Perfluorinated Cyclic and Acyclic Keto−Enol Systems: A Remarkable Contrast

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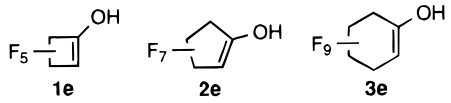
Received November 1, 1996[⊗]

Abstract: Recent reports from this laboratory have revealed that highly fluorinated 4- and 5-membered-ring enols are comparable in stability to, or more stable thermodynamically than, the corresponding ketones, even in non-Lewis-basic media. Work on perfluorinated keto−enol systems has now been extended to 2*H*-perfluorocyclohexanone plus its enol and to a series of acyclic analogues. In carbon tetrachloride, $K_{E/K} = 0.33$ (22 °C) for the six-ring system, but only enol is detectable in Lewis-basic solvents. This shift is attributable to strong hydrogen-bond formation between the enol and Lewis base. A perfluoroenol has been shown to form significantly stronger hydrogen bonds than the potent hexafluoroisopropyl alcohol. Acyclic systems (e.g., 3*H*-perfluoro-2-butanone and its enol) contrast sharply with the cyclic, as no enol is detectable at equilibrium even in powerfully Lewis-basic media. Ab initio quantum mechanical calculations indicate that it is principally the enols, not the ketones, that are responsible for the difference between the two types of keto−enol systems, i.e. acyclic perfluoroenols are strongly destabilized relative to cyclic counterparts.

Introduction

In an intriguing series of papers published mostly in the 1970s, Bekker, Knunyants, and their co-workers described a series of highly fluorinated keto−enol systems with striking properties.[2] Unlike their hydrocarbon counterparts,[3−5] the enols displayed great kinetic stability, resisting ketonization under the influence of both strong acids and high temperatures. In the case of pentafluoroacetone, though, the Russian researchers showed that the keto form is thermodynamically more stable than the enol.[6] They regarded all of their enols as metastable, in fact, separated from lower energy keto forms by high barriers to interconversion.

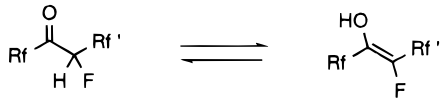
We recently reported, however, that two of the fluorinated enols (**1e** and **2e**) studied by these researchers are more stable *thermodynamically* than their ketones in all media. Among



1e **2e** **3e**

unconjugated and unhindered enols, these are the most stable relative to their ketones that have ever been investigated.[7] It was difficult to reconcile this finding with an earlier report by the Russian chemists claiming that enol **3e** isomerizes to its ketone **3k** in water.[8] We have revisited system **3** and will report the relative stabilities of the keto−enol tautomers in a variety of media.

With work on the cyclic systems complete, our attention was drawn to the fact that highly fluorinated *acyclic* keto−enol systems have remained largely unexplored. Several α-hydrogen bearing perfluorinated ketones of this type have been reported in the literature,[9] but with the exception of pentafluoroacetone,[6] there are no examples of equilibration with their enols. For this reason, keto−enol pairs **4**, **5**, and **6** were synthesized and



System	Rf	Rf '
4	CF_3	F
5	CF_3	CF_3
6	C_3F_7	C_2F_5

the tautomers were equilibrated. We report here that cyclic and acyclic keto−enol systems differ in important ways. Quantum mechanical calculations have been particularly useful in exposing some of the differences, and these will be discussed first.

Results and Discussion

Computational Results. Quantum mechanical calculations we have carried out on a series of highly fluorinated keto−enol systems have underestimated the relative stability of fluorinated enols, but since the degree of underestimation is reasonably consistent, useful comparisons can be made between two systems.[7] Our work on the new keto−enol

[⊗] Abstract published in *Advance ACS Abstracts,* March 15, 1997.

(1) Walter H. Stockmayer Fellow, 1995−96.

(2) For a concise summary of this work, see: Hart, H.; Rappoport, Z.; Biali, S. E. In ref 3, pp 502−514.

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(4) Keeffe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1990**, *112*, 4862.

(5) Toullec, J. In *Advances in Physical Organic Chemistry*; Gold, V.; Bethell, Eds.; Academic Press: London, 1982; Vol. 18, pp 1−77. Chiang, Y.; Hojatti, M.; Keeffe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000.

(6) Bekker, R. A.; Melikyan, G. G.; Dyatkin, B. L.; Knunyants, I. L. *Zh. Org. Khim.* **1975**, *11*, 2370; English translation, p 2415. (b) Bekker, R. A.; Melikyan, G. G.; Dyatkin, B. L.; Knunyants, I. L. *Zh. Org. Khim.* **1975**, *11*, 1370; English translation, p 1356.

(7) (a) Correa, R. A.; Lindner, P. E.; Lemal, D. M. *J. Am. Chem. Soc.* **1994**, *116*, 10795. (b) Lindner, P. E.; Correa, R. A.; Gino, J.; Lemal, D. M. *J. Am. Chem. Soc.* **1996**, *118*, 2556. (c) Lindner, P. E.; Lemal, D. M. *J. Org. Chem.* **1996**, *61*, 5109.

(8) (a) Bekker, R. A.; Popkova, V. Ya.; Knunyants, I. L. *Dokl. Akad. Nauk SSSR* **1977**, *233*, 591; English translation, p 187. (b) Bekker, R. A.; Popkova, V. Ya. *Izv. Akad. Nauk SSSR* **1978**, *12*, 2775; English translation, p 2476.

(9) (a) Martini, T.; Schumann, C. *J. Fluorine Chem.* **1976**, *8*, 525. (b) Saoutina, L. V.; Zapevalov, A. Ya.; Kodess, M. I.; Kolenko, I. P.; German, L. S. *Izv. Akad. Nauk SSSR* **1982**, *11*, 2615. (c) Wiley, D. W.; Simmons, H. E. *J. Am. Chem. Soc.* **1964**, *29*, 1876.

S0002-7863(96)03788-2 CCC: $14.00

Table 1. Ab Initio Energy Differences for Systems **1**, **2**, and **3** at the HF/6-311G**//3-21G Level of Theory

system	*E*(ketone)	*E*(enol)	ΔE (kcal/mol)[a]
1	−724.223 21	−724.221 11	1.3
2	−961.054 76	−961.052 98	1.1
3	−1197.858 27	−1197.852 90	3.4

[a] $\Delta E = E$(enol) − E(ketone).

Table 2. Ab Initio Energy Differences for Systems **1**, **2**, **4**, and **5** at the HF/6-31G**//6-31G** Level of Theory

system	*E*(ketone)	*E*(enol)	ΔE (kcal/mol)[a]
1	−724.040 09	−724.036 01	3.1 (3.3)[b]
2	−960.814 60	−960.810 18	2.8 (2.9)
4	−686.228 51	−686.204 37	15.2
5	−922.987 09	−922.964 46	14.2

[a] $\Delta E = E$(enol) − E (ketone). [b] The values in parentheses are corrected for zero-point vibrational energies, 298 K, and estimated entropy difference. The corrections are based on the HF/6-31G** calculations with frequencies larger than 500 cm^{-1} scaled by 0.893.[25]

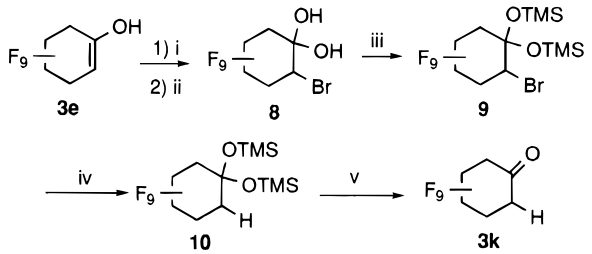
systems was therefore initiated by calculating the keto−enol energy gaps.

All calculations were performed with Gaussian 92.[10] The initial geometry optimizations were carried out at the HF/3-21G level of theory, and the coordinates were used as starting points for the final optimizations at the HF/6-31G** level of theory. An exception to this was system **3**, which was too large to be optimized at the higher level. The lowest energy conformation for ketone **3k** at the HF/6-311G**//3-21G level of theory was a chair structure with the hydrogen atom in the equatorial position. The keto−enol energy gap for system **3** at this level of theory, along with those for systems **1** and **2**, is shown in Table 1. A modest shift toward the ketone in system **3** is predicted relative to systems **1** and **2**. The nearly identical values for systems **1** and **2** show, however, that ring strain does not have a profound effect on relative enol stability.

In contrast to that for system **3**, HF/6-31G** optimization for systems **1**, **2**, **4**, and **5** was not problematic. Two minima for ketone **5k** were examined, one with the trifluoromethyl groups cisoid and the other with them transoid with respect to the single bond connecting the carbonyl carbon and the carbon bearing the hydrogen. The latter was found to have the lower energy as would be anticipated on steric grounds. For all cyclic enols the syn conformers were lower in energy than the anti conformers. On the other hand, the anti conformer of enol **4e** was more stable than the syn by 1.0 kcal/mol. The lowest energy isomer of enol **5e** was the *E* syn conformer.

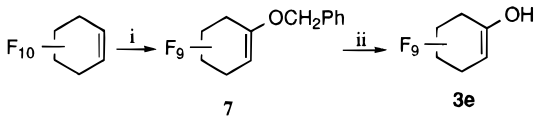
The keto−enol energy gaps for systems **1**, **2**, **4**, and **5** calculated at the HF/6-31G**//6-31G** level of theory are shown in Table 2. Detailed analyses for systems **1** and **2**, including higher level calculations, have been given elsewhere.[7] The data in Table 2 reveal a striking difference in the calculated keto−enol energy gaps for cyclic versus acyclic systems. For example, the gap for system **4** is about 12 kcal/mol larger than for systems **1** and **2**. This could be partly rationalized by the "gem-difluoro effect",[11] the special stabilization of geminal fluorines bound to *saturated* carbon. It is therefore all the more surprising that the keto−enol energy gap for system **5**, where the difluoromethylene group has been eliminated, is about 11 kcal/mol larger than for the cyclic systems.

Scheme 1[a]



[a] Key: (i) Br_2, CH_3CN; (ii) H_2O; (iii) *N*,*O*-bis(trimethylsilyl)acetamide, CH_2Cl_2; (iv) isopropyl alcohol/acetone, *hν*; (v) H_2SO_4, CCl_4.

Synthesis of Keto−Enol Systems 3−6. System 3. Perfluorocyclohex-1-enol (**3e**) was prepared in the 1970s by Bekker and co-workers[8] by the high-temperature acid-induced cleavage of benzyl enol ether **7**. Our work on systems **1** and **2** showed



Key: (i) $KOCH_2Ph$; (ii) H_2SO_4, 1,2,4-$C_6H_3Cl_3$

that this procedure results in significant amounts of dehydrofluorination of the enol but that the enol ethers cleave smoothly with sulfuric acid at room temperature in 1,2,4-trichlorobenzene. The same is true in system **3** as enol **3e** was obtained in 70% yield from compound **7**.

Ketone **3k** was also prepared by the same workers, but in very low yield. We recently reported a high-yield synthesis of 2*H*-perfluorocyclopentanone (**2k**) via bromination of its enol.[7c] The same procedure has been applied to the synthesis of ketone **3k** and appears in Scheme 1.

System 4. The enol of pentafluoracetone has been known for more than 20 years, but the most successful syntheses start with either hexafluoroacetone[12] or chloropentafluoroacetone,[6b] which are highly toxic and expensive. We have now prepared it from the much cheaper and safer hexafluoroisopropyl alcohol.

Qian and Nakai have shown that the lithium enolate of enol **4e** can be generated from hexafluoroisopropyl alcohol with 2 equiv of butyllithium. They claimed that "in reactions with reagents bearing active hydrogens, the initial protonation occurs at the β-carbon, not at oxygen." [13] This is surprising, for hard electrophiles such as proton donors with high-lying LUMOs prefer to attack enolates at oxygen.[14] The enolate of pentafluoroacetone should be no exception, as quantum mechanical calculations of high quality carried out by Dixon and Smart[15] indicate that the negative charge on oxygen is about the same for the enolate anions of pentafluoroacetone and acetone.

Indeed, when the enolate of **4**e was treated with concentrated sulfuric acid in tetrahydrofuran, we found only O-protonation. Qian and Nakai based their conclusion on the reaction of the enolate with water which gave the hydrate of pentafluoroacetone.

(10) Gaussian 92, Revision C.3: Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schelegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian, Inc.; Pittsburgh, PA, 1992.

(11) See, for example: Smart, B. E. In *Molecular Structure and Energetics*; Liebman, J. F.; Greenberg, A., Eds.; VCH Publishers: Deerfield Beach, FL, 1986; Vol. 3, p 141.

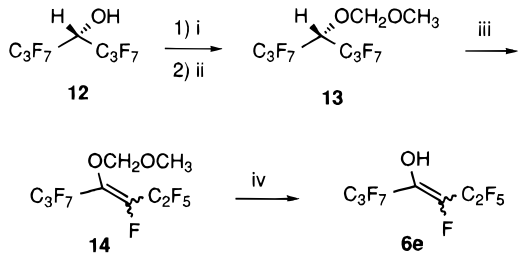
(12) Postovoi, S. A.; Vol'pin, I. M.; Mysov, E. I.; Zeifman, Yu. V.; German, L. S. *Izv. Akad. Nauk SSSR* **1989**, *5*, 1173; English translation, p 1067.

(13) Qian, C. P.; Nakai, T. *Tetrahedron Lett.* **1988**, *29*, 4119.

(14) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976; Chap. 3.

(15) Qian, C. P.; Nakai, T. Dixon, D. A.; Smart, B. E. *J. Am. Chem. Soc.* **1990**, *112*, 4602.

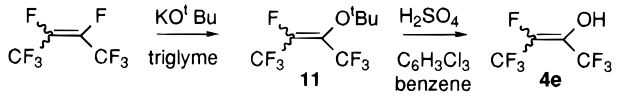
Scheme 2[a]



[a] Key: (i) NaH, Et_2O; (ii) CH_3OCH_2Cl; (iii) LDA, Et_2O; (iv) H_2SO_4, CCl_4.

It seems likely that kinetic protonation in this case also occurred at oxygen but that the enol subsequently hydrated to the gem-diol.[16]

System 5. Enol **5e** was prepared from its *tert*-butyl enol ether as shown:

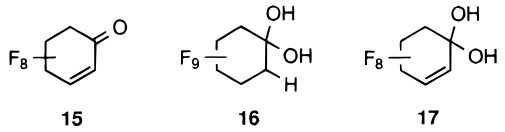


Thus, treating a mixture of (*E*)- and (*Z*)-perfluoro-2-butene (4:1) with potassium *tert*-butoxide in triglyme produced a mixture of (*E*)- and (*Z*)-2-*tert*-butoxyperfluoro-2-butene (1:1) (**11**). The enol was generated by adding a drop of sulfuric acid to the *E* and *Z* enol ethers in 1,2,4-trichlorobenzene as solvent containing a slight excess of benzene to serve as a *tert*-butyl cation trap. The most notable difference between the ^{19}F NMR spectra of the enol ethers and the enols is that the vinyl fluorines of the *E* and *Z* enols appear 21.3 and 19.2 ppm further upfield than the corresponding fluorines in the *E* and *Z* enol ethers.

System 6. Ketone **6k** was prepared in 1964 by Wiley and Simmons.[9c] Prior to the present work the enol had never been detected, however. Throughout our research on related keto−enol systems we have been frustrated by the fact that a method used to prepare one enol is not adaptable to the synthesis of another. Enol **6e** proved to be no exception. The *tert*-butyl enol ether route employed in system **5** was not feasible because perfluoro-3-heptene was not readily available and because it would give a mixture of regio- as well as stereoisomers. We therefore focused on trapping the enolate of **6e**, generated from perfluoro-4-heptanol,[17] with sulfuric acid as in the synthesis of **4e**. This route failed to produce the desired enol, however, because β-elimination of fluoride from the enolate was so facile, even at −78 °C, that it could not be trapped by sulfuric acid.

Perfluoro-4-heptanol was therefore protected as its methoxymethyl ether, **13**, with the hope that its dehydrofluorination would proceed smoothly. Indeed, treating compound **13** with lithium diisopropylamide (LDA) in ether produced enol ether **14** with a *Z*:*E* ratio of 1:4.[18] The mixture of enol ethers was cleaved at room temperature by sulfuric acid to give enol **6e** with complete retention of configuration (Scheme 2).

Keto−Enol Equilibration Studies. Equilibration of System 3. As noted above, Bekker, Knunyants, and co-workers reported that enol **3e** isomerizes in water to ketone **3k**, together with enone **15**.[8] Their conclusion was based on an experiment in which the enol was treated with water, followed by distillation from concentrated sulfuric acid to give ketone **3k** and enone **15**, in approximately equal amounts. This experiment does not prove that the keto−enol equilibrium lies far toward the ketone, however, as ketone **3k** surely hydrated[19] in the aqueous medium; hydration should drive ketonization powerfully. We have confirmed this expectation by showing that treating enol **3e** with water generates gem-diols **16** and **17**, with no detectable amount of either ketone.



We therefore set out to determine the position of the keto−enol equilibrium for system **3**. Establishment of equilibrium in systems **1** and **2** was facile at 25 °C in carbon tetrachloride containing a trace of the very weak base *N*-methylpyrrolidone (NMP) as catalyst. Carbon tetrachloride was chosen as solvent because it should provide for meaningful comparisons between experiment and the gas phase calculations. Subjecting enol **3e** to these conditions resulted in the gradual rise of signals for the ketone. After 12 h, a constant keto−enol ratio of 3:1 was achieved. The same composition was obtained when the equilibrium was approached from the ketone side to give a reliable equilibrium constant of $K_{\mathbf{3e/3k}} = 0.33 \pm 0.02$ (22 °C). This shift toward the keto form with respect to systems **1** and **2** is consistent with the calculated keto−enol gaps in Table 1.

Since Table 1 indicates a difference in keto−enol gap of only about 2 kcal/mol between systems **1/2** and **3**, the new result suggests that ketones **1k** and **2k** lay just beyond our detection limits in the earlier equilibration studies with their enols. Thus, we decided to revisit these experiments and carry out the equilibrations at higher concentrations with the hope of detecting trace amounts of the ketones. Indeed, in the case of system **2**, by using long accumulation times and 0.5 M solutions, we could pull signals for **2k** out of the baseline of the ^{19}F NMR spectrum. Careful integration of the appropriate signals revealed that $K_{\mathbf{2e/2k}} = 130 \pm 20$ in carbon tetrachloride at 22 °C. In a parallel experiment starting with **1e**, no ketone could be detected; the lower limit for $K_{E/K}$ was thereby extended to 250. Though data in Tables 1 and 2 predict slightly greater relative stability for **2e** than for **1e**, calculations at the MP2/6-311G**//6-31G** level (which begin to take into account electron correlation) predict the opposite.[7b,c] At this level **1e** is predicted to be 1.2 kcal/mol lower in relative energy than **2e**, consistent with the experimental result.

Interestingly, the keto−enol gap for 2*H*-perfluorocyclopropanone (**18k**) and its enol (**18e**) is only 4.1 kcal/mol at the HF/6-31G**//6-31G** level of theory. Since this is nearly equal to the energy gaps for systems **1** and **2**, the enol should be present in substantial concentration at equilibrium in the 3-membered-ring system as well. This represents a sharp contrast with the hydrocarbon parents, as the keto−enol energy gap for cyclopropanone and its enol is calculated to be 27.1 kcal/mol at the same level of theory.

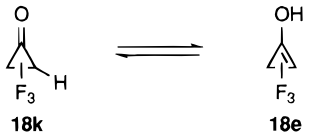
Earlier work in this laboratory has shown that the equilibrium compositions in cyclic, fluorinated keto−enol systems are dramatically shifted toward the enols by Lewis basic solvents because of strong hydrogen bonding between the enol and the Lewis base. This effect is seen clearly in system **3**, as addition

(16) We have shown that treating enol **4e** with water gives the gem-diol.

(17) The alcohol was obtained in 65% yield by $LiAlH_4$ reduction of perfluoro-4-heptanone, which was prepared by the method of Tamborski. Chen, L. S.; Chen, G. J.; Tamborski, C. J. *J. Fluorine Chem.* **1984**, *26*, 341.

(18) The enol ether prepared from $CF_3CH(OMEM)CF_2CF_3$ with LDA in THF showed a *Z*:*E* ratio of 1:3 (ref 15).

(19) Fluorinated ketones exist as their hydrates in water. See, for example: Guthrie, J. P. *Can. J. Chem.* **1975**, *53*, 898.



18k **18e**

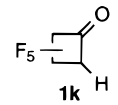
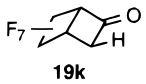
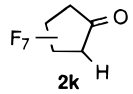
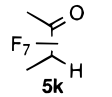
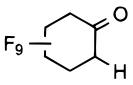
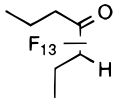
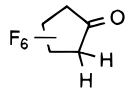
of 10 equiv of dry tetrahydrofuran to the equilibrium mixture in carbon tetrachloride shifts the equilibrium such that no ketone is detectable by ^{19}F NMR spectroscopy. Since hydrogen bonding is so important in these systems, we set out to determine the strength of the hydrogen bond between the enol **1e** and tetrahydrofuran in carbon tetrachloride. We have previously reported that the chemical shift of the vinyl fluorine of the enols is very sensitive to hydrogen bonding interactions.[7b] For example, the vinyl fluorine of **1e** shifts 4.2 ppm upfield when 1 equiv of THF is added to a 0.13 M solution of the enol in carbon tetrachloride. This feature has been used to assess the enol's hydrogen-bonding ability.

Enthalpies and entropies of hydrogen-bond formation are most conveniently extracted from van't Hoff plots where the association constant for the hydrogen-bond equilibrium is calculated at several temperatures.[20] It is well documented, however, that the calculation of association constants is littered with many pitfalls. In particular, only data points that are between 20% and 80% saturation should be used in calculating K_{assoc}.[21] This made our measurements difficult as the enol and THF bind so tightly in CCl_4 that the measurements had to be made at enol concentrations less than 50 mM. Working at high dilution caused a problem in that adventitious water competed with the THF for hydrogen bonding to the enol. Large uncertainties in $\Delta H°$ and $\Delta S°$ of hydrogen-bond formation therefore resulted.

With the hope of obtaining useful information at higher concentrations, our focus changed to comparing the hydrogen-bond strength of enol **1e** with that of the well-studied, powerful hydrogen-bond-donor hexafluoroisopropyl alcohol.[22] All of the thermodynamic data for the hydrogen bonding of hexafluoroisopropyl alcohol to various Lewis bases is in methylene chloride as solvent. A competition experiment was therefore set up in which equimolar amounts of hexafluoroisopropyl alcohol and enol **1e** competed for 1 equiv of acetonitrile in methylene chloride. The ratio of association constants for hydrogen-bond formation of acetonitrile to the enol and alcohol was found to be 13:1 (22 °C). In other words, *the free energy of hydrogen-bond formation with acetonitrile in methylene chloride solution is 1.5 kcal/mol more negative for the enol than for hexafluoroisopropyl alcohol.*[23] In the nonpolar solvent carbon tetrachloride the hydrogen-bond strengths would be greater yet.

Equilibration of Acyclic Keto−Enol Systems. The most interesting result from the ab initio calculations in Table 2 was the finding that, in striking contrast to cyclic enols, acyclic enols were *much less stable* than their ketones. Bekker and coworkers have shown that this is the case for system **4**, as the enol ketonized completely over the course of several days in refluxing methylene chloride.[6,24] We now report that the same is true for system **5**: adding a trace of NMP to a 0.5 M solution of enol **5e** in carbon tetrachloride resulted in complete ketonization after 12 h.

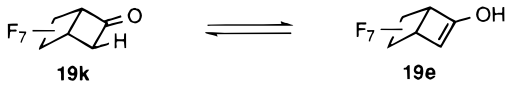
Table 3. Keto−Enol Equilibrium Constants in CCl_4[a]

Ketone[b]	$K_{E/K}$	Ketone[b]	$K_{E/K}$
 **1k**	>250	 **19k**	0.07 ± 0.01
 **2k**	130 ± 20	 **5k**	<0.005
 **3k**	0.33 ± 0.02	 **6k**	very small
 **20k**	0.15 ± 0.01		

[a] Measurements were made at 22 °C. [b] For systems **1** and **19**, see ref 7b; for **2** and **20**, see ref 7c. [c] It is not known whether $K_{E/K}$ for **6** is larger or smaller than that for **5**.

One difference between enol **5e** and the cyclic enols, of course, is that the former has a double bond which is flanked by CF_3 groups whereas the latter have CF_2 groups attached to the double bond. To determine whether this difference has a critical effect on the equilibrium, enol **6e**, in which each end of the double bond bears CF_2 groups, was synthesized. As expected, when **6e** was treated with a trace of NMP in carbon tetrachloride, complete ketonization was observed. The sharp contrast in relative enol stabilities between cyclic and acyclic systems is therefore quite general.

As discussed earlier, Lewis-basic solvents shift the keto−enol equilibrium dramatically toward the enol. In the case of system **19**, for example, little enol was present at equilibrium



19k **19e**

in carbon tetrachloride, but no ketone was detectable in Lewis-basic media such as acetonitrile and tetrahydrofuran. Stabilization of enols **5e** and **6e** by acetonitrile was not enough, however, to make any enol detectable at equilibrium in those systems. In the case of system **5**, 0.5% enol would have been found. Furthermore, there was no detectable amount of **5e** at equilibrium in a powerfully Lewis-basic pyridine/NMP (1:5 (v/v)) solvent system.

Summary and Analysis of Keto−Enol Equilibria. Equilibrium constants for all of the keto−enol systems we have studied are presented in decreasing order in Table 3. *The >50 000-fold range convincingly confirms the existence predicted by the ab initio calculations of a gulf between acyclic and certain cyclic systems.* From Table 2, the difference of 11.1 kcal/mol between the ΔE's for systems **1** and **5** would translate into a difference in equilibrium constants by a factor of 1.7×10^8 if $\Delta S°$ were the same for both systems. Even

(20) Gellman, S. H.; Dado, G. P.; Liang, G. B.; Adams, B. R. *J. Am. Chem. Soc.* **1991**, *113*, 1164.

(21) Deranleau, D. A. *J. Am. Chem. Soc.* **1969**, *91*, 4044.

(22) (a) Purcell, K. F.; Stikeleather, J. A.; Brunk, S. D. *J. Mol. Spectrosc.* **1969**, *32*, 202. (b) Purcell, K. F.; Stikeleather, J. A.; Brunk, S. D. *J. Am. Chem. Soc.* **1969**, *91*, 4019.

(23) The enthalpy of hydrogen-bond formation between hexafluoroisopropyl alcohol and acetonitrile is 5.9 kcal/mol in methylene chloride (ref 22b). We cannnot assign a corresponding value for the enol because the entropy of hydrogen-bond formation for the two donors may differ considerably. $\Delta S°$ for the bulky hexafluoroisopropyl alcohol may be significantly more negative than for the enol (Kivinen, Murto, J.; Liljequist, S.; Vaara, S. *Acta Chem. Scand.* **1975**, *A29*, 911).

(24) The Russian group also prepared the enol of 3*H*-perfluoro-2-pentanone and reported that it ketonizes in water. As in the case of **3k**, however, hydration of the ketone must have driven the equilibrium, so this result does not reveal the relative energies of the keto and enol forms. Bekker, R.A.; Popkova, V. Ya.; Snegirev, V. G.; Knunyants, I. L. *Izv. Akad. Nauk SSSR* **1983**, *3*, 620; English translation, p 560.

with allowance for a substantial $\Delta\Delta S°$ between the cyclic and acyclic systems, the quantum mechanical calculations indicate that the lower limit determined experimentally for the difference in equilibrium constants is very conservative. The value of $K_{E/K}$ given in Table 3 for system **5**, <0.005, is the upper limit which we measured directly in carbon tetrachloride. However, the true equilibrium constant must be far smaller yet in light of our failure to detect enol even in strongly Lewis-basic media. Thus, the ab initio calculations are probably not far from the mark in their prediction of the magnitude of the cyclic−acyclic gulf.

In that regard, the three systems in Table 3 for which both experimental and HF/6-31G**//6-31G** energies are available, *viz.* **2**, **19**, and **20**, provide a measure of the value of the calculations for comparing keto−enol systems. The discrepancies between experiment and theory are large for all three systems, *viz.* 5.8, 6.3, and 5.4 kcal/mol, respectively. Although only the calculated values for **2** and **20** were corrected for zero-point energy, temperature, and entropy differences, those corrections were just 0.1−0.2 kcal/mol. *The close agreement among the three discrepancies inspires confidence that calculations at this level predict $\Delta\Delta G°$ fairly accurately in comparing one keto−enol system with another. They therefore make possible a reasonable estimate of $K_{E/K}$ for systems in which this constant is so large or small as to be experimentally inaccessible.*

Though we were only able to measure a lower limit for $K_{E/K}$ in the case of system **1**, the calculations leave little doubt that the true equilibrium constant lies close to that limit. At the HF/6-31G**//6-31G** level of theory, **2e** is actually predicted to enjoy slightly greater relative stability than **1e**, contrary to the small difference of opposite sign revealed by experiment. As noted above, at the higher MP2/6-311G**//6-31G** level, the ΔE values are correctly ordered, 1.1 kcal/mol for system **1** and 2.3 kcal/mol for **2**.

Comparing **19** with **1** and **20** with **2** in Table 3 reveals the importance of α-fluorines in determining the magnitude of $K_{E/K}$. The substantial difference in $K_{E/K}$ between system **3** and **1** or **2** can be understood if one assumes that, as ring size increases, the factors which make acyclic systems so different begin to come into play. Support for this interpretation is provided in the following paper.

Reason for the Cyclic−Acyclic Contrast. Are the large differences in keto−enol energy gaps between cyclic and acyclic systems attributable to the ketones, the enols, or both? We first considered the ketones. The energy changes for the set of isodesmic reactions in Figure 1 were calculated at the HF/6-31G**//6-31G** level. Those very small changes reveal that, referenced to saturated compounds, cyclic fluoroketones are not significantly destabilized relative to acyclic counterparts.

We therefore turned our attention to the enols and carried out similar calculations on the following set of isodesmic reactions (Figure 2). The same saturated reference compounds were employed, but this time large energy differences emerged. Clearly, as compared with the reference compounds, acyclic perfluoroenols are strongly destabilized relative to cyclic ones.

Also of interest is the question of how the fluorocarbon systems which have been discussed compare with corresponding hydrocarbon-derived keto−enol pairs. The isodesmic reactions in Figure 3, again calculated at the HF/6-31G**//6-31G** level, address this question for the set of ketones. As anticipated, the ΔE's are all large and positive because fluorination destabilizes ketones. The fact that the ΔE's are all similar to one another shows that it makes little difference whether the ketone be cyclic or acyclic. A dichotomy appears in Figure 4, however, where enols are compared analogously. In the cyclic cases the ΔE's are relatively small compared with those for the acyclic examples. Thus, in comparison with hydrocarbon counterparts, the cyclic/acyclic contrast is again attributable primarily to differences in the enols, not the ketones. Reasons for this unexpected finding, the implications of which extend beyond the realm of keto−enol chemistry, are discussed in the following paper.

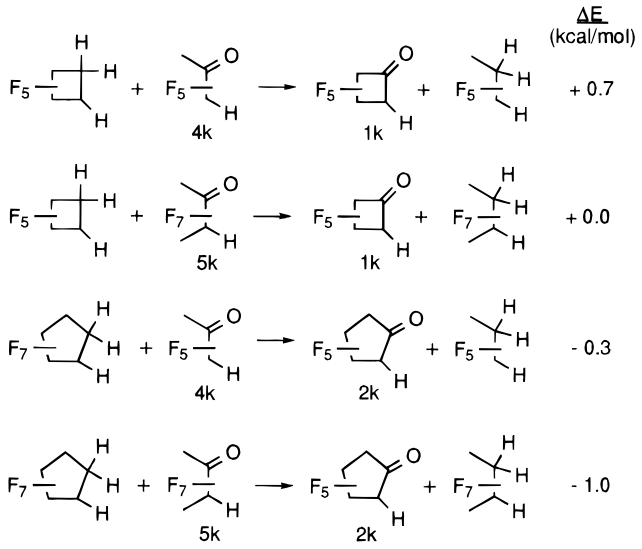


Figure 1. Carbonyl group transfer reactions between cyclic and acyclic molecules.

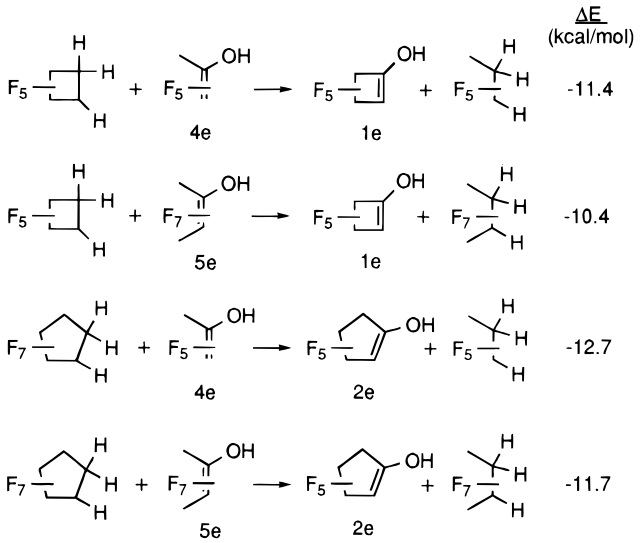


Figure 2. Enol group transfer reactions between cyclic and acyclic molecules.

Conclusion

Though perfluorocyclohexen-1-ol enjoys somewhat less stability relative to its ketone than is the case for its 4- and 5-membered-ring analogues, all three cyclic systems contrast markedly with acyclic counterparts. The acyclic enols are much less stable than their ketones even in Lewis-basic solvents, to which fluoroenols have been shown to form unusually strong hydrogen bonds. High-level ab initio calculations anticipate this surprising difference and show that it arises not from the ketones but from destabilization of acyclic relative to cyclic perfluoroenols. The large destabilization is found whether saturated fluorocarbon derivatives or the hydrocarbon analogues of the fluorinated keto−enol pairs are chosen as reference compounds. Reasons underlying this phenomenon are presented in the paper which follows.

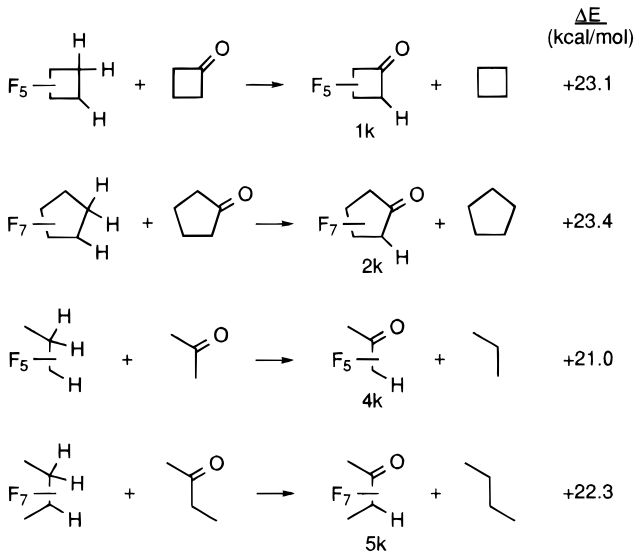


Figure 3. Carbonyl group transfer reactions between hydrocarbon and fluorocarbon derivatives.

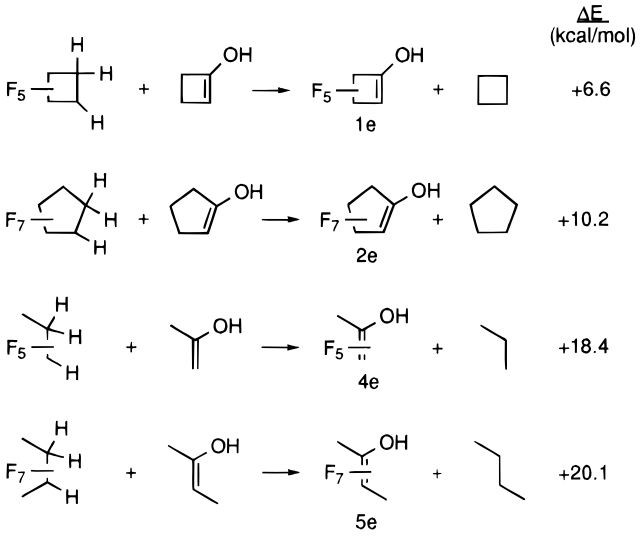


Figure 4. Enol group transfer reactions between hydrocarbon and fluorocarbon derivatives.

Experimental Section

^{19}F NMR spectra were recorded at 282.2 MHz, and all chemical shifts are reported on the Φ scale (ppm from internal trichlorofluoromethane, upfield negative). The ^{1}H NMR spectra were recorded at 300 MHz with tetramethylsilane as the internal standard; chemical shifts are reported on the δ scale. Carbon tetrachloride was distilled from phosphorus pentoxide and acetonitrile from calcium hydride. Diethyl ether and tetrahydrofuran were distilled from potassium benzophenone ketyl. Perfluoro-2-butene was obtained from PCR, Inc., as a mixture of cis and trans isomers.

Analytical gas chromatograms were obtained with a 25 m methyl silicone capillary column and flame ionization detector. The standard program was as follows: carrier pressure 25 psi; injector 150 °C; detector 200 °C; column temperature is noted in text. Isolation of pure compounds was done by preparative GC using a thermal conductivity detector. The column used was 25 ft × $^{1}/_{8}$ in, 20% QF-1 on 80/100 mesh Chromosorb-W HP. The standard program was as follows: injector 190 °C; detector 210 °C; column temperature is noted in text. Isolated yields were corrected for purity. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

The quantum mechanical calculations were performed on Gaussian 92, Revision C.3.[10] Vibrational frequencies were calculated at the HF/6-31G** level of theory and those >500 cm^{-1} were scaled by 0.893.[25]

Hydrogen-Bonding Competition. To a 5 mL round-bottom flask containing ca. 0.1 g of P_2O_5 was added 500 μL of methylene chloride. The flask was attached to a vacuum line, and the contents were degassed by two freeze−pump−thaw cycles. The methylene chloride was statically transferred (20 °C, 30 mTorr) to a flame-dried NMR tube. Freshly prepared enol **1e**[7b] was then transferred in vacuo to the same tube. The contents of the tube were carefully thawed under nitrogen, and the tube was capped with a rubber septum. As an internal standard, 1.0 μL of hexafluorobenzene (8.9×10^{-3} mmol) was added; ^{19}F NMR integration of the hexafluorobenzene-to-enol signals revealed 4.8×10^{-2} mmol of **1e** (96 mM). The initial chemical shift for the vinyl fluorine of **1e** was $\Phi_{free} = -139.27$ ppm.

An equimolar quantity (4.8×10^{-2} mmol) of acetonitrile was introduced by adding 2.5 μL to the enol solution. The new chemical shift of the vinyl fluorine was $\Phi = -140.65$ ppm. Hexafluoroisopropyl alcohol (5.0 μL, 4.8×10^{-2} mmol) was added to the tube; the vinyl fluorine shifted to $\Phi = -140.55$ ppm. A separate experiment revealed that hexafluoroisopropyl alcohol itself does not perturb the vinyl fluorine signal. The saturation chemical shift of the enol complex was determined by adding acetonitrile until the chemical shift of the vinyl fluorine no longer changed; a total of 20 μL was required to give $\Phi_{sat} = -141.34$ ppm.

From these data the fraction of enol complexed in the presence of equimolar acetonitrile was first calculated (0.67), and from this value, the equilibrium constant for complexation was obtained ($K_e = 64$). The chemical shift following addition of hexafluoroisopropyl alcohol revealed the new fraction of enol that was complexed (0.62), from which the concentration of free acetonitrile (0.025 M) was calculated using K_e. From the difference between the total acetonitrile concentration and the sum of the enol-bound and free concentrations, the concentration of complexed hexafluoroisopropyl alcohol was obtained (0.011 M). This allowed determination of the equilibrium constant for complexation of the alcohol ($K_a = 5.0$). Thus, $K_e/K_a = 13$, with the error estimated to be ±1. It follows that the free energy of hydrogen bonding of acetonitrile to the enol is 1.5 kcal/mol greater than that to hexafluoroisopropyl alcohol in methylene chloride at 22 °C.

Equilibration of 2e and 2k. A solution of ketone **2k** in 500 μL of CCl_4 was prepared as described previously.[7c] The concentration was determined by adding 51.0 μL (8.9×10^{-3} mmol) of a 0.17 M solution of hexafluorobenzene in CCl_4 to the ketone solution. Integration of the hexafluorobenzene-to-ketone signals revealed $3.5(5) \times 10^{-1}$ mmol of ketone. Care must be taken to use delay times of at least 8 s in the NMR acquisition to allow full relaxation of all nuclei. Then 150 μL (1.52×10^{-3} mmol) of a 0.010 M solution of NMP in CCl_4 was added to catalyze the enolization. The initial ketone concentration was 0.50 M. The reaction was followed by ^{19}F NMR spectroscopy until the keto-to-enol ratio remained constant. Three different integral regions were averaged for the enol signal at $\Phi = -161$ ppm (vinyl F) and the ketone signal $\Phi = -218$ ppm (F geminal to H). This experiment was repeated three times in the concentration range 0.26−0.50 M to give an equilibrium constant of $K_{2e/2k} = 130 \pm 20$. The error is the standard deviation in the measurements.

Equilibration of 1k and 1e. From Ketone. Ketone **1k** was statically transferred at −23 °C (30 mTorr) to a cold NMR tube (−196 °C) containing 2.0 mL of dry CCl_4 and 1.0 μL (8.7×10^{-3} mmol) of hexafluorobenzene as an internal standard. After the tube had been carefully warmed under a nitrogen atmosphere, integration of the ketone and hexafluorobenzene signals revealed 2.6×10^{-3} mmol of **1** (1.3 mM). A 1.3 μL aliquot of a 0.020 M solution of 1-methyl-2-pyrrolidone (2.6×10^{-5} mmol) in CCl_4 was added via syringe. After 24 h, no ketone was detectable by ^{19}F NMR spectroscopy. This experiment had to be carried out at very low concentration to avoid hemiketal formation, but that problem does not arise starting from the enol.

From Enol. Freshly prepared enol **1e** was statically transferred to a flame-dried NMR tube containing 500 μL of dry carbon tetrachloride. The concentration was determined by adding 1.0 μL (8.7×10^{-3} mmol) of hexafluorobenzene to the tube. Integration of the hexafluorobenzene-to-enol signals revealed 2.0×10^{-1} mmol of enol (0.40 M). Then 10 μL (1.0×10^{-3} mmol) of a carbon tetrachloride solution that was 0.10

(25) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. S. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

M in both perfluoromethylcyclohexane and *N*-methylpyrrolidone was added. The purpose of the perfluoromethylcyclohexane was to have an area standard close in chemical shift to the ketone signal to ensure optimal integration. After 4 h, integration of the enol (Φ −139.0)-to-perfluoromethylcyclohexane (Φ −190.2) signals revealed a (140 ± 20)-to-1 ratio, but the signal at Φ −205.8 ppm for ketone **1k** was not detectable. The same was true after 16 h. On the basis of the signal-to-noise ratio of the perfluoromethylcyclohexane resonance, which had approximately the same line width as the ketone signal, the ratio of enol-to-ketone was clearly >250.

Perfluorocyclohex-1-enol (3e). To a dry 50 mL round-bottom flask containing 15 mL of 1,2,4-trichlorobenzene and a stir bar was added 3.2 g (9.1 mmol) of 1-benzoxyperfluorocyclohexene.[8] The reaction vessel was attached to the vacuum line, and two U-traps cooled to −13 °C (ethylene glycol/CO_2(s)) and −78 °C (isopropyl alcohol/CO_2(s)) were attached in series. Concentrated sulfuric acid (10 mL, 0.19 mol) was added, and the heterogeneous liquids were stirred vigorously for 2 min. All volatile products were removed under reduced pressure (30 mTorr) and collected in the U-traps. The −13 °C U-trap contained only 1,2,4-trichlorobenzene and the −78 °C U-trap contained 1.7 g (77% yield) of enol **3e** (95%) and enone **15** (5%). The ^{19}F and ^{1}H NMR spectra of both compounds were consistent with those reported elsewhere.[8]

2-Bromoperfluorocyclohexane-1,1-diol (8). Freshly prepared enol **3e** (3.0 g, 12 mmol) was statically transferred at 15 mTorr to a 25 mL round-bottom flask containing 10 mL of dry acetonitrile. With the vessel cooled in an ice bath, bromine (3 mL, 60 mmol) was added at once, followed by 20 mL of water. Residual bromine was quenched with 10 mL of a saturated solution of sodium thiosulfate, and the product was extracted with 3 × 15 mL of diethyl ether. The solvents were removed first on a rotary evaporator and then with a vacuum pump at 1 Torr. Analysis of the ^{1}H NMR spectrum revealed 0.6 equiv of acetonitrile complexed to the hydroxyl groups. Otherwise, the light yellow oil was shown to be pure by ^{19}F NMR spectroscopy (3.5 g, 82% yield). ^{19}F NMR (CD_2Cl_2): Φ −109.5, −128.8 (AX q, J = 270 Hz, 2F); −119.8, −135.8 (AX q, J = 278 Hz, 2F); −121.4, −140.6 (AX q, J = 280 Hz, 2F); −122.1, −137.5 (AX q, J = 285 Hz, 2F); −132.2 (m, 1F). ^{1}H NMR (CD_2Cl_2): δ 5.5 (bs, 2H); 2.01 (s, 3H).

2-Bromo-1,1-bis(trimethylsiloxy)perfluorocyclohexane (9). To a dry 25 mL round-bottom flask equipped with a Teflon stir bar was added 2 mL of *N*,*O*-bis(trimethylsilyl)acetamide (8 mmol) and 20 mL of methylene chloride. At ambient temperature 0.90 g (2.5 mmol) of diol **8** dissolved in 5 mL of methylene chloride was added dropwise with stirring to the reaction vessel. After 15 min the reaction mixture was washed with one 10 mL portion of water, and the methylene chloride layer was separated and dried over $MgSO_4$. The solution was concentrated and the resulting liquid passed through a silica gel column with methylene chloride as the eluting solvent to remove residual silating agent. After removal of the solvent in vacuo, 1.1 g of **9** was obtained as a clear, colorless liquid (88% yield). ^{19}F NMR ($CDCl_3$): Φ −109.5, −127.8 (AX q, J = 280 Hz, 2F); −117.2, −133.0 (AX q, J = 273 Hz, 2F); −120.6, −140.1 (AX q, J = 281 Hz, 2F); −121.6, −137.8 (AX q, J = 277 Hz, 2F); −130.8 (m, 1F). ^{1}H NMR ($CDCl_3$): δ 0.14 (s, 9H); 0.24 (s, 9H). MS: *m/e* 395 ($C_9H_{10}{}^{81}BrF_8OSi^+$), 393 ($C_9H_{10}{}^{79}BrF_8OSi^+$), 147 ($C_5H_{15}OSi_2^+$), 73 ($C_3H_9Si^+$). HRMS: calcd for $C_{12}H_{18}{}^{79}BrF_9O_2Si_2$, 499.9885; found, 499.9876.

2*H*-1,1-Bis(trimethylsiloxy)perfluorocyclohexane (10). A solution consisting of 300 mg (0.600 mmol) of compound **9**, 8 mL of isopropyl alcohol, and 1 mL of acetone was irradiated in a Pyrex tube with a 450 W medium-pressure Canrad-Hanovia mercury lamp for 30 min. Pentane (20 mL) was added, and the product was washed with 20 mL of water to remove isopropyl alcohol and hydrogen bromide. The pentane layer was separated, dried over $MgSO_4$, and filtered. After the solvent was removed by short-path distillation, a dynamic vacuum transfer at 25 °C (30 mTorr) left behind all high-boiling material. The volatile fraction contained 180 mg of compound **10** as a clear, colorless oil (71% yield). The liquid was obtained analytically pure by preparative GC (170 °C, t_R = 10.4 min). ^{19}F NMR (C_6D_6, 25 °C): −120.0, −128.0 (AB q, J = 283 Hz, 2F); −129.0 to −134.0 (broad m, 6F); −212.0 to −216.0 (broad s, 1F). The ^{19}F NMR spectrum sharpens considerably at 70 °C as chair−chair interconversion occurs faster, but certain peaks in the −129 to −134 ppm range are still not resolvable. The spectrum remains broad down to −50 °C. ^{1}H NMR (C_6D_6, 25 °C): 0.24 (s, 18H); 4.60 (broad d, J = 48 Hz, 1H). MS: *m/e* 422 (M^+), 147 ($C_5H_{15}OSi_2^+$), 73 ($C_3H_9Si^+$). Anal. Calcd for $C_{12}H_{19}F_9O_2Si_2$: C, 34.12; H, 4.53; F, 40.48. Found: C, 34.44; H, 4.68; F, 40.29.

2*H*-Perfluorocyclohexanone (3k).[8] To a 5 mL round-bottom flask containing 63 mg of compound **10** (0.15 mmol) and 2.0 mL of carbon tetrachloride was added 0.1 mL of concentrated sulfuric acid (2.0 mmol). The contents were well-stirred for 20 h under nitrogen, and then all volatiles were removed at 30 mtorr to a U-trap cooled to −78 °C. The contents of the U-trap were statically transferred (25 °C, 30 mTorr) to a flame-dried NMR tube; the total volume was 1.0 mL. After the tube had been carefully thawed under nitrogen, 1.0 μL (8.7×10^{-3} mmol) of hexafluorobenzene was added. Integration of the ketone-to-hexafluorobenzene signals in the ^{19}F NMR spectrum revealed 0.12 mmol of ketone **1k** (80% yield). ^{19}F NMR ($CDCl_3$): Φ −115.2, −139.7 (AX q, J = 291 Hz, 2F); −124.3, −144.2 (AX q, J = 290 Hz, 2F); −125.6, −143.8 (AX q, J = 280 Hz, 2F); −126.2, −130.6 (AB q, J = 268 Hz, 2F); −226.7 (d, J = 47 Hz, 1F).

Equilibration of 3e and 3k. To the 0.12 M solution of **3k** in CCl_4 prepared above was added 120 μL (0.0012 mmol) of a 0.010 M NMP solution in CCl_4. The reaction was monitored by ^{19}F NMR spectroscopy for 12 h, i.e. until well after the keto:enol ratio had become constant. Starting with the ketone, K_E values of 0.35 and 0.33 were obtained in separate runs. When equilibrium was approached from the enol side, the enol/ketone ratio was found to be 0.32, leading to an average value of 0.33 for $K_{3e/3k}$.

(*E*)- and (*Z*)-2-*tert*-Butoxyperfluoro-2-butene (11). With the aid of a dry ice condenser, 5.0 g (25 mmol) of (*E*)- and (*Z*)-perfluoro-2-butene (4:1) was distilled into a dry 100 mL three-neck round-bottom flask containing 15 mL of freshly distilled triglyme. A 1.2 M solution of potassium *tert*-butoxide in triglyme was added dropwise to the reaction vessel with efficient stirring at 0 °C. The progress of the reaction was monitored by ^{19}F NMR spectroscopy. After all of the olefin was consumed, the volatile products were removed at 20 °C (1 Torr) to a U-trap cooled to −78 °C (isopropyl alcohol/CO_2(s)). The contents of the U-trap were thawed to produce 1.5 g (24% yield) of a 50:50 mixture of the *E* and *Z* isomers of **11**, which were not separated. ^{19}F NMR ($CDCl_3$).[26] *Z* isomer: −64.4 (q, J = 15 Hz, 3F); −66.8 (q, J = 15 Hz, 3F); −132.2 (s, 1F). *E* isomer: −65.6 (d, J = 23 Hz, 3F); −67.7 (s, 3F); −142.5 (q, J = 23 Hz, 1F). ^{1}H NMR ($CDCl_3$). *E* and *Z* isomers: 1.32 (s); 1.34 (d, J = 1.2 Hz), respectively. Anal. Calcd for $C_8H_9F_7O$: C, 37.82; H, 3.57; F, 52.18. Found (both isomers): C, 37.53; H, 3.47; F, 52.16.

(*E*)- and (*Z*)-Perfluoro-2-buten-2-ol (5e). A 50:50 mixture of *E* and *Z* isomers of **11** (50 mg, 0.20 mmol) was added to an NMR tube containing 0.5 mL of $CDCl_3$/benzene (95:5 v/v). Two drops of concentrated sulfuric acid were added, and the NMR tube was shaken vigorously for 1 min. The organic layer was decanted from the acid and transferred to a dry NMR tube. The ^{19}F NMR showed clean and quantitative conversion to a 50:50 mixture of *E* and *Z* isomers of **5e**. ^{19}F NMR ($CDCl_3$). *Z* isomer: −65.5 (q, J = 15 Hz, 3F); −66.2 (q, J = 15 Hz, 3F); −153.7 (s, 1F). *E* isomer: −66.8 (s, 3F); −68.9 (d, J = 23 Hz, 3F); −163.5 (q, J = 23 Hz, 1F). ^{1}H NMR ($CDCl_3$). *E* and *Z* isomers: 4.6 (broad s).

Equilibration of 5e and 5k. The enol was prepared as above except CCl_4 and bibenzyl were substituted for $CDCl_3$ and benzene, respectively. The enol/CCl_4 solution was removed from the acid by a dynamic vacuum transfer at 20 °C (30 mTorr) with the volatiles collected in a U-trap cooled to −78 °C. The contents of the trap were statically transferred to an NMR tube and carefully thawed under nitrogen. To catalyze the equilibration, 5 μL of NMP was added and the reaction

(26) Assignment of the *Z* and *E* enol ethers was established by analysis of the ^{19}F NMR spectrum. The trifluoromethyl groups of the *Z* isomer split each other into quartets with a coupling constant of 15 Hz as a consequence of through-space interaction of the CF_3 groups. The vinyl fluorine appears as a sharp singlet at −132.2 ppm. For the *E* isomer the splitting pattern is different, as one CF_3 group appears as a singlet at −67.7 ppm and the other as a doublet (J = 23 Hz) centered at −65.6 ppm. This doublet splitting arises from through-space coupling between the trifluoromethyl group and the vinyl fluorine that is cis to that CF_3 group. Splitting of the vinyl fluorine into a quartet (J = 23 Hz) also reflects this coupling. The *E* and *Z* isomers of the enol (**5e**) were assigned analogously.

was monitored by ^{19}F NMR spectroscopy. After 12 h, complete and clean conversion to ketone **5k**[9a,b] was observed.

4*H*-Perfluoro-4-heptyl Methoxymethyl Ether (13). Perfluoro-4-heptanol[17] (1.5 g, 3.6 mmol) was added dropwise to a slurry of 87 mg of NaH (60% dispersion in mineral oil, 3.6 mmol) in 15 mL of ethyl ether. After 30 min of efficient stirring, 270 μL (3.2 mmol) of chloromethyl methyl ether was added dropwise over a 5 min period. The contents of the vessel were well stirred for 30 min and then filtered. The ether solution was washed with 2 × 10 mL of water and dried over $MgSO_4$. Concentration of the solution at 20 °C (100 Torr) was followed by a dynamic transfer at 20 °C (30 mTorr) to remove mineral oil. The product was found to decompose on distillation, but 600 mg (40% yield) was obtained pure by preparative GC (130 °C, t_R = 2.3 min). ^{19}F NMR ($CDCl_3$): Φ −81.0 (m, 6F); −116.6, −118.5 (AB q, J = 299 Hz, 4F); −125.5, −126.8 (AB q, J = 287 Hz, 4F). ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3H); 4.70 (m, 1H); 4.84 (s, 2H). MS: *m/e* 412 (M^+), 381 ($C_8H_3F_{14}O^+$), 169 ($C_3F_7^+$), 69 (CF_3^+). Anal. Calcd for $C_9H_6F_{14}O_2$: C, 26.24; H, 1.47; F, 64.56. Found: C, 25.73; H, 1.49; F, 64.89.

(*E*)- and (*Z*)-Perfluoro-4-hept-3-enyl Methoxymethyl Ether (14). To a flame-dried 25 mL round-bottom flask filled with argon was added 320 mg (0.78 mmol) of compound **13** and 10 mL of dry ethyl ether. The vessel was cooled in an ice bath and 10 mL (1 mmol) of a 0.1 M LDA solution in hexanes/Et_2O was added via cannula. After 2 h, the reaction mixture was washed with 2 × 15 mL of 5% HCl and then once with 15 mL of water. The ether layer was dried over $MgSO_4$ and filtered; the filtrate was concentrated at 20 °C and 100 Torr. After a vacuum transfer to leave behind high molecular weight material, analysis of the product by ^{19}F NMR revealed a *Z*-to-*E* ratio of 1:4.[27] The isomers were separated by preparative gas chromatography (110 °C, $t_R{}^E$ = 5.6 min, $t_R{}^Z$ = 5.8 min); total recovered mass was 107 mg (35% yield). ^{19}F NMR ($CDCl_3$). *E* isomer: Φ −81.3 (t, J = 8 Hz, 3F, C_7); −84.2 (s, 3F, C_1); −116.0 (m, 2F, C_5); −119.7 (d, 2F, C_6); −127.9 (d, J = 16 Hz, 2F, C_2); −140.2 (m, 1F, C_3). *Z* isomer: Φ −81.0 (t, J = 11 Hz, 3F, C_7); −83.7 (s, 3F, C_1); −113.7 (m, 2F, C_5); −115.3 (m, 2F, C_2); −125.6 (t, J = 8 Hz, 2F, C_6); −133.2 (m, 1F). ^{1}H NMR ($CDCl_3$): δ 3.55 (s, 3H); 5.02 (m, 2H). IR (thin film, cm^{-1}).[27] *E* isomer: 2975, 2842, 1336, 1224, 1135, 1119, 1032, 957, 913, 882. *Z* isomer: 2975, 2842, 1670 (C═C), 1352, 1332, 1228, 1158, 1124, 1040. MS: *m/e* 392 (M^+), 391 (M^+ − H), 169 ($C_3F_7^+$), 69 (CF_3^+). HRMS: calcd for $C_9H_5F_{13}O_2$, 392.0082; found, 392.0068.

(*E*)-Perfluorohept-3-en-4-ol (6e). A solution containing 30 mg of (*E*)-perfluoro-4-hept-3-enyl methoxymethyl ether **(14)** in 0.7 mL of CCl_4 was treated with a drop of concentrated sulfuric acid in an NMR tube. The tube was shaken for 30 s, and the ^{19}F NMR spectrum showed complete and clean conversion to the enol. *E* isomer: Φ −81.2 (t, J = 10 Hz, 3F); −84.7 (s, 3F); −118.9 (m, 2F); −120.6 (d, J = 10 Hz, 2F); −128.4 (d, J = 10 Hz, 2F); −159.0 (m, 1F).

Equilibration of 6e and 6k. Enol **6e** was prepared as above except that a dynamic vacuum transfer at 20 °C (30 mTorr) was used to remove **6e** and CCl_4 from the acid. The contents of the trap were statically transferred to an NMR tube and carefully thawed under nitrogen. Then 5 μL of NMP was added and the reaction was monitored by ^{19}F NMR spectroscopy. After 12 h, complete and clean conversion to ketone **6k**[9a,b] was observed.

Acknowledgment. The authors thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation for support of this research. P.E.L. is grateful to DuPont for a Walter H. Stockmayer Fellowship. Thanks are due to the Keck and the Dreyfus Foundations for grants to the Chemistry Department which enabled purchase of the computer hardware and software used in this work. High-resolution mass spectra were run by Dr. Andrew Tyler at the Harvard University Mass Spectrometry Laboratory, supported by NSF Grant CHE 9020043 and NIH Grant 510-RR06716.

Supporting Information Available: Tables of final optimized geometries (6-31G**) in Cartesian coordinates for the acyclic keto−enol systems (2 pages). See any current masthead page for ordering and Internet access instructions.

JA963788N

(27) The absence of a C═C stretch in the infrared spectrum for the major product identified it as the *E* isomer, as it is well documented that structurally similar *E* enol ethers lack this band.[9c] The *Z* isomer, on the other hand, shows a weak band in the IR at 1670 cm^{-1}, which is consistent with the literature values. For a discussion of the infrared spectra, see: Kurbakova, A. P.; Leites, L. A.; German, L. S.; Kurykin, M. A. *J. Fluorine Chem.* **1996**, *77*, 169.