A Study of the Stereochemical Factors Involved in Multistep 1,2-Hydride Transfers

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Abstract: Synthetic routes to the *all-cis*- and the *all-trans*-1,2,3,4,5-pentamethylcyclopentyl cation have been developed. These cations both undergo very rapid multiple 1,2-hydride shifts, but the rate of this process is about 40 times faster in the all-trans case. This implies that the stereochemistry of the penultimate hydride in the rearrangement cascade can affect the rate of a given 1,2-hydride shift, i.e. that it is better if this penultimate hydride is located trans to the migrating one. A further implication of this work is that the hydride shifts in the parent cyclopentyl cation may be partially ordered and that rapid multiple hydride shifts in general may be subject to the same criteria.

A degenerate 1,2-hydride or alkyl shift in a carbocation may have an enormous range of activation barriers (varying from 3–20 kcal mol^{-1}), depending on the cation structure and the geometry of the shift. Where these barriers are in the lower part of this range, it is consequently not unusual to find organic systems where *multiple* 1,2-hydride or alkyl shifts have occurred during the course of some acid catalyzed rearrangement,[1] or in proposed biosynthetic carbocationic rearrangements.[2] These multiple rearrangements often maintain some stereochemical control, usually as a result of geometric constraints within those systems.

This paper therefore considers the possibility that the rate of a single 1,2-hydride shift within a series of multiple 1,2-hydride shifts may depend in some way on the overall stereochemistry associated with those multiple shifts. In order to probe this question, we required two comparable systems that undergo multiple 1,2-hydride shifts in which the individual hydride shifts differed *only* in the stereochemistry of the subsequent hydride shift.

The simplest model system one could imagine would be the two-step shift process depicted in Scheme I.

One can ask the following question here. Is the rate of the first step in this two-step process *dependent* on the stereochemistry associated with the second hydride shift, or alternatively, is there concertedness associated with the overall process?

The Scheme I system is assumed to be constrained in some way so that in this hypothetical model one directs the stereochemistry of these hydride shifts. For the more general consideration of an unconstrained case, one can consider the cyclopentyl cation **4**, which is known[3] to undergo extremely rapid 1,2-hydride shifts. The stereochemistry associated with these multiple shifts is completely unknown, but one can imagine two extreme cases, both of which would have a very stereochemically ordered sequence of events: (a) all shifts occur from one face of **4**, or (b) each hydride shift alternates faces of the cation.

These possibilities are shown in Scheme II. There are of course any number of intermediate situations. What distinguishes a and b is the *same considerations* that we have just outlined.

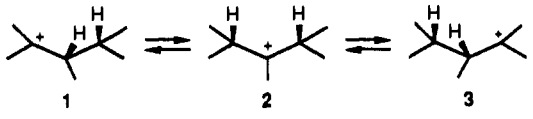
We can think of no practical way of probing the stereochemical details of the multiple hydride shifts in **4** so in this paper we propose a model system study which is an amalgamation of the ideas shown in Schemes I and II.

The 1,2,3,4,5-pentamethylcyclopentyl cation **5** is a potentially workable system for study if one could prepare the two isomers shown below in Scheme III. The following considerations apply: (1) The multiple hydride shifts are totally degenerate in both **5a** and **5b**. This is not the situation in the Scheme I model, but it is a necessary requirement to make the kinetic NMR line-broadening studies feasible. In considering various ring sizes, one can note that the all-cis migrations are degenerate for any ring size, whereas the all-trans shifts are degenerate *only* in odd-membered rings.[4] (2) Competing 1,2-methyl shifts are not expected to be rapid since these would produce a secondary cation in the first instance. The methyl groups are present simply to "direct" the hydride shifts.

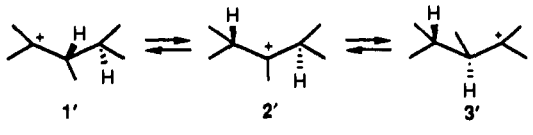
Our intention then was to prepare both **5a** and **5b** as observable carbocations and to measure quantitatively the rate of the de-

Scheme I

Case 1

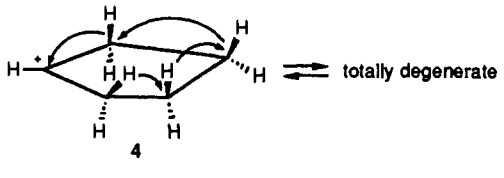


Case 2

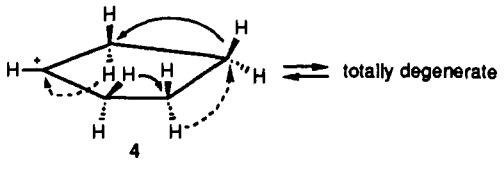


Scheme II

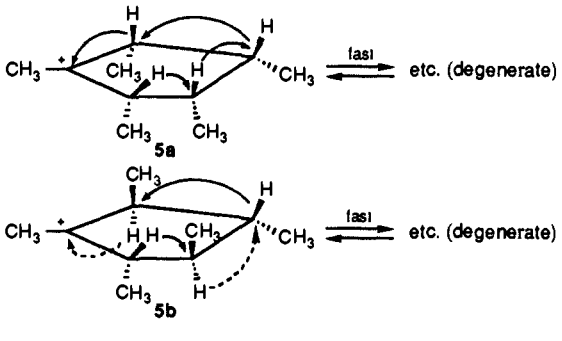
Case a



Case b



Scheme III



(1) Whitlock, H. W.; Overman, L. E. *J. Am. Chem. Soc.* **1971**, *93*, 2247.
(2) King, J. F.; de Mayo, P. In *Molecular Rearrangements*; de Mayo, P., Ed.; Interscience: New York, NY, 1964; Part 2.
(3) (a) Olah, G. A., Lukas, J. *J. Am. Chem. Soc.* **1968**, *90*, 933–938. (b) Olah, G. A.; White, A. M. *Ibid.* **1969**, *91*, 3954–56.

(4) Cyclopropyl cations are unstable, opening to allyl cations, and cycloheptyl cation is also unstable, giving the 1-methylcyclohexyl cation.

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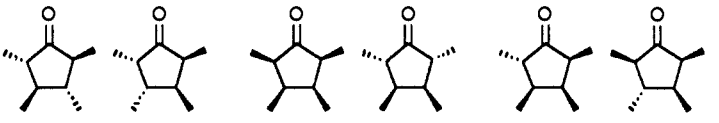


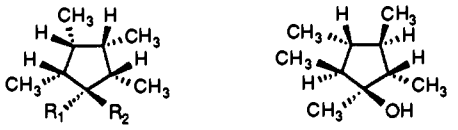
ketone	7b	7c	7a	7d	7f	7g
ketone point group	C_2	C_2	C_s	C_s	C_1	C_1
methyl alcohol(s) point group	C_1	C_1	C_s	C_s	C_1	C_1

Figure 1. Six possible 2,3,4,5-tetramethylcyclopentenones (only CH_3 groups shown)

generate multiple hydride shifts in each case to see if one situation was indeed preferred over the other.

Results

Synthesis of Starting Alcohols. The cations **5a** and **5b** were prepared under standard superacid conditions by the protonation and subsequent ionization of alcohols **6a** (or **6c**) and **6b**, respectively. The alcohols **6a** and **6b** were prepared from the respective ketones **7a** and **7b**, two of the six possible 2,3,4,5-tetramethylcyclopentanones shown in Figure 1.

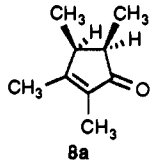


6a: $R_1 = OH$, $R_2 = CH_3$
6c: $R_1 = CH_3$, $R_2 = OH$

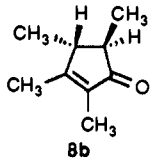
6b (racemic)

We have included all of the isomers of **7** in Figure 1 because partial epimerization, presumably via the enolates, turned out to be a not totally inconsequential problem in the syntheses and the NMR spectra of five-membered rings are rather ambiguous for assigning vicinal cis and trans proton coupling constants. For example, all four of the ketone isomers with higher symmetry, i.e. C_2 or C_s, would be expected to have rather similar NMR spectra.

Although none of the ketones **7** have been reported previously, the α,β-unsaturated analogues **8a** and **8b** are known,[5] and these proved to be convenient starting materials. The trans isomer **8b** was obtained pure from the 1:9 **8a**/**8b** equilibrium mixture by spinning band distillation, and lithium/ammonia reduction of this enone followed by quenching with a variety of proton sources gave predominantly a single product (ca. 80%). Stability considerations and literature precedent[6] would predict the preferential formation of the all-trans ketone **7b**, and this is confirmed on the basis of the NMR symmetry of this ketone (C_2 or C_s) and that of the single alcohol product produced on methyllithium treatment, and showing C_1 symmetry (Figure 1). The only other **7** isomer with the above characteristics is **7c**, and this would have required among other things an unlikely isomerization of the original trans methyls in **8b** to the less stable cis orientation.



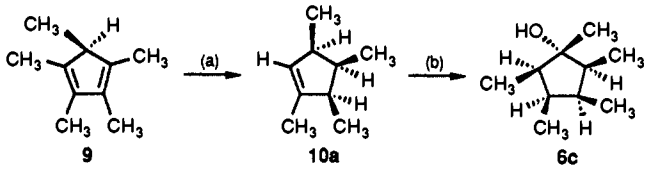
8a



8b

Although the trans enone **8b** could be easily isolated by distillation, the cis isomer **8a** always accounted for about 10% of the undistilled material, presumably epimerizing to the more stable trans isomer under distillation conditions. Flash chromatography of the mixture on silica gel gave an unsatisfactory separation of **8a**; however an analytical sample was isolated by preparative GLC. The best approach to obtaining **8a** in quantity was to perform a kinetic quench on the common cross-conjugated enolate produced from **8a** or **8b**.[7] Of a number of quench conditions, a *tert*-butyl

Scheme IV



9 **10a** **6c**

alcohol/THF mixture proved best, giving an **8a**/**8b** ratio of ca. 6:4. This enriched mixture was used directly, and catalytic hydrogenation gave a major product of C_s or C_2 symmetry. Hydrogenation from the least hindered face would give the required all-cis ketone **7a**; however a possible subsequent epimerization of the two methyl groups adjacent to the ketone would give **7d**, of the same symmetry type. That some epimerization could occur under the hydrogenation conditions (assuming that hydrogen added cis) was already illustrated by the formation of some of the all-trans ketone **7b** from the catalytic hydrogenation of the trans enone **8b**. Ketones **7f** and **7g** are also produced in this latter reaction. However, the epimerization of **7a** to **7d** would be expected to proceed via the intermediacy of **7f** and since none of the product assigned to **7f** was observed in the hydrogenation of **8b**, we conclude that the major product was the all-cis ketone **7a**. Methyl lithium give a single alcohol (C_s symmetry) assigned the stereochemistry **6a**.

The alcohol **6c** (the alcohol epimer of **6a**) would give an identical all-cis carbocation, and so to avoid any possible ambiguity in the previous assignment, this was prepared according to Scheme IV.

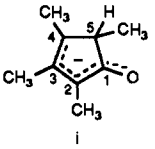
The diene **9** was mono-hydrogenated to give predominantly (70%) the all-cis alkene **10a** (either by a 1,2- or 1,4-addition of hydrogen). Two other alkenes, assigned structures **10b** and **10c** were produced in minor amounts (19 and 7%, respectively). All three were isolated pure as analytical samples by preparative GLC and characterized by ^1H NMR. Alkene **10c** is unsymmetrical and easily distinguished from **10a** and **10b**. Alkenes **10a** and **10b** were assigned as follows: (1) **10a** is expected on steric hydrogenation grounds to be the major isomer and (2) on hydroboration–oxidation, a symmetric (C_s) alcohol is expected (and observed), whereas for **10b** an unsymmetrical alcohol would be produced.

Preparation of Carbocations 5a and 5b. In both cation cases, the tertiary alcohols were used as the carbocation precursor. We had some initial concern that a dehydration–reprotonation sequence, on first contact of the alcohol with the superacid, might epimerize the carbocations, but this did not happen. Magic acid

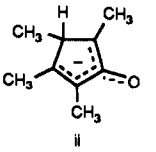
(5) (a) Campbell, P. H.; Chiu, N. W. K.; Deugau, K., Miller, I. J.; Sorensen, T. S. *J. Am. Chem. Soc.* **1969**, *91*, 6404–6410. (b) Kohl, F. X., Jutzi, P. *J. Organomet. Chem.* **1984**, *243*, 119.

(6) Samson, M.; De Clerq, P.; Vandewalle, M. *Tetrahedron* **1975**, *31*, 1233–1235.

(7) The formation of either the conjugated enolate i or the cross-conjugated enolate ii (or a mixture of both) could be involved in this epimerization

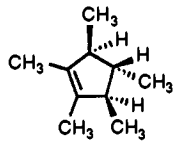


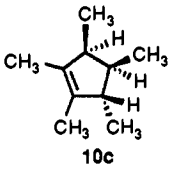
i



ii

reaction. Quenching the enolate with D_2O/THF at −78 °C led mainly to the replacement of the low-field δ 2.75 methine proton in **8a** and the high-field methine proton at δ 1.85 in **8b**, but a totally unambiguous assignment of the methine protons in either **8a** or **8b** is not possible from the simple spectra. We therefore carried out a ^{13}C INADEQUATE (one-dimensional) experiment with use of the trans ketone **8b**. This allows the carbon connectivity to be traced and unequivocally assigned. A HETCOR experiment then unambiguously identifies the methine protons. The residual ^1H peak in **8b**, referred to above, is located on C4, proving that the deuterium is on C5 and identifying the cross-conjugated enolate ii as the species formed.


10b


10c

(1:1 FSO_3H-SbF_5) in a SO_2ClF/SO_2F_2 solvent mixture was used as the cation supporting medium, in order to reach the lowest possible temperatures. Some preliminary trial experiments using a 1,2,5-trimethylcyclopentyl 1-chloride and $SbF_5/SO_2ClF/SO_2F_2$ showed that oxidation of the methylated cyclopentyl cation to methylated cyclopentenyl (allyl) cations was a competing reaction, but that this oxidation was virtually nonexistent in magic acid solutions.

Cation 5b. This cation proved relatively robust to irreversible rearrangements. It could be prepared at −120 °C and was stable up to −80 °C for extended periods of time (although a slow decomposition was occurring). The ^{13}C and ^1H NMR data are given in Table I. In the ^1H NMR spectra at −100 °C, one sees only two peaks, an averaged methine peak and an averaged methyl peak, both very sharp. On progressive cooling to −145 °C, both peaks begin to broaden slightly. The methyl peak is somewhat broader than the methine peak, contrary to the expectations for an NMR dynamic line-broadening process and indicative of a shorter T_2 relaxation for the averaged methyls in this somewhat viscous medium.

In the ^{13}C NMR spectra, one also sees two peaks, i.e. the averaged methine carbons and the averaged methyl carbons. On progressive cooling, one begins to see significant line broadening of the methine carbon at −140 °C. This peak is broader at −144 °C and broader still at −148 °C. One also sees some broadening of the averaged methyl peak at this lowest temperature. The line broadening is clearly due to a slowing down of the 1,2-hydride shifts since viscosity broadening would have affected the methyl ^{13}C more than the methine ^{13}C, as indicated in related work with nonexchanging systems.

The methine ^{13}C line broadening was computer modeled by assuming "frozen-out" chemical shift positions estimated from various static cyclopentyl cations. Even moderate uncertainties in making these estimates do not have an appreciable effect on the rate constants obtained. This data is given in Table II, including a crude estimate of E_a. One can also show that the lack of observable dynamic broadening in the ^1H spectra is consistent with the derived rate constants in Table II.[8]

Cation 5a. This cation proved to be extremely unstable and much effort was needed to generate the cation (use of very low temperature conditions). Even in the best cases, however, the starting cation solution was never completely free of small rearrangement ion peaks. That some of these "impurity" peaks were due to other geometric isomers of **5a** was shown by preparing cation solutions starting with either of the corresponding tertiary alcohols from ketones **7f** and **7g** (the resultant cations are interconverted by a single 1,2-hydride shift). Interestingly, cation **5b** was not observed as one of the rearrangement species.

The ^{13}C NMR spectra of cation **5a** (Table I) showed much more extensive line-broadening than **5b** when comparisons were made at the same temperature. At −132.5 °C, the averaged methine carbons already form a very broad peak and this was the lowest temperature at which one could obtain a line-shape before the methine carbon peak broadened into the baseline. On warming to −123 °C, one sees progressive sharpening of this peak, but irreversible decomposition sets in at about −120 °C. The line-broadening data was treated in the same way as for **5b** to obtain the exchange rate constants (Table II).

Although both **5a** and **5b** exhibit very low barriers for the multiple hydride shifts, the shifts in **5b** are nevertheless about *40 times faster* at −132 °C.

(8) For a given rate constant, the line broadening of an "averaged" NMR peak depends on the $\Delta\delta$ separation (in hertz) of the individual sites and this is naturally much larger for ^{13}C resonances than for ^1H ones.

Table I. ^{13}C and ^1H Chemical Shifts

cation	$^{13}CH_3$(av)[a]	^{13}CH(av)[a]	C^1H_3(av)[b]	C^1H(av)[b]
5a	16.2	110.8	*c*	*c*
5b	16.95	114.8	1.825	2.24

[a] Relative to internal $CFCl_3$ = 117.9. [b] Relative to external TMS in $(CD_3)_2O$ and approximately corrected for bulk diamagnetic susceptibility effects (based on pure SO_2ClF) by adding +0.416 ppm to the measured values. [c] The ^{13}C results were obtained in 10-mm NMR tubes which were added quickly and directly to the precooled probe of the Bruker WH-90 spectrometer (iron magnet). In the ^1H results, 5-mm tubes were used with a Varian XL-200 (supercon) and the combination of a smaller sample volume and nondirect access to the precooled probe caused enough rearrangement of the cation that ^1H assignments were not unambiguous.

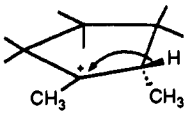
Table II. Rates of 1,2-Hydride Shifts

cation	temp,[a] °C	rate:[b] k, s^{-1}
5a	−132.0	2×10^5
	−127.9	4×10^5
5b	−148.2	4×10^5
	−144.1	7×10^5
	−140.4	2×10^6
	(−132.0)[c]	(8×10^6)

[a] Considered accurate to ±0.5 °C. [b] In the kinetic matrix, the following values of chemical shifts (in hertz) were used for the line-broadening computations: 7580, 1700, 850, 1700, 795, 410, 270, 270, 410. The first five are ring carbons starting from the C^+ center, the last five are methyls, also starting from the $C^+ - CH_3$. These values are based on data for the 1-methyl-, the 1,2-dimethyl-, and the 1,3-dimethyl-1-cyclopentyl cations. [c] Extrapolated values, using E_a = 5.9 kcal/mol. There is considerable uncertainty in this extrapolation, but this would not materially affect the conclusions drawn in this paper.

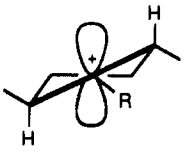
Discussion

A single hydride shift in either **5a** or **5b** has a seemingly identical local environment if one focuses on the two carbon atoms involved here (see below):


5a or 5b local structure

Therefore, in rationalizing why the all-trans cation **5b** undergoes faster 1,2-hydride shifts than in **5a**, one has to consider other factors.

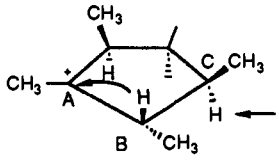
The most attractive explanation relates to the probable conformational structure of cyclopentyl cations. Recent experimental work by the Forsyth[9] and Sunko[10] groups on 1-methyl-1-cyclopentyl cation, together with theoretical calculations on the secondary ion by Schleyer, Koch, et al.,[11] suggests that a "twist" C_2 conformer is the stable ground-state structure. The C–H hyperconjugation involves one β-hydrogen from each face of the cation, as shown below:


R = H or CH_3

In the case of our all-trans isomer **5b**, the β-hydrogens have this favorable orientation. In considering the transition state for a 1,2-hydride shift (see diagram below), one is developing a "new" carbocation center at B and a "new" β-hydrogen interaction at C (i.e. this is the hydrogen which would be involved in the next

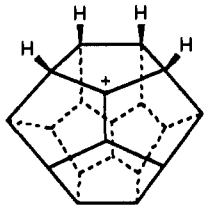
(9) Botkin, J. H.; Forsyth, D. A.; Sardella, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 2797–2802.
(10) Vančik, H.; Sunko, D. E. *J. Am. Chem. Soc.* **1989**, *111*, 3742–3744.
(11) Schleyer, P. v. R.; Carneiro, J. W. de M.; Koch, W.; Raghavachari, K. *J. Am. Chem. Soc.* **1989**, *111*, 5475–5477.

hydride shift proceeding in the same circular direction). It seems quite plausible that the transition state would be made more favorable if this "new" β-hydrogen at C were so aligned that it could move easily into the hyperconjugating position concerted with the hydride shift process on the neighboring carbon B. In the all-cis cation, one does not have both β-CH bonds in an appropriate location to stabilize a "twist" conformation and one may need extra reorganization of the conformation in this case prior to a second 1,2-hydride shift taking place (and hence slower).

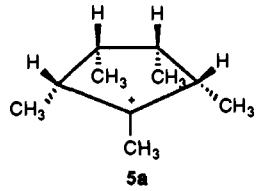


← this hydrogen is favorably disposed to stabilize developing charge at B

A second rationalization of the results involves the possibility that **5a** and **5b** are solvated in a somewhat different way. Since one face of **5a** is very hindered, one would expect preferential solvation on the C–H face. In **5b**, both faces are identical in this C_2 structure. Cations **5a** bears a superficial resemblance to the dodecahedryl cation **11**, which has no possibility of solvation from the backside.



11

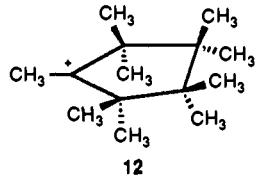


5a

Cation **11** has very high barriers for the 1,2-hydride shifts.[12] In the main, these high barriers are probably due to ring-strain effects which place the migrating C–H bonds in an unfavorable orientation.[13] However, there seems some possibility that the lack of backside solvation could also be a factor, and in this case the comparison with **5a** is valid, although the differences observed in this work between **5a** and **5b** are minute compared to the large difference between **5a** and **11**.

Overall, we tend to favor the steric argument for the **5a**/**5b** rate difference.

In concluding this discussion, we would first like to compare our data to that recently obtained by Mayr and Koschinsky[14] for the nonamethylcyclopentyl cation **12**, and then to finally comment on the hydride shift possibilities in the cyclopentyl cation itself.



12

Cation **12** shows a low temperature ^{13}C NMR spectrum in which the methyls appear as *two* peaks, area 4:5. At higher temperatures, these broaden and coalesce to a single peak. The ring carbons form a single sharp peak unchanged over this temperature range. These observations can only be rationalized by postulating very rapid and stereospecific 1,2-methyl shifts, either as a consequence of a partially bridged structure or because of conformational effects which favor such a process. Our work might suggest that a sequential trans migration would be preferred over a sequential cis process in explaining the results.

The NMR spectrum of the parent cyclopentyl cation **4** exhibits one proton and one carbon peak in solution, indicating complete averaging via 1,2-hydride shifts.[3] Even at the lowest possible solution temperature no line broadening is observed for either peak. Although this result would be consistent with either a localized cation or a hydrogen-bridged structure, Yannoni, Myhre, et al.[15] on the basis of a 70 K MAS NMR solid spectrum, showed that the localized cation was the ground state. The recent calculations of Schleyer, Koch, et al.[11] are in agreement and show that a C_2 "twist" structure is the computationally most stable form of the cyclopentyl cation. In this structure, as mentioned previously, one hydrogen from each face is involved in the hyperconjugated stabilization. On the basis of our work with the tertiary ions **5a** and, in particular **5b**, we believe that there is now some real possibility that the hydride shifts in the cyclopentyl cation could show some stereospecificity, ie. sequential trans shifts, as shown earlier in Scheme II, case b.[16]

Conclusions

The further implication of the present work is that sequential hydride shifts occurring during acid-catalyzed, etc. rearrangements may indeed be kinetically more favorable with certain sterically fixed orientations that with others, ie. as in **5a** and **5b**, or that in unconstrained systems where there is a multiple choice of migration pathways, a specific migration course will dominate.

Experimental Section

Infrared spectra were recorded on a Nicolet 5-DX FT-IR machine. ^1H NMR (200 MHz) spectra were recorded on a Varian XL-200 spectrometer. ^{13}C NMR (22.63 MHz) spectra were recorded on a Bruker WH-90 spectrometer; low-temperature spectra were recorded with use of a ^{19}F lock, and chemical shifts were referenced to the lowfield peak of $CFCl_3$ (125.0 ppm). Temperature calibrations were performed as previously described.[17] Mass spectra were recorded on either a Kratos-MS80 or VG-7070 spectrometer.

2,3,4,5-Tetramethylcyclopent-2-enone was prepared according to the procedure of Kohl and Jutzi.[5] Spinning band distillation gave the pure trans isomer (bp 62 °C, 7 mmHg). 1,2,3,4,5-Pentamethylcyclopentadiene was prepared by treatment of the enone with methyllithium, followed by acidic (aqueous HCl) workup and distillation from calcium hydride. THF was distilled under argon from potassium/benzophenone ketyl. All alkyllithiums were titrated according to the procedure of Kofron and Baclawski[18] immediately before use. Flash chromatography was performed by eluting with hexane/ethyl acetate mixtures.

Cations for ^{13}C NMR spectroscopy were prepared by the slow addition of the appropriate alcohol (ca. 50 mg in $CFCl_3$) to a 20-fold excess of 1:1 FSO_3H·SbF_5 (Aldrich) dissolved in a ca. 2:1 mixture of sulfuryl chloride fluoride and sulfuryl fluoride. All additions were made while cooling the solutions to −130 °C in a pentane/liquid nitrogen slush bath.

Synthetic Experimental. 2α,3β,4α,5β-Tetramethylcyclopentanone (7b). To a stirred solution of anhydrous ammonia (100 mL) at −78 °C in a 250-mL round-bottomed flask (flame dried) was added lithium wire (57.1 mg, 8.83 mmol). A solution of *trans*-2,3,4,5-tetramethylpent-2-enone (0.541 g, 3.92 mmol) in THF (2 mL) was added to the deep blue ammonia solution over a period of 2 min during which time the blue color persisted. After an interval of several minutes, the reaction mixture was quenched with anhydrous ethanol in THF, the cloudy white solution was diluted with ether, and the ammonia was allowed to evaporate. After 1 h water was added, and the aqueous phase washed with ether (3 × 20 mL); the organic portions were combined and dried (K_2CO_3), and the solvent was removed under vacuo to give a pale yellow oil (466.5 mg,

(12) Olah, G. A.; Surya Prakosh, G. K., Kobayashi, T.; Paquette, L. A. *J. Am. Chem. Soc.* **1988**, *110*, 1304–1305.

(13) The dihedral angle is favorable but the H–C–C$^+$ angle is large and relatively rigid.

(14) Mayr, H.; Koschinsky, R. *J. Am. Chem. Soc.* **1989**, *111*, 2305–2306.

(15) Myhre, P. C.; Kruger, J. D.; Hammond, B. L.; Lok, S. M.; Yannoni, C. S.; Macho, V.; Limbach, H. H.; Vieth, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 6079–6080.

(16) The cyclopentyl cation **4** has of course no built-in constraints such as exist in **5a** and **5b**, and there will be a process which interconverts the two C_2 "twist" structures. If this process is faster than the hydride shifts one would lose any stereospecificity. From the lack of line broadening in solution ^{13}C NMR spectra, one can put an upper limit of ca. 3 kcal/mol for a 1,2-hydride shift in **4**. The barrier for the "twist" ⇄ "twist" degenerate interconversion has not been computed directly but the C_{2v} planar structure of **4** is calculated to lie about 3–3.5 kcal/mol above the "twist" structure.[11] Given that transition states are involved here rather than ground states, it is quite possible that this "twist" ⇄ "twist" interconversion could indeed be higher than that for a 1,2-hydride shift. The situation is more complex than this, however, because the envelope C_s structure for **4** is computed to be only marginally higher in energy than the "twist" conformer, although the $C_2 \rightleftarrows C_s$ interconversion barrier may also still involve a planar transition state (i.e. ≥ 3 kcal/mol).

(17) Kirchen, R. P., Sorensen, T. S. *J. Am. Chem. Soc.* **1978**, *100*, 1487.

(18) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

85%), consisting mainly of (**7b**). Flash chromatography allowed the isolation of this ketone as a single component by GLC along with a minor ketone component corresponding to either **7f** or **7g**. NMR δ_H (200 MHz, C_6D_6): 0.75 (8 H, bd, $(AB_3X)_2$ system (the methine hydrogen and the methyl are virtually overlapped)), 0.99 (6 H, d, J = 7.0 Hz), 1.26 (2 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 12.5 (CH_3), 16.1 (CH_3), 44.9 (CH), 51.0 (CH), 221.8 (quat). IR (neat) ν/cm^{-1}: 2960 (s), 2930.6 (m), 2873 (m), 1742 (vs), 1460 (m), 1375 (m), 1168 (m), 977 (m). MS (EI) m/e: 140 (M^+, 10.4), 125 (2.7), 111 (2.9), 83 (48.0), 69 (12.9), 56 (36.0), 41 (21.8), 32 (100.0). Anal. $C_9H_{16}O$ requires 140.1201, found 140.1195.

Minor Ketone 7f or 7g. NMR δ_H (200 MHz, $CDCl_3$): 0.88 (3 H, d, J = 7.9 Hz), 0.97 (3 H, d, J = 6.8 Hz), 1.02 (3 H, d, J = 7.0 Hz), 1.07 (3 H, d, J = 6.3 Hz), 1.75 (2 H, m), 2.80 (2 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 11.0 (CH_3), 12.9 (CH_3), 13.1 (CH_3), 17.1 (CH_3), 40.0 (CH), 43.6 (CH), 45.6 (CH), 51.3 (CH), 223.0 (quat). IR (neat) ν/cm^{-1}: 2963 (s), 2929 (m), 2875 (s), 1740 (vs), 1457 (s), 1371 (w), 1172 (w), 963 (w); MS (EI) m/e: 140 (M^+, 8.3), 125 (2.8), 111 (3.0), 83 (20.0), 69 (10.4), 57 (4.7), 56 (100.0), 53 (11.3), 41 (20.5).

1α,2α,3β,4α,5β-Pentamethylcyclopentan-1-ol (6b). To a cooled (0 °C) solution of **7b** (863.3 mg, 6.17 mmol) in ether (10 mL) was added an etherial solution of methyllithium (10 mL, 1 M, 10 mmol), over a period of 10 min. The solution was allowed to stir for 10 min at 0 °C and then for 10 min at room temperature, the reaction was then quenched by the addition of aqueous K_2CO_3 and then water. The organic phase was washed with ether (3 × 10 mL), the organic portions were combined and dried (K_2CO_3), and the solvent was removed under vacuo to give a pale yellow oil (828.9 mg, 86%).

NMR δ_H (200 MHz, $CDCl_3$): 0.92 (9 H, m), 0.98 (3 H, d, J = 6.2 Hz), 1.08 (3 H, s), 1.1–1.3 (3 H, m), 1.40 (1 H, quin, J = 7.5 Hz). NMR δ_C (22.63 MHz, $CDCl_3$): 11.8 (CH_3), 15.3 (CH_3), 16.9 (CH_3), 17.6 (CH_3), 24.2 (CH_3), 46.1 (CH), 47.9 (CH), 50.9 (CH), 52.9 (CH), 80.4 (quat); IR (neat) ν/cm^{-1}: 3446 (s), 2957 (vs), 2871 (vs), 1457 (s), 1375 (s), 1134 (s), 1037 (s), 1017 (m), 919 (s). MS (EI) m/e: 156 (M^+, 10.2), 138 (44.6), 123 (77.7), 99 (77.1), 83 (67.5), 81 (64.3), 55 (56.7), 43 (100.0). Anal.: $C_{10}H_{20}O$ requires 156.1514, found 156.1512.

***cis*-2,3,4,5-Tetramethyl-2-cyclopenten-1-one (8a).** To a cooled (0 °C) solution of diisopropylamine (1.2 mL, 0.86 g, 8.52 mmol) in THF (10 mL) was added *n*-butyllithium (9.6 mL, 0.88 M, 8.45 mmol) dropwise. The solution was cooled to −78 °C, and a solution of the enone **8** (predominantly trans) (1.0634 g, 7.71 mmol) in THF (5 mL) was added over a period of 1 min. The solution was allowed to stir for 5 min and then transferred via a cannula into a cooled solution of *tert*-butyl alcohol (10 mL) in THF (50 mL) and immediately diluted with water (100 mL) and ether (50 mL). The aqueous phase was extracted with ether (2 × 20 mL), the organic portions were combined and washed with diluted HCl (2 × 30 mL), and the ether was removed under vacuo; the resultant oil was diluted with dichloromethane and washed with water (2 × 100 mL), the organic phase dried (K_2CO_3), and the solvent removed under vacuo to give a colorless oil (1.0151 g, 7.36 mmol, 95%) that contained the enone in a cis to trans ratio of 56:44 (by GLC).

2α,3α,4α,5α-Tetramethylcyclopentanone (7a). A ca. 1:1 mixture of the cis and trans enones was dissolved in ether and cooled to 0 °C. Palladium on alumina (5%) was added, a hydrogen atmosphere admitted above the solution, and the resultant mixture rapidly stirred until GLC analysis showed that the starting material had disappeared (several days). The solution was filtered through Celite, and the solvent was removed in vacuo to give a colorless oil containing a mixture of isomeric ketones. Flash chromatography gave a ca. 25% recovery of the ketone **7a**.

NMR δ_H (200 MHz, $CDCl_3$): 0.87 (6 H, d, J = 6.7 Hz), 1.02 (6 H, d, J = 7.0 Hz), 2.40 (4 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 10.9 (CH_3), 11.4 (CH_3), 36.9 (CH), 46.2 (CH), 223.2 (quat). IR (neat) ν/cm^{-1}: 2972 (s), 1736 (vs), 1458 (m), 1385 (m), 1168 (m), 1120 (m). MS (EI) m/e: 140 (M^+, 60.6), 125 (27.9), 111 (21.2), 83 (100.0), 69 (72.1), 56 (100.0), 41 (82.7). Anal.: $C_9H_{16}O$ requires 140.1201, found 140.1199.

1α,2β,3β,4β,5β-Pentamethyl-1-cyclopentanol (6a). To a cold (0 °C) ethereal solution (10 mL) containing mainly the all cis ketone (**7a**) (186.1 mg, 1.33 mmol) was added methyllithium (3 mL, 1.1 M, 3.3 mmol) over a period of 5 min. The solution was allowed to warm to room temperature and then quenched by the addition of aqueous K_2CO_3, the organic phase was removed, the aqueous phase was washed with ether (3 × 10 mL), and the organic portions were combined and dried (K_2CO_3), and the solvent was removed in vacuo to give a pale yellow oil (197.4 mg, 1.27 mmol, 95%). Flash chromatography gave a colorless oil (105.3 mg, 0.675 mmol, 51%).

NMR δ_H (200 MHz, $CDCl_3$): 0.87 (6 H, d, J = 7.2 Hz), 0.94 (6 H, d, J = 7.2 Hz), 1.16 (3 H, s), 1.86 (2 H, m), 2.13 (2 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 9.7 (CH_3), 11.8 (CH_3), 27.6 (CH_3), 39.0 (CH), 46.4 (CH), 79.2 (quat). IR (neat) ν/cm^{-1}: 3626 (m), 3544 (m), 2963 (vs), 2879 (vs), 1455 (s), 1374 (s), 1127 (s), 1063 (m), 1022 (m), 921 (s). Anal.: $C_{10}H_{20}O$ requires 156.1514, found 156.1511.

1,2,3α,4α,5α-Pentamethylcyclopent-1-ene (10a). 1,2,3,4,5-Pentamethylcyclopentadiene (0.88 g, 6.29 mmol) was dissolved in diethyl ether (10 mL) and cooled to 0 °C. Pd/Al_2O_3 (5%) was added, and hydrogen gas was admitted. The solution was then stirred until GLC analysis showed complete removal of starting material (ca. 10 min). The solution was filtered through Celite, and the solvent was removed under reduced pressure to give a pale yellow oil (0.80 g, 5.71 mmol, 91%). GLC analysis showed three components a, b, and c; in the ratio 73:19:7, which was used without purification in the following step. Analytical samples of each were obtaned by preparative GLC.

(a) NMR δ_H (200 MHz, $CDCl_3$): 0.83 (3 H, d, J = 6.7 Hz), 0.85 (6 H, d, J = 6.8 Hz), 1.55 (6 H, s), 2.30 (3 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 11.0 (CH_3), 12.0 (CH_3), 15.5 (CH_3), 37.5 (CH), 46.6 (CH), 134.8 (quat). IR (neat) ν/cm^{-1}: 2960 (vs), 2870 (s), 1446 (m), 1377 (m), 1042 (w), 913 (w). MS (EI) m/e: 138 (M^+, 5.0), 124 (6.2), 123 (100.0), 81 (14.5), 57 (8.5), 53 (26.3), 43 (15.6), 41 (12.2).

(b) NMR δ_H (200 MHz, $CDCl_3$): 0.95 (6 H, d, J = 6.9 Hz), 1.01 (4 H, d, AB_3X_2 system with the methine and methyl at virtually the same chemical shift), 1.51 (6 H, s), 1.93 (2 H, m). MS (EI) m/e: 138 (M^+, 4.6), 124 (7.7), 123 (100.0), 81 (10.6), 57 (6.5), 55 (6.5), 53 (26.5), 43 (47.0), 41 (7.9).

(c) NMR δ_H (200 MHz, $CDCl_3$): 0.78 (3 H, d, J = 7.1 Hz), 0.91 (3 H, d, 7.1 Hz), 0.93 (3 H, d, J = 6.9 Hz), 1.49 (3 H, bs), 1.54 (3 H, bs), 1.65 (1 H, sextet, J = 7.5 Hz), 2.02 (1 H, bs), 2.31 (1 H, m). MS (EI) m/e: 138 (M^+, 3.5), 124 (7.6), 123 (100.0), 81 (11.8), 57 (7.6), 55 (8.7), 53 (50.5), 43 (44.6).

1α,2α,3α,4α,5α-Pentamethylcyclopentan-1-ol (6c). To a cold (−25 °C) solution of borane/THF (20 mL, 1.0 M, 20 mmol), was added pentamethylcyclopentene (1.3415 g, 9.45 mmol) (>70% **10a**) over a period of 5 min. The solution was allowed to stand for 5 min and then was quenched with aqueous NaOH (8 mL, 3 M) and methanol (2 mL). Hydrogen peroxide (8 mL, 30%) was added and cooling removed, and the reaction quenched with ether and water. The organic phase was removed, the aqueous phase was washed with ether (3 × 20 mL), the organic portions were combined and dried (K_2CO_3), and the solvent was removed under reduced pressure. Flash chromatography gave a 31% (based on 70% **10a**) recovery (321.5 mg, 2.06 mmol) of the all-cis alcohol **6c**.

NMR δ_H (200 MHz, $CDCl_3$): 0.76 (6 H, d, J = 7.0 Hz), 0.86 (6 H, d, J = 7.3 Hz), 1.01 (3 H, s), 2.0 (2 H, quintet, J = 7.8 Hz), 2.30 (2 H, m). NMR δ_C (22.63 MHz, $CDCl_3$): 10.9 (CH_3), 11.6 (CH_3), 21.0 (CH_3), 37.2 (CH), 48.4 (CH), 82.3 (quat); IR (neat) ν/cm^{-1}: 3369 (s), 2971 (vs), 1448 (m), 1389 (s), 1376 (m), 1106 (m), 975 (m), 917 (s). MS (EI) m/e = 138 (M − 18, 42.6), 123 (77.1), 99 (69.1), 81 (62.7), 72 (65.6), 57 (64.3), 43 (100). Anal.: $C_{10}H_{20}O$ requires 156.1514, found 156.1522.

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