts in which the alcohol function was protected.[5] Those models can also be used to help delineate the oxidative pathways. Several issues need to be resolved. One concerns whether the oxidation of an aldehyde to an acyl equivalent takes place by a series of two single-electron-transfer steps, or by a concerted two-electron transfer. A second issue is whether the oxidation involves a distinct covalent intermediate between the oxidant and the reductant. Yet a third concerns the true substrate for oxidation.

We here report that the enamines derived from a number of 2-alkyl and 2-benzylthiazolium salts, and not the salts themselves, undergo facile electrochemical oxidation in Me_2SO.

Experimental Section

Synthesis of 2-alkyl and 2-benzylthiazolium salts was reported elsewhere.[4a,5,6] Briefly, to synthesize the 2-(1-hydroxybenzyl)thiazolium ions, the thiazole was condensed with the appropriate benzaldehyde, the hydroxy functional group was methylated with NaH/MeI then the ni-

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