Simple Enols

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I. Introduction

Despite the impression conveyed by most organic textbooks, certain enols can exist free of and not in equilibrium with their aldehyde or ketone tautomers. I use the adjective "simple" in the title of this article to describe those enols which contain none of the special types of functionality well known to stabilize enols;[1] thus 1,3-diketones, β-keto esters, α-nitro, cyano, or sulfonyl ketones, phenols, and related substances which exist, sometimes entirely, as enols are excluded from our discussion.[2]

There now exists a rather large number of simple enols, usually formed as the kinetic products of a reaction, which can be prepared either in isolation (for example, in the gas phase or in a matrix) or in condensed phases (pure or in solution), free of the corresponding keto form. The kinetic energy barrier for conversion to the generally more stable keto form sometimes can be quite high.

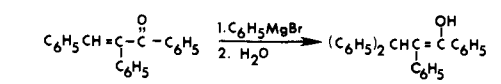
It is my main purpose to review here known structural types of simple enols, their properties, and the methods by which they can be prepared. Conversely, certain keto forms of relatively simple phenols have been synthesized, and I include a brief section on this topic.

Previous reviews of enolization or keto–enol tautomerism deal primarily with factors that affect the equilibration of tautomers[1-4] or with special features such as photoenolization[5] or the use of enolates in synthesis.[6] I hope that this review, which focuses on the structure and properties of the individual (and usually the less stable) tautomer, will provide a fresh view of this subject.

II. Enols with Bulky Aryl Groups

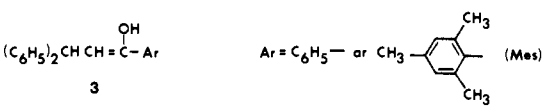
A. Fuson's Classic Studies

Early in this century, there were indications that some simple enols might be isolable. For example, in 1906 Kohler isolated a crystalline compound, mp 95–100 °C, thought to be the enol **2**, from conjugate addition of phenylmagnesium bromide to the unsaturated ketone **1**.[7] The compound, not obtained pure, was



1 **2**

rapidly converted to its keto form. Later,[8] Kohler found that in compounds of type **3**, when Ar was mesityl (Mes), conversion

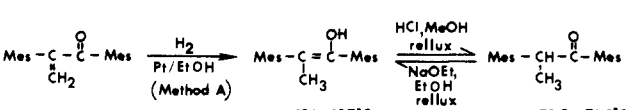


3

to the keto form was slower than when Ar = phenyl, but he had evidence for the existence of these enols only in solution and could not isolate them. Also, taking advantage of Mes groups, Lutz[9] was able to isolate the crystalline enol **4** and even the dienol **5**.[10] These were isolated studies, however, and it remained for Fuson, in a classic series of papers, to investigate the problem more systematically.

4 (m.p.132°C) 5 (m.p.73°C)

The first crystalline simple enol reported by Fuson was **7**, prepared by 1,4-addition of hydrogen to the enone **6**.[11] Only a single product was obtained, and though the stereochemistry was never established, the bulky mesityl groups are probably trans to each other. The keto form **8** could be prepared from **7** by refluxing with acid, whereas the enolate prepared from **8** and base gave the enol **7** on protonation.[12] The presence of a hydroxyl group in **7** was demonstrated by an infrared spectrum (3623 cm^{-1}).



m.p.126–127°C m.p. 73.5–74.5°C

6 **7** **8**

Within just a few years, a rather large number of enols similar to **7** were prepared. These are listed in Table I, with their methods of preparation.[13] In enols **7** and **9–18**, the carbon–carbon double bond is tetrasubstituted, but some enols with only trisubstitution were also stable (**19–26**). The first of these to be described was **19**, obtained through a pinacol-type rearrangement of **28**.[14] The IR spectrum of **19** showed bands for the hydroxyl group. Not only could esters (acetate, benzoate) be prepared in the usual way,

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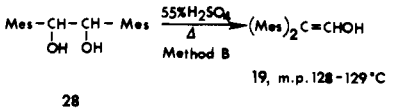
TABLE I. Stable Hindered Enols $R_1R_2C{=}C(OH)R_3$[a]

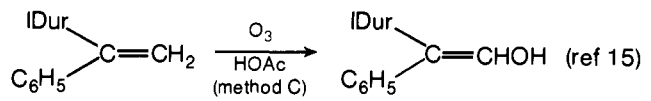
compd	R_1	R_2	R_3	prep[b]	ref
7	Mes	CH_3	Mes	A	11, 12
9	Mes	C_2H_5	Mes	E	17
10	Mes	$C_6H_5CH_2$	Mes	A, E	17
11	Mes	C_6H_5	Mes	D	16
12	Mes	Mes	Mes	D	22
13	Mes	CH_3	Dur	A	19
14	Mes	CH_3	IDur	A	19
15	Dur	CH_3	Mes	A	19
16	IDur	CH_3	Mes	A	19
17	Mes	Mes	CH_3	D	21
18	Mes	Mes	C_6H_5	D	21
19	Mes	Mes	H	B, F	14, 18
20	IDur	IDur	H	B	14c
21	Tip	Tip	H	B	22
22	Mes	C_6H_5	H	B, C, F	20, 15, 18
23	3-BrMes	C_6H_5	H	F	18
24	Dur	C_6H_5	H	F	18
25	IDur	C_6H_5	H	C	15
26	Mes	*p*-$CH_3C_6H_4$	H	C	15
27	Mes	C_6H_5	CHO		23

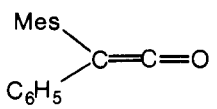
[a] Abbreviations: Mes = mesityl (2,4,6-trimethylphenyl); Dur = duryl (2,3,5,6-tetramethylphenyl); IDur = isoduryl (2,3,4,6-tetramethylphenyl); 3-BrMes = 3-bromomesityl; Tip = 2,4,6-triisopropylphenyl. [b] A: 1,4-addition of hydrogen to an enone; see 7 in text. B: acid-catalyzed rearrangement of a 1,2-diol; see **19** from **28** in text. C: ozonolysis of a 1,1-diarylethylene; see **25** in text. D: Grignard addition to a ketone; see **11** in text. E: 1,4-addition of a Grignard to an enone; see **9** in text. F: reduction of a ketene with a Grignard reagent; see **19** from **31** in text.

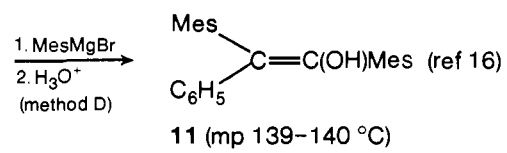


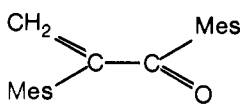
but treatment with HCl/ROH (R = CH_3, C_2H_5) gave the corresponding vinyl ethers.

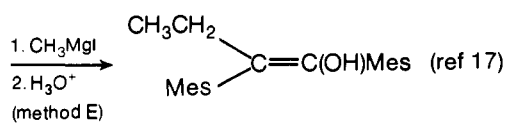
Other general methods used by Fuson to prepare stable "hindered" enols are illustrated by the following examples:

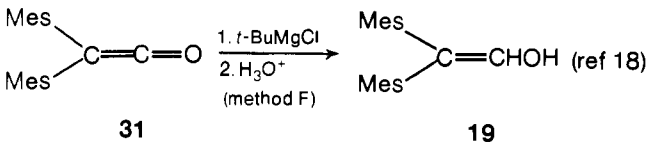






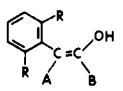






Also, certain of these enols (i.e., **7, 11, 18, 22**) could be obtained from the corresponding keto forms by acidification of the enolates, or by hydrolysis of the enol esters.

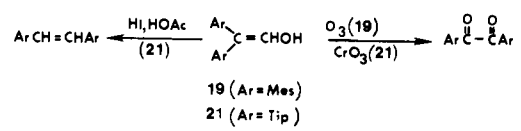
Fuson extended these methods to substituents other than those listed in Table I. In some instances, he obtained evidence that the enols were formed in solution but could not be isolated; in others, only keto structures were produced. From these studies, he generalized that for enol E to be stable (i.e., isolable),



E (R=alkyl)

B may be any alkyl group or hydrogen if A is a hindered aryl group (i.e., mesityl, duryl, etc.). But if B is a hindered aryl group, A may be aryl, alkyl, or hydroxyl but *not* hydrogen. No stereochemistry is implied by structure E, since the stereochemistry of these enols was not determined.

The reactions of enols of the type listed in Table I were studied to only a limited extent by Fuson, and for the most part have not been investigated since. Most of the reactions are typical for the two functional groups—formation of esters or ethers from the alcohol function, ketonization, hydrogenation, and oxidative cleavage at the double bond. Certain of the reactions, however, have novel aspects. For example, oxidation of **7** with potassium permanganate or with bromanil resulted in 1,4-dehydrogenation to **6.** Oxidation of **19** with ozone, or **21** with chromic acid, pro-

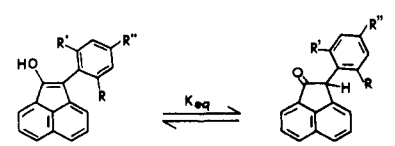


ceeded with aryl rearrangement, as did the reduction of **21** with HI in acetic acid. Not all of the enols could be converted to the corresponding ketones; for example, all attempts to convert **12** to the keto form failed. Most of the experiments on the enols listed in Table I were performed to determine their structures. A systematic study of their chemistry has never been undertaken and might be worthwhile.

B. Recent Work

Although Fuson's classic studies revealed some of the structural limitations of these stable enols, they did not include any quantitative measurements. Indeed, it is not clear from his work whether the enols were isolable because they were stabilized or the keto forms were destabilized, or the barrier to their interconversion was high. Only recently have modern physical methods been applied to the problem.

Miller[24] studied by NMR the acenaphthene systems shown. In the keto forms (**33, 35**) groups R and R′ are not equivalent but they may become so by either of two processes: (a) 180°



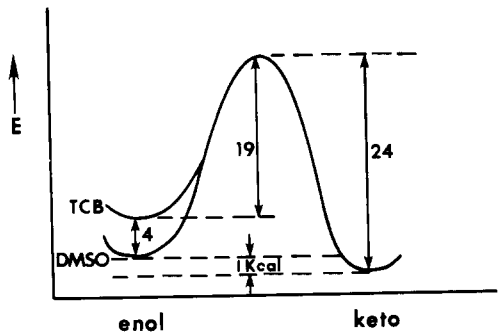


Figure 1. Approximate energy diagram for **32** ⇄ **33**, using data and estimations in ref 24.

rotation about the C_{sp^3}–C_{Ar} bond, or (b) enolization, followed by ketonization of the symmetric enol (in the following equations, ketone* refers to site-exchanged ketone). The observed rate constant for the exchange process as measured by NMR

$$\text{(a) ketone} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{ketone*}$$

$$\text{(b) ketone} \underset{k_{-1}'}{\overset{k_1'}{\rightleftharpoons}} \text{enol} \underset{k_1'}{\overset{k_{-1}'}{\rightleftharpoons}} \text{ketone*}$$

(for example, by observing the coalescence temperature T_c for the two methyl singlets in **33**), is given by

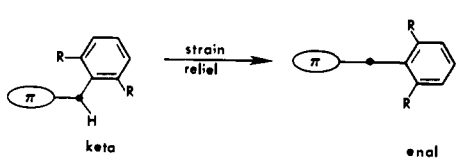
$$k_{obsd} = k_1 + k_1'/2$$

(k_1' must be divided by 2 because, once formed, the enol can revert to unexchanged ketone or site-exchanged ketone with equal probability). The observed T_c for **33** in 1,2,4-trichlorobenzene (TCB) was 183 °C, corresponding to a rate constant of 147 s^{-1}. From the fact that there was no significant change in T_c when the solvent contained as much as 2% trichloroacetic acid (which should catalyze the enolization), the author concluded that the $k_1'/2$ term must be less than 25 s^{-1} (this value would have resulted in a 3° drop in coalescence temperature, which would have easily been observable). Thus the maximum value of k_1' would be 50 s^{-1} which, at 183 °C, corresponds to a $\Delta G^{\ddagger}$ for enolization of at least 24 kcal/mol.

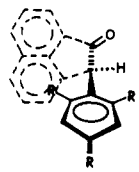
The equilibrium constant (enol/keto) for **32** ⇄ **33** was also measured (by NMR) and was 0.3 in Me_2SO-d_6, corresponding to a ΔG of about 1 kcal/mol. The free energy of the enol's hydrogen bond to Me_2SO is estimated at 4 kcal/mol. Thus we can draw the approximate energy diagram shown in Figure 1.

The even higher barrier to rotation for **35** ($T_c \geq 200$ °C) suggested that **34** should be isolable, and indeed the author isolated this enol as orange needles, mp 182–186 °C. The NMR spectrum in Me_2SO-d_6 showed a singlet at δ 3.33 for the O–H proton, and the infrared spectrum had an OH band at 3540 cm^{-1} and no carbonyl absorption.

After considering a variety of factors, Miller concluded that the major reason for the relative thermodynamic stability of enols **32** and **34** is the steric destabilization of the keto forms. This effect is demonstrated by the increase in K_{eq} (from 0.3 for **32** to 2.6 for **34** in Me_2SO) when methyl groups are replaced by isopropyl groups. Strain is relieved when the keto form is converted to the enol, since in the latter structure the R groups can



straddle the acenaphthenol π system. In the keto form, the R groups strongly interact in a destabilizing manner with that π system, as seen in the following drawing:

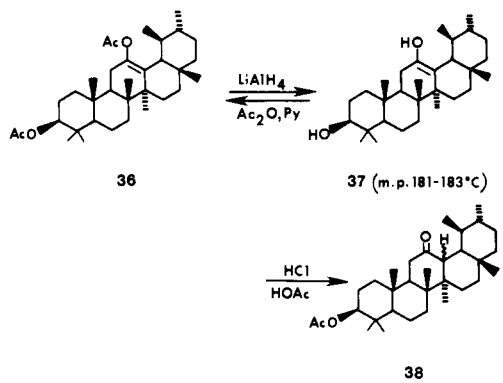


Resonance stabilization of the enol (relative to the ketone) due to the double bond in the five-membered ring is considered to be unimportant.

III. Other Highly Substituted Enols

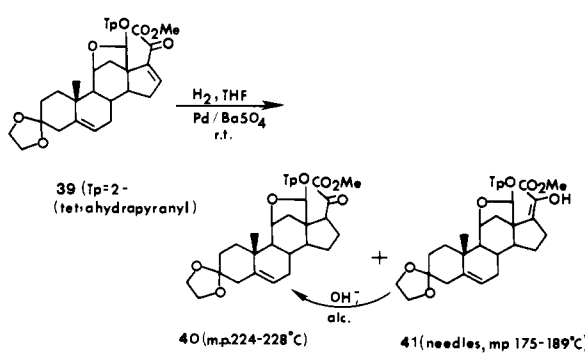
A. Steroidal Enols

Hindered aryl substituents are not required for an enol to be isolable. For example, several steroidal enols have been isolated in crystalline form. The carbon–carbon double bond in these enols is usually tetrasubstituted and the hydroxyl group is in a somewhat crowded environment, thus slowing ketonization. Perhaps the first example is that of Kaye and the Fiesers[25] who obtained enol **37** from the lithium aluminum hydride reduction of diester **36.** The enol was characterized by its infrared and ultraviolet spectra and by acetylation in pyridine to the original diacetate. Acetylation in acid, however, converted **37** to the keto acetates **38** (epimeric at C_{13}). Although the reason for the slow

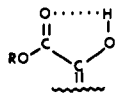


ketonization of **37** is not known, we note that the environment of C_{13} contains one α-axial and two β-axial methyls which could hinder delivery of a proton to that carbon.

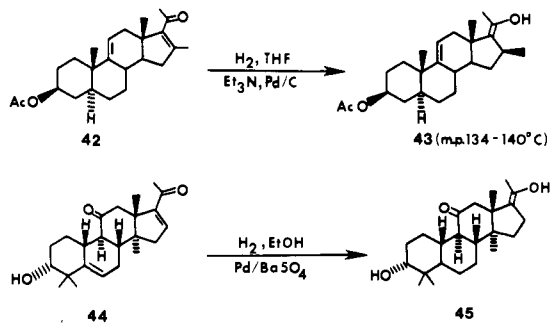
Catalytic hydrogenation of **39** gave not only the saturated ketone **40** but its enol **41** as well.[26] Presumably hydrogenation involves 1,4-addition to the enone. Enol **41** was characterized by its spectral properties and conversion to an enol acetate with acetic anhydride–pyridine and to ketone **40** with alcoholic base.



One might argue that **41** derives some stabilization from conjugation of the enol double bond with the ester carbonyl group, and perhaps also from some intramolecular hydrogen bonding, as shown. However, the enolic hydroxyl is not suffi-



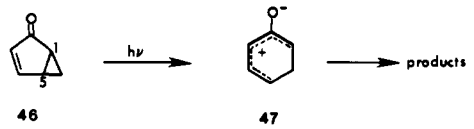
ciently acidic to react with diazomethane, and two similar examples are known where the ester function is replaced by a methyl group. Hydrogenation of **42** gave enol **43**[27] and similar reduction of **44** gave enol **45.**[28] Thus the C_{21} ester group is not



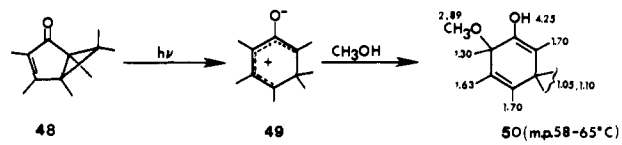
essential. We suspect that once again steric factors retard the ketonization (the C_{13}, C_{16} methyl substituents in **43** and the C_{13}, C_{14} methyl substitutents in **45**). The broad melting ranges of **41** and **43** may be due to thermal ketonization during the melting point determination. When **43,** for example, was heated for 2 h at 100 °C, it was converted to a mixture of the 17α- and 17β-C_{20} ketones. Enol **45** and similar enols were not isolated pure, but subjected to autoxidation, providing a route to 17-keto steroids.[28]

B. Other Cyclic Enols

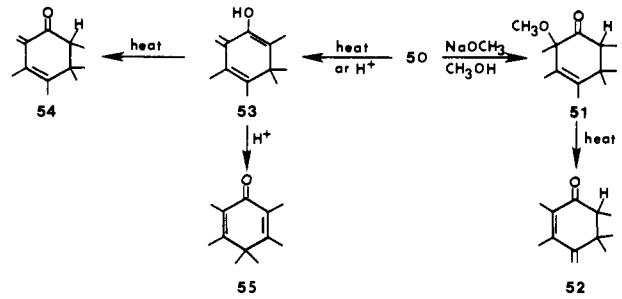
Evidence for the existence of much simpler enols with tetrasubstituted double bonds was obtained in cyclic systems by Hart and Swatton.[29] Most photochemical reactions of bicyclo[3.1.0]hex-3-en-2-ones **46** involve breaking the C_1–C_5 bond and can be rationalized in terms of a dipolar intermediate **47.** For



example, irradiation of the hexamethyl derivative **48** in cold methanol gave the crystalline enol **50,** presumably by trapping the dipolar intermediate **49.** The structure of **50** was clearly

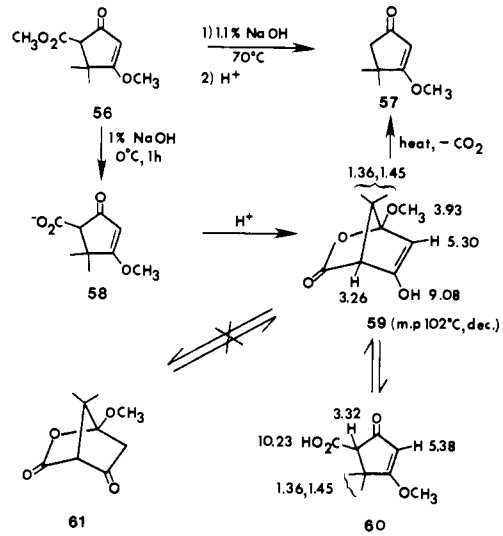


established by its NMR (see structure) and other spectral properties and by further transformations. For example, dilute base converted **50** quantitatively at 0 °C to the keto form **51** whose structure was established by its spectra and conversion to **52** by methanol loss. (NOTE: Only one stereoisomer of **51** was formed; its stereochemistry is not known.) Thus **50** is the kinetic product from **49,** whereas the keto form **51** is thermodynamically favored. Heat or a trace of acid causes 1,2-elimination of methanol from **50** to give another enol **53.** Although **53** was an oil which was difficult to purify and much less stable than **50,** its identity as an enol was clear from its spectra and conversion on heating to the keto form **54,** or on rearrangement in acid to the dienone **55.**



The reasons for the stability of **50** and **53** are not known. Their stability relative to the keto forms is certainly kinetic rather than thermodynamic. Tetrasubstitution of the enolic double bond and the bulk of the *gem*-dimethyl group adjacent to the carbon which must be protonated to give the keto form undoubtedly play a role.[30]

A novel crystalline bicyclic enol **59** has been described.[31] Saponification of β-keto ester **56** at 70 °C proceeded with decarboxylation to give **57,** but when the reaction was carried out under milder conditions, a crystalline intermediate was isolated, assigned the enol lactone structure **59,** formed through an intramolecular Michael addition of carboxylate to the enone moiety in **58.** The product showed a lactone carbonyl band at 1780 cm^{-1} and had an NMR spectrum (see structure) consistent with the structure. In solution, **59** is in equilibrium with the keto acid **60,** as shown by NMR, ultraviolet spectroscopy, and reconversion to **56** with diazomethane. Equilibration with the keto form **61** was

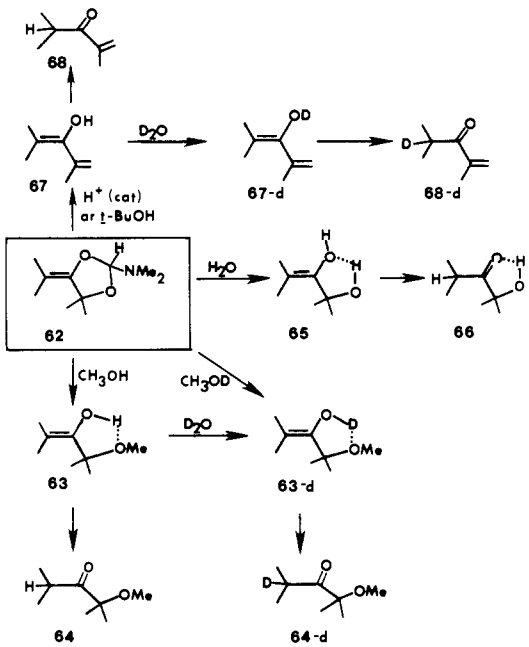


not observed, however. Apparently relief of strain obtained through a retro-Michael is favored over ketonization. On melting, **59** loses CO_2 to form **57.**

The isolation of **59** is quite surprising in view of the inherent strain associated with the bicyclo[2.2.1]heptene ring system. But **59** is insoluble in the aqueous acid in which it is formed, and this may account for its isolation. The authors depict some intramolecular hydrogen bonding between the hydroxyl and carbonyl groups, but this seems unlikely in view of the molecular geometry.

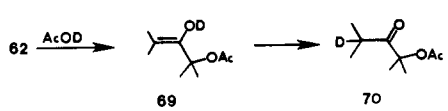
C. Acyclic Enols

In the acyclic series, simple tetrasubstituted enols have not been isolated in pure form, but evidence for their rather long lifetimes in solution was presented in elegant fashion.[32] Hydrolysis of 2-dimethylamino-4-methylene-1,3-dioxolanes[33] gives a variety of enols depending on the reaction conditions. For example, when the highly reactive heterocycle **62** was treated in CCl_4 solution with methanol, enols **63** and **67** were formed; both were identified by their NMR spectra. Each enol gradually

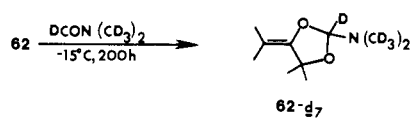


ketonizes (to **64** and **68,** respectively). Enol **63** was formed faster than **67** and was kinetically the more stable of the two. Apparently intramolecular hydrogen bonding, possible with **63,** outweighs the added conjugation present in **67.** With *tert*-butyl alcohol in place of methanol, only **67** was formed from **62.** Enol **67** could also be obtained from **62** in Me_2SO containing traces of moisture or acid; under these conditions, **67** was remarkably stable and could still be observed in solution after 8 days. Even the hydroxy enol **65** could be observed, formed very rapidly from **62** and water. It quickly ketonized to **66,** however.

Hoffmann used a nice trick to prolong the lifetimes of these enols. Exchange with D_2O or use of deuterated solvent (i.e., CH_3OD) produced the deuterated enols **63**-*d* and **67**-*d*. Because of the isotope effect in deuteron vs. proton transfer, these deuterated enols had longer lifetimes than their protio analogs. For example, the rearrangement of **63**-*d* to **64**-*d* required about 20 days for completion at room temperature in carbon tetrachloride; the comparable time for **63** → **64** was about 15 min. Also, treatment of **62** in carbon tetrachloride with *O*-deuterioacetic acid permitted the enol **69** to be observed before rearrangement to **70** was complete, whereas with ordinary acetic acid the only observable product was the protio analog of the keto form **70.**

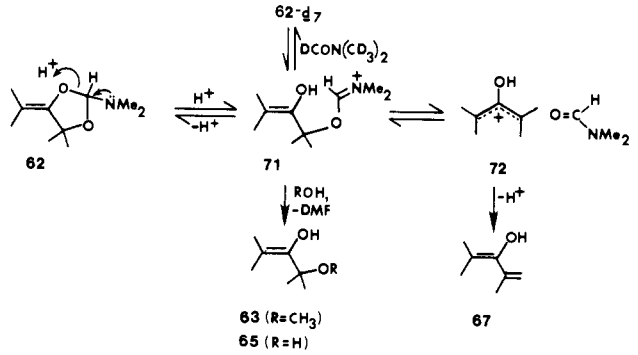


Compounds of the type **62** exchange amide moieties more rapidly than they form enols. For example, treatment of **62** at −15 °C with $DCON(CD_3)_2$ gave the deuterio analog **62**-d_7 with

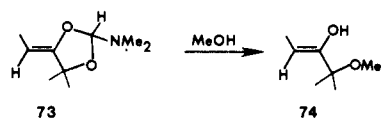


very little enol formation. To account for these observations, the authors suggest that two intermediates are involved in enol formation. Protonation and C–O bond cleavage gives immonium ion **71** which through nucleophilic attack may either exchange amide or form α-substituted enol (**63, 65**) in an S_N2-like process. Alternatively, loss of DMF would give the hydroxyallyl cation **72** which, in an E1-type process, could give dienol **67.**

What are the reasons for the stability of enols of the type **63**

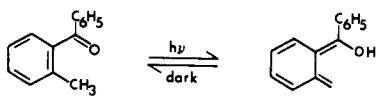


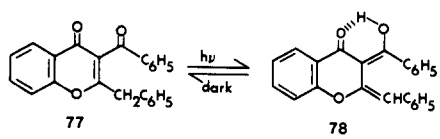
and **67**? One reason, of course, has to do with their method of formation. Compounds of the type **62** are highly reactive with a good leaving group (DMF), and can be hydrolyzed with very weak acids (alcohols, water) in stoichiometric amounts, so that the acidity of the reaction medium is kept low. In this way, catalysis of ketonization is minimized. Furthermore, polar aprotic solvents can be used, and these stabilize the enols through hydrogen bonding. Enols of type **63** may also be stabilized through intramolecular hydrogen bonding, whereas **67** may derive some stabilization through conjugation (although the all-planar s-trans geometry does have some problems because of 1,3-methyl interactions). Finally, the degree of substitution appears to be important. Thus when one methyl group in **63** was replaced by hydrogen,[34] the resulting enol **74** was more difficult to detect, since it rearranged very rapidly to the corresponding ketone.[35,36]



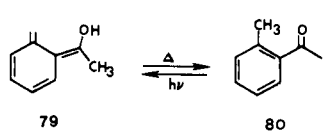
IV. Photo Enols

The light-catalyzed enolization of a wide variety of ketones is a general phenomenon which has long been recognized. Important examples which were studied early include **75** → **76**[37] and **77** → **78.**[38] The ground-state existence of enols such as **76**



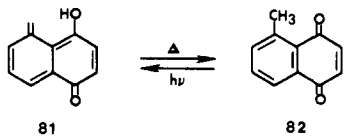


was demonstrated by trapping with dienophiles, by deuterium incorporation into the ortho alkyl substituent, and in many other ways. This subject has been recently reviewed[5] and will not be discussed here in detail. In most cases, the enols formed in this way are short-lived in terms of isolation as stable molecules at room temperature. For example, the rate constant for reketonization of **79** to **80** (from which **79** can be formed, through irra-



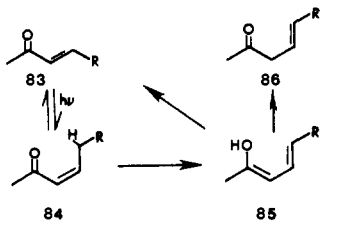
diation) is about 10^8 s^{-1} in cyclohexane and even in hydrogen bond acceptor solvents which stabilize the enol is still about 10^4 s^{-1}.[39] Ways of prolonging the lifetimes of such enols have been explored through appropriate substitution (for example, **81** →

82 has a rate constant of only 10^1 s^{-1} in hexamethylphosphoric triamide (HMPA)),[40] but in general most enols of this type are not isolable at room temperature because of the strong driving force for rearomatization.



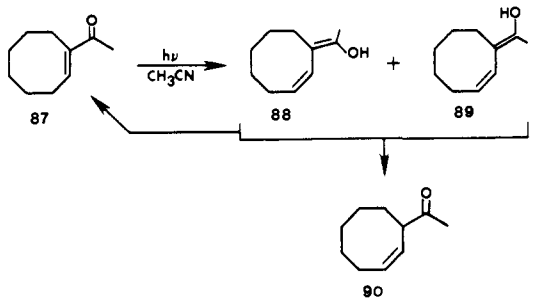
81 **82**

Analogous enols are involved in the photoisomerization of α,β- to β,γ-unsaturated ketones. Initial cis–trans isomerism about the double bond is followed by hydrogen abstraction leading to a dienol **85** which may then tautomerize to either type of ketone, **83** or **86**.[41] Recent application of this reaction to a



83 **84** **85** **86**

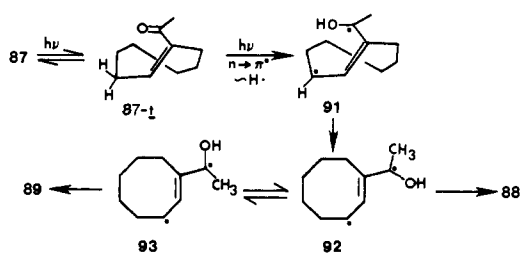
cyclic system led to remarkably stable enols.[42] Irradiation of a 5% solution of 1-acetylcyclooctene in acetonitrile in a nitrogen atmosphere with light of wavelength >350 nm gave an 80% yield of enols **88** and **89** in a 5:1 ratio. The enols were thoroughly characterized by their IR and NMR spectra, by acetylation to the corresponding enol acetates, and by isomerization (thermal, acid- or base-catalyzed) to a mixture of **87** and 3-acetylcyclooctene **90.** Although highly air sensitive, the enols were stable



87 **88** **89** **90**

in dilute solution and an inert atmosphere, and had not isomerized to the keto forms even after 3 days at room temperature in acetonitrile. They could also be generated by irradiation in methanol, and when the solvent was deuterated, conversion to the ketone **90**-*3d* required 4 days at room temperature.

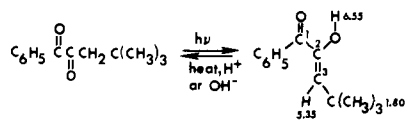
The mechanism by which enols **88** and **89** are formed follows the general pattern for acyclic enones. The eight-membered ring is large enough to permit cis–trans isomerism, and models show that only in this isomer is the geometry right for γ-hydrogen abstraction. The twisted biradical **91** which is formed initially relaxes to the less strained equilibrating biradicals **92** and **93** which then give the observed dienols.



87-*t* **91** **93** **92**

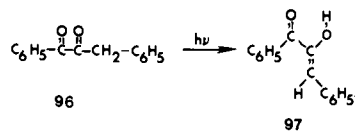
At least three factors are thought to contribute to the stability and long lives of **88** and **89.** Unlike acyclic enols which initially have an s-cis configuration, **88** and **89** are formed with a fairly rigid s-trans geometry which maximizes double bond conjugation. Also, the isomerization of the enols to the corresponding ketones is accompanied by a decrease in the number of sp^2-hydridized carbons in the eight-membered ring, a process known to add strain due to additional nonbonded interactions.[43] Finally, hydrogen bonding with the solvent must play a role, since irradiation of **87** in nonpolar solvents (benzene, carbon tetrachloride, cyclohexane, etc.) did not give any enol or **90.**[44]

Irradiation of certain phenyl 1,2-diketones has recently been shown to produce enols. For example **94** gave **95,**[45a] whose



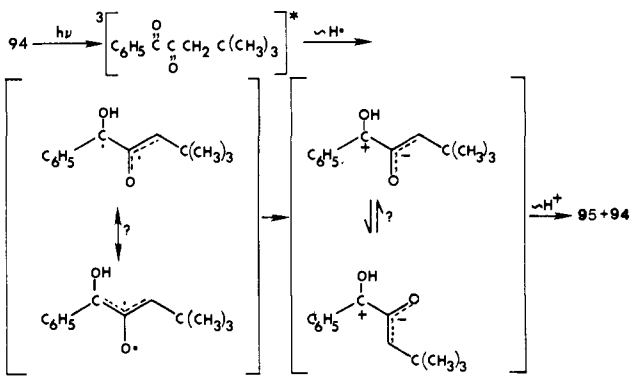
94 **95**

dilute solutions in carbon tetrachloride were stable at room temperature for days. The NMR spectrum showed a vinyl proton and a hydroxyl proton (exchangeable with D_2O), and the IR spectrum showed a concentration-independent hydroxyl band at 3410 cm^{-1}. The enol was converted back to the keto form by acid, base, or injection at 200 °C in a gas chromatograph. Conjugation, steric hindrance at C_3 due to the *tert*-butyl group, and possibly intramolecular hydrogen bonding stabilize **95.** Enol **97**[10c,46] has been similarly prepared.[45]



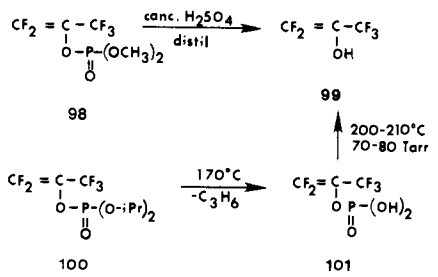
96 **97**

The process by which **95** is formed is somewhat different from most photoenolizations, since it involves β- rather than γ-hydrogen abstraction. The reaction goes through a triplet state of the diketone, possible via a dipolar intermediate in which rotation about the single bond joining the oppositely charged moieties is possible.

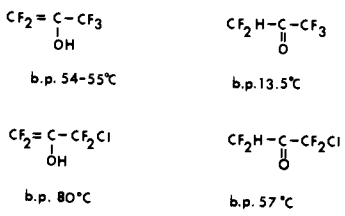


V. Fluorinated Enols

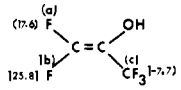
Perhaps the most remarkably stable simple enols are a group of highly fluorinated compounds prepared recently by Bekker, Knunyants, and co-workers in Russia. For example, the enol of pentafluoroacetone **99** is a distillable liquid, bp 54–55 °C, obtained in 90% yield from the enol phosphate **98** by heating with concentrated sulfuric acid.[47,48] The corresponding diisopropyl ester **100** can also be converted to **99** (72% yield) thermally. The enol in which the CF_3 group is replaced by CF_2Cl has been similarly prepared.[47,48] The boiling points of these enols are



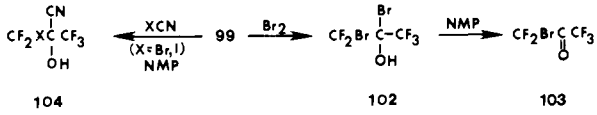
appreciably higher than those of the corresponding ketones, as expected:



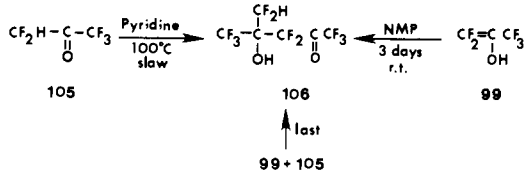
The structure of **99** was clear from its infrared spectrum (ν_{O-H} 3420 cm^{-1}, $\nu_{C=C}$ 1778 cm^{-1}), its ^{19}F NMR spectrum (chemical



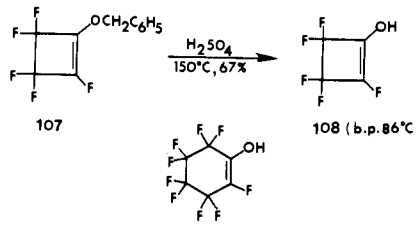
shifts are in ppm from CF_3CO_2H used as an external reference; J_{ab} = 56.2, J_{ac} = 9.7, J_{bc} = 24.2 Hz), and conversion to the ketone in various ways (for example, heating with trifluoroacetic acid or in acetonitrile at 100 °C, or on standing in water for several days). Enol **99** was converted to esters and ethers in fairly standard ways; addition of bromine to give **102,** which could be converted to the ketone **103** with *N*-methylpyrrolidone (NMP), or of cyanogen halides to give **104** has been claimed.[47] The



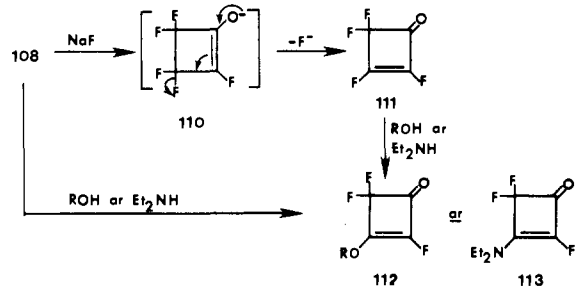
reaction with weak bases is interesting.[48] Either the ketone **105** or the enol **99** could be converted to the condensation product **106,** but in both cases the reaction was very slow. In contrast, when **99** and **105** were mixed, formation of **106** was virtually instantaneous.[48] Consequently the slow step in the first processes must be enolization of **105** or ketonization of **99.**



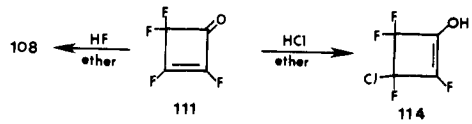
Several cyclic fluorinated enols have also been prepared. For example, acid-catalyzed cleavage of the enol ether **107** (readily prepared from perfluorocyclobutene, benzyl alcohol, and



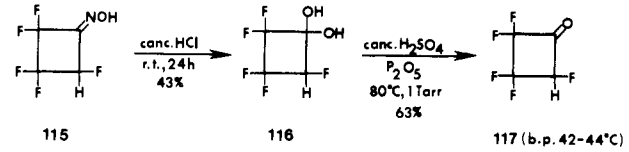
aqueous KOH) gave the cyclobutenol **108** in good yield.[49] The six-membered analog **109** was similarly prepared.[50] These enols were stable toward acid, could be stored for long periods without ketonizing, and formed stable distillable complexes with diethyl ether (for example, **108**·Et_2O could be stored in glass, and had a boiling point of 63–64 °C at 48 Torr) as do many other fluorinated alcohols.[51] However, they are very sensitive to base. For example, the weak base fluoride ion converts **108** to the cyclobutenone **111,** presumably via the enolate **110.**[49] More nucleophilic bases (alcohols or amines) displace another fluoride, presumably through addition–elimination to **111.** In some



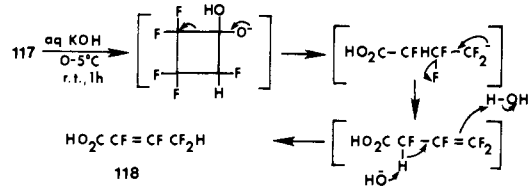
cases, addition to **111** without elimination is possible, and this can occur in a 1,4-manner to provide yet another route to enols. For example, **111** can be converted to **108** or the chlorinated enol **114.**[52]



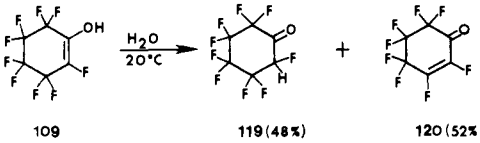
Enol **108** neither equilibrates with its keto form **117** in acid nor can it be converted by base to the keto form because of



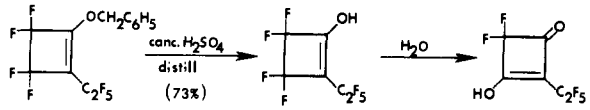
facile base-catalyzed elimination of fluoride ion from the enolate **110.** Consequently, it was of interest to synthesize the keto form by an independent route. This has been done from the oxime **115.**[53,54] Like the enol **108,** ketone **117** was stable to acid. With base, ring cleavage occurred to give **118.** Since the enol, under



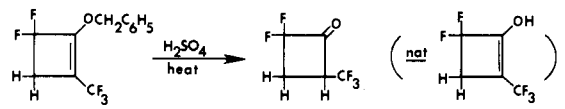
similar conditions, gave **112** (R = H) and CFH=CFCF$_2$CO$_2$H, it is clear that **108** and **117** do not equilibrate either in acid or in base. When the ring is larger (i.e., **109**), the enol can be converted to its keto form but equilibration by acid or base does not occur.[50]



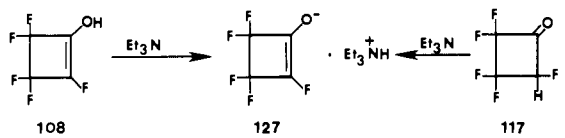
The fluorine on the double bond in enols of this type can be replaced by a perfluoralkyl group without losing the stability of the enol. Thus enol **122** was prepared in a manner analogous to **108.**[55] The enol is distillable, but reacts exothermically with



water to give **123.** Attempts to replace the CF_2 in the 3 position by CH_2, however, gave only the keto form (**124** → **125**).[55]



Although equilibration studies at present are lacking, it seems likely that the fluorinated enols possess kinetic rather than thermodynamic stability relative to their keto forms. The enolic carbon–carbon double bond, being substituted with strongly electron-withdrawing substituents, is not readily susceptible attack by a proton, thus slowing acid-catalyzed conversion to the keto form. It is thought[48] that the enolate anions are also destabilized by the unshared electron pairs of fluorines on the α carbon, and in the case of cyclic enols (**108, 109**) other reactions occur, such as loss of fluoride ion (**108** → **111**) or ring cleavage (**117** → **118**), which interfere with enol–keto equilibration. In one case, an enolate salt (or complex) **127** has been prepared from both the ketone and its enol.[52,53] It is stable for



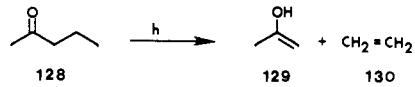
1–2 h and can be acylated (on oxygen) but gradually decomposes to resinous products on prolonged standing. Careful acidification of **127** (to determine the ratio of **108/117**) has not been described, and it might be worthwhile to determine the protonation site of the enolate.

It will be of interest to see, as research progresses, to what extent other enols stabilized by strongly electron-withdrawing substitutents can be synthesized, and to further study the chemistry of these novel compounds.

VI. Enols of Acetaldehyde, Acetone, and Other Simple Carbonyl Compounds

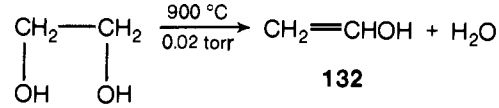
The most recent estimate[56] for the equilibrium constant of vinyl alcohol/acetaldehyde in dilute aqueous solution is about 5×10^{-6}, and for propen-2-ol/acetone the value is even smaller (6×10^{-8}). An indirect experimental estimate gives 13.2 kcal/mol as the difference between the heats of formation of vinyl alcohol and acetaldehyde in the gas phase,[57] which agrees reasonably well with a recent ab initio calculation (11.7 kcal/mol).[58] The energy difference between acetone and its enol is comparable, estimated experimentally at 13.9 kcal/mol.[59] These values are also approximately what one calculates from bond energies. Although vinyl alcohol, propen-2-ol, and other simple enols are thermodynamically substantially less stable than their keto tautomers, they can nevertheless have considerable kinetic stability. Vinyl alcohol is predicted to be stable with respect to *intra*molecular rearrangement (an activation energy of 85 kcal/mol is calculated for the unimolecular vinyl alcohol → acetaldehyde transformation). Vinyl alcohol survives long enough in the gas phase for its bond angles and distances and preferred conformation to be determined, and long enough in solution for its NMR spectrum to be accurately measured.

The enol of acetone was first observed directly in the gas phase.[60] Irradiation of 2-pentanone (1.6 Torr) in nitrogen (750 Torr) with a mercury arc produced propen-2-ol and ethylene by a Norrish type II process. The enol **129** was detected by its in-

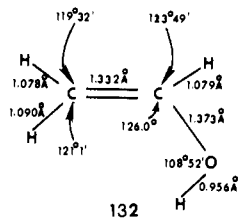


frared spectrum (ν_{O-H} 3628 cm^{-1}). Its identity was established by showing that the rate of disappearance of this O–H band was equal to the rate of appearance of the carbonyl band of acetone. The half-life of **129** at 750 Torr total pressure in a glass vessel lined with aluminum foil was 3.3 min at 21 °C. Ketonization occurred on the vessel walls, as shown by deuterium incorporation in the acetone when the reaction vessel surface was pretreated with D_2O.

Vinyl alcohol has been prepared by dehydration of ethylene glycol at 0.02–0.04 Torr and 900 °C.[61] It had a half-life of about

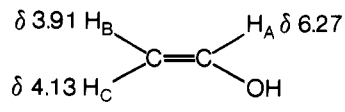


30 min in a Pyrex flask! From the microwave spectrum, the following structural parameters were derived:

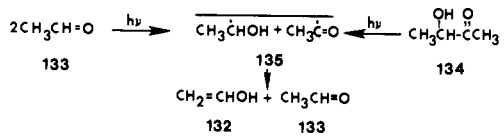


The C–O bond distance is appreciably shorter than that of ordinary alcohols (about 1.43 Å) suggesting that the C–O bond in **132** has some π character. The syn conformation, as shown, is preferred, confirming experimentally a prior theoretical calculation.[62]

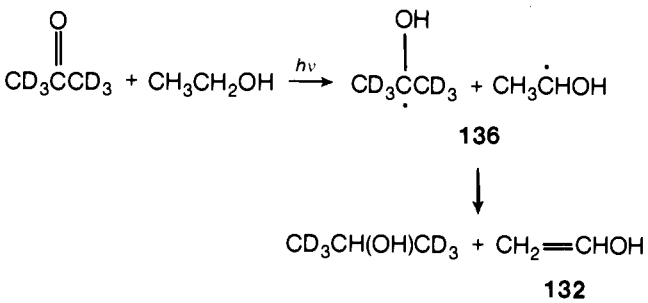
Chemically induced dynamic nuclear polarization (CIDNP) has provided a technique for measuring the ^1H and ^{13}C NMR spectra of a variety of enols, and for determining their rates of ketonization in solution. The technique involves generating in a modified NMR spectrometer, either photochemically or thermally, a pair of radicals which have structures such that, when they react in a subsequent step, an enol is produced with nuclear spins polarized and therefore detectable, even though the enol concentration may be quite low. For example, irradiation of either acetaldehyde or acetoin in benzene or other nonpolar solvents produced radical pair **135**[63] which subsequently disproportionated to vinyl alcohol and **133.**[64] The ^1H NMR spectrum of **132** was assigned as follows:



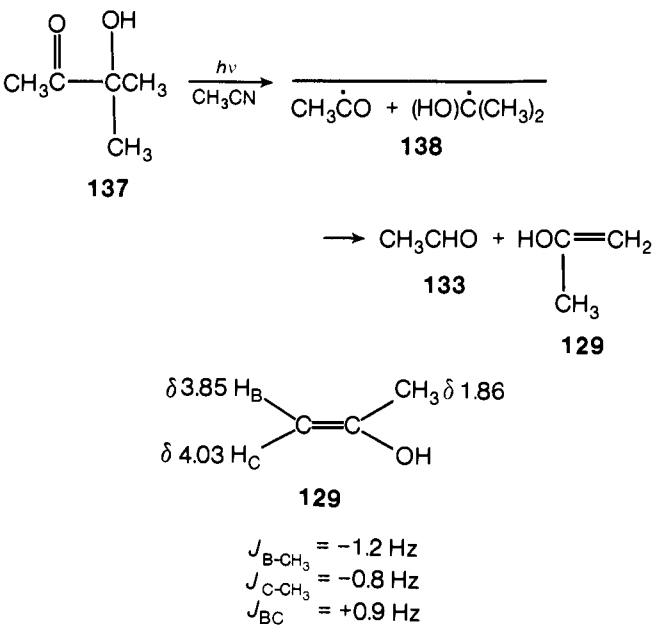
J_{AB} = 6.5 Hz
J_{AC} = 14.0 Hz
J_{BC} = −1.8 Hz



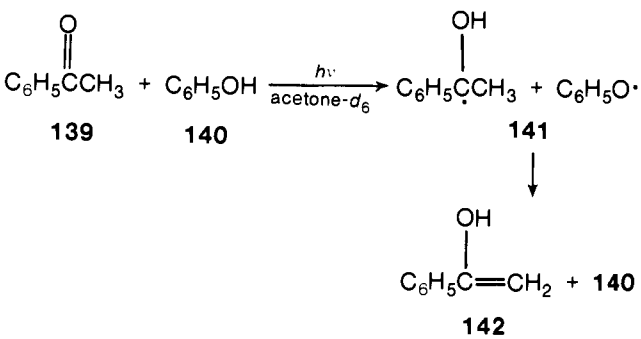
The lifetime of **132**, determined from the disappearance of H_c after irradiation, was as long as 25 s in these solutions,[65] but if a little *p*-toluenesulfonic acid was added to the solution (to catalyze ketonization), **132** could not be detected. Later,[66] the NMR spectrum of vinyl alcohol was confirmed by irradiating hexadeuterioacetone in ethanol; the radical pair **136** dissociated to **132** and hexadeuterio-2-propanol, giving the same NMR spectrum for **132** as determined previously.[58]



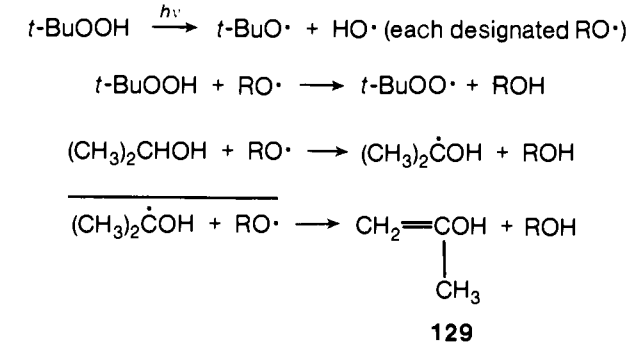
The enol of acetone has also been prepared and studied by these techniques. In acetonitrile, its lifetime is about 14 s.[65,67]



The enol of acetophenone was observed by irradiating the ketone in phenol.[68,68a] The suggested mechanism is

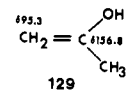


SCHEME I



The vinyl protons of **142** were observed at δ 4.5. Other enols have been detected in this way.[65,66,69] In general, the stationary enol concentration achieved is about 10^{-4} M and the half-lifetimes under these circumstances are about 10–20 s.

^{13}C NMR spectra of simple enols have also been observed by the CIDNP technique.[70] For example, irradiation of 10–50% solutions of *tert*-butyl hydroperoxide in isopropyl alcohol produced acetone enol **129**, probably via a sequence such as in Scheme I. Although the methyl carbon was not observed, both vinyl carbon signals were readily identified. The hydroxyl-bearing carbon of vinyl alcohol appears at δ 148.1, whereas in **129** ho-

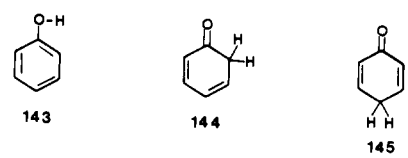


mologs (CH_3 replaced by ethyl, propyl, butyl) that carbon appears at δ 160– 162. Thus replacement of a vinyl proton by OH shifts the vinyl carbon resonance downfield about 25 ppm, whereas the comparable figure for a saturated carbon is about 48 ppm. Attempts have been made to explain these differences.[70]

It seems clear from these studies that enols, even simple enols, can be quite long-lived if they are generated in a manner which slows down the proton transfer mechanism for ketonization.

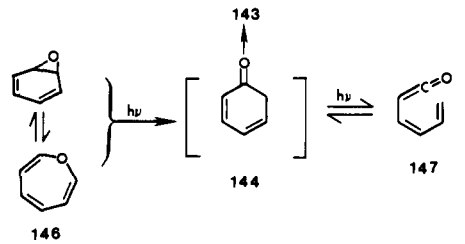
VII. Keto Forms of Phenols

Phenol exists in the enolic form **143** rather than in either of the two possible keto forms **144** and **145** primarily because the



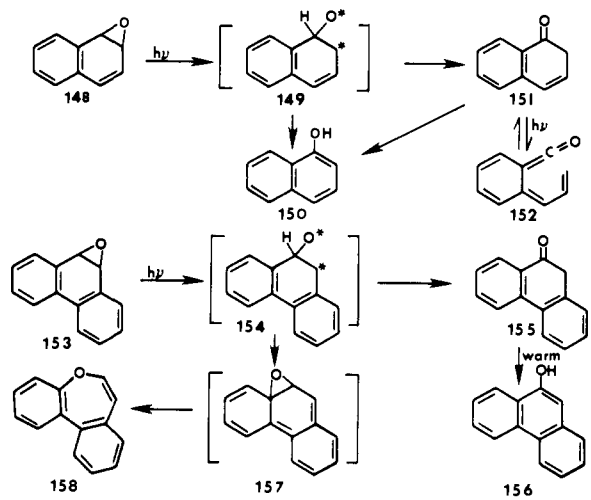
resonance energy gained through aromatization is considerably greater than the bond-energy difference which ordinarily favors keto over enol structures. Structural modifications which either destabilize the phenolic structure or stabilize the ketonic structure can lower this energy gap and permit the keto form to be observed, particularly if it is the kinetic product of a reaction. If the structural modification is sufficient, the keto form may even predominate at equilibrium. This is an old subject which has been reviewed,[71-74] and the treatment here will be illustrative rather than exhaustive, with emphasis on recent work and on the principles involved.

Neither keto form of phenol itself has yet been detected, although there is strong evidence for the existence of **144** as a short-lived intermediate. Irradiation through Pyrex of benzene oxide–oxepin **146** as a thin film at 77 K caused a decrease in its absorption at 1660 cm^{-1} and appearance of a sharp band at 2112 cm^{-1} due to ketene **147**.[75] Shortly a photostationary state was reached in which the concentration of **147** remained constant and phenol **143** began to appear (1590 cm^{-1}) at the ex-

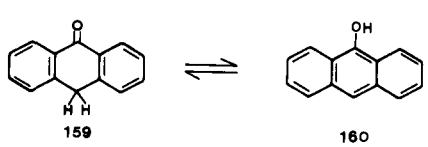


pense of **146.** Since the photoisomerization of 2,4-cyclohexadienones to ketenes is well known,[76] and since both a ketene and phenol were formed, it seems reasonable that the keto tautomer **144** was present, though in too low a concentration to be detected.

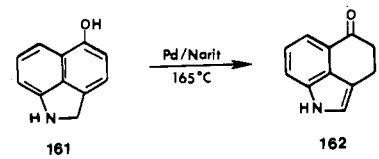
Fusion of one or two benzo rings to the arene oxide **146** allowed the keto forms **151** and **155** to be detected. Irradiation of naphthalene 1,2-oxide (**148,** Nujol suspension, quartz, 77 K) was followed by infrared spectroscopy, and a strong carbonyl band due to **151** (1674 cm^{-1}) was readily observed, as well as bands for 1-naphthol (1595 cm^{-1}) and ketene **152** (2112 cm^{-1}). The bands due to **151** and **152** disappeared in favor of the 1-naphthol band when the sample was warmed to −100 °C. Similar irradiation of phenanthrene 9,10-oxide (**153**) led to a new band at 1695 cm^{-1} attributed to 9-phenanthrone (**155**). As the solution was allowed to warm to room temperature, the band due to **155** disappeared in favor of 9-phenanthrol (**156,** 1600 cm^{-1}). In this case no ketene was detected (its formation would require loss of aromaticity in both benzene rings), but the dibenzooxepin **158** was another product of the photoisomerization.



Although no quantitative data are available, it seems likely from the manner in which these experiments were carried out that the keto tautomers have stabilities in the order **155** > **151** > **144** relative to their corresponding phenolic tautomers. The principle involved is that increasing benzo substitution diminishes the gain in resonance energy achieved through aromatization, thus diminishing the energy gap between the keto and phenolic tautomers. Perhaps the best known example of this principle is 9-anthrone/9-anthrol, where the keto form predominates at equilibrium (89% in ethanol at room temperature).[77,78]

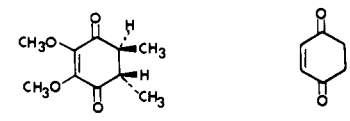


One may also stabilize the keto form of a phenol by trading the aromaticity of the phenolic ring for aromaticity in another ring. An example is the conversion of naphthol **161** to indole **162.**[79]

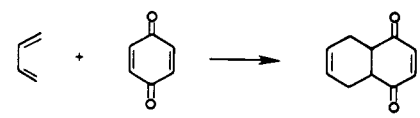


The generality of this idea does not seem to have been widely exploited.

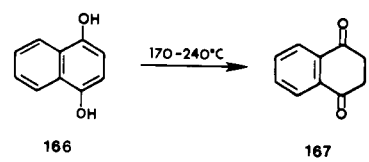
Another way to overcome the aromatic resonance energy of phenolic forms is to introduce a second ketonizable hydroxyl group; if both hydroxyls ketonize, twice the bond-energy difference which favors keto over enol structures becomes available to balance against the resonance energy of the aromatic form. Many diketo structures of this type are known, although their stability is usually kinetic rather than thermodynamic. The antibiotic gliorosein (**163**) occurs in nature as such a diketo structure, though it is readily aromatized by bases.[80] Whereas **163** is sufficiently stable at room temperature to permit its isolation from the natural source, the parent compound **164** (the



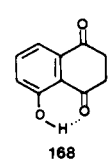
diketo form of hydroquinone) is appreciably less stable. It can be kept below 10 °C in crystalline form (mp 54 °C), but rearranges to hydroquinone slowly in nonpolar and very rapidly in polar solvents.[81] Although **164** had to be synthesized indirectly, many diketo forms of hydroquinones such as **165** are readily



accessible and isolable in one step through the cycloaddition of quinones to dienes.[82] In the naphthalene series, they may also be obtained by fusing the corresponding 1,4-naphthalene-

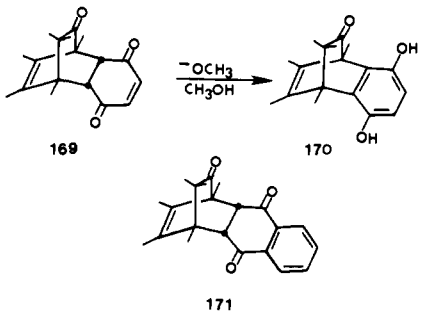


diols.[83,84] Most of these diones are kinetically stable but are converted by base to the phenolic form. However, other structural features may cause the diketo form to be thermodynamically stable. Thus **168** is the stable form of 1,4,5-naphthalenetriol.[84]

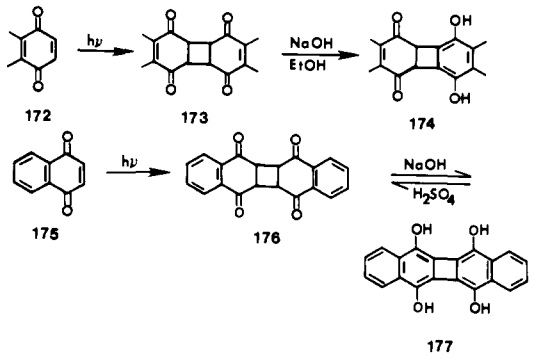


Whereas the adduct of 1,4-benzoquinone and hexamethyl-2,4-cyclohexadienone, **169,** is readily aromatized to **170,** the analogous naphthoquinone adduct **171** is recovered unchanged when its alkaline solutions (inert atmosphere) are acidified.[85] Apparently the difference between benzenoid and naphthalenoid resonance energy is sufficient to determine thermodynamic stability.

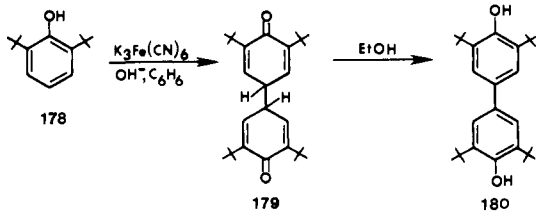
The converse situation appears in the quinone photodimers **173** and **176.** Treatment of **173** with base aromatizes only one



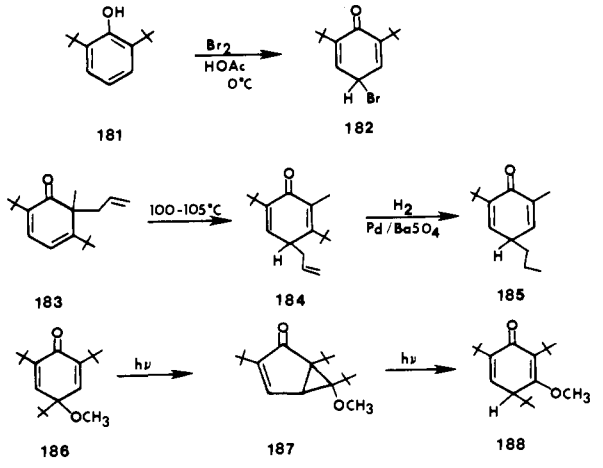
of the six-membered rings,[86] presumably to avoid the destabilization associated with the biphenylene that would otherwise result. In the naphthalene, where further delocalization is possible, both rings are aromatized (**176** → **177**).[87]



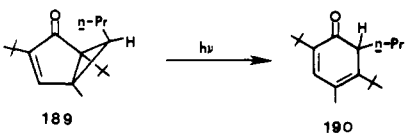
Finally, steric factors may permit the isolation of keto forms of phenols. Oxidation of 2,6-di-*tert*-butylphenol (**178**) with alkaline ferricyanide in benzene gave diketone **179**, which was



stable as the solid or in nonpolar solvents, but rapidly aromatized in ethanol.[88] Other examples of this type included **182**,[89] **184**,[90] **185**,[90] and **188**[91] which are substituted derivatives of the "para"



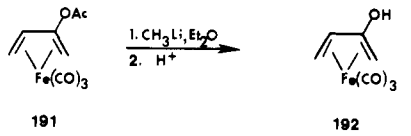
keto form **145**, and **190** which is a substituted "ortho" keto form **144**. In all these cases the keto form is kinetically stable, probably due to steric hindrance to reagents required for proton



transfer, but the phenolic forms are thermodynamically more stable.

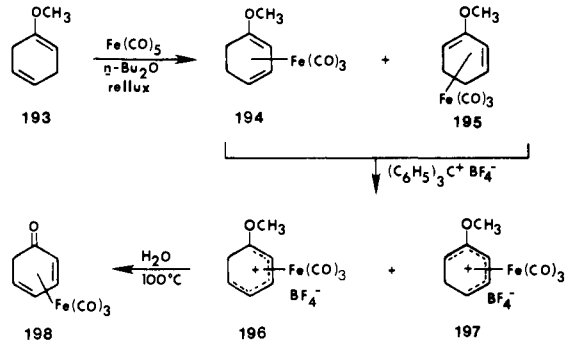
VIII. Stabilization of Enols and Keto Forms of Phenols through Coordination with Metals

Dienes form stable complexes with a variety of metals, and advantage of this has been taken to prepare complexes of ligands which in a formal sense are either enols or keto forms of phenols. For example, treatment of 2-acetoxy-1,3-butadiene with $Fe_2(CO)_9$ in benzene gave the yellow crystalline complex **191**; the acetoxy group was then converted to a hydroxyl group to give **192**, air sensitive but stable in solution.[92] Compound **192** is a



complex of the enol form of methyl vinyl ketone. Its structure was established by NMR and by conversion with benzoyl bromide to a crystalline benzoate. The pK_a of **192** is 9.24 in 48% aqueous ethanol corresponding to about 8.5 in water. Thus it is a much stronger acid than would be expected for the enol itself, probably because of electron withdrawal by the metal. Similar complexes with the hydroxyl at C_1 of the butadiene moiety have also been prepared.[92]

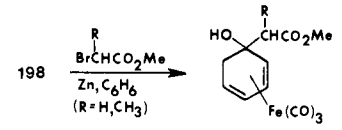
At about the same time, the iron tricarbonyl complex of **144**, the conjugated tautomer of phenol, was also prepared.[93,94] The vinyl ether **193** (obtained by lithium–ammonia reduction of anisole[94]) was refluxed with iron pentacarbonyl in di-*n*-butyl ether to give a mixture of **194** and **195** which was treated with trityl tetrafluoborate. Hydride abstraction (the other organic product is triphenylmethane) gives a mixture of carbonium ion salts **196** and **197**. When this mixture is heated with water on a steam bath,



crystals of complex **198** separate; this arises from hydrolysis of **196**, and unreacted **197** can be recovered as the hexafluorophosphate by adding ammonium hexafluorophosphate to the aqueous solution. Complexes similar to **198**, but with a methyl at C_3 or a methoxyl at C_4 of the dienone ligand, have also been prepared.[93] The structure of **198** was established by its spectra; the ^1H NMR spectrum shows two sets of vinyl protons at δ 5.84 ($C_{3,4}$) and 3.26 ($C_{2,5}$) and a methylene group at δ 2.35, and the ultraviolet spectrum (λ_{max} 230 nm, ϵ 13,100) is consistent with a dienone moiety. The mass spectral fragmentation pattern is also consistent with the structure.[95]

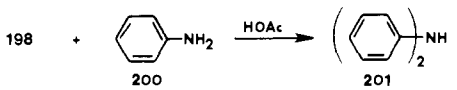
Ketone **198** undergoes a number of ordinary carbonyl reactions. For example, it gives an oxime[96] (which, however, does

not undergo Beckmann rearrangement) and it undergoes the Reformatsky reaction,[97] but the reaction with organolithium reagents or Grignard reagents led only to decomposition. At-



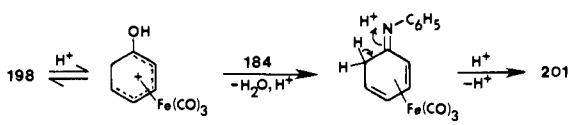
199

tempts to exchange the α-methylene protons with CH_3OD/CH_3O^- also caused decomposition of the complex. However in acidic solution **198** can be used to phenylate the nitrogen of primary aromatic amines.[98] Presumably the reaction involves



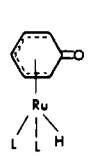
200 201

nucleophilic attack on protonated ketone **202** to give the imine complex **203** which in acid aromatizes and discards the metal to give **201.**

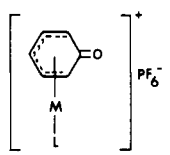


202 203

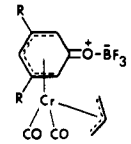
Finally, mention might be made of several complexes which have been described recently that include the ruthenium complex **204,**[99] the rhodium and iridium complexes **205,**[100] and the chromium complex **206.**[101] In each of these complexes phenoxide ion is coordinated to the metal through the π bonds of its ketonic tautomer. The chemistry of these novel complexes remains to be explored.



204 (L = $(C_6H_5)_3$ P)



205 (L = pentamethyl-cyclopentadiene, M = Rh, Ir)



206 (R = H, CH_3)

IX. Summary

Simple enols are not inherently unstable, as the independent existence of many of their simple derivatives testifies (i.e., enol esters, enol ethers), although they are usually thermodynamically less stable than their corresponding keto forms. The problem, then, in producing an enol not in equilibrium with its keto form involves generating the enol as a kinetic reaction product by a method that retards or prevents the proton transfer which converts it to the keto form. In this review, several ways of accomplishing this goal are described.

The earliest examples involved placing large groups (i.e., mesityl) at one or both ends of the enolic carbon–carbon double bond. This substitution retards proton removal from the hydroxyl group and proton delivery to the α carbon. It may also, in some instances, diminish the energy gap between enol and keto forms, through destabilization of the latter. Most of this work was done many years ago, before the NMR era of organic chemistry, and there are indications[24] that reinvestigation using modern techniques could be worthwhile. The reactions of these enols have barely been studied.

More recently, simple enols with less bulky groups have been prepared (section III), and even simple alkyl substitution clearly enhances the kinetic stability of these compounds. It is important that the enol-forming reaction be fast, faster than the proton transfer which brings about ketonization, if the enols are to be detected or isolated. Photochemical methods (section IV) are particularly good in this regard. But thermal methods can also do, as the synthesis of vinyl alcohol in the gas phase strikingly illustrates.[61] The long lifetime of this simplest of enols, which permitted its bond angles, distances, and preferred conformation to be accurately measured, should encourage further efforts in this direction.

Application of the CIDNP technique has permitted the NMR spectra of several enols to be measured, although so far the lifetimes of enols generated in this way have been comparatively short, less than a minute. Even so, this represents a very substantial displacement from the equilibrium concentration.

Perhaps most striking are the recently prepared, long-lived, and distillable fluorinated enols (section V). Since equilibration studies are as yet lacking, it is not known whether their stability with respect to the keto forms is kinetic or thermodynamic.

Keto forms of phenols in a sense are the counterpart of simple enols of carbonyl compounds. Although there is evidence for the "ortho" keto form of phenol itself (**144**) as a short-lived intermediate,[75] there are no data yet on the corresponding "para" keto form (**145**). Some of the same techniques used to prepare stable forms of enols have been used to stabilize these keto forms of phenols (for example, use of bulky substituents to retard proton transfer and to destabilize the phenolic form), and many examples are now known (section VII). Finally, enols and the keto forms of phenols have been stabilized through complexation with metals (section VIII). Although this method of stabilization alters the properties of the uncomplexed species rather drastically, it nevertheless leads to novel structures whose chemistry has as yet only barely been studied.

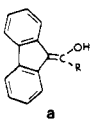
It is hoped that this review will dispel the myth that simple enols are known only as minor components of an equilibrium with their keto forms.

Acknowledgment. I am indebted to Dr. Michio Sasaoka for collecting some of the references used in this review. I also thank Michigan State University for a sabbatical leave (April–June, 1979) during which time the review was written.

X. References

(1) G. W. Wheland, "Advanced Organic Chemistry", 3rd ed., Wiley, New York, 1960, pp 663–702. Wheland refers to "simple" carbonyl compounds as those which in their keto form contain only an isolated carbonyl group, and whose enolic forms are not phenolic.
(2) Also excluded are enediols

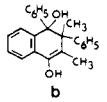
For a review, see G. Hesse in "Methoden der Organischen Chemie" (Houben-Weyl), Vol. VI/1d, Georg Thieme Verlag, Stuttgart, 1978, p 217.
(3) S. Forsen and M. Nilsson in "The Chemistry of the Carbonyl Group", Vol. 2, J. Zabicky, Ed., Interscience, New York, 1970, pp 158–240.
(4) G. S. Hammond in "Steric Effects in Organic Chemistry", M. S. Newman, Ed., Wiley, New York, 1956, pp 442–454.
(5) P. G. Sammes, *Tetrahedron*, **32**, 405 (1976).
(6) G. Hesse in ref 2, p 1.
(7) E. P. Kohler, *Am. Chem. J.*, **36**, 177 (1906).
(8) E. P. Kohler, M. Tishler, and H. Potter, *J. Am. Chem. Soc.*, **57**, 2517 (1935); E. P. Kohler and R. B. Thompson, *ibid.*, **59**, 887 (1937).
(9) R. E. Lutz and C. J. Kibler, *J. Am. Chem. Soc.*, **62**, 360 (1940).
(10) Other early examples of stable enols are the following.



a

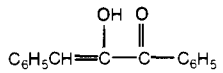
a: (R = H) W. Wislicenus and M. Waldmüller, *Chem. Ber.*, **42**, 785 (1909); (R = C_6H_5) K. H. Meyer and H. Gottlieb-Billroth, *ibid.*, **54**, 577 (1921). Neither enol was obtained pure. For R = H, the compound was obtained by the base-catalyzed condensation of ethyl formate with fluo-

rene; it was a distillable yellow oil which readily polymerized but gave a crystalline acetate, benzoate, and other derivatives. For R = C_6H_5, the corresponding ketone gave an enolate with aqueous alkali which, on acidification with cold hydrochloric acid, gave crystals of the enol.



b

b: H. M. Crawford, *J. Am. Chem. Soc.*, **57**, 2000 (1935); **61**, 3310 (1939). This compound, mp 208 °C, was obtained from the reaction of 2,3-dimethyl-1,4-naphthoquinone with excess phenylmagnesium bromide. The stereochemistry at the adjacent sp^3 carbons is not known.



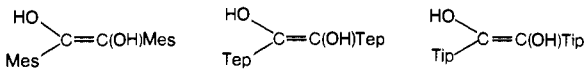
c

c: E. P. Kohler and R. P. Barnes, *J. Am. Chem. Soc.*, **56**, 211 (1934). This crystalline enol, mp 89–90 °C, is undoubtedly stabilized by conjugation of the carbon–carbon double bond with the carbonyl group (compare with **1**).

(11) R. C. Fuson, J. Corse, and C. H. McKeever, *J. Am. Chem. Soc.*, **62**, 3250 (1940).

(12) R. C. Fuson, D. J. Byers, and N. Rabjohn, *J. Am. Chem. Soc.*, **63**, 2639 (1941).

(13) Fuson also prepared the following crystalline, stable enediols:



where Mes = mesityl, Tep = 2,4,6-triethylphenyl, and Tip = 2,4,6-triisopropylphenyl. For Mes, see R. C. Fuson and J. Corse, *J. Am. Chem. Soc.*, **61**, 975 (1939); R. B. Thompson, *ibid.*, **61**, 1281 (1939); R. C. Fuson, C. H. McKeever, and J. Corse, *ibid.*, **62**, 600 (1940). For Tep, see R. C. Fuson, J. Corse, and C. H. McKeever, *ibid.*, **61**, 2010 (1939). For Tip, see R. C. Fuson and E. C. Horning, *ibid.*, **62**, 2962 (1940).

(14) (a) R. C. Fuson and S. P. Rowland, *J. Am. Chem. Soc.*, **65**, 992 (1943); (b) R. C. Fuson, L. J. Armstrong, and W. J. Shenk, Jr., *ibid.*, **66**, 964 (1944); (c) R. C. Fuson, P. L. Southwick, and S. P. Rowland, *ibid.*, **66**, 1109 (1944).

(15) R. C. Fuson, M. D. Armstrong, W. E. Wallace, and J. W. Kneisley, *J. Am. Chem. Soc.*, **66**, 1274 (1944).

(16) R. C. Fuson, L. J. Armstrong, J. W. Kneisley, and W. J. Shenk, Jr., *J. Am. Chem. Soc.*, **66**, 1464 (1944).

(17) R. C. Fuson, D. J. Byers, S. P. Rowland, P. L. Southwick, and C. A. Sperati, *J. Am. Chem. Soc.*, **66**, 1873 (1944).

(18) R. C. Fuson, R. E. Foster, W. J. Shenk, Jr., and E. W. Maynert, *J. Am. Chem. Soc.*, **67**, 1937 (1945).

(19) R. C. Fuson and C. A. Sperati, *J. Am. Chem. Soc.*, **63**, 2643 (1941).

(20) R. C. Fuson, N. Rabjohn, and D. J. Byers, *J. Am. Chem. Soc.*, **66**, 1272 (1944).

(21) R. C. Fuson, L. J. Armstrong, D. H. Chadwick, J. W. Kneisley, S. P. Rowland, W. J. Shenk, Jr., and Q. F. Soper, *J. Am. Chem. Soc.*, **67**, 386 (1945).

(22) R. C. Fuson, D. H. Chadwick, and M. L. Ward, *J. Am. Chem. Soc.*, **68**, 389 (1946).

(23) R. C. Fuson and T-L. Tan, *J. Am. Chem. Soc.*, **70**, 602 (1948).

(24) A. R. Miller, *J. Org. Chem.*, **41**, 3599 (1976).

(25) I. A. Kaye, M. Fieser, and L. F. Fieser, *J. Am. Chem. Soc.*, 77, 5936 (1955).

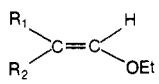
(26) K. Heusler, P. Wieland, and A. Wettstein, *Helv. Chim. Acta*, **42**, 1586 (1959).

(27) J. Attenburrow, J. E. Connett, W. Graham, J. F. Oughton, A. C. Ritchie, and P. A. Wilkinson, *J. Chem. Soc.*, 4547 (1961).

(28) P. R. Enslin, *Tetrahedron*, **27**, 1909 (1971).

(29) H. Hart and D. W. Swatton, *J. Am. Chem. Soc.*, **89**, 1874 (1967).

(30) Increasing alkyl substitution increases the kinetic stability of enol ethers, as shown by the following relative hydrolysis rates in 80% aqueous dioxane (25 °C):



R_1	R_2	k_{rel}
H	H	34.0
H	CH_3	13.3
CH_3	H	4.1
CH_3	CH_3	1.0

Data are from T. Okuyama, T. Fueno, H. Nakatsuji, and J. Furukawa, *J. Am. Chem. Soc.*, **89**, 5826 (1967). It seems reasonable to expect that enol stability would be affected by substitution in a similar manner to enol ether stability.

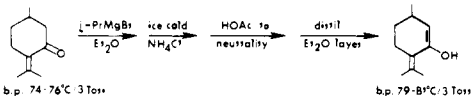
(31) J. M. Landesberg, *J. Org. Chem.*, **40**, 2688 (1975).

(32) H. M. R. Hoffmann and E. A. Schmidt, *J. Am. Chem. Soc.*, **94**, 1373 (1972); E. A. Schmidt and H. M. R. Hoffmann, *ibid.*, **94**, 7832 (1972).

(33) H. M. R. Hoffmann, K. E. Clemens, E. A. Schmidt, and R. H. Smithers, *J. Am. Chem. Soc.*, **94**, 3201 (1972).

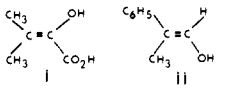
(34) H. M. R. Hoffmann and E. A. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **12**, 239 (1973).

(35) V. Grignard and J. Savard, *Bull. Soc. Chim. Belg.*, **36**, 97 (1927), claim to have prepared and distilled the enol form of pulegone, prepared from pulegone according to the following sequence:



The strongest evidence for the enol is that whereas pulegone liberates only 26% of the theoretical amount of methane on treatment with CH_3MgI, the "enol" liberated methane in 100% yield; also, treatment with benzoyl chloride gave the enol benzoate. Preparation of menthone enol is also claimed. Although these results have been accepted (ref 6, p 90) and pulegone may be a candidate for forming a relatively stable enol (compare with **67**), we believe that these experiments should be repeated using modern methods for structure determination, particularly NMR.

(36) Several enols have been detected by ultraviolet spectroscopy as intermediates with finite lifetimes in certain reactions. For example, the enolic acid i is an intermediate in the decarboxylation of dimethyloxaloacetic



acid (R. Steinberger and F. H. Westheimer, *J. Am. Chem. Soc.*, **73**, 429 (1951)) and the even simpler enol ii was detected as an intermediate in the decarboxylation of 3-phenyl-2,3-epoxybutanoic acid (V. J. Shiner, Jr., and B. Martin, *ibid.*, **84**, 4824 (1962)). Distillation of glyceraldehyde from sulfuric acid (1 M) affords initially the enol of pyruvaldehyde, indicated by a band at about 250 nm which decays in about 15 min (10^{-2} M solution) as the spectrum of pyruvaldehyde develops (B. J. Thornton and J. C. Speck, Jr., *Anal. Chem.*, **22**, 899 (1950)), and private communication from J. C. Speck, Jr.). No attempt has been made to carry out such reactions in a manner which might permit isolation of these enols.

(37) N. C. Yang and C. Rivas, *J. Am. Chem. Soc.*, **83**, 2213 (1961).

(38) K. R. Huffman, M. Loy, and E. F. Ullman, *J. Am. Chem. Soc.*, **87**, 5417 (1965).

(39) R. Haag, J. Wirz, and P. J. Wagner, *Helv. Chim. Acta*, **60**, 2595 (1977).

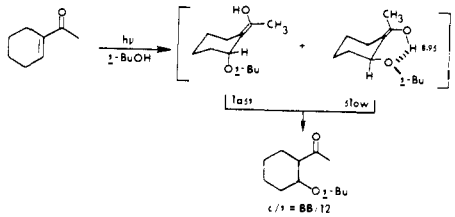
(40) E. Rommel and J. Wirz, *Helv. Chim. Acta*, **60**, 38 (1977).

(41) N. C. Yang and M. J. Jorgenson, *Tetrahedron Lett.*, 1203 (1964).

(42) R. Noyori, H. Inoue, and M. Katô, *Bull. Chem. Soc. Jpn.*, **49**, 3673 (1976).

(43) E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, 1962, pp 267 ff.

(44) Irradiation of the six-membered analog of **87** in *tert*-butyl alcohol resulted in addition of the alcohol to the carbon–carbon double bond (B. J. Ramey and P. D. Gardner, *J. Am. Chem. Soc.*, **89**, 3949 (1967)). It is thought that the initial products are enols, one of which has an intramolecular hydrogen bond and is appreciably longer lived than the other. When followed by NMR, a peak at δ 8.95 was observed, ascribed to the hydroxylic proton in that enol. The lifetimes of these enols appear to be considerably less than those of **88** and **89**.



(45) (a) P. J. Wagner, R. G. Zepp, K-C. Liu, M. Thomas, T-J. Lee, and N. J. Turro, *J. Am. Chem. Soc.*, **98**, 8125 (1976). (b) There is only NMR and IR spectral evidence for photochemical formation of **97** from **96**. In contrast the reverse reaction (to give the 1,2-diketone) occurred on irradiation of the enol 1,4-diphenyl-2-hydroxy-1-buten-3-one, prepared by copper acetate/acetic acid oxidation of *sym*-diphenylacetoin: private communication from N. J. Turro.

(46) H. Moureu, *Ann. Chim. (Paris)*, **14** [10], 283 (1930).

(47) R. A. Bekker, G. G. Melikyan, É. P. Lur'e, B. L. Dyatkin, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **217**, 1320 (1974); English (Plenum), p 572.

(48) R. A. Bekker, G. G. Melikyan, B. L. Dyatkin, and I. L. Knunyants, *Zh. Org. Khim.*, **11**, 1370 (1975); English (Plenum), p 1356.

(49) R. A. Bekker, V. Ya. Popkova, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **229**, 870 (1976); English (Plenum), p 514.

(50) R. A. Bekker, V. Ya. Popkova, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **233**, 591 (1977); English (Plenum), p 187.

(51) W. J. Middleton and R. V. Lindsey, *J. Am. Chem. Soc.*, **86**, 4948 (1964); R. Filler and R. M. Schure, *J. Org. Chem.*, **32**, 1217 (1967).

(52) R. A. Bekker, V. Y. Popkova, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **231**, 864 (1976); English (Plenum), p 700.

(53) R. A. Bekker, V. Y. Popkova and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **235**, 103 (1977); English (Plenum), p 370.

(54) I. L. Knunyants, É. G. Bykhovskaya, and V. N. Frosin, *Zh. Vses. Khim. Ova.*, **9**, 598 (1964); *Chem. Abstr.*, **62**, 2700c (1965).

(55) R. A. Bekker, V. Y. Popkova and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1193 (1978); English (Plenum), p 1038.

(56) J. P. Guthrie and P. A. Cullimore, *Can. J. Chem.*, **57**, 240 (1979); J. P. Guthrie, *ibid.*, **57**, 797, 1177 (1979). These papers contain references to earlier experimental and calculated values for the enol content of simple carbonyl compounds.

(57) J. L. Holmes, J. K. Terlouw, and F. P. Lossing, *J. Phys. Chem.*, **80**, 2860 (1976).
(58) W. J. Bouma, D. Poppinger, and L. Radom, *J. Am. Chem. Soc.*, **99**, 6443 (1977).
(59) S. K. Pollack and W. J. Hehre, *J. Am. Chem. Soc.*, **99**, 4845 (1977). These authors state that "it has not been possible to prepare the enol forms of molecules such as acetone independently of their thermodynamically more stable keto tautomers. Therefore, all that is, in fact, known about the stabilities of such species derives from experiments on two-component equilibria in which the enol is by far the minor component." These statements, though incorrect, as demonstrated by the many examples described here in this review, are nevertheless fairly representative of the general misperception of the situation by most chemists, and indeed provide one raison d'être of this review.
(60) G. R. McMillan, J. G. Calvert, and J. N. Pitts, Jr., *J. Am. Chem. Soc.*, **86**, 3602 (1964). A species thought to be the enol of crotonaldehyde was similarly detected: J. W. Coomber, J. N. Pitts, Jr., and R. R. Schrock, *Chem. Commun.*, 190 (1968).
(61) S. Saito, *Chem. Phys. Lett.*, **42**, 399 (1976).
(62) S. Samdal and H. M. Seip, *J. Mol. Struct.*, **28**, 193 (1975).
(63) Intermediate radicals in many of these studies have been detected and identified by ESR spectrometry.
(64) B. Blank and H. Fischer, *Helv. Chim. Acta*, **56**, 506 (1973).
(65) B. Blank, A. Henne, G. P. Laroff, and H. Fischer, *Pure Appl. Chem.*, **41**, 475 (1975).
(66) J. Bargon and K-G. Seifert, *Chem. Ber.*, **108**, 2073 (1975).
(67) G. P. Laroff and H. Fischer, *Helv. Chim. Acta*, **56**, 2011 (1973).
(68) S. M. Rosenfeld, R. G. Lawlor, and H. R. Ward, *J. Am. Chem. Soc.*, **95**, 946 (1973).
(68a) The acidity of acetophenone enol in aqueous solution has recently been measured directly by a flash photolysis technique: P. Haspra, A. Sutter and J. Wirz, *Angew. Chem., Int. Ed. Engl.*, **18**, 617 (1979).
(69) H. E. Chen, S. P. Vaish, and M. Cocivera, *J. Am. Chem. Soc.*, **95**, 7586 (1973).
(70) S. A. Sojka, C. F. Poranski, Jr., and W. B. Moniz, *J. Am. Chem. Soc.*, **97**, 5953 (1975); *J. Magn. Res.*, **23**, 417 (1976).
(71) R. H. Thomson, *Q. Rev. Chem. Soc.*, **10**, 27 (1956).
(72) V. V. Ershov and G. A. Nikiforov, *Russ. Chem. Rev.*, **35**, 817 (1966).
(73) Reference 3, pp 168–198.
(74) K. F. Wedemeyer in "Methoden der Organischen Chemie" (Houben-Weyl), Vol. VI/1c, Part 2, Georg Thieme Verlag, Stuttgart, 1976, esp. pp 717–735.
(75) D. M. Jerina, B. Witkop, C. L. McIntosh, and O. L. Chapman, *J. Am. Chem. Soc.*, **96**, 5578 (1974).
(76) D. H. R. Barton and G. Quinkert, *J. Chem. Soc.*, 1 (1960); G. Quinkert, *Angew. Chem., Int. Ed. Engl.*, **4**, 211 (1965); O. L. Chapman and J. D. Lassila, *J. Am. Chem. Soc.*, **90**, 2449 (1968); J. Griffiths and H. Hart, *ibid.*, **90**, 3297 (1968).
(77) K. H. Meyer, *Ann.*, **379**, 37 (1911); K. H. Meyer and A. Sander, *ibid.*, **396**, 133 (1913); **420**, 113 (1920); H. Baba and T. Takemura, *Bull. Chem. Soc. Jpn.*, **37**, 124 (1964).
(78) The reason why equilibrium favors the keto form in the anthracene (**159** > **160**) but the enol form in the phenanthrene series (**156** > **155**) probably involves two factors. In valence-bond terms, 9-phenanthrol has all aromatic rings benzenoid whereas in 9-anthrol, one ring is quinoid; also in 9-anthrone, the carbonyl group is conjugated with both aryl rings, whereas in 9-phenanthrone it is conjugated directly with only ring. Thus whereas 9-anthrone has been known for many years, 9-phenanthrone went undetected until 1974.
(79) C. A. Grob and J. Voltz, *Helv. Chim. Acta*, **33**, 1796 (1950); C. A. Grob and B. Hofer, *ibid.*, **35**, 2095 (1952).
(80) J. F. Grove, *J. Chem. Soc. C*, 985 (1966); E. B. Vischer, *J. Chem. Soc.*, 815 (1953).
(81) E. W. Garbisch, *J. Am. Chem. Soc.*, **87**, 4971 (1965).
(82) L. W. Butz and A. W. Rytina, *Org. React.*, **5**, 136 (1949).
(83) R. H. Thomson, *J. Chem. Soc.*, 1737 (1950); D. B. Bruce and R. H. Thomson, *ibid.*, 275 (1952).
(84) M. S. Pearson, B. J. Jensky, F. X. Greer, J. P. Hagstrom, and N. M. Wells, *J. Org. Chem.*, **43**, 4617 (1978).
(85) H. Hart and K. Takagi, *J. Org. Chem.*, in press.
(86) R. C. Cookson, D. A. Cox, and J. Hudec, *J. Chem. Soc.*, 1717 (1962).
(87) J. M. Bruce, *J. Chem. Soc.*, 2782 (1962); see also J. Dekker, P. J. van-Vuuren, and D. P. Venter, *J. Org. Chem.*, **33**, 464 (1968); D. P. Venter and J. Dekker, *ibid.*, **34**, 2224 (1969).
(88) M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957).
(89) V. V. Ershov and A. A. Volo'kin, *Izv. Akad. Nauk SSSR*, **730**, 2022 (1962); in English, p 680, 1931.
(90) B. Miller, *J. Am. Chem. Soc.*, **89**, 1685 (1967).
(91) T. Matsuura and K. Ogura, *J. Am. Chem. Soc.*, **89**, 3846 (1967).
(92) C. H. DePuy, R. N. Greene, and T. E. Schroer, *Chem. Commun.*, 1225 (1968); C. H. DePuy, T. Jones, and R. L. Parton, *J. Am. Chem. Soc.*, **96**, 5602 (1974).
(93) A. J. Birch, P. E. Cross, J. Lewis, D. A. White, and S. B. Wild, *J. Chem. Soc. A*, 332 (1968).
(94) A. J. Birch and K. B. Chamberlain, *Org. Syn.*, **57**, 107 (1977).
(95) J. Calleja, R. Davis, and I. A. O. Ojo, *Org. Mass Spectrom.*, **12**, 109 (1977).
(96) J. Lewis and A. W. Parkins, *Chem. Commun.*, 1194 (1968).
(97) R. J. H. Cowles, B. F. G. Johnson, J. Lewis, and A. W. Parkins, *J. Chem. Soc., Dalton Trans.*, 1768 (1972).
(98) A. J. Birch and I. D. Jenkins, *Tetrahedron Lett.*, 119 (1975).
(99) D. J. Cole-Hamilton, R. J. Young, and G. Wilkinson, *J. Chem. Soc. Dalton Trans.*, 1995 (1976).
(100) C. White, S. J. Thompson, and P. M. Maitlis, *J. Organomet. Chem.*, **127**, 415 (1977).
(101) W. S. Trahanovsky and R. A. Hall, *J. Am. Chem. Soc.*, **99**, 4850 (1977).