Novel Keto−Enol Systems: Cyclobutane Derivatives

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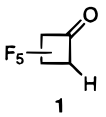
Abstract: 3*H*-Perfluorobicyclo[2.2.0]hexan-2-one (**3**) has been synthesized from hexafluorobenzene and equilibrated with its enol form (**4**). In carbon tetrachloride $K_{e/k} = 0.07 \pm 0.01$ (25 °C), but in Lewis basic solvents (e.g. acetonitrile, ether, and tetrahydrofuran) only enol is detectable at equilibrium because of its strength as a hydrogen bond donor. In the monocyclic counterpart of this keto−enol system, 2*H*-perfluorocyclobutanone (**1**) and perfluorocyclobut-1-enol (**2**), the enol is more stable yet. Here ketone is undetectable under equilibrating conditions in all media examined, including carbon tetrachloride. Among unhindered and unconjugated enols, **2** and **4** are more stable relative to their ketones than any others that have been reported. Ab initio quantum mechanical calculations support the conclusion that destabilization of the ketones, but not stabilization of the enols, by fluorine substitution is responsible for the unique relative stability of these enols.

Introduction

Keto−enol equilibria have been investigated since the 19th century, and the subject is regarded as very well understood.[2] Enols derived from unhindered, unconjugated ketones are present in miniscule amount at equilibrium; e.g. for acetone 4.7 × 10^{-7}% and for cyclopentanone 1.1 × 10^{-6}% (in water at 25 °C).[3,4] Establishment of equilibrium in such a keto−enol system is facile with either acid or base catalysis. In a little-known series of 19 papers published mostly in the 70's, however, Bekker, Knunyants, and their co-workers described the synthesis of an array of highly fluorinated simple keto−enol systems with dramatically contrasting properties.[5] They found the enols to be amazingly stable kinetically, resisting the influence of powerful acids such as sulfuric and triflic. The Russian researchers reported impressive thermal stability for the enols as well; the enol of pentafluoroacetone, for example, was claimed to ketonize only slowly at 180 °C. The authors regarded all of their fluorinated enols as thermodynamically unstable with respect to the corresponding ketones, and attributed the enol stability to high interconversion barriers.

In the case of the keto−enol system **1** and **2**, they reported that neither form can be isomerized to the other by either heat or catalysts.[6] Both molecules were said to be stable to acids and to decompose in the presence of bases.



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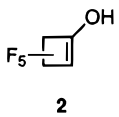
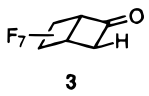


2

Our attention was drawn to this work by the finding that ketone **3**, prepared in our laboratory as an intermediate in a synthetic scheme, was accompanied by a persistent impurity which proved to be its enol **4**. Subsequent study of the relationship between these isomers yielded surprising results which led us to reinvestigate keto−enol system **1** and **2**, the monocyclic analog of our keto−enol pair. A preliminary account of our research on these two systems has appeared.[7] Herein the synthetic and mechanistic work are presented in full.



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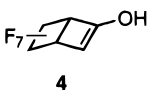

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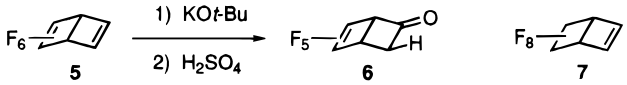
Results and Discussion

Synthesis of Ketone 3. In earlier work in our laboratory, perfluoro(Dewar benzene) (**5**) had been transformed into bicyclo[2.2.0]hexenone **6** via its 2-*tert*-butoxy derivative.[8] We therefore planned to synthesize ketone **3** in analogous fashion from perfluoroolefin **7**. This compound had been prepared by vapor-phase photolysis of perfluoro-1,3-cyclohexadiene,[9] but since the diene is not readily available an alternative route was sought. Perfluoro(Dewar benzene) (**5**) is formed in high yield when perfluorobenzene is irradiated in the vapor phase.[10] Since **5** is a dangerous compound which detonates capriciously as a neat liquid, it is handled exclusively in solution in our laboratory



5 **6** **7**

[⊗] Abstract published in *Advance ACS Abstracts,* March 1, 1996.

(1) Walter H. Stockmayer Fellow, 1995−6.

(2) *The Chemistry of Enols*; Rappoport, Ed.; John Wiley and Sons: Chichester, 1990.

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

(4) Toulec, 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.

(5) For a concise summary of this work, see: Hart, H.; Rappoport, Z.; Biali, S. E. In ref 1, pp 502−14.

(6) (a) Bekker, R. A.; Popkova, V. Ya.; Knunyants, I. L. *Dokl. Akad. Nauk SSSR* **1976**, *229*, 870; *Dokl. Akad. Nauk SSSR, Engl. Transl.* **1976**, *229*, 514. (b) Bekker, R. A.; Popkova, V. Ya.; Knunyants, I. L. *Dokl. Akad. Nauk SSSR* **1976**, *231*, 864; *Dokl. Akad. Nauk SSSR, Engl. Transl.* **1976**, *231*, 700. Bekker, R. A.; Popkova, V. Ya.; Knunyants, I. L. *Dokl. Akad. Nauk SSSR* **1977**, *235*, 103; *Dokl. Akad. Nauk SSSR, Engl. Transl.* **1977**, *235*, 370.

(7) Correa, R. A.; Lindner, P. E.; Lemal, D. M. *J. Am. Chem. Soc.* **1994**, *116*, 10795.

(8) Soelch, R. R.; McNierney, E.; Tannenbaum, G. A.; Lemal, D. M. *J. Org. Chem.* **1989**, *54*, 5502.

(9) Feast, W. J.; Musgrave, W. K. R.; Weston, R. G. *J. Chem. Soc., Chem. Commun.* **1970**, 1337.

(10) Camaggi, G.; Gozzo, F.; Cevidalli, G. *J. Chem. Soc., Chem. Commun.* **1966**, 313. Haller, J. *J. Am. Chem. Soc.* **1966**, *88*, 2070.

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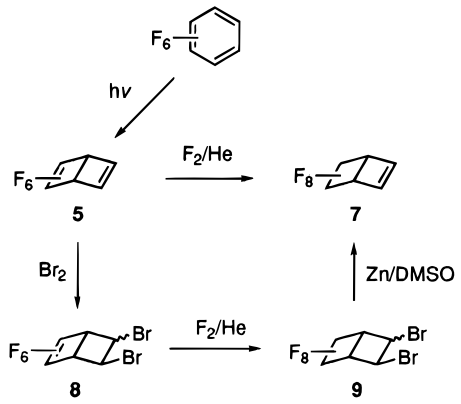
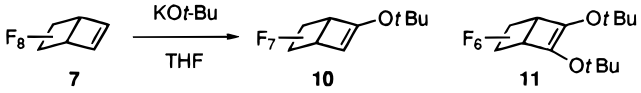
Scheme 1



after its creation in the gas phase. Direct fluorination of the Dewar benzene gives olefin **7**, but the yield is poor as a consequence of oligomerization and overfluorination. Thus, a more circuitous path was chosen (Scheme 1).

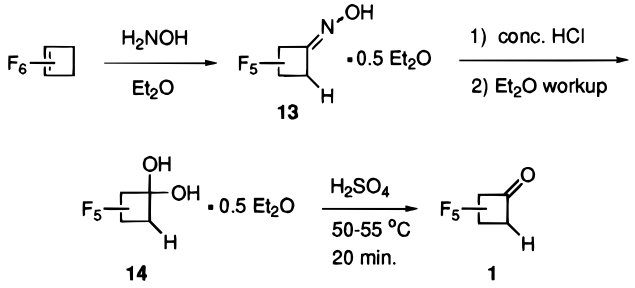
Bromination of **5** by a modification of Haszeldine's procedure[11a] gave a 2.3:1 mixture of the exo,cis and trans dibromides **8**. Hydrogen bromide also reacts with **5** to yield exo,cis and trans adducts, but the bromine is exclusively exo in both. Both HBr and Br_2 addition are radical chain processes in which the initial attack on the olefin is by a bromine atom. Therefore, in the bromination the first bromine is introduced exclusively exo, presumably for steric reasons, and the subsequent attack on Br_2 occurs at both faces of the molecule. The contribution from endo attack suggests that (weak) bridging by the exo bromine comes into play in the intermediate radical.[11b]

Direct fluorination of the isomer mixture **8** in $CFCl_3$ yielded the cis and trans octafluoro dibromides **9**, which gave the desired olefin **7** upon treatment with activated zinc in dimethyl sulfoxide. Enol ether **10** was formed in high yield when **7** was treated with 1 equiv of potassium *tert*-butoxide in THF at −65 °C.[12] The vinyl fluorine signal at Φ −121.8 in the ^{19}F NMR spectrum confirmed that monosubstitution had taken place. Addition of 2 equiv of *tert*-butoxide yielded the symmetrical di-*tert*-butoxy derivative **11**.

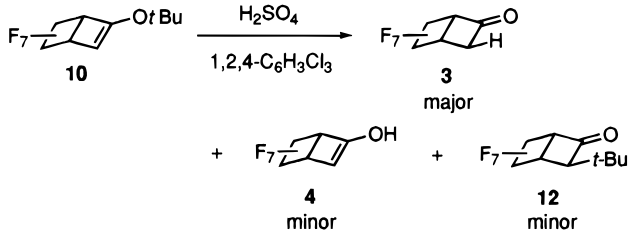


When enol ether **10** was stirred with excess concentrated sulfuric acid in 1,2,4-trichlorobenzene for several minutes, followed by trap-to-trap distillation, the major component of the distillate was ketone **3.** The ^{19}F NMR spectrum of the ketone reveals its configuration as well as structure. Now the fluorine at C_3 which resonated at Φ −121.8 in **10** appears as a subsplit doublet at −186.0 ppm. The doublet splitting of ∼50 Hz is caused by the geminal hydrogen, and further splitting of this signal results from through-space interaction with the endo fluorine at C_5.[13] Thus, the hydrogen at C_3 must be on the exo face of the molecule. Fluorines at C_5 give rise to an AB quartet at Φ −116.0 and −125.6 (J = 229 Hz); selective broadening of the downfield half of the quartet shows that it corresponds to the endo fluorine. Presumably the AB quartet for the C_6 fluorines at Φ −111.8 and −130.8 can be assigned accordingly,

Scheme 2



the downfield half to the endo and the upfield half to the exo fluorine. Resonances at Φ −182.0 and −182.6 ppm reveal the bridgehead fluorines. A strong carbonyl stretching band in the IR spectrum at 1838 cm^{-1}, typical for fluorinated cyclobutanone rings,[8,14] confirmed the structure assignment of the ketone.



Even under conditions where ketone **3** equilibrates with its enol, none of the stereoisomeric ketone in which the hydrogen at C_3 is endo is observed. Thus, the exo-H configuration is by far the more stable one. Probably the chief reason is smaller dipole−dipole repulsion in this stereoisomer between the C_3−F bond and neighboring C−F bonds.[15]

In the enol ether cleavage, two impurities accompanied the ketone; one of these could be left behind in a subsequent static vacuum transfer at 0 °C and 30 mTorr. This impurity proved to be enol **4**, as revealed by the ^{19}F NMR spectrum which closely resembles that of the enol ether precursor. It comprises a doublet at Φ −126.8 (J = 22 Hz) for the vinyl fluorine, bridgehead fluorine signals at −191.5 and −197.3, and two AB quartets for the CF_2 groups.

The other impurity was *exo*-3-*tert*-butylbicyclo[2.2.0]hexan-2-one (**12**), presumably formed via alkylation of the enol by *tert*-butyl cation. It also was identified by its ^{19}F NMR spectrum, the most notable feature of which is a doublet at Φ −163, J = 38 Hz. This resonance was assigned to the fluorine geminal to the *tert*-butyl group. The large size of this coupling constant is probably a consequence of the bulkiness of the *tert*-butyl group, which (crowded by the bridgehead fluorine at C_4) forces the geminal fluorine into close proximity to the endo fluorine at C_5.[13] Formation of the C-alkylation product can be eliminated by carrying out the enol ether cleavage in the presence of several equivalents of bibenzyl. The background for this finding is discussed below.

Synthesis of Ketone 1 and Enol 2. A slightly modified version of the route developed by Bekker and Knunyants[6] was used to synthesize 2*H*-perfluorocyclobutanone, **1** (Scheme 2). The reaction between perfluorocyclobutene and the free base hydroxylamine was previously reported to give oxime **13** and its tautomer, **13a**.[16] However, a closer examination of the reaction products by ^{19}F NMR revealed that the two isomers were the *Z* and *E* oximes as evident from two separate doublets

(11) (a) Barlow, M. G.; Haszeldine R. N.; Morton, N. O.; Woodward, D. R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2170. (b) Skell, P. S.; Shea, K. J. In *Free Radicals*; Kochi, J. K., Ed.; Wiley & Sons: New York, 1973; Vol. II, p 809 *et seq*.

(12) For examples of reactions of perfluoroolefins with alkoxides see: Smart, B. E.; Krespan, C. G. *J. Am. Chem. Soc.* **1977**, *99*, 1218.

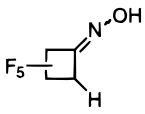
(13) Barefoot, A. C., III; Saunders, W. D.; Buzby, J. M.; Grayston, M. W.; Lemal, D. M. *J. Org. Chem.* **1980**, *45*, 4292.

(14) England, D. C. *J. Am. Chem. Soc.* **1961**, *83*, 2205.

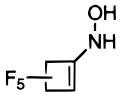
(15) Rahman, M. M.; Secor, B. A.; Morgan, K. M.; Shafer, P. R.; Lemal, D. M. *J. Am. Chem. Soc.* **1990**, *112*, 5986.

(16) Knunyants, I. L.; Bykhowskay, E. G.; Frosin, V. N. *Zh. Vses. Khim. Obshch.* **1964**, *9*, 598.

at −200 and −195.6 ppm, corresponding to the fluorine geminal to hydrogen in the two isomers. The previously assigned



13

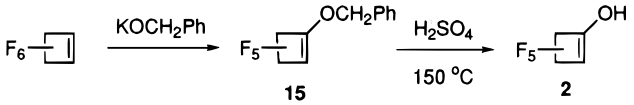


13a

tautomer, **13a**, would not possess a signal in this high field region of the spectrum, nor would it show the 46-Hz doublet splitting from coupling to a geminal hydrogen.

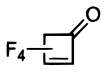
The mixture of oximes was hydrolyzed with concentrated hydrochloric acid to the ketone hydrate, which was distilled as a hydrogen-bonded 2:1 complex with ether. The ketone was generated by treating this *gem*-diol with concentrated sulfuric acid. Ketone **1** is an extremely hygroscopic compound, and atmospheric exposure results in the immediate formation of the ketone hydrate as white crystals.[17] Due to the sensitive nature of ketone **1**, the compound was handled in vacuo and stored at −78 °C in silated vessels under a nitrogen atmosphere.

The enol of ketone **1** was independently synthesized by Bekker[6a] as shown below.



15 **2**

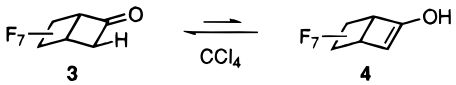
Our attempts to cleave the benzyl enol ether **15** in this manner were unsuccessful, as the enol readily dehydrofluorinated at the elevated temperatures. This decomposition pathway was suppressed by performing the reaction at room temperature with 1,2,4-trichlorobenzene as solvent, but a small amount of enone **16** (5−10%) still accompanied the enol.



16

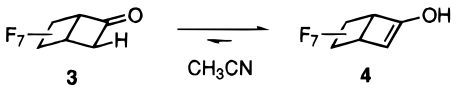
Since enol **2** is so labile it was stored in silated vessels at −60 °C. Under these conditions it survived for extended periods of time. In contrast to enol **2**, enol **4** is quite resistant to dehydrofluorination because that process would introduce a highly strained double bond.

Keto−Enol Equilibration Studies. (a) Equilibration of 3 and 4. The addition of 0.01 equiv of the extremely weak base *N*-methylpyrrolidone (NMP) to ketone **3** in carbon tetrachloride resulted in the rise of enol signals from the baseline in the ^{19}F NMR spectrum. After 24 h the ratio of ketone to the enol remained constant at 93:7. This experiment was repeated three times, confirming that $K_{enol/ketone} = 0.07 \pm 0.01$. [The amount of NMP present was too small to perturb the equilibrium significantly.]



3 **4**

The position of equilibrium is altered dramatically by the addition of Lewis basic solvents. Thus, when several equivalents of acetonitrile, diethyl ether, or tetrahydrofuran are added to the ketone in carbon tetrachloride, only enol is detectable by ^{19}F NMR after several minutes. This can be rationalized as the result of selective stabilization of the enol form by hydrogen bond formation to the Lewis base. Enol **4** is apparently the first example of an unhindered, unconjugated enol which has been shown to be the exclusive form at equilibrium in any medium.[18]



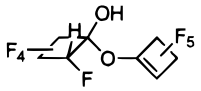
3 **4**

The potency of enol **4** as a hydrogen-bond donor is apparent in the fact that $K_{e/k} = 1.94 \pm 0.10$ in carbon tetrachloride containing 1.6% acetonitrile (v/v). Dilution of this solution with carbon tetrachloride diminishes the enol/acetonitrile interaction, allowing the ketone to be the dominant form again.

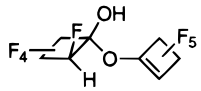
The hydrogen-bonding interaction between the enol and Lewis bases such as acetonitrile, THF, and NMP is sensitively reflected in the chemical shift of the vinyl fluorine of the enol. As an example, the addition of 1 equiv of NMP to the enol (0.2 M) in carbon tetrachloride caused the vinyl fluorine of the enol to shift 5.2 ppm upfield. On the chance that this shift may have been the result of stoichiometric deprotonation of the enol by NMP, the same experiment was performed with the much stronger base triethylamine. Indeed, the same direction of shift was observed, but the magnitude of the shift was much greater. Thus, when 1 equiv of triethylamine was added to the enol (0.1 M) at −23 °C in carbon tetrachloride the vinyl fluorine shifted 19 ppm upfield. This large shift suggests deprotonation of the enol to form the triethylammonium salt. A shift of similar direction and magnitude was reported when monocyclic enol **2** was treated with triethylamine at −78 °C.[6b] An attempt to measure the pK_a of enol **4** in water failed because of rapid hydration of the enol, giving the *gem*-diol.

(b) Equilibration of 1 and 2. All attempts to convert enol **2** into its keto form were unsuccessful. On the chance that the enol might be the more stable form, we focussed our attention on approaching the equilibrium from the side of the ketone. A significant breakthough was quickly realized as treatment of a solution of **1** in chloroform-*d* with excess acetonitrile, tetrahydrofuran, or diethyl ether resulted in the immediate and complete formation of enol **2**. The relative stability of **1** and **2** was still unknown, however, because the equilibrium was undoubtedly driven toward the enol by formation of a strong hydrogen bond between the enol and the Lewis base.

Conditions were sought under which the interconversion would be facile but the equilibrium would not be perturbed by enol hydrogen bond formation with the base or solvent. Again, a trace of *N*-methylpyrrolidone (NMP) as catalyst in the non-hydrogen bonding medium carbon tetrachloride met these criteria nicely. Therefore, to a 0.03 M solution of ketone **1** (1 equiv) in carbon tetrachloride was added 0.01 equiv of NMP. Excitingly, tautomerization was fast but enol **2** was accompanied by the diastereomeric hemiketals **17** and **18**.[19] The formation of the two diastereomers, a consequence of the bimolecular reaction of enol **2** (or enolate) with ketone **1**, was reversible, for the the final reaction mixture contained only enol **2** and a small amount of enone **16**.



17



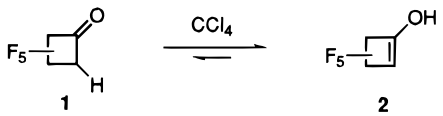
18

(17) Hexafluorocyclobutanone is also highly hygroscopic, and it forms a very stable hydrate (see ref 14).

(18) Remarkable enols stabilized by oxygen and chlorine substituents have recently been described; they approach **3** in stability. Ettlinger, M. G.; Watson, K. J.; Jaroszewski, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 1557. See also: Nadler, B.; Rappoport, Z.; Arad, Y.; Apeloig, Y. *J. Am. Chem. Soc.* **1987**, *109*, 7873.

The lability of **17** and **18** prevented their isolation, but their formation was revealed by the two high field doublets at −211.7 and −215.9 ppm in the ^{19}F NMR spectrum corresponding to a fluorine geminal to hydrogen in each diastereomer. The downfield region consisted of many overlapping signals making explicit assignments difficult. The identities of **17** and **18** were confirmed by showing that the same hemiketals were formed when separately prepared enol and ketone are combined in carbon tetrachloride. Furthermore, **17** and **18** revert to the enol and the ketone, which subsequently hydrates, when treated with water.

The bimolecular reaction was concentration dependent, of course, and was avoided by carrying out the equilibration at higher dilution. Thus, with 0.01 equiv of NMP in a 0.0013 M solution of **1** in carbon tetrachloride, enolization was clean and after 24 h no ketone was detectable by ^{19}F NMR. Thus, the enol is much more stable than its ketone even in a solvent of extremely low Lewis basicity. *This is the first example of an unhindered and unconjugated keto−enol system in which the enol has been demonstrated to be more stable than the ketone even in non-hydrogen-bonding solvents.*



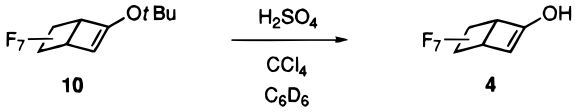
1 **2**

Though they used NMP as a base for catalyzing reactions of various perfluoro enols,[20] the Russian group apparently never subjected ketone **1** to traces of an extremely weak base such as NMP or acetonitrile. They mention only stronger bases such as triethylamine which give enone **16** as the only observed product. Deprotonation of the ketone is of course necessary, but the key to enolization in this sensitive system is that the conjugate acid of the base must be acidic enough to reprotonate the enolate anion. The use of a strong base extends the lifetime of the enolate anion, ultimately allowing dehydrofluorination to dominate.

We reinvestigated the question of acid catalysis of enolization. After several attempts with varying amounts of sulfuric acid in carbon tetrachloride, no enol was observed. This supports the Russian workers' claim that acids do not catalyze interconversion of **1** and **2**.

Mechanism of Acid-Catalyzed Cleavage of Enol Ether 10. The acid induced cleavage of hydrocarbon-derived enol ethers with sulfuric acid has been shown to proceed by protonation at carbon as the first and rate-determining step.[21] We have found that the same is not true of fluorinated enol ether **10**. The mechanism of this reaction was probed with an NMR tube experiment in which the bicyclic enol ether was dissolved in carbon tetrachloride containing 5% benzene-d_6 (as an NMR lock) and then treated with concentrated sulfuric acid. The mixture was shaken thoroughly[22] and the evolution of the reaction was monitored by ^{19}F NMR.

Addition of the acid resulted in the immediate disappearance of the signals for **10** with concomitant appearance of signals for enol **4**. The shift of the vinyl fluorine, which had been at −121.8 ppm in **10**, to −126.8 ppm provided a convenient way to follow the progress of the reaction. The electron deficient nature of the fluorinated double bond in **10** is probably responsible for the enol's lack of reactivity at carbon.[23]



10 **4**

When the same experiment was repeated in the *absence* of benzene-d_6 we were surprised to find that a significant amount of enol ether remained after several minutes. Furthermore, *tert*-butyl ketone **12** was present, whereas it had not been observed in the previous experiment. The reason for these differences is that benzene efficiently intercepted the *tert*-butyl cation, giving *tert*-butyl benzene-d_5 and 1,4-di-*tert*-butylbenzene-d_4 by electrophilic aromatic substitution.[24] Gas chromatographic analysis confirmed the formation of the substituted benzenes by coinjection of authentic samples of *tert*-butyl benzene and 1,4-di-*tert*-butylbenzene with the reaction mixture. Benzene's ability to considerably accelerate the (net) enol ether cleavage reaction reveals that the process is reversible, and that by capturing the *tert*-butyl cation benzene suppresses not only C-alkylation of the enol, which gives **12**, but also a much faster O-alkylation, which regenerates the starting material. For the purpose of preparing pure ketone **3**, the nonvolatile bibenzyl is substituted for benzene as the cation trap since the ketone is isolated by vacuum transfer.

Agitating the NMR tube containing enol **4** caused it to slowly tautomerize to ketone **3**, indicating that thermodynamic control of the reaction can be achieved at longer reaction times. Since tautomerization was slow it was possible to obtain a relatively stable solution of enol by separating the acid and organic layers before ketonization occurred to a significant degree. Ketonization in the acid solution presented the interesting challenge of determining the tautomerization catalyst. A solution of enol and ketone (90:10) in carbon tetrachloride was separated into two different NMR tubes, one containing trifluoroacetic acid and the other containing no acid. The rate of ketonization in both tubes was the same, indicating that trifluoroacetic acid does not catalyze ketonization. This does not eliminate sulfuric acid as a potential catalyst, however, because sulfuric acid is approximately ten orders of magnitude more acidic than trifluoroacetic acid.

In attempting to pinpoint the catalyst further, we were frustrated by the fact that the rate of ketonization varied capriciously in the two-phase carbon tetrachloride/sulfuric acid mixture. The weakly basic glass surface of the reaction vessel or the bisulfate anion generated in the reaction may be the catalyst. Both possibilities are feasible since extremely weak bases (e.g. acetonitrile) have been shown to catalyze interconversion in this system. Whatever the exact catalyst, there is no evidence to reject the Russian claim that acids do not effect equilibration in perfluorinated keto−enol systems.

Properties of Ketone 3 and Its Derivatives. Ketone **3** is a highly unstable molecule, undergoing significant decomposition at room temperature in a dry vessel after 2 h. This instability

(19) In contrast, there was no evidence of a bimolecular reaction between enol **4** and ketone **3** at a concentration of 0.03 M.

(20) Bekker, R. A.; Melikyan, G. G.; Lur'e, É. P.; Dyatkin, B. L.; Knunyants, I. L. *Dokl. Akad. Nauk SSSR* **1974**, *217*, 1320; *Dokl. Akad. Nauk SSSR, Engl. Transl.* **1974**, *217*, 572. Bekker, R. A.; Melikyan, G. G.; Dyatkin, B. L.; Knunyants, I. L. *Zh. Org. Khim.* **1975**, *11*, 1370; *Zh. Org. Khim., Engl. Transl.* **1975**, *11*, 1356. Bekker, R. A.; Melikyan, G. G.; Dyatkin, B. L.; Knunyants, I. L. *Zh. Org. Khim.* **1975**, *11*, 2370; *Zh. Org. Khim., Engl. Transl.* **1975**, *11*, 2415. Bekker, R. A.; Badanyan, Sh.O.; Melikyan, G. G.; Knunyants, I. L. *Zh. Org. Khim.* **1977**, *13*, 1582; *Zh. Org. Khim., Engl. Transl.* **1977**, *13*, 1461.

(21) Kresge, A. J.; Chen, H. J. *J. Am. Chem. Soc.* **1972**, *94*, 2818. Kresge, A. J.; Sagatys, D. S.; Chen, H. C. *J. Am. Chem. Soc.* **1977**, *99*, 7228.

(22) The reaction mixture was heterogeneous, with the acid layer settling to the bottom of the tube. For efficient reaction the tube had to be shaken vigorously.

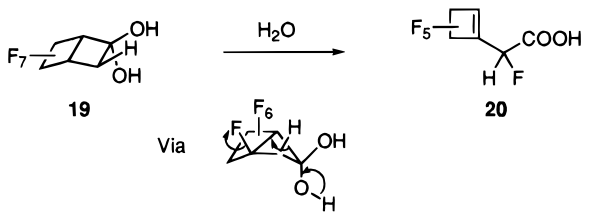
(23) Fluorine atoms attached to sp^2 carbons substantially decrease the reactivity of the double bond toward electrophilic reagents. See, for example: Polishchuk, V. R.; Mysov, E. I.; Stankevitch, I. V.; Chistyakov, A. L.; Potechin, K. A.; Struchkov, Yu.T. *J. Fluorine Chem.* **1993**, *65*, 233.

(24) For the reaction of benzene with *tert*-butyl cation, see: March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley & Sons: New York, 1992; p 535.

is probably due to a combination of high ring strain and fluorine substitution. The great reactivity of the ketone is manifested in the fact that it hydrates voraciously, transforming a volatile liquid into the nonvolatile, crystalline *gem*-dihydroxy compound **19**. In fact, if the glassware and reagents used to prepare the ketone are not thoroughly dried then a significant amount of hydrate accompanies ketone in the product.

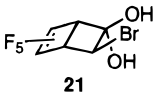
Addition of 1 equiv of water to the ketone trapped from the reaction mixture causes the hydrate **19** to crystallize; the impurities are then pumped off, leaving behind pure hydrate. The high-field portion of the ^{19}F NMR spectrum of **19** showed three signals in a 1:1:1 ratio at −184.7, −194.8, and −198.6 ppm, the last a subsplit doublet with $J_{HF} = 51.0$ Hz. The first two signals are attributable to the bridgehead fluorines and the last to the fluorine geminal to the hydrogen. A strong, broad band at 3320 cm^{-1} in the IR spectrum revealed the presence of the hydroxyls. This diol can be prepared in reproducible yields of 80−85% starting from enol ether **10**.

The diol is sensitive to water, as it rapidly decomposed to acid **20** in wet solvents or upon standing in the atmosphere. We suggest that the cleavage occurs both because C_1 can tolerate carbanionic character and because the molecule can attain an approximately antiperiplanar conformation which makes concert possible. The carboxylic acid is stable, for crystals of it were unchanged after three months' exposure to the atmosphere. The ^{19}F NMR spectrum showed three signals at −103.9, −115.4,

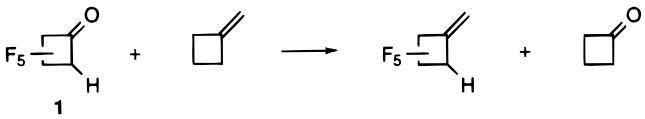


and −118.5 ppm in a 1:2:2 ratio which were assigned to the vinyl and methylene fluorines, respectively. The fluorine atom α to the carboxyl group appeared as a doublet centered at −198.5 ppm with $J_{HF} = 47.0$ Hz, indicating that it is geminal to a hydrogen. A broad peak at 3030 cm^{-1} and a strong band at 1730 cm^{-1} in the IR spectrum provided confirmatory evidence for the acid functionality.

It is interesting that diol **21**, similar in structure to **19**, is quite stable in water[8] despite the apparent opportunity for allylic stabilization[25] in the transition state for ring opening. [Concerted loss of HF as suggested for **19** would not be expected, of course, because it would yield a cyclobutadiene.] The presence of additional fluorines to stabilize developing negative charge in the transition state, greater skeletal flexibility to make concerted reaction possible, and less destabilization of the developing carbonyl function (H instead of Br) may all contribute to the greater lability of **19**.

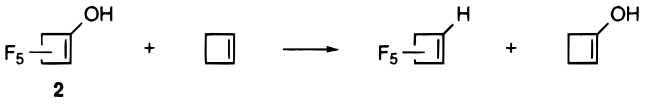


Quantum Mechanical Calculations.[26] What are the reasons for the unprecedented stability of the enols presented above? We have attempted to answer this question with two isodesmic reactions. The first is the reaction of ketone **1** and methylenecyclobutane to give 2*H*-perfluoromethylenecyclobutane and cyclobutanone.

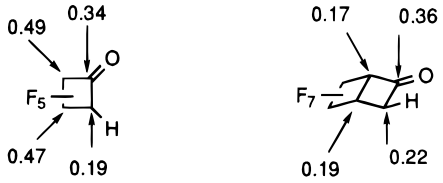


The heat of the reaction at the HF/6-31G**//6-31G** level of theory is −17.4 kcal/mol, indicating that fluorination of cyclobutanone is energetically a very unfavorable process. This result supports previous work that points to the same conclusion.[27]

One must also inquire whether perfluorination stabilizes cyclic enols such as **2**. The isodesmic reaction below suggests the contrary, as the calculated heat of reaction is −5.5 kcal/mol. We therefore propose that the remarkable enol stability in the systems discussed above is a consequence of ketone destabilization without a contribution from enol stabilization.



With the focus narrowed, we inquired why enol **2** is more stable with respect to its ketone than bicyclic enol **4**. A calculation of the charge distribution in each ketone afforded a plausible explanation. The charges on carbons shown below were calculated at the HF/6-31G** level; they are based on fits to electrostatic potentials, but the charges based on natural orbitals lead to the same conclusion.



The α-carbons bearing hydrogen were calculated to have approximately the same charge in the monocyclic **1** and bicyclic **3** ketones (the same is true of the carbonyl carbons and oxygens). However, the calculated charge at the other α-carbon is almost three times as great and that at the β-carbon of the cyclobutanone ring more than twice as great in the monocyclic as in the bicyclic ketone. Most of this difference is attributable to the presence of two fluorines at these carbons in ketone **1** as opposed to only one fluorine in ketone **3**. Since a positive charge adjacent to a carbonyl is destabilizing, it follows that monocyclic ketone **1** should be more destabilized than bicyclic ketone **3**, as implied by our experimental and computational results. This rationalization based on ketone charge distributions must be considered tentative, however, because it does not always make the correct prediction in comparing two keto−enol systems.

The neighboring positive charges of ketone **1** are partially relieved on enolization as shown by a calculation of the charge distribution at carbon in enol **2** at the HF/6-31G** level of

(25) Little would be gained from the allylic interaction, as judged from calculations which predict that the perfluoroallyl anion will be grossly nonplanar, and that the classical planar structure will lie far higher and not even be a potential energy minimum. Dixon, D. A.; Fukunaga, T.; Smart, B. E. *J. Phys. Org. Chem.* **1988**, *1*, 153.

(26) The calculations were carried out using (a) the Spartan package of programs (Hehre, W.; Wavefunction, Inc.: 188401 Von Karman, Suite 370, Irvine, CA 92717) and (b) 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).

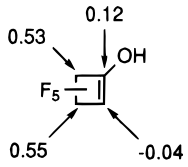
(27) See, for example: Smart, B. E. In *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: Deerfield Beach, FL, 1986; Vol. 3, p 141.

Table 1. Ab Initio Energy Differences for Ketone **1** and Enol **2**

level of theory[a]	energy (hartrees) **1**	energy (hartrees) **2**	ΔE (kcal/mol)[b]
HF/6-31G*//6-31G*	−724.039038	−724.029111	6.2
HF/6-31G**//6-31G**	−724.040884	−724.036011	3.1 (3.3)[c]
HF/6-311G**//6-31G**	−724.231243	−724.227548	2.3
MP2/6-311G**//6-31G**	−725.961465	−725.959469	1.1

[a] The geometries were optimized with Gaussian 92.[26b] Initial optimizations were at the 3-21G level of theory, and the coordinates were used as starting points for the higher level geometry optimizations. [b] $\Delta E = E$(syn enol) − E(ketone). [c] The value in parentheses is corrected for zero-point vibrational motion, 298 K and estimated entropy difference. The corrections are based on the HF/6-31G** calculation with frequencies larger than 500 cm^{-1} scaled by 0.893.

theory. In particular, the vinyl carbon bearing the fluorine of enol **2**, which was positively charged in ketone **1**, now possesses



a small negative charge. The relief of adjacent positive charges is likely to be an important driving force for enolization.

Ab initio calculations of the keto−enol energy gaps in the systems discussed in this paper as well as their hydrocarbon counterparts were carried out at various levels of theory. The results for ketone **1** and enol **2** are shown in Table 1. The thermodynamic stability of the fluorinated enols relative to their ketones was badly underestimated at the lower levels of theory.[28] This is particularly clear in the case of **1** and **2** where we have shown that the enol is substantially more stable than its ketone in carbon tetrachloride, a weakly interacting medium which should allow for meaningful comparisons between the gas-phase calculations and the experimental results. It is encouraging, however, that the calculated keto−enol gap shrinks monotonically as the quality of theory improves.[29]

Despite their limitations, ab initio calculations at every level examined rightly predict enol **2** to be more stable relative to its ketone than enol **4**; at the HF/6-31G**//6-31G** level the difference in size of the two keto−enol gaps is 4.8 kcal/mol. At every level of theory the calculations also correctly predict the fluorinated enols to be far more stable (relative to ketones) than their hydrocarbon analogs. An HF/6-31G**//6-31G** calculation gives this difference as 16.5 kcal/mol for enol **2** versus cyclobut-1-enol,[30] and 15.3 kcal/mol for enol **4** versus bicyclo[2.2.0]hex-2-en-2-ol.

The geometry of enols has been the focus of several quantum mechanical studies in recent years.[31] In general, the syn planar conformers are the most stable. Particularly intriguing calculations by Dixon and Smart[31b] using a triple-ζ basis set (TZ + P) found the cis, syn conformer for the enol of 2-fluoroacetaldehyde to be 4.2 kcal/mol more stable than the cis, anti conformer. This was attributed, at least in part, to the stabilization of the cis, syn conformer by the formation of an intramolecular hydrogen bond between the hydroxyl hydrogen and the vinyl fluorine. The main piece of evidence supporting this conclusion was the short r(H−F) distance of 2.37 Å; the sum of the H and F van der Waals radii is 2.67 Å.[32]

The syn conformer of enol **2** is also more stable than the anti form, but only by 0.5 kcal/mol at the HF/6-31G**//6-31G** level. In fact, the slight energetic preference for the syn conformer is not the result of intramolecular hydrogen bonding, for the r(H−F) distance is 3.02 Å. The absence of intramolecular hydrogen bonding in **2** may be a reflection of the geometric constraints imposed by the cyclobutene ring. The barrier to rotation about the C−O bond is quite low, as a structure rotated by 90° was located as a transition state that lies only 3.1 kcal/mol above the syn conformer.

At the HF/6-31G** level ketone **1** is puckered such that the β-carbon is 22° out of the plane of the two α-carbons and the carbonyl carbon. The puckering presumably relieves eclipsing interactions present in the planar structure. Otherwise, the bond lengths and bond angles are not unusual. The C═O bond length is 1.17 Å, and the two α-carbons make an angle of 90.3° with the carbonyl carbon.

Conclusion

While earlier Russian work had shown that highly fluorinated enols are surprisingly stable kinetically, the present research has revealed that such enols can also be remarkably stable thermodynamically relative to the corresponding ketones. Among unhindered, unconjugated enols, those discussed here are the most stable in this sense that have ever been reported. Enol **4** is much lower in energy than its ketone in Lewis basic solvents as a result of hydrogen bonding; in the weakly interacting medium carbon tetrachloride it is present to the extent of 7% at equilibrium. Enol **2** is much more stable than its ketone even in carbon tetrachloride. Quantum mechanical calculations indicate that the striking stability is attributable solely to destabilization of the ketones, not to stabilization of the enols, by fluorine substitution.

Experimental Section

The ^{19}F NMR spectra were obtained at 282.2 MHz on a Varian Unity Plus spectrometer with trichlorofluoromethane (Freon 11) as an internal standard. Chemical shifts are reported on the Φ scale (ppm from internal trichlorofluoromethane, upfield negative). The ^{1}H NMR spectra were recorded at 300 MHz on the Varian Unity Plus spectrometer. Tetramethylsilane was used as an internal standard and chemical shifts are reported on the δ scale.

Analytical gas chromatograms were obtained with a Hewlett-Packard Model 5880A gas chromatograph with a methylsilicone capillary column, flame ionization detector, and electronic integration and were not corrected for differential detector response. Unless otherwise specified, all analyses were carried out using a 25 or 12 m methylsilicone capillary column. The standard program was the following: carrier pressure 15 psi; injector 150 °C; detector 200 °C; column 30 °C for 5 min, then 10 °C/min to 180 °C. Yields were corrected for purity as found by GC. Isolation of pure compounds was done by preparative GC on a Hewlett-Packard 5750 instrument 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 the following: flow 5 mL/min; injector 150 °C; detector 200 °C; column 55 °C for 6 min, then 15 °C/min to 220 °C.

Infrared spectra were measured on a Perkin Elmer 599 spectrophotometer calibrated with polystyrene, or on a IR-Bio-Rad Digilab FTS-40 Fourier transform spectrophotometer. Mass spectra were determined on a Finnigan 4023 Quadrupole Mass Spectrometer. Microanalytical data were obtained from Galbraith Labs, Knoxville, TN, and Spang Microanalytical Laboratory, Eagle Harbor, MI. Melting points were

(28) At the HF/STO-3G//STO-3G level the energy gap for **1**/**2** is 13.0 kcal/mol.

(29) The change in size of the energy gap in progressing from the 6-31G* to the 6-31G** level seems surprising, as the only change in basis set is the addition of polarization functions on the lone hydrogen.

(30) At this level of theory, cyclobutanone itself is more stable than its enol by 19.6 kcal/mol. On the basis of thermochemical group equivalents, this energy difference was estimated to be 18.7 kcal/mol (Brickhouse, M. D.; Squires, R. R. *J. Phys. Org. Chem.* **1989**, *2*, 389).

(31) (a) Apeloig, Y. In ref 2, Chapter 1, p 1. (b) Dixon, D. A.; Smart, B. E. *J. Phys. Chem.* **1991**, *95*, 1609. (c) Turecek, F.; Cramer, C. J. *J. Am. Chem. Soc.* **1995**, *117*, 12243.

(32) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

determined in open capillary tubes with a Thomas-Hoover "Uni-Melt" and are uncorrected.

All solvents and reagents used in this work were reagent grade. Carbon tetrachloride was distilled from P_2O_5 before use in equilibration studies. Zinc was activated by stirring with 1 N hydrochloric acid for 5 min, washing with water, ethanol, and diethyl ether, and drying under vacuum; it was then stored under nitrogen. NMR tubes were silated by adding a few drops of *N*,*O*-bis(trimethylsilyl)acetamide and heating the tube with a heat gun in the hood while the liquid made contact with all inner surfaces; the tube was washed out with acetone and dried under vacuum. Fluorine gas in helium (20/80) was purchased from Matheson and was passed over a bed of sodium fluoride before use. Perfluorobenzene was purchased from Fairchild Chemical and chlorotrifluorethylene came from PCR. Perfluorocyclobutene was prepared by the method of Tatlow,[33] and should be handled in a well-ventillated hood due to its high toxicity.

2-Hydroperfluorocyclobutanone Oxime Etherate (13).[16] To ethyl ether (120 mL) at 0 °C was added freshly prepared hydroxylamine[34] (10.6 g, 0.32 mol) in a three-necked round-bottom flask equipped with a dry ice condenser. The solution was stirred under nitrogen for 10 min to dissolve as much as possible of the hydroxylamine. Perfluorocyclobutene (26 g, 0.16 mol) was condensed into the reaction vessel over a 15-min period. After 8 h of additional stirring, the yellow precipitate was removed by filtration and the ether removed under reduced pressure. The oxime distilled at 32−42 °C/12 Torr (lit. bp 47 °C/12 Torr) complexed with 0.5 equiv of ether. A total of 12 g, 42%, was isolated. ^{19}F NMR($CDCl_3$): Major isomer Φ −115.4, −116.6 (AB q, J = 234 Hz, 2F); −122.2, −131.9 (AB q, J = 226 Hz, 2F); −200.0 (d, J = 46 Hz, 1F). Minor isomer Φ −133.3, −122.4 (AB q, J = 226 Hz, 2F); −118.7 (s, 2F); −195.6 (d, J = 46 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ 1.22 (t, 3H); 3.60 (q, 2H); 5.65 (m, 1H); 12.2 (s, 1H).

2-Hydroperfluorocyclobutanone-1,1-diol Etherate (14).[6] To a 100-mL round-bottom flask equipped with a magnetic stir bar was added 50 mL of concentrated hydrochloric acid. Oxime **13** (13.3 g, 80 mmol) was added dropwise over the course of 10 min. After 20 h of stirring at ambient temperature the solid was removed by filtration and the filtrate was diluted with 30 mL of distilled water. The product was extracted with three 40-mL portions of diethyl ether and dried over $MgSO_4$. The solvent was removed under reduced pressure and the product distilled at 40−45 °C/0.5 Torr to give a clear, colorless liquid. ^{19}F NMR(CD_2Cl_2): Φ −120.4, −134.1 (AB q, J = 231 Hz, 2F); −127.9, −132.6 (AB q, J = 215 Hz, 2F); −213.9 (d, J = 47 Hz, 1F). ^{1}H NMR (CD_2Cl_2): δ 1.22 (t, 3H); 3.60 (q, 2H); 5.01 (s, 2H); 5.06 (d of multiplet, J = 47 Hz, 1H).

2-Hydroperfluorocyclobutanone (1).[6] Concentrated sulfuric acid (130 mL, 2.4 mol) was added to a dry 250-mL three-necked round-bottom flask attached to a 25-mL U-trap equipped with stopcocks at each port. The acid was heated to 40 °C and 2-hydroperfluorcyclobutanone-1,1-diol−0.5 diethyl ether (19 g, 0.09 mol) was added to the reaction vessel via syringe. After 20 min of magnetic stirring at 55 °C the pressure was reduced as the volatile components were dynamically removed and trapped at −196 °C. Distillation of the reaction mixture through a 10 cm Vigreux column at 42 °C under an argon atmosphere produced 7.2 g (50%) of **3** as a clear, colorless liquid. ^{19}F NMR(CCl_4): Φ −122.5, −130.6 (AB q, J = 273 Hz, 2F); −128.7, −135.6 (AB q, J = 234 Hz, 2F); −205.8 (d, J = 47 Hz, 1F). ^{1}H NMR (CCl_4): δ 5.80 (d of multiplet, J = 47 Hz, 1H).

2-Hydroperfluorocyclobutanone-1,1-diol. Ketone **1** (0.5 g, 3 mmol) was statically transferred to a round bottom flask containing 50 μL (3 mmol) of distilled water. After the mixture had warmed to room temperature, the quantitative formation of white crystals was observed. The solid was sublimed at 40 °C/2 Torr, to give clear, colorless crystals that were free of ether. Mp 52.5−54.5 °C. ^{19}F NMR (CD_2Cl_2): Φ −120.6, −133.7 (AB q, J = 231 Hz, 2F); −127.7, −132.8 (AB q, J = 215 Hz, 2F); −213.5 (d, J = 47 Hz, 1F). ^{1}H NMR (CD_2Cl_2): δ 3.60 (s, 1H); 3.82 (s, 1H); 5.12 (d of multiplet, J = 47 Hz, 1H).

1-Hydroxyperfluorocyclobut-1-ene (2).[6] A 25-mL three-necked round-bottom flask was charged with benzyl enol ether **12** (1g, 4 mmol) and 1,2,4-trichlorobenzene (10 mL). A magnetic stir bar was added and the reaction vessel was connected to a vacuum line. The solution was treated with concentrated sulfuric acid (0.4 mL, 8 mmol) at ambient temperature. The immiscible liquids were vigorously stirred for 1 min and then the products were passed through a series of two traps. The first trap at −13 °C (ethylene glycol, $CO_{2(s)}$) collected the solvent and the second trap cooled to −78 °C (2-propanol, $CO_{2(s)}$) collected the enol. The enol (95% pure, 0.5 g, 72% yield) was statically transferred to a silated glass bulb and stored at −78 °C. ^{19}F NMR (CCl_4): Φ −116.5 (m, 2F); −120.2 (m, 2F); −139.0 (s, 1F). ^{1}H NMR (CCl_4): δ 5.8 (s).

Equilibration of Ketone 1 and Enol 2. Ketone **1** 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 μL (8.7×10^{-6} mol) 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^{-6} mol of **1** (1.3 mM). A 1.3-μL aliquot of a 0.02 M solution of 1-methyl-2-pyrrolidone (2.6×10^{-8} mol) in CCl_4 was added via syringe. The ^{19}F NMR spectra were recorded every 6 h.

5,6-Dibromoperfluorobicyclo[2.2.0]hex-2-ene (8). A 250-mL three-necked round-bottom flask containing 19.5 g of 94% pure perfluoro-(Dewar benzene) (**5**, 0.098 mol) in 40 mL of Freon 11 was placed in an ice bath. Bromine (5.0 mL, 0.098 mol) was added dropwise from a pressure-equalizing dropping funnel with good stirring, while the reaction vessel was irradiated with a 75-W sunlamp. A water-cooled condenser connected to a bubbler was attached to the flask. The bromine color was discharged almost immediately after entering the solution. Its presence is an indication of the end point of the reaction. The solvent was short-path distilled, and fractional distillation through a 10 cm Vigreux column of the remaining material under reduced pressure (60−65 °C/40 Torr) afforded 31.7 g (90% yield) of a colorless liquid. This fraction was found to be 96% dibromoolefin **25** (0.088 mol, 2.33/1 exo, cis/trans) by gas chromatography (25 m methylsilicone; exo,cis t_R = 4.17; trans t_R = 3.59 min). The dibromo adducts were separated by preparative gas chromatography. ^{19}F NMR ($CDCl_3$): exo, cis Φ −113.3 (s, 2 F); −115.7 (d, 2F); −173.9 (s, 2 F); trans Φ −102.1 (s, 1F), −108.1 (s,1F); −115.1 (s, 1F); −117.9 (s, 1F); −171.7 (s, 1F); −191.8 (s, 1F). IR (thin film): exo,cis 1760, 1370, 1125, 970, 850, 750 cm^{-1}; trans 1760, 1370, 1140, 970, 850, 800, 770, 695 cm^{-1}. MS (same for both isomers) (*m*/*e*): 346(M^+), 265 ($C_6F_6Br^+$), 186 ($C_6F_6^+$, base), 155 ($C_5F_5^+$), 117 ($C_5F_3^+$).

2,3-Dibromoperfluorobicyclo[2.2.0]hexane (9). To 45 g of dibromoolefin **8** (93% pure, 0.12 mol) was added 450 mL of Freon 11 in a 500-mL heavy-walled Pyrex cylinder with 2-holed Teflon cap for gas inlet and outlet tubes. The temperature of the reaction was kept at −23 °C by immersing the reaction vessel in a dewar flask containing methanol cooled by means of an external refrigerating unit. Fluorine gas (F_2/He, 20/80) was bubbled through the solution (40 mL/min) for 22 h. The fluorine flow was stopped and the system was flushed with argon for 2 h. The solvent was removed by short-path distillation and the product was fractionally distilled through a 10-cm Vigreux column (48−53 °C/60 Torr) to recover 41.2 g of 85% pure dibromo compounds **9** (0.091 mol, 76%). The products were isolated pure by preparative gas chromatography. ^{19}F NMR ($CDCl_3$): exo, cis Φ −119.5 (m, 2F); −119.5, −124.5 (AB q, J = 230 Hz, 2F); −171.3 (s, 2F); trans Φ −104.1 (m, 1F); −119.7, −126.9 (AB q, J = 225 Hz, 2F); −119.1, −125.5 (AB q, J = 225 Hz, 2F); −171.4 (d, 1F); −189.3 (d, 1F). IR (gas phase): exo,cis 1390, 1310, 1280, 1220, 1080, 1000, 860, 710 cm^{-1}; trans 1380, 1310, 1270, 1210, 960, 870, 710 cm^{-1}. MS (same for both isomers) (*m*/*e*): 303 ($C_6F_8Br^+$), 222 ($C_4F_5Br^+$), 191 ($C_3F_4Br^+$, base), 155 ($C_5F_5^+$), 124 ($C_4F_4^+$). Anal. Calcd for $C_6F_8Br_2$: C, 18.76; Br, 41.64; F, 39.60. Found trans: C, 18.80; Br, 41.36; F, 39.29. Mixture of isomers: C, 18.89.

Perfluorobicyclo[2.2.0]hex-2-ene (7). To a 250-mL three-necked round-bottom flask was added 120 mL of DMSO and 30.0 g of activated zinc (0.46 mol). A pressure equalizing dropping funnel and 50-mL U-trap cooled to −196 °C were connected to the reaction vessel. The pressure was reduced to 150 Torr and 11.6 g (0.026 mol) of 86% dibromoolefin was added dropwise over a 2-h period. A total of 4.7 g (0.021 mol, 81% yield) of 100% pure perfluoroolefin (**7**) was recovered (GC, 12 m methylsilicone; t_R = 0.6 min). ^{19}F NMR ($CDCl_3$): Φ −116.6 (d, 2F); −115.1, −126.1 (subsplit AB quartet, J = 219.2 Hz, 2F); −196.8 (s, 2F). IR (gas phase): 1750, 1370, 1330,

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1270, 1200, 1060, 1020, 930, 860, 840, 710 cm^{-1}. MS (*m*/*e*): 224 (M^+), 206 ($C_6F_7^+$), 174 ($C_5F_6^+$), 155 ($C_5F_5^+$, base), 124 ($C_4F_4^+$).

2-*tert*-Butoxyperfluorobicyclo[2.2.0]hex-2-ene (10). To a dry 250-mL three-necked round-bottom flask equipped with a pressure equalizing dropping funnel was added 35 mL of tetrahydrofuran and 8.5 g of perfluoroolefin **7** (0.038 mol). The reaction vessel was cooled to −78 °C (CO_2(s), 2-propanol) and flushed with nitrogen for 10 min. A 1.0 M solution of potassium *tert*-butoxide was slowly added dropwise until the ^{19}F NMR spectrum of the reaction mixture showed complete consumption of the starting material.

The reaction was quenched with 30 mL of ice cooled water, transferred into a 250-mL separatory funnel, and extracted with pentane (3 × 50 mL). The organic phase was backextracted with water, and then dried with sodium sulfate. Distillation at room temperature while reducing the pressure slowly from 760 to 40 Torr removed the solvent. Fractional distillation (63 °C/40 Torr) in the presence of $CaCO_3$ afforded 6.6 g of a colorless liquid, 93% pure (GC, 12 m methylsilicone; t_R = 3.7 min) perfluoro enol ether **10** (0.022 mol, 58%). The enol ether was isolated pure by preparative gas chromatography. ^{19}F NMR ($CDCl_3$): Φ −121.8 (d, 1F); −118.5, −125.3 (AB q, J = 222 Hz, 2F); −119.4, −125.8 (AB q, J = 214 Hz, 2F); −191.3 (s, 1F); −197.1 (s, 1F). ^{1}H NMR ($CDCl_3$): δ 1.4 (s, 9H). IR (neat): 2990, 1710, 1360, 1180, 1020, 940, 900, 845 cm^{-1}. MS (*m*/*e*): 278 (M^+), 263 ($C_9H_6F_7O^+$), 155 ($C_5F_5^+$), 143 ($C_4F_5^+$), 124 ($C_4F_4^+$), 93 ($C_3F_3^+$), 57 ($C_4H_9^+$). Anal. Calcd for $C_{10}H_9F_7O$: C, 43.17; H, 3.24; F, 47.84. Found: C, 43.45; H, 3.32; F, 47.57.

2,3-Di-*tert*-butoxyperfluorobicyclo[2.2.0]hex-2-ene (11). The same method described above for the mono-*tert*-butoxy derivative (**10**) was employed. A dry 250-mL three-necked round-bottom flask containing 7.3 g of 100% pure perfluoroolefin **7** (0.033 mol) dissolved in 30 mL of freshly distilled THF was cooled to −65 °C under nitrogen atmosphere. A total of 2.0 equiv of potassium *tert*-butoxide (2.0 M) was added dropwise with vigorous stirring. After 2.5 h, the contents of the reaction vessel were dynamically transferred (25 °C/30 mTorr) to a U-trap. The leftover solid was washed with pentane and methylene chloride, and the mixture was filtered through a bed of filter aid. This filtrate was combined with the contents of the U-trap, and the solvents were removed by distillation as the pressure was slowly lowered from 760 to 30 Torr at room temperature. Fractional distillation (63 °C/50 Torr) afforded a light brown crystalline compound. These crystals were washed with pentane to give 9.0 g of 95% pure (12 m methylsilicone; t_R = 10.4 min) diether **11** (0.026 mol, 78% yield). These colorless, transparent crystals were purified by preparative gas chromatography. Mp 52.5−54 °C. ^{19}F NMR ($CDCl_3$): Φ −119.8, −124.0 (subsplit AB q, J = 219 Hz, 4F); −184.7 (m, 2F). ^{1}H NMR ($CDCl_3$): δ 1.5 (s, 18H). IR: 2990, 1670, 1350, 1260, 1175, 950, 810 cm^{-1}. MS (*m*/*e*): 332 (M^+), 276 ($C_{10}H_{10}F_6O_2^+$), 261 ($C_9H_7F_6O_2^+$), 57($C_4H_9^+$). Anal. Calcd for $C_{14}H_{18}F_6$: C, 50.60; H, 5.42; F, 34.34. Found: C, 50.54; H, 5.42; F, 34.42.

3*H*-Perfluorobicyclo[2.2.0]hexan-2-one (3). (a) From Enol Ether 10. A 10-mL side-arm round-bottom flask containing 30 mg (0.11 mmol) of 100% pure perfluoro enol ether **10** and excess bibenzyl (8−10 equiv) dissolved in 1.5 mL of dry 1,2,4-trichlorobenzene was attached to a vacuum line. Two traps in series at temperatures of −5 °C (ice/NaCl) and −78 °C (2-propanol/CO_2(s)) were installed to trap the reaction products. Concentrated sulfuric acid (0.2 mL, 30 equiv) was added via syringe, and the reaction was thoroughly mixed for 10 min. To allow the reaction products to distill at room temperature, the pressure was reduced to 0.01 Torr for 30 min. The content of the −5 °C trap was found to be solely 1,2,4-trichlorobenzene; the −78 °C trap contained a mixture of ketone **3** and enol **4** (90/10). A static transfer (0 °C/0.03 Torr) to an NMR tube containing dry chloroform-*d* and 1 μL of hexafluorofluorobenzene (8.7 × 10^{-3} mmol) separated the more volatile ketone from its enol. Integration of the ketone and hexafluorobenzene signals revealed 9.6 × 10^{-2} mmol of ketone **3** (85% yield). ^{19}F NMR ($CDCl_3$) of **3**: Φ −111.8, −130.8 (AB q, J = 222 Hz, 2F); −116.0, −125.8 (AB q, J = 229 Hz, 2F); −182.0 (s, 1F); −182.6 (s, 1F); −186.0 (subsplit d, 1F). IR (gas phase) of **3**: 2910, 1838, 1404, 1360, 1292, 1204, 1061, 996, 926, 865, 829 cm^{-1}.

(b) From Diol 20. The same procedure as above was employed except that 0.50 g of enol ether **10** (1.8 mmol) and 3.5 mL of 1,2,4-trichlorobenzene was treated with 30 equiv of concentrated sulfuric acid. The content of the −78 °C trap was transferred to a 5-mL round-bottom flask containing 50 μL of distilled water. Formation of white crystals was instantaneous. These crystals were subjected to reduced pressure (0 °C/0.01 Torr) to remove excess water. A total of 0.35 g of diol **20** was recovered (1.5 mmol, 83% yield). ^{19}F NMR ($CDCl_3$) of **20**: Φ −118.2, −129.2 (AB q, J = 217 Hz, 2F); −121.9, −126.3 (AB q, J = 224 Hz, 2F); −184.7 (m, 1F); −194.7 (m, 1F); −198.6 (subsplit d, 1F). IR (CH_3CN) of **20**: 3320, 2990, 1300, 1190, 960, 920, 870, 830 cm^{-1}. MS (*m*/*e*) of **20**: 222 ($C_6HF_7O^+$), 175 ($C_5HF_6^+$), 156 ($C_5HF_5^+$), 109 ($C_3F_3O^+$).

Seventy-five milligrams of **20** (0.31 mmol) was transferred in a nitrogen-filled glovebag to a 5-mL side-arm flask. The flask was attached to a vacuum line and 0.5 mL (30 equiv) of concentrated sulfuric acid was added. Reaction was allowed to proceed at room temperature until diol **20** completely dissolved in the acid. The pressure was reduced to 0.01 Torr and product was collected at −78 °C; it was statically transferred (25 °C/0.01 Torr) into a well-dried NMR tube containing dry chloroform-*d*. A total of 60 mg of hydroperfluoro ketone **3** (0.27 mmol, 87% yield from **20**) was obtained. ^{19}F NMR and IR data for **3** were identitical to those reported above.

2-Hydroxyperfluorobicyclo[2.2.0]hex-2-ene (4). (a) Method A. Hydroperfluoro ketone **3** was statically transferred (25 °C/0.03 Torr) to a well-dried NMR tube containing 0.2 mL of dry acetonitrile. ^{19}F NMR (CD_3CN): Φ −116.9, −124.7 (AB q, J = 207 Hz, 2F); −117.9, −124.7 (AB q, J = 219 Hz, 2F); −131.1 (d, J = 22 Hz, 1F); −189.7 (m, 1F); −196.5 (s, 1F). IR (CH_3CN): 3100, 1730, 1320, 1180, 920, 870 cm^{-1}. MS (*m*/*e*): 222 (M^+), 175 ($C_5HF_6^+$), 156 ($C_5HF_5^+$), 106 ($C_4HF_3^+$, base).

(b) Method B. To a dry NMR tube containing 0.5 mL of CCl_4 and 0.05 mL of benzene-d_6 was added 30 mg (0.1 mmol) of enol ether **10**. An initial ^{19}F NMR spectrum was recorded and then 4−5 drops of concentrated sulfuric acid were added. The NMR tube was shaken vigorously, with pauses only to record ^{19}F NMR spectra. After complete disappearance of **10**, the organic layer was poured away from the acid to produce a solution of **4** and **3** (90/10) in CCl_4. ^{19}F NMR (CCl_4) of **4**: Φ −117.4, −126.1 (AB q, J = 212 Hz, 2F); −118.3, −125.8 (AB q, J = 212 Hz, 2F); −126.8 (d, J = 23 Hz, 1F); −191.5 (s, 1F); −197.3 ppm (s, 1F). ^{1}H NMR (CCl_4): δ 4.8 (s, 1H).

Equilibration of Ketone 3 and Enol 4. Ketone **3** was statically transferred at 25 °C (30 mTorr) to a cold NMR tube (−196 °C) containing 0.5 mL of dry CCl_4 and 2 μL (1.7 × 10^{-5} mol) of hexafluorobenzene as an internal standard. After the tube had been carefully warmed, integration of the ketone and hexafluorobenzene signals revealed 1.5 × 10^{-5} mol of **3** (3 mM). A 9.0-μL aliquot of a 0.02 M solution of 1-methyl-2-pyrrolidone (1.8 × 10^{-7} mol) in CCl_4 was added to the NMR tube via syringe. The ^{19}F NMR spectrum was recorded every 10 h until a constant **3**-to-**4** (93/7) ratio was established.

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Supporting Information Available: Tables of final optimized geometries (6-31G**) in Cartesian coordinates for ketone **1** and enol **2** (syn and anti) (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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