HINDERED AND CHELATED 1,2-ENEDIOLS

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CONTENTS

CONTENTS (*Continued*)

I. INTRODUCTION

Benzoins, containing the group –COCHOH–, are assumed to tautomerize to enediols, containing the group HO—C=C—OH. Perhaps the most convincing evidence in support of this assumption is provided by many reactions in alkaline solution, such as acylation, in which derivatives of the enediol are produced. As a rule the enediols are much less stable than the corresponding benzoins, and isolation becomes difficult, if not impossible. In the last 25 years, exceptions to this statement have arisen. If certain structural effects are present, enediols become so stable that isolation can be accomplished with ease. In fact in some cases, both the benzoin and enediol are isolable and interconvertible (13).

An attempt has been made in the present review to cover the literature up through the 1962 *Chemical Abstracts.*

II. SCOPE OF THE REVIEW

The most recent monograph (23) on enediols covers all types, whether isolable or not. Of concern in this work are general subjects such as methods of detection and analysis, and tautomerism. The enediols covered are those which are tautomeric with the acyloins and benzoins, those obtainable from sugars, those having other functional groups, those in which there are thiol or amino instead of hydroxyl groups, those in which the unsaturation is part of an aromatic ring, and those in which there is additional unsaturation. The emphasis in the monograph is on reductone and L-ascorbic acid for which the physical and chemical properties and the biochemistry are given in some detail.

In the present review an attempt has been made to cover the 1,2-enediols in greater detail. Those of interest are sufficiently stable to be isolated and they are isomeric with the benzoins. Aliphatic enediols of biochemical importance, such as reductone and L-ascorbic acid, and those in which the doubly bonded carbon atoms are part of an aromatic ring, such as in catechol, are omitted. Most of the enediols included have the functional group attached to two rings, although in a few cases there is an intervening carbonyl group. Usually the hindered enediols possess two aromatic rings, while the chelated ones have instead two heterocyclic rings.

The reader interested in the entire field of enediols should consult the monograph as well as the present review in order to bring the subject up-to-date.

III. NOMENCLATURE

The general term "enediol" is being used for the type being reviewed, although the name "dienol" is sometimes employed. In the literature many of the compounds of interest are named as glycols of acetylene. For example, 2,4,6-$(CH_3)_3C_6H_2C(OH)$=$C(OH)C_6H_2$-$(CH_3)_3$-2,4,6 would be called 1,2- or α,β-dimesitylacetylene glycol. This compound is also referred to as 2,2′,4,4′,6,6′-hexamethystilbenediol. By the I.U.C. nomenclature, which will be used in this review, this enediol would be called 1,2-(di-2,4,6-trimethylphenyl)-1,2-ethenediol.

The first German publications on 2-heterocyclic enediols listed them as benzoins (38, 45). This situation resulted because of mistaken identity. A benzoin would normally be expected on heating 2-pyridine aldehyde with sodium or potassium cyanide, and the product was called pyridoin, but it is actually the enediol, 1,2-di-(2-pyridyl)-1,2-ethenediol. Unfortunately, the Germans have retained the benzoin terminology.

There is also a tendency, particularly among German biochemists, to use the term "reductones." This name undoubtedly arose from the fact that the specific compound reductone is an important member of the class.

IV. METHODS OF PREPARATION

A. GENERAL METHODS

The enediols which have been prepared are listed in Tables I and II. Often they are produced by methods employed for the preparation of the isomeric benzoins

TABLE I
AROMATIC ENEDIOLS, R—C(OH)=C(OH)—R′

No.	R	R′	Method of preparation	% yield	Color	Form	M.p., °C.	Reference
1	C_6H_5	CF_3	IVB1		Colorless		148–150	51
2	C_6H_5	C_6H_5CO	IVB1		Yellow			3
3	C_6H_5	2,4,6-$(CH_3)_3C_6H_2CO$	IVB1	95	Yellow		79–80	2
4	2,6-$(CH_3)_2C_6H_3$	2,6-$(CH_3)_2C_6H_3$	IVA1b	Nearly quant.	White	*cis*	123–124	27
			IVA1b	Nearly quant.	White	*trans*	151–152	27
5	2,4,6-$(CH_3)_3C_6H_2$	2,4,6-$(CH_3)_3C_6H_2$	IVA1b	70			149–151	55
			IVA1a	35	White			26
			IVA1a	60	White			26
			IVA1b	85–95	White			26
			IVA1b			*trans*	166–168	27
6	2,4,6-$(C_2H_5)_3C_6H_2$	2,4,6-$(C_2H_5)_3C_6H_2$	IVA1a	29	White	*cis*	154–155	25
			IVA1b			*cis*	154–155.5	25
			IVA1b		White	*trans*	181.5–183.5	27
			IVC1	56	White	*trans*		27
7	2,3,4,6-$(CH_3)_4C_6H$	2,3,4,6-$(CH_3)_4C_6H$	IVA1b	Nearly quant.		*cis*	142–144	29
			IVA1b			*trans*	183–185	29
8	2,3,5,6-$(CH_3)_4C_6H$	2,3,5,6-$(CH_3)_4C_6H$	IVA1a			*cis*	167–169	29
			IVA1b			*trans*	214–215	29
9	2,4,6-$[(CH_3)_2CH]_3C_6H_2$	2,4,6-$[(CH_3)_2CH]_3C_6H_2$	IVA1a	37		*cis*	175–176	28
			IVA1b			*trans*	259–260.5	28
			IVC1	20–40		*trans*	259–260.5	28
10	2,6-$(CH_3)_2$-4-BrC_6H_2	2,6-$(CH_3)_2$-4-BrC_6H_2	IVA1b	Nearly quant.	White	*cis*	124–125	30
			IVA1b	Nearly quant.		*trans*	183–184	30
11	2,4,6-$(CH_3)_3$-3-BrC_6H	2,4,6-$(CH_3)_3$-3-BrC_6H	IVA1b			*cis*	158–160	30
			IVA1b			*trans*	204.5–205.5	30
12	2,4,6-$(C_2H_5)_3$-3-BrC_6H	2,4,6-$(C_2H_5)_3$-3-BrC_6H	IVA1a			*cis*	138–139	30
			IVA1b			*trans*	179.5–180.5	30
13	2,4,6-$(CH_3)_3$-3-OCH_3C_6H	2,4,6-$(CH_3)_3$-3-OCH_3C_6H	IVA1a	55		*cis*	138.5–139.5	31
			IVA1b			*trans*	232–233	31
14	2,6-$(CH_3)_2$-3-$NH_2C_6H_2$	2,6-$(CH_3)_2$-3-$NH_2C_6H_2$	IVA1b	95	Orange		229–230 dec.	33
15	2-$CH_3OC_6H_4$	2,4,6-$(CH_3)_3C_6H_2CO$	IVB1	86	Colorless		105	4
16	2-$CH_3C_{10}H_6$	2-$CH_3C_{10}H_6$	IVA1b		White	*cis*	184–187	32
			IVA1a	26	White	*cis*	186–188	32
			IVA1b			*trans*	Indef.	32
17	9-$C_{14}H_9$	9-$C_{14}H_9$	IVB2	25	Yellow		283[a]	6

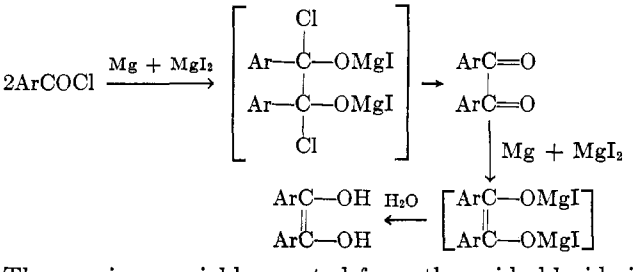
[a] This compound to which an enediol structure was ascribed (41) was later (21) found to be the phenanthril; the phenanthroin was also obtained, but the isomeric enediol was too unstable to be isolated.

(40). The enediol may be an intermediate and, if it is sufficiently stable, conversion to the benzoin may not occur.

1. *Reduction of Acid Chlorides or Benzils*

a. With Magnesium–Magnesium Iodide

Aromatic acids and their derivatives, such as the chlorides, esters, peroxides, and benzils, may be reduced by a mixture of magnesium and magnesium iodide in a mixed solvent of ether and benzene (35). This method is particularly valuable if aldehydes are not readily available. It has been applied to the preparation of hindered enediols by starting either with the acid chloride or benzil. The action of the reagent bears a resemblance to that of the Grignard reagent in that addition of $Mg^{I}I$ is involved. For acid chlorides the reaction appears to proceed through the benzil as an intermediate.



The maximum yield reported from the acid chloride is 55% (31); from the benzil, 60% (26). The acid

TABLE II

HETEROCYCLIC ENEDIOLS, R—C(OH)=C(OH)—R′

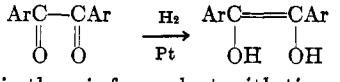
No.	R	R′	Method of preparation	% yield	Color	M.p., °C.	Reference
1	C_6H_5	2-C_5H_4N	IVA1b		Yellow	61	12
2	C_6H_5CO	2-C_5H_4N	IVB2	35–45	Orange to red-brown	93	20
			IVA1c	72	Orange-red	90–93	20
3	2-C_5H_4N	2-C_5H_4N	IVB2		Yellow	156	37
			IVB3c				45
			IVB4			156	45
			IVB3b	34		153	44
			IVB3a	Almost quant.		156	38
			IVA1b	95		153–154	17
			IVB2	95	Yellow-orange	156	12
4	2-(6-$CH_3C_5H_3N$)	2-(6-$CH_3C_5H_3N$)	IVB4		Red-yellow	198 dec.	45
5	2-[4,6-$(CH_3)_2C_5H_2N$]	2-[4,6-$(CH_3)_2C_5H_2N$]	IVB2		Yellow-red	221–222	47
6	2-(5-$C_2H_5C_5H_3N$)	2-(5-$C_2H_5C_5H_3N$)	IVB2		Yellow-brown	140	47
7	2-(6-$HOCH_2C_5H_3N$)	2-(6-$HOCH_2C_5H_3N$)	IVB2	Nearly quant.	Bright red	187	48
8	2-(6-$HOOCC_5H_3N$)	2-(6-$HOOCC_5H_3N$)	IVB2		Red-brown	250 dec.	46
9	2-C_9H_6N	2-C_9H_6N	IVB2	90	Dark purple	232–233 dec.	10
			IVA1b		Dark purple	232–233 dec.	10
			IVB2		Purple	231–232 dec.	57
			IVB3d	25–46		228–230	1
10	2-(6-$CH_3C_9H_5N$)	2-(6-$CH_3C_9H_5N$)	IVB2	60	Dark brown	258 dec.	11
11	2-Pyridyl N-oxide	2-Pyridyl N-oxide	IVB2		Orange	167	49
12	2-(6-Methylpyridyl N-oxide)	2-(6-Methylpyridyl N-oxide)	IVB2		Orange	191	49
13	2-Quinolyl N-oxide	2-Quinolyl N-oxide	IVB2		Brick red	193–194 dec.	13
			IVB6	15	Brick red	192–193 dec.	13
			IVB5	75	Brick red	190–191 dec.	13
14	2-Thiazolyl	2-Thiazolyl	IVB2	53	Orange	169	7
15	2-(5-Methylthiazolyl)	2-(5-Methylthiazolyl)	IVB2	63	Orange	194	7
16	2-(4,5-Dimethylthiazolyl)	2-(4,5-Dimethylthiazolyl)	IVB2	64	Deep orange	211	7
17	2-Benzothiazolyl	2-Benzothiazolyl	IVB2	90	Orange-red	280–282 dec.	57
18	2-Benzoselenazolyl	2-Benzoselenazolyl	IVB2	90	Red	274–275 dec.	58
19	2-Benzimidazolyl	2-Benzimidazolyl	IVB2	84	Yellow	240 dec.	54
20	2-(6-Chlorobenzimidazolyl)	2-(6-Chlorobenzimidazolyl)	IVB2	80	Bright yellow	252 dec.	54

chloride is readily available from the acid, but the benzil may be difficult to acquire if the corresponding aldehyde is not at hand. Most of the benzils reduced in the literature came from benzoins produced as by-products in the enediol synthesis.

Both the *cis* and *trans* forms of the aromatic enediols may be produced by these methods. However, the greatest success in obtaining the *cis* form has been achieved by the magnesium–magnesium iodide reduction of the acid chloride.

b. With Molecular Hydrogen

Molecular hydrogen, in the presence of platinum, has been employed widely in the reduction of hindered benzils. The yields in the reaction, which is 1,4-addition, are often almost quantitative. Usually the



first product is the *cis* form, but with time, particularly in the presence of a base like piperidine, the *cis* is converted into the *trans* form. For example, 2,2′,6,6′-tetramethylbenzil when hydrogenated in methanol containing a drop of acetic acid gave the *cis*-enediol almost quantitatively in 10 min. (27). In the absence of acid, the same procedure gave the *trans* form almost quantitatively in 12 hr.

c. With Hydrogen Sulfide

Several of the chelated enediols have been produced by the reduction of the benzil with hydrogen sulfide. Thus 1-benzoyl-2-(2-pyridyl)-1,2-ethenediol has been obtained in 72% yield (20).

B. METHODS FOR CHELATED ENEDIOLS

1. Hydrolysis of α-Bromodesoxybenzoins, Mono- or Diacetates of the Enediols

In a few cases rather unstable enediols have been obtained either from the α-bromodesoxybenzoins or

the mono- or diacetates produced from the benzoin or the α-bromodesoxybenzoin. A case in point is that of 1-phenyl-2-(2,4,6-trimethylbenzoyl)-1,2-ethenediol, obtained by the acid hydrolysis of the monoacetate (2).

2. Condensation of Aldehydes with Alkali Cyanides

For the chelated enediols in the N-heterocyclic series, the best method of preparation is from the aldehyde by treatment with an alkali cyanide in alcoholic or pyridine solution. As is shown in Table II, the yields vary from 9 to 95%. The best yields were obtained for the enediols which resist low pressure hydrogenation and which are not directly convertible into the isomeric benzoins. Other products isolated in this reaction were the glycol, the carboxylic acid, and the benzoin.

There is a temptation to regard the mechanism of this reaction as that of the normal benzoin condensation. The final product could be the benzoin or the enediol depending on the relative stabilities of the two. Two facts may be cited which throw some doubt on this view: (1) other reagents such as glacial acetic acid, boron trifluoride, hydrogen cyanide, and certain methyl heterocycles produce enediols from 2-N-heterocyclic aldehydes; and (2) any reagent other than an alkali cyanide yields little or no benzoin from aromatic aldehydes. To date the mechanism of enediol formation by this particular reaction has not been studied.

The glycol and acid are probably produced by a mixed Cannizzaro reaction between the enediol and the original aldehyde. It is interesting to note that these compounds are the main products in the condensation of 4-N-heterocyclic aldehydes with an alkali cyanide (52).

3. Condensation of Aldehydes with Other Reagents

a. Acetic Acid

2-Pyridinealdehyde when mixed with glacial acetic acid at room temperature produced the enediol in almost quantitative yield (38). The reaction is accelerated by bromine, iodine, and the iodide anion. Neither benzaldehyde, 3-pyridinealdehyde, nor 4-pyridinealdehyde formed the benzoin under similar conditions.

b. Boron Trifluoride

2-Pyridinealdehyde with boron trifluoride gave the enediol, the yield in the presence of acetone being 34% (44). No condensation occurred with the 3- and 4-isomers.

c. Hydrogen Cyanide

Dry hydrogen cyanide introduced into pure 2-pyridinealdehyde followed by warming gave the enediol (45). No yield was given, and benzaldehyde under similar conditions produced no benzoin.

d. Methyl Heterocycles

A solution of 2-quinaldehyde and certain methyl heterocycles (2-picoline, quinaldine, lepidine, and 1-methylisoquinoline) in ethanol, when heated in a sealed tube, gave the enediol, glycol, and acid of the aldehyde (1). The yields of the enediol varied from 25 to 46%. It is suggested that the anion of the methyl heterocycle, formed by the loss of a methyl proton, plays a role similar to that of the cyanide anion in the benzoin condensation. These basic catalysts do not yield benzoin from benzaldehyde.

4. Oxidation of 2-Methylpyridines

The vapor of 2-methylpyridine, water, and air passed over a catalyst of vanadium pentoxide–molybdenum trioxide, impregnated on silica at 380–400°, yielded 1,2-di-(2-pyridyl)-1,2-ethenediol (45). The other products of the reaction were 2(1H)-pyridone and 2-pyridinealdehyde. No yields were given. The enediol is in all probability produced through the aldehyde as an intermediate. Although the originators of the method attribute the conversion to the presence of traces of hydrogen cyanide, other substances may be responsible since it has been shown that a variety of substances or heat alone will convert 2-pyridinealdehyde into the enediol (12).

This same procedure with 2,6-dimethylpyridine yielded 1,2-di-(6-methylpyridyl-2)-1,2-ethenediol.

5. Conversion of the Potassium Salt of the Enediol into the Free Enediol

This method is of limited value, but it was employed in the case of the potassium salt of 1,2-di-(2-quinolyl)-1,2-ethenediol N,N′-dioxide (13). Treatment with benzoyl chloride, doubtless due to the acid present, gave the enediol in a 75% yield.

6. Conversion of the Benzoin into the Enediol

This transformation is rare, but it was applied successfully to quinaldoin N,N′-dioxide, which was converted in 15% yield to the isomeric enediol by aqueous pyridine (13).

C. METHODS FOR HINDERED ENEDIOLS

1. Conversion of the cis to the trans Form

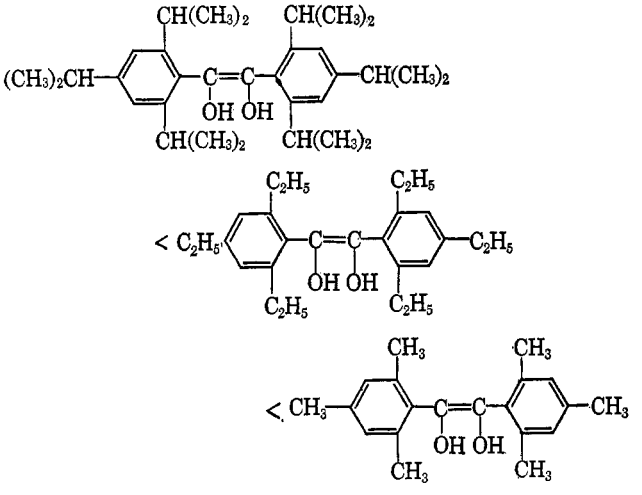
In the methods for producing hindered enediols, the more unstable *cis* form is often isolated first. Conversion into the more stable *trans* form is possible. For example, *cis*-1,2-di-(2,4,6-triethylphenyl)-1,2-ethenediol has been converted into the *trans* form with a 56%

yield by agitating the methanolic solution with platinum oxide in an atmosphere of hydrogen (27).

V. STRUCTURAL EFFECTS NECESSARY FOR STABILITY

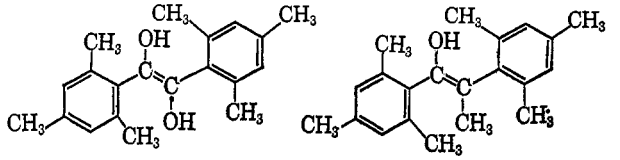
A. HINDERED ENEDIOLS

Two principal factors appear to be responsible for the stability of hindered enediols: (1) The system is highly conjugated, the two rings being in conjugation through the double bond of the enediol group, and (2) the substituents in the *ortho* positions are of sufficient size to interfere with the normal reactivity of the hydroxyl groups. The importance of the size of the interfering substituents has been the subject of considerable study. It has been found, for example, that the ease of oxidation by air increases as the size of the alkyl group decreases (28). Interfering substituents,



even though large, are not sufficient to produce stability when present in only one of the rings (34).

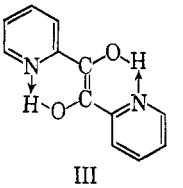
If sufficient steric hindrance exists, the enediol as formed may be isolated as such, not because it is more stable than the isomeric benzoin, but because the *o*-substituents interfere with the conversion to the keto form (62). This explanation indicates why the size of the *o*-substituents is important. There is a parallelism between the enediols (I) and enols (II), in that the latter also are convertible into the keto form with difficulty.



I II

B. CHELATED ENEDIOLS

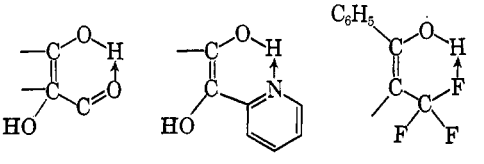
Two principal factors are also responsible for the stability of the chelated enediols: (1) The system is highly conjugated, as in the case of the hindered aromatic enediols, and (2) these compounds are chelated, as is shown in the structural formula for 1,2-di-(2-pyridyl)-1,2-ethenediol (III). Maximum stability is achieved



III

in that the conjugated system is planar. Only one form has been isolated, and it is in all probability the *trans*, since the *cis* could not be uniplanar, and chelation, if at all possible, would be extremely difficult. These enediols exist only in cases in which the functional group is attached to the 2-positions in the heterocyclic rings, a fact which lends further support to the chelated structure.

The rather unstable enediols listed 2 and 3 in Table I, and 1 in Table II, contain one carbonyl group or one 2-N-heterocyclic ring and suggest that some stability is achieved by a single chelated ring as in IV and V.



IV V VI

The stability of 1-phenyl-2-trifluoromethyl-1,2-ethenediol, 1 (51), Table I, has also been explained on this basis, as in VI. In this case support for the structure is available, in that two different hydroxyl infrared absorption bands, 3077 and 3410 cm.$^{-1}$ in the solid state and 3363 and 3617 cm.$^{-1}$ in chloroform solution, are exhibited.

Some evidence has been advanced which opposes this view (17, 20). 1,2-Di-(2-pyridyl)-1,2-ethenediol in solution forms a monoacetyl derivative and a monourethane. These facts are interpreted to mean that under these conditions ketonization occurs immediately after one chelate ring is broken. The solid enediol, in contrast, forms a diurethane when heated slightly above the melting point of the isocyanate.

Upon the basis of present evidence it appears that a single chelate ring can produce sufficient stability to permit isolation. Such enediols, however, often exist only for short periods of time under ordinary laboratory conditions.

VI. *cis* AND *trans* FORMS

A. ISOLATION

cis and *trans* forms have been obtained for the hindered aromatic enediols. Either of these forms may be prepared as indicated in sections IVA1a and IVA1b.

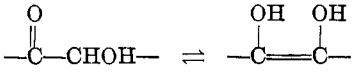
Isolation of the *trans* has also been achieved through an interconversion of the *cis* form as shown in section IVC1. No reference to the reverse interconversion of the *trans* to the *cis* form has been found.

B. DETERMINATION OF CONFIGURATION

The precise physical methods now available for the determination of configuration have not been applied to the hindered aromatic enediols. Although it was assumed in all cases that the low melting form was the *cis*, there were other indications that this assumption was correct. The first form obtained on catalytic hydrogenation, which would be expected to be the *cis*, was the low melting form. As is to be expected, this form could be converted into the higher melting *trans* by simply shaking its solution in methanol in the presence of platinum oxide and hydrogen. In some cases a higher degree of activity was noted for the *cis* form. For example, *cis*-1,2-di-(2,4,6-triisopropylphenyl)-1,2-ethenediol decolorized Tillman's reagent more rapidly than the *trans* isomer (28), and *cis*-1,2-di-(2,6-dimethylphenyl)-1,2-ethenediol was oxidized in air more rapidly than the *trans* form (27).

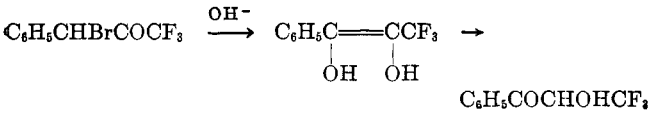
VII. INTERCONVERSION OF ENEDIOLS AND BENZOINS

In the benzoin–enediol equilibrium



acidic conditions would be expected to favor the benzoin while basic conditions would favor the enediol. In agreement with this principle, 1,2-di-(2,6-dimethylphenyl)-1,2-ethenediol in methanolic hydrogen chloride has been converted into the corresponding benzoin in good yield (27). The simplest chelated enediols in the N-heterocyclic series are not affected in this way. In fact, the benzoins of 2-pyridine-, 2-quinoline-, and 6-methyl-2-quinolinealdehydes are not known (the 2-quinaldoin described (42) could not be obtained by Hammick (36) or the author). The chelated ring in 1,2-di-(2-quinolyl)-1,2-ethenediol N,N′-dioxide is less stable since this compound was converted into the benzoin with methanolic hydrogen chloride, while the reverse effect was accomplished with a mixture of pyridine and water (13).

An interesting rearrangement occurs in preparing the benzoin from 2-bromobenzyl trifluoromethyl ketone by treatment with sodium carbonate (51). Not the expected phenyltrifluoroacetylcarbinol, but the enediol, 1-phenyl-2-trifluoromethyl-1,2-ethanediol, and benzoyl trifluoromethylcarbinol, were obtained.



VIII. PHYSICAL PROPERTIES

The color and melting points of the enediols prepared are listed in Tables I and II. The color varies from white to a deep red, and they are all solids. Some of the *trans* hindered enediols are yellow, while the *cis* isomers are white. The intensely colored ones are the chelated members in which a conjugated, four-ring system is present, which, especially if planar or nearly so, could be expected to absorb in the visible region.

The dipole moment has been determined for only one enediol, 1,2-di-(2-pyridyl)-1,2-ethenediol (43). Its value is 1.13 D. while benzoin gave a value of 3.56 D. and furoin, 4.10 D. If formula III is correct, the dipole moment should be 0. Although a nonplanar structure could account for the difference, it has been attributed to the presence of 2,2-pyridil as an impurity.

IX. MOLECULAR SPECTRA

A. ULTRAVIOLET SPECTRA

As is shown in Table III, the ultraviolet spectra are available for six enediols. It is unsafe to generalize on such limited data. It does appear, however, that the enediols of the 2-N-heterocyclic series possess two bands, one with a wave length around 250 mμ of high intensity and another with a more variable wave length (300–440 mμ) at a lower intensity.

TABLE III
ULTRAVIOLET SPECTRA OF ENEDIOLS

Compound	Solvent	λ	Log ε	Reference
1-Benzoyl-2-(2-pyridyl)-1,2-ethenediol	Hexane	405	4.2	20
1,2-Di-(2-pyridyl)-1,2-ethenediol	Cyclohexane	260	4.3	17
	Cyclohexane	400	3.92	
1,2-Di-(2-quinolyl)-1,2-ethenediol[a]	Chloroform	440	4.5	58
1,2-Di-(6-methylquinolyl-2)-1,2-ethenediol	Dioxane	253	4.73	11
	Dioxane	300	4.28	
1,2-Di-(2-benzothiazolyl)-1,2-ethenediol[a]	Chloroform	270	4.15	58
	Chloroform	410	4.6	
	Chloroform	430	4.4	
1,2-Di-(2-benzoselenazolyl)-1,2-ethenediol[a]	Chloroform	280	3.95	58
	Chloroform	417	4.5	
	Chloroform	440	4.4	

[a] These values are approximations since they were estimated, for the most part, from published curves.

B. INFRARED SPECTRA

The significant bands for the limited number of infrared spectra which have been determined for enediols are given in Table IV. These results for the chelated enediols show conclusively that the com-

TABLE IV
INFRARED SPECTRA OF ENEDIOLS[a]

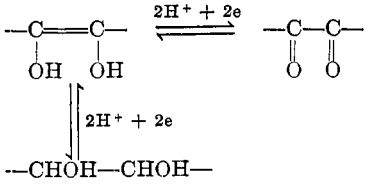
Compound	Bands, cm.$^{-1}$: C=O as in benzoin 1684 (43)	OH as in benzoin 3400 (43)	Chelate compounds 3200–2500 (5)	Reference
1-Phenyl-2-trifluoromethyl-1,2-ethenediol	None	3410	3077	51
		3617[b]	3363[b]	51
1,2-Di-(2,4,6-triethylphenyl)-1,2-ethenediol		3550		25
		3600		
1-Benzoyl-2-(2-pyridyl)-1,2-ethenediol	1603[c]		[d]	20
1,2-Di-(2-pyridyl)-1,2-ethenediol	None	None	~2750 (weak)	43
	None	None	~2740[e]	43
			2670	44
1,2-Di-(2-quinolyl)-1,2-ethenediol	None	None	~2700 (weak)	63
1,2-Di-(2-pyridyl)-1,2-ethenediol N,N′-dioxide	None	None	~2900 (weak)	9
	None	None	~3100 (weak)	49
1,2-Di-(2-quinolyl)-1,2-ethenediol N,N′-dioxide	None	None	~3100 (weak)	9
1,2-Di-(2-thiazolyl)-1,2-ethenediol	None	None	3125–2747	7
1,2-Di-(5-methylthiazolyl-2)-1,2-ethenediol	None	None	3125–2747	7
1,2-Di-(4,5-dimethylthiazolyl-2)-1,2-ethenediol	None	None	3125–2747	7

[a] All determinations were made on solids unless otherwise indicated. [b] Chloroform solution. [c] Chelated carbonyl. [d] A broad flat band (no wave number was given) appears in the chelated hydroxyl region. [e] Carbon tetrachloride solution.

pounds are not benzoins since the carbonyl and hydroxyl bands characteristic of this type are missing. Some significance has been attached to a broad, weak band (2700–2750 cm.$^{-1}$), which occurs in the chelated region of enediols of nonoxygenated heterocyclic types. Attention was called to this band first in a study of 1,2-di-(2-pyridyl)-1,2-ethenediol, and later in the case of 1,2-di-(2-quinolyl)-1,2-ethenediol, with which compound it appeared in measurements made using a potassium bromide pellet, a mineral oil mull, or a solution of carbon tetrachloride and bromoform. This band appears to occur at higher wave lengths if the hydrogen bond of the chelate ring is joined to the oxygen atom of an amine oxide group rather than to the nonoxygenated nitrogen atom. However, more determinations need to be made before any great significance can be attached to these higher values, particularly since CH stretching vibrations for pyridine and quinoline occur near 3020 cm.$^{-1}$. The single hindered enediol, 1,2-di-(2,4,6-triethylphenyl)-1,2-ethenediol, for which measurements are available, gave two bands (3550 and 3600 cm.$^{-1}$) which have been attributed to the hydroxyl groups in the compound.

X. POLAROGRAPHIC STUDIES

Two chelated enediols, 1,2-di-(2-pyridyl)-1,2-ethenediol and its N,N′-oxide, have been studied at the dropping mercury electrode (39). The reversible reactions involved here may be represented as



In contrast to benzoin which is reduced in a two electron wave of constant height, the height of the wave of 1,2-di-(2-pyridyl)-1,2-ethenediol varies with the pH. In the latter case, at higher pH concentrations two distinct waves appear. These facts, the similarity of the polarographic behavior with that of 1,2-di-(2-pyridyl)-ethylene, and other observations are cited in support of the enediol structure.

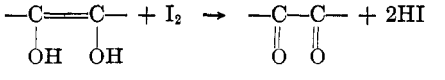
Similar effects were obtained in the polarographic behavior of 1,2-di-(2-pyridyl)-1,2-ethenediol N,N′-dioxide when allowance was made for the reducible amine oxide groups.

XI. COLOR TESTS

Many color tests are available for enediols since, being unsaturated, they are easily oxidized. The tests listed are ordinarily positive with enediols and negative with isomeric benzoins.

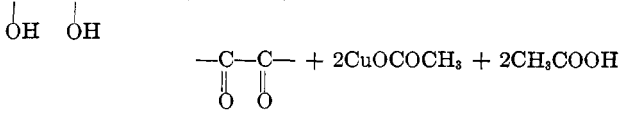
A. IODINE

An alcoholic solution of iodine and the enediol react with the disappearance of the violet color (15).



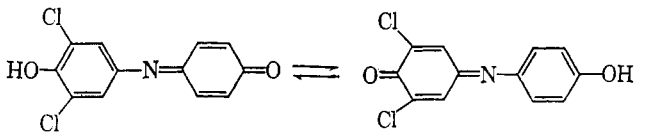
B. COPPER ACETATE

The blue color of cupric acetate disappears at low temperature in the presence of an enediol as the cupric is reduced to cuprous ion.

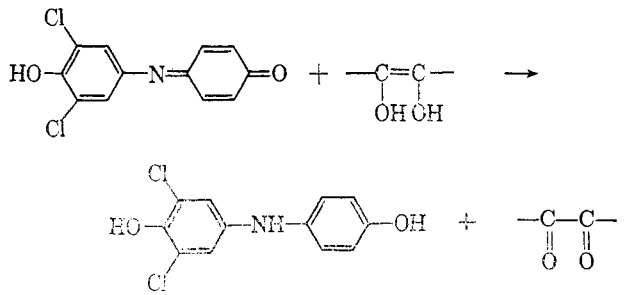


C. N-(3,5-DICHLORO-4-HYDROXYPHENYL)-*p*-QUINONIMINE (TILLMAN'S REAGENT)

This reagent appears under names such as 2,6-dichloroindophenol, 2,6-dichlorophenolindophenol, or 2,6-dichlorobenzeneoneindophenol. Perhaps a more appropriate name would be one in which it is labeled as a derivative of *p*-quinonimine, *i.e.*, N-(3,5-dichloro-4-hydroxyphenyl)-*p*-quinonimine. The compound exists in two tautomeric forms.

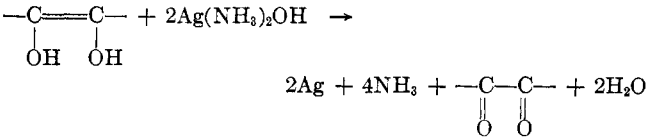


It is colored red in the acidic form or blue as the sodium salt and in the presence of an enediol the color is destroyed (15).



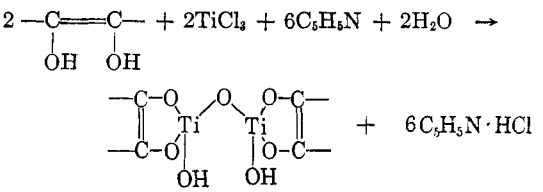
D. AMMONIACAL SILVER NITRATE (TOLLEN'S REAGENT)

Ammoniacal silver nitrate reacts with enediols, as it does with aldehydes, in that a finely divided black precipitate of silver or a silver mirror is formed.



E. TITANIUM CHLORIDE

Titanium chloride in a mixture of pyridine and methanol gives a black-brown precipitate which becomes light in color when shaken in air. However, if an enediol is present, the black-brown precipitate becomes brick red or blood red in color (61).



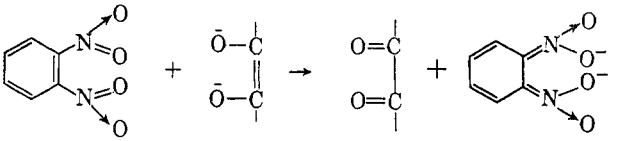
This test is not positive for phenols, with the exception of the *o*-polyhydric phenols.

F. PIPERAZINE

Piperazine alone gives a color with enediols, although no reaction is given (53). The test promises to be useful in the identification of enediols by paper chromatography.

G. *o*-DINITROBENZENE

Enediols such as ascorbic acid are oxidized by *o*-dinitrobenzene in the cold to give a substance having a violet color in alkaline solution (24).



On acidification the violet nitroxylic ion changes to the yellow nitroxylic acid. Besides ascorbic acid, pyrogallol and 1,3-dihydroxyacetone react positively. Aldoses and ketoses respond after being kept in alkaline solution for some time to permit enolization.

XII. REACTIONS OF ENEDIOLS

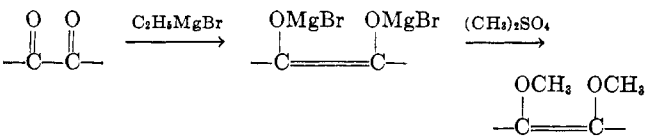
A. GENERAL REACTIONS

1. Salt Formation

The enediols, being acidic, form salts with alkali metals (14). In some cases these salts have been obtained directly on condensing the aldehyde with an amount of the metallic cyanide more than sufficient to produce a maximum yield of the enediol (13).

2. Alkylation

The alkylation of enediols is difficult. When the conventional methods failed for 1,2-di-(2,4,6-triisopropylphenyl)-1,2-ethenediol, success was achieved by the indirect method of reducing the benzil with ethylmagnesium bromide and treating the reaction mixture with methyl sulfate (28).



Various investigators have attempted unsuccessfully to methylate 1,2-di-(2-pyridyl)-1,2-ethenediol (12, 14, 17).

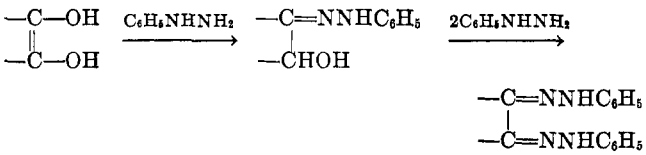
3. Acylation

In contrast to alkylation, the acylation of enediols usually occurs readily with acetic anhydride or benzoyl chloride in pyridine. The *cis* and *trans* forms of the diacetates of most of the hindered enediols have been prepared by the anhydride method. As has been indicated previously, this treatment on 1,2-di-(2-pyridyl)-1,2-ethendiol gave the monoacetate of 2-pyridoin (12, 14, 17), while acetyl chloride in excess (no other solvent), gave two diacetates, presumably the *cis* and *trans* forms (17). These forms are of interest since they rep-

resent the only case of geometrical isomers reported among the 2-N-heterocyclic enediols and their derivatives. Benzoyl chloride in pyridine on 1,2-di-(2-quinolyl)-1,2-ethenediol and the 6,6′-dimethyl homolog produced dibenzoates (10, 11).

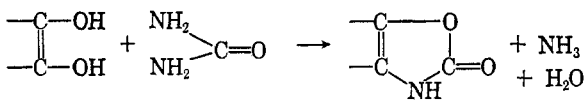
4. Phenylhydrazone and Osazone Formation

It has already been shown that enediols sometimes undergo reactions which involve the tautomeric benzoin form. This situation prevails in the case of 1,2-di-(2-pyridyl)-1,2-ethenediol, which with one mole of phenylhydrazine gave the phenylhydrazone (45%), but with three moles, the osazone was formed in 70% yield (14).



5. Oxazolone Formation

Refluxing 1,2-di-(2-pyridyl)-1,2-ethenediol with urea in glacial acetic acid produced the oxazolone in 72% yield (14).

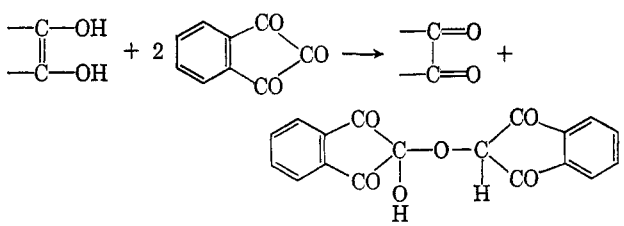


6. Urethane Formation

Enediols react with phenyl isocyanate in benzene solution to give the monourethanes, but if the solvent is omitted, diurethanes are obtained (17). By heating in ethanol or aniline, the diurethane gave the monourethane of the ketol form.

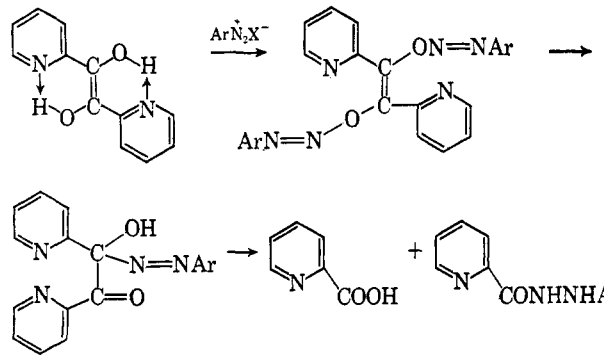
7. With Ninhydrin

Water-soluble enediols in aqueous solution gave insoluble crystalline precipitates of hydrindantin with ninhydrin (60).



8. With Diazonium Salts

Enediols, such as 1,2-di-(2-pyridyl)-1,2-ethenediol, react with diazonium salts to form a product, which on hydrolysis yields 2-pyridinecarboxylic acid and its aryl hydrazide, each in yields of around 60% (16, 18). Through a study of intermediates a mechanism has been suggested.



9. Hydrogenation

a. With Molecular Hydrogen

The factors which contribute to the stability of enediols (steric hindrance and chelation) interfere with catalytic hydrogenation at low pressure. Not only did low pressure hydrogenation of hindered diketones not proceed beyond the enediol stage (55), but chelated enediols such as 1,2-di-(2-quinolyl)-1,2-ethenediol were not affected under these reducing conditions (10). However, by the use of palladium asbestos, aqueous alcoholic hydrogen chloride, and low pressure hydrogen, both 1,2-di-(2-pyridyl)-1,2-ethenediol and its 6,6′-homolog were reduced to the corresponding glycols (45).

By using higher temperatures and pressures and other catalysts, it has been possible to obtain ethanes from hindered enediols. Such reductions do not appear to have been attempted on the enediols as such, but they have on diketones, in which cases the enediols were probably intermediates. The hydrogenation of 1,2-di-(2,3,5,6-tetramethylphenyl)- and 1,2-di-(2,3,4,6-tetramethylphenyl)-1,2-ethanediones with molecular hydrogen, at 230° and 5500 p.s.i. pressure in the presence of copper chromite, produced the corresponding ethanes (29).

b. With Other Reducing Agents

The use of the Grignard reagent has already been mentioned in section XIIA2. In addition, chelated enediols have been reduced to the glycol with zinc and acetic acid (14).

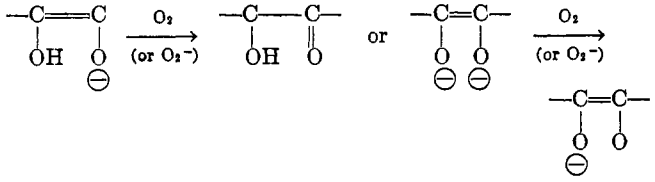
10. Oxidation

a. With Air

As has already been indicated, enediols are readily oxidized by air to the diketone. In the preparation of 1,2-di-(2,4,6-triethylphenyl)-1,2-enediol, the benzil was recovered as well as the enediol (25). The clue which led to the discovery of 1,2-di-(2-quinolyl)-1,2-ethenediol was the fact that the dark purple compound produced differed from a benzoin in that its solution oxidized quickly in air to a yellow benzil. By oxidizing in a boiling solution of dioxane, a yield of 83% was obtained (10). The product is not always the benzil. In the presence of ferric chloride, oxygen at low pressure pro-

duced 2-pyridinecarboxylic acid from 1,2-di-(2-pyridyl)-1,2-ethenediol (no yield was given) (45).

The mechanism of the oxidation of enediols by oxygen has been studied (50, 59). It is a two-step reaction, which begins either with a singly or doubly charged anion.



The proof for the existence of the semiquinone radical seems well established in the case of the oxidation of benzoin in alkaline solutions. The variation of the rate of oxidation of l-ascorbic acid with pH has been interpreted by assuming the presence of both singly and doubly charged anions.

b. With Other Oxidizing Agents

The benzil has also been produced by oxidizing agents other than oxygen. Sodium hypoiodite gave a 90% yield from *cis*-1,2-di-(2,4,6-triisopropylphenyl)-1,2-ethenediol, and hydrogen peroxide in alkaline solution led to an 80% yield from the *trans* isomer (28).

With chelated enediols the oxidation product using 30% hydrogen peroxide is different. 1,2-Di-(2-pyridyl)-1,2-ethenediol, for example, gave 2-pyridinecarboxylic acid N-oxide (no yield is reported) (45).

11. Hydroxylation

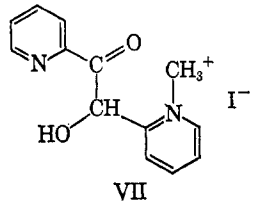
Enediols, in the presence of the ferrous ion, ethylenediaminetetraacetate, and oxygen, introduce hydroxyl groups into aromatic or heterocyclic rings (8, 56). The reaction is electrophilic and the ordinary rules of substitution apply. Yields, using ascorbic acid as the enediol, vary from 9% in converting aniline to *p*-aminophenol to 55% in converting salicylic acid to 2,5-dihydroxybenzoic acid.

B. REACTIONS OF N-HETEROCYCLIC ENEDIOLS

1. Addition

a. With Alkyl Halides

1,2-Di-(2-pyridyl)-1,2-ethenediol in acetic acid solution forms a quaternary ammonium salt with methyl iodide (17). On the basis of its ultraviolet spectrum and inability to affect Tillman's reagent in acidic or neutral solution, it was assigned the keto structure VII.



VII

b. With Aromatic Nitro Compounds

1,2-Di-(2-pyridyl)-1,2-ethenediol in absolute ether forms 1:1 molecular compounds with 2,4-dinitrofluorobenzene and 2,4-dinitrochlorobenzene (17).

2. Metal Chelates

A dark violet copper complex of 1,2-di-(2-pyridyl)-1,2-ethenediol (one atom of Cu for each hydroxyl H) is formed in treating the enediol with copper acetate and sodium acetate (19).

XIII. ANALYTICAL METHODS

These methods take advantage of the color reactions listed under XI.

A. TITRATION WITH IODINE

The enediol was dissolved in 95% ethanol, acidified with sulfuric acid, and an excess of standard iodine solution was added. The unreacted iodine was titrated immediately with standard thiosulfate (2, 20).

B. TITRATION WITH N-(3,5-DICHLORO-4-HYDROXYPHENYL)-*p*-QUINONIMINE (TILLMAN'S REAGENT)

This method is the most widely used of the analytical procedures. The enediol is titrated with the commercial sodium salt of the substituted quinonimine in a buffered phosphate solution, under an atmosphere of nitrogen, either directly, or an excess of the reagent may be employed. In the latter case back titration is accomplished with a standard solution of ascorbic acid or some other enediol (22).

In a second procedure (14) a weighed quantity of the benzoin or enediol is dissolved in ethanol under an atmosphere of nitrogen, after which 0.1 *N* sodium hydroxide, buffered phosphate at pH 7, or 0.1 *N* acetic acid is added. The solution is then titrated, still under nitrogen, with Tillman's reagent. Only the stabler enediols will survive under neutral and acidic conditions. Results obtained by this procedure are given in Table V.

TABLE V

ANALYSIS OF BENZOINS AND ENEDIOLS BY TITRATION WITH TILLMAN'S REAGENT

	% enediol when titrated in presence of		
Compound	0.1 *N* NaOH	buffered phosphate, pH 7	0.1 *N* CH_3COOH
Benzoin	76.9	0	
Furoin	80.6	0	
1,2-Di-(2-pyridyl)-1,2-ethenediol	98.3	94.8	93.3

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