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Aromatic and heterocyclic semidiones

Charles Louis Myers
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**MYERS, Charles Louis, 1941-
AROMATIC AND HETEROCYCLIC SEMIDIONES.**

**Iowa State University, Ph.D., 1968
Chemistry, organic**

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AROMATIC AND HETEROCYCLIC SEMIDIONES

by

Charles Louis Myers

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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Ames, Iowa

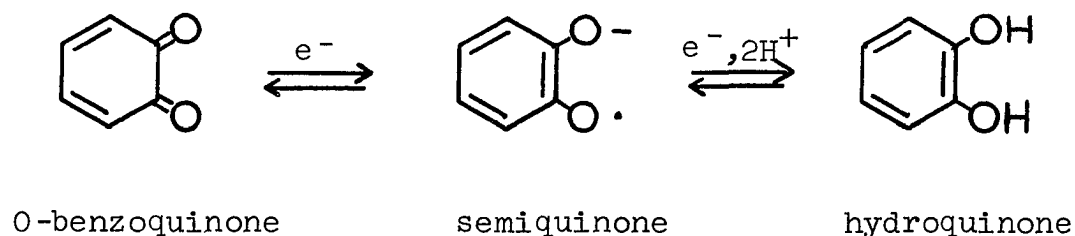
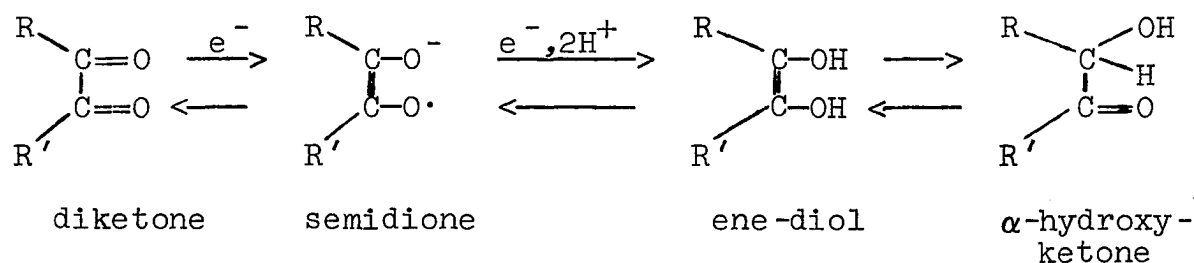
1968

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I. INTRODUCTION

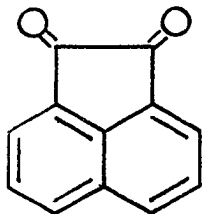
Semidiones are radical anions derived from diketones by a one electron reduction (1). They are analogous to the semiquinone radical anions derived from quinones and the equilibria which involve semidiones are essentially the same as the equilibria which involve semiquinones. The distinction



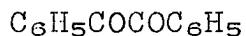
between the two types of radicals is more one of semantics than of chemistry. In both aliphatic dicarbonyl systems (1, 2) and benzenoid aromatic systems (1,3), both terminologies have been used for the same radicals by different workers. The two terminologies are useful to distinguish those easily reduced compounds, such as benzoquinones, which gain unusual stability by achieving aromaticity upon reduction, from those diketones, such as biacetyl, which do not gain aromaticity upon reduction. Russell defines semiquinones as those radical

anions in which two mutually conjugated oxygens are bonded to carbon atoms of an aromatic ring, whether benzenoid or not (4). The radicals discussed in this work include both semidione and semiquinone types by this definition.

The dicarbonyl moiety in benzoquinones is only a part of the entire potential aromatic system, which is the actual electrophile. As one proceeds to larger aromatic quinones, such as naphthoquinones and anthraquinones, the potential gain in resonance energy becomes relatively less important and the reduction potentials of the dicarbonyl compounds increase to more negative numbers (5). Those "quinones" or diketones which have a dicarbonyl moiety conjugated with an aromatic system, but which have no possibility for achieving aromaticity upon reduction, have even greater negative reduction potentials. This class of compounds includes acenaphthenequinone (5) and benzil (6) which have reduction potentials intermediate in magnitude between those of potentially aromatic quinones and those of aliphatic diketones such as biacetyl (6). The presence of a diketo group



acenaphthenequinone

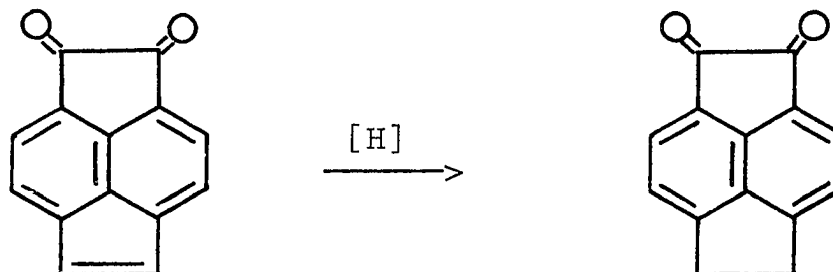


benzil



biacetyl

in a molecule does not necessarily indicate that reduction will occur at that moiety. For example, the most reducible group in pyracycloquinone is the antiaromatic π system, and the radical anion of this compound has the properties of a hydrocarbon radical anion rather than a semiquinone (3).

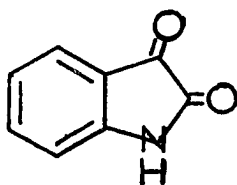


pyracycloquinone

1,2-diketopyracene

Attempts to prepare the hydroquinone produced only 1,2-diketopyracene (3).

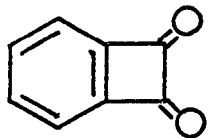
Of the compounds to be discussed in this thesis the only extensive previous studies of reduction potentials were of isatin and the substituted isatins (7, 8). These studies were performed in aqueous solution primarily for comparison with aqueous biological dehydrogenation reactions (7).



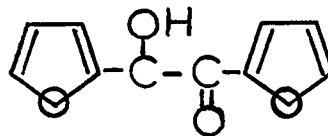
isatin

Aqueous conditions are not suitable for comparison of redox potentials with structure for a wide variety of dicarbonyl compounds since the equilibria involved are very strongly pH dependent (5). The use of neutral non-aqueous conditions mitigates this problem and allows comparison among the results of different workers. Such a technique has been applied previously to the study of diketones, triketones and α -ketoesters (6) and to studies of nitroaromatic radical anions (9, 10) and phthalimide radical anions (11).

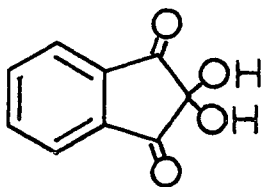
A large amount of literature has accumulated on the electron spin resonance (ESR) spectroscopy of semiquinones and semidiones. Jones has reviewed some of the recent quinone literature (12) and Russell has reviewed the chemistry of semidiones (1, 4). Most semidione studies have been of the aliphatic semidiones. These efforts have been principally directed toward the elucidation of spin delocalization mechanisms (13) and the application of ESR to the study of conformational and structural problems in organic chemistry (1, 4, 14, 15). Some aromatic semidiones which have been studied by ESR are those derived from benzocyclobutenedione (16), acenaphthenequinone (17), benzil (17), 1-phenylpropane-1,2-dione (18) and furil (19). Some reported aromatic semitrones are those derived from ninhydrin (20) and 1,5-diphenylpropanetrione (6).



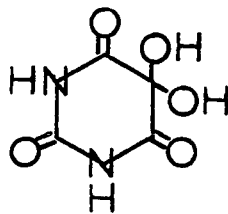
benzocyclobutenedione



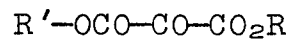
furil



ninhydrin

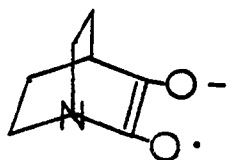


alloxan hydrate

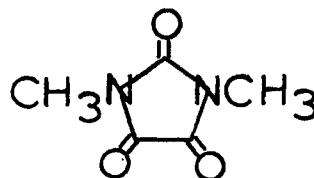


mesoxalate ester

The examples of semidiones or semitriones which have heteroatoms bonded to the dicarbonyl moiety are the radical anions of ethyl benzoylformate (18), the mesoxalate esters (6), 1,2-benzoxalate (6) and alloxan (20). The most recent examples of α -heterosemidiones are those derived from autoxidation of 3-quinuclidinone (21) and from reduction of dimethylparabanic acid (21). The latter result is part of the present study.



quinuclidine-2,3-semidione



dimethylparabanic acid

Several previous studies of aromatic heterocyclic radical anions, other than semidiones, have been made which are related to a discussion of the present work. These include studies of the phthalimide and related radical anions (11, 22, 23), azo-type radical anions (24), 2,1,3-benzoxadiazole and congeneric radical anions (25), and the radical anions of dibenzothiophene and its congeners (26). A large number of heterocyclic radical ions have been prepared and the chemistry of aromatic radical ions has been reviewed (12).

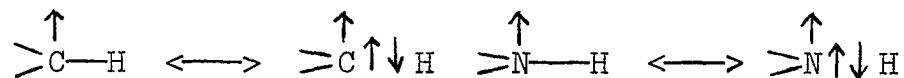
Aromatic radicals have often been of interest because of the proportionality of the proton hyperfine splitting constant a^H , and the π spin density, ρ_C , on the carbon atom bearing the proton. This relationship was expressed by McConnell by the following equation (27). The best numerical value of Q_{CH}^H has been somewhat dependent on the particular system

$$a^H = Q_{CH}^H \rho_C$$

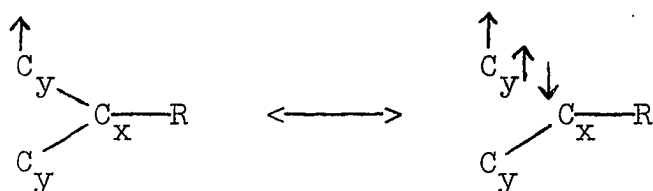
studied, but generally has been within the range of -22.5 to -30 gauss (28). An experimental spin density at a particular carbon in a π radical is obtained by merely dividing a^H at that carbon by Q_{CH}^H .

In a π radical, isotropic hyperfine splitting of an atom in the nodal plane must arise from a polarization of the electrons of the σ bond system because the π system has no

electron density at the nuclei. Splitting by a proton occurs by polarization of the C-H or N-H bond. Such polarization



places a negative spin (opposite in sign to the spin of the unpaired π electron) on the proton, accounting for the negative sign of Q_{CH}^H . This σ bond polarization places a positive spin on the carbon or nitrogen and contributes to C^{13} and N^{14} hyperfine splittings in addition to proton splittings. Just as σ bond polarization by an adjacent atom in a π system causes negative proton splittings, so it is predicted to cause negative C^{13} and N^{14} splittings. Therefore,



splitting by C_{13} and N_{14} atoms in a π system are dependent on both their own π spin density, the "direct effect", and on the π spin density on adjacent atoms, the "adjacent effect" (28). These two effects are opposite in sign if all of the positions involved have positive π spin densities. The adjacent effect is obviously most important at positions of low π spin density adjacent to positions of high π spin density.

The sum of the direct and adjacent effects has been expressed as the Karplus-Fraenkel equation (29), a simplified

form of which is indicated. The adjacent atom σ - π spin polarization parameter for carbon, Q_{C-C}^{Cx} , has been shown to be a

$$a^{Cx} = Q_C^C \rho_{C_x} + \sum_y Q_{C-C}^{Cx} \rho_{C_y}$$

significant contribution to C^{13} splittings, with Q_{C-C}^{Cx} amounting to -14 gauss (28). However, the analogous parameter for nitrogen, Q_{CN}^N , is much smaller and its magnitude has often been debated. The majority of estimates of Q_{CN}^N have been approximately ± 3 gauss in magnitude (30, 31, 32, 21, 33).

The adjacent effect is a negligible contribution to the nitrogen splitting in radicals which have an unpaired spin density on nitrogen of similar magnitude to the spin density on adjacent atoms. In such radicals the nitrogen hyperfine splitting constant is proportional to the π spin density on nitrogen with a proportionality constant, Q_N^N , of 25 gauss (34). The subject of the relationship between hyperfine

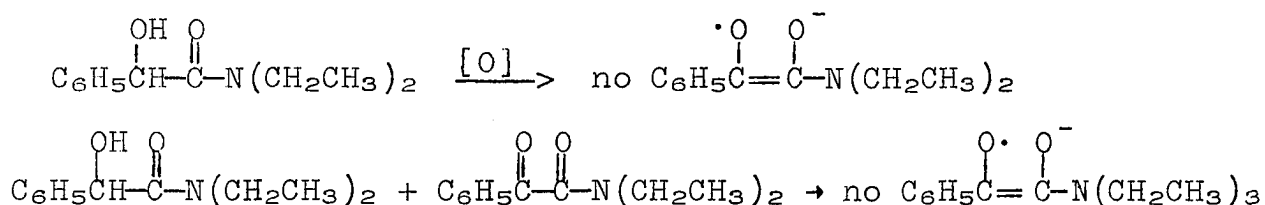
$$a^N = Q_N^N \rho_N$$

splitting constants and spin densities has been reviewed (35).

The purpose of the present work is to extend the study of the chemistry of aromatic and α -hetero semidiones. Emphasis is placed on the relationship between structure and stability and on spin density distribution. In addition, the results are considered in terms of their pertinence to the application of the Karplus-Fraenkel equation (20) to nitrogen

radicals. Therefore, α -nitrogen semidiones are of particular interest.

Several previous attempts to prepare certain α -nitrogen semidiones were not successful (36). For example, N,N-diethyl-2-hydroxy-2-phenylacetamide could not be converted to the semidione either by oxidation in basic DMSO or by mixing with the dicarbonyl compound in basic DMSO (36).



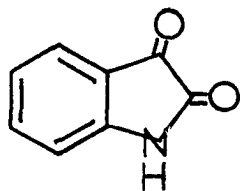
Other workers in this group have had similar negative results in attempts to make semidiones from amides.

One can imagine an infinite number of α -heterodicarbonyl compounds which might be reducible to semidiones. However, common keto amides and oxamides have relatively high reduction potentials and semidione generation from them is not expected to be facile. The corresponding esters have been found difficult to reduce to the semidiones (6) and amides often have higher redox potentials than the corresponding esters (5). Furthermore, a primary or secondary amide can deprotonate in basic media instead of accepting an electron. The high redox potentials are probably due to resonance stabilization of the amide or ester.

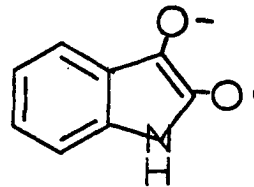
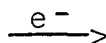


It is expected, however, that incorporation of the amide or oxamide moiety into certain cyclic systems can lead to some stabilization of the semidione.

An ideal series of compounds to begin this work was suggested by a study of indigo chemistry, which brought to attention isatin and related aromatic compounds. These systems were expected to yield semidiones which would be stabilized by a gain of aromaticity of the indole type. From this series the work proceeded to less stable α -hetero semidiones.



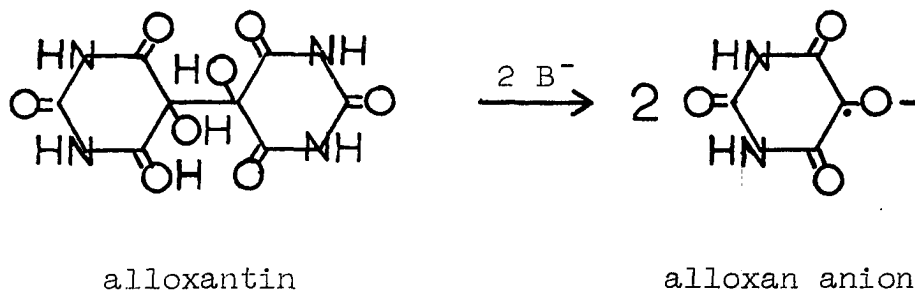
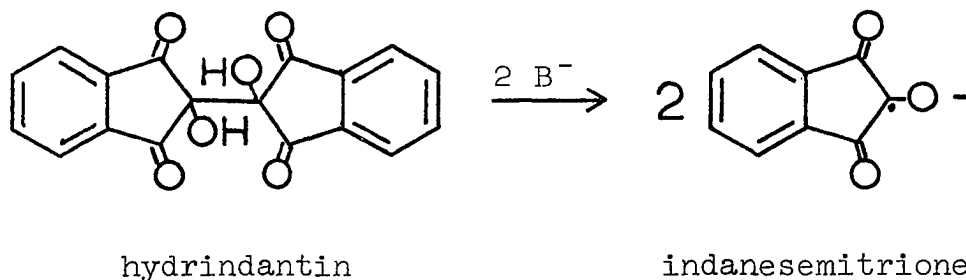
isatin



indole-2,3-semidione

The general techniques used to generate semidiones in previous work have included reduction of diketones in basic solution, electrolytic reduction of diketones, disproportionation or oxidation of α -hydroxyketones in basic solution and autoxidation of monoketones having an α -methylene group (1, 4). In certain cases radical anions have been produced by dissociation of pinacol-type dimers having the same oxidation

state as the radical anions. The semitriones of indanetrione and alloxan have been prepared by this method (20). All of these methods have been used in the present work. An additional method, which has not been used in this work, is direct



semidione generation by the acyloin condensation (39).

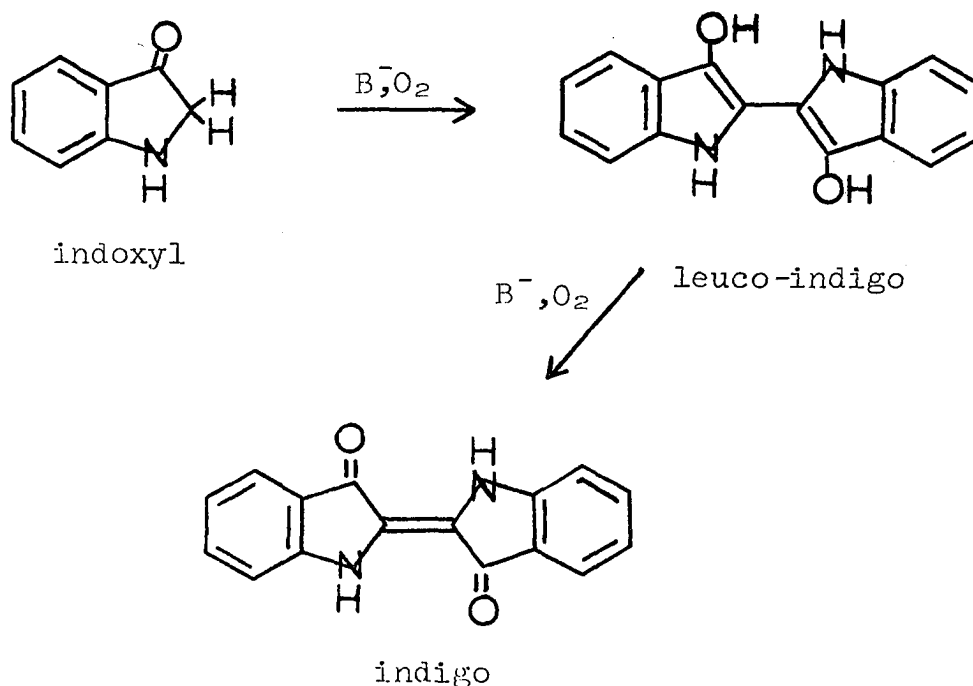
The solvents used in ESR studies of semidiones have usually been high dielectric aprotic solvents such as dimethyl sulfoxide (DMSO), dimethylformamide (DMF) or hexamethylphosphoramide (HMPA). These solvents, especially DMSO, solvate cations strongly and so eliminate many of the complications which arise from ion-pairing phenomena. Most semidione ESR work has been performed in DMSO or DMSO-*t*-butyl alcohol 80:20. These conditions are known to be ideal for

electron transfer reactions (39). The bases usually employed in semidione work have been the alkali metal alcoholates with potassium t-butoxide used most frequently. Ion pairing phenomena are less likely for potassium, rubidium and cesium salts than for lithium and sodium salts. This has been demonstrated for various radical ions including ketyls (40) and semidiones (41).

II. ELECTRON SPIN RESONANCE

A. Radicals Derived from Isatin

The series of heterocyclic semidiones having the indole, thiophene and benzofuran ring systems might be predicted to be most readily available either by reduction of the corresponding dicarbonyl compounds or by autoxidation of the corresponding monocarbonyl compounds. The latter method is often convenient since only one oxygen function need be introduced before the ESR experiment. However, for this particular series the ketonic monocarbonyl compounds are the indoxyls, which do not autoxidize to the monomeric semidiones but very easily undergo oxidative dimerization to the indigos.



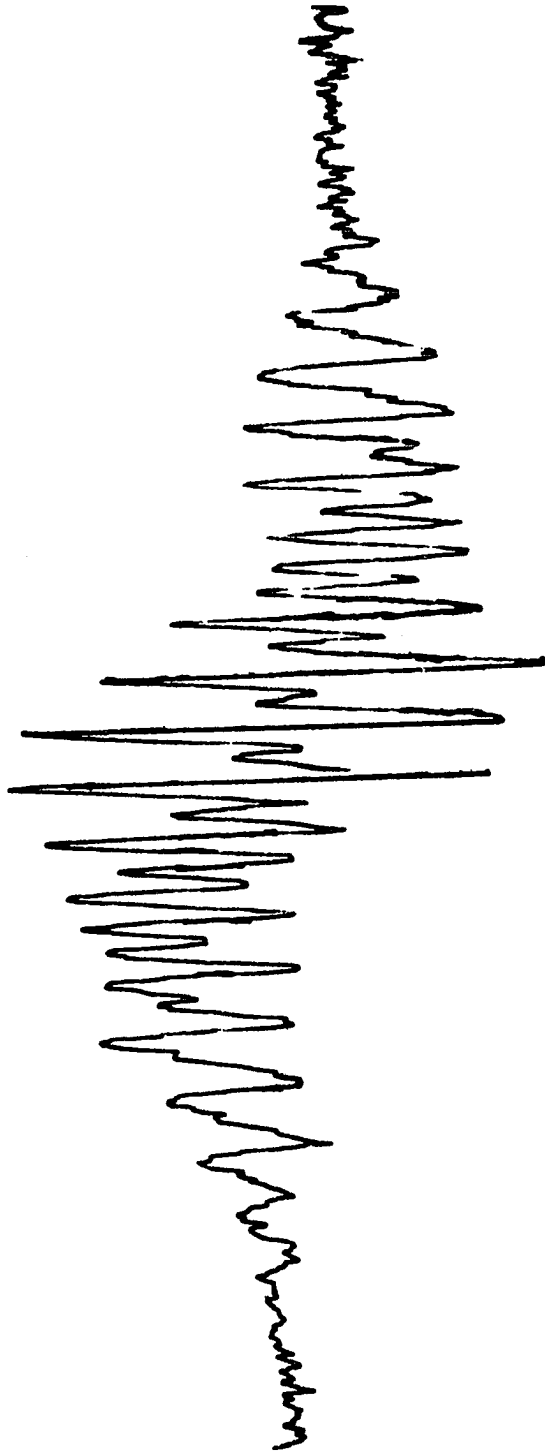
This reaction has been studied recently from a mechanistic point of view by G. A. Russell and G. Kaupp and has been the commercial source of synthetic indigo dye since the nineteenth century (37).

The enol acetate of indoxyl was hydrolyzed and autoxidized in an ESR cell in aqueous sodium hydroxide. A green solution of the indigo radical anion was produced, the ESR spectrum of which is shown in Figure 1. This radical was previously prepared by the reduction of indigo and by oxidation of leuco-indigo (42, 43). The radical has also been prepared in these laboratories by Dr. G. Kaupp by the oxidation of indoxyl by electron acceptors other than oxygen.

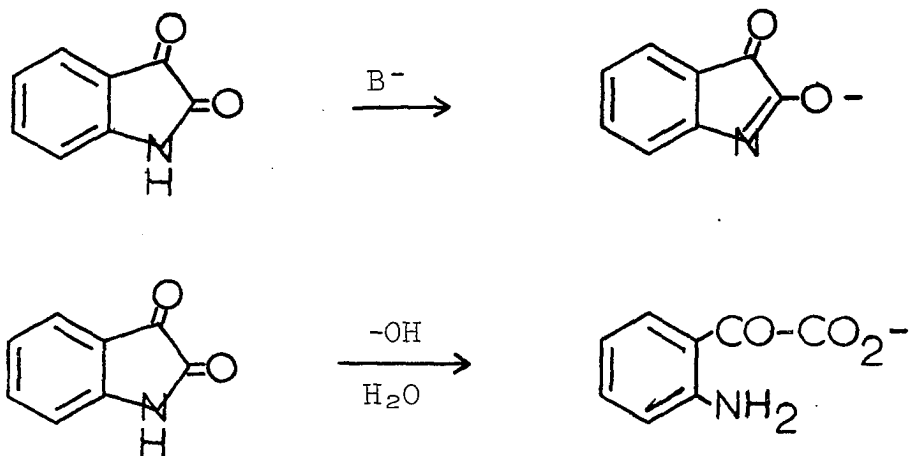
Since isatin and some ring substituted isatins were commercially available the most convenient preparation of the desired semidione seemed to be the reductive method. Isatin was reduced to the radical anion by reaction with potassium t-butoxide in DMSO and by the reaction with propiophenone and potassium t-butoxide in DMSO. The propiophenone enolate had been used previously as a reducing agent in semidione work (1). Although the ESR spectrum of the isatin radical anion could be resolved under these conditions, reduction in basic solution gave a relatively poor yield of radical anion.

Isatin is capable of forming a relatively stable purple enolate anion in nonaqueous basic solutions (8) and this

Figure 1. First-derivative ESR spectrum of the indigo radical anion produced by the hydrolysis and autoxidation of indoxyl acetate in aqueous sodium hydroxide solution.

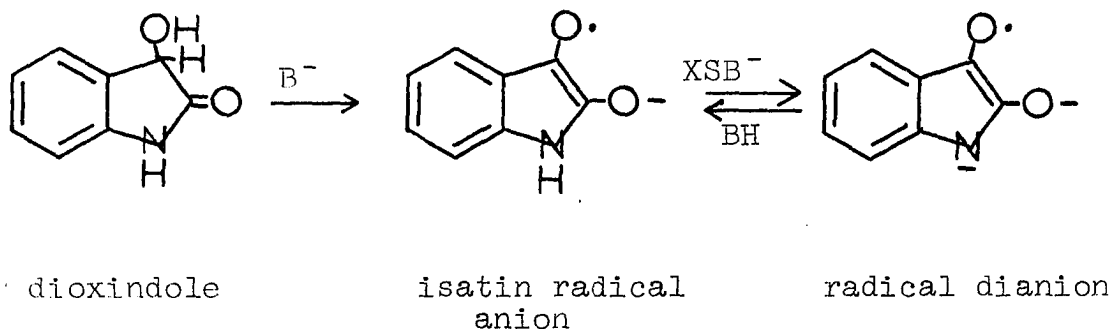


enolate formation competes quite effectively with semidione formation. In aqueous base isatin is readily hydrolyzed to



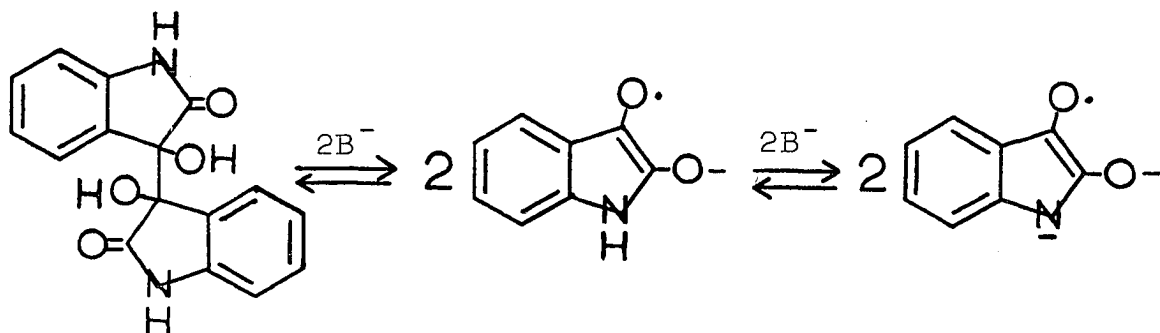
the ring-opened carboxylate (8).

Much better yields of the radical anion were obtained by oxidation of dioxindole. When dioxindole was treated



with an excess of potassium t-butoxide in DMSO, the dianion radical was produced. When moist air was allowed to enter the ESR cell some protonation occurred and a mixture of the radical anion and dianion was observed.

The best method of generating the isatin radical ions is the dissociation of the isatide dimer, which has the same oxidation state as the semidione. Reaction of the dimer with an equivalent amount of potassium t-butoxide in DMSO produces

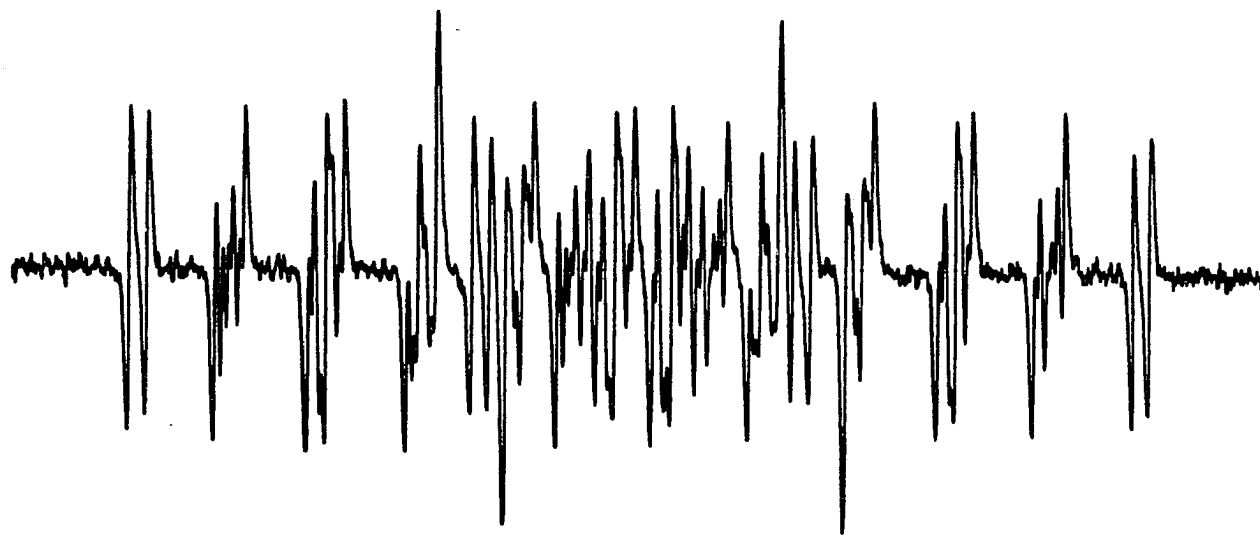


isatide

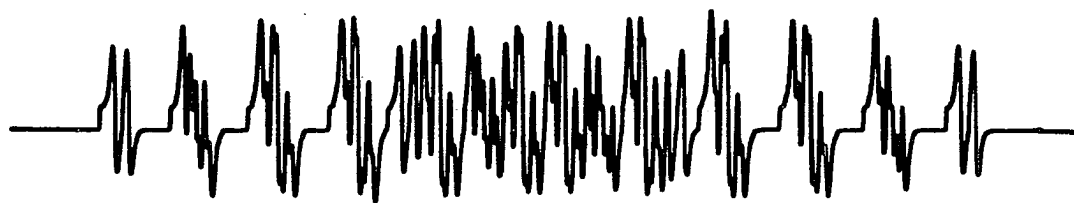
the radical anion in high yield. The use of slightly more than one equivalent of potassium t-butoxide in DMSO produces a mixture of anion and dianion radicals and the use of an excess of potassium t-butoxide produces only the radical dianion. When oxygen is added to a solution of the radical anion, the radical signal disappears and the red color of the semidione is replaced by the purple color of the isatin enolate anion. All of the reactions involved are apparently reversible.

The ESR spectra of the isatin radical anion in DMSO-t-butyl alcohol 80:20 and the dianion in DMSO are shown in Figures 2 and 3, respectively. The hyperfine splitting constants of these and related radicals are indicated in Table I. The isatin radical anion spectrum exhibits proton hyperfine splittings of 3.73 gauss (1H), 3.17 gauss (1H),

Figure 2. First-derivative ESR spectrum of the isatin radical anion (top) in DMSO-t-butyl alcohol 80:20; calculated spectrum for Lorentzian line width (bottom) of 0.10 gauss and splitting constants from text performed by Japan Electron Optics Laboratory Co. (JEOLCO) JNM-RA-1 spectrum accumulator.



GAUSS
0 2



GAUSS
0 2

Figure 3. First-derivative ESR spectrum of the isatin dianion radical (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

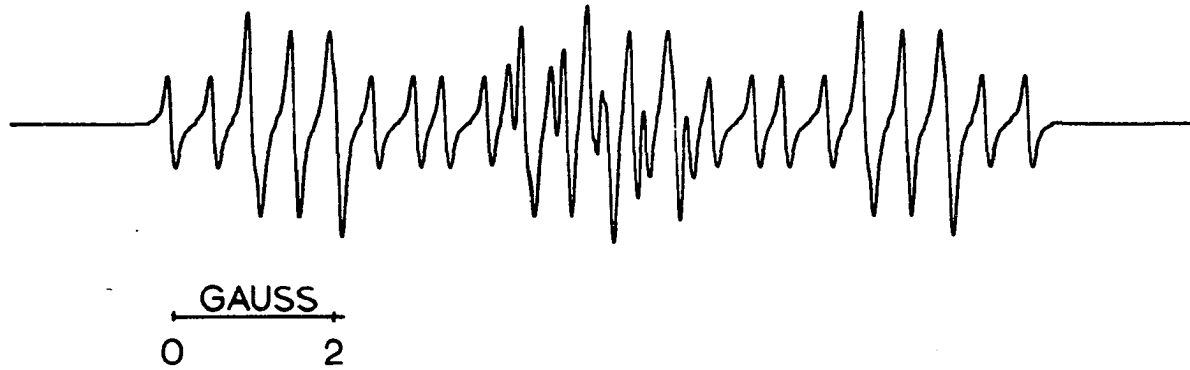
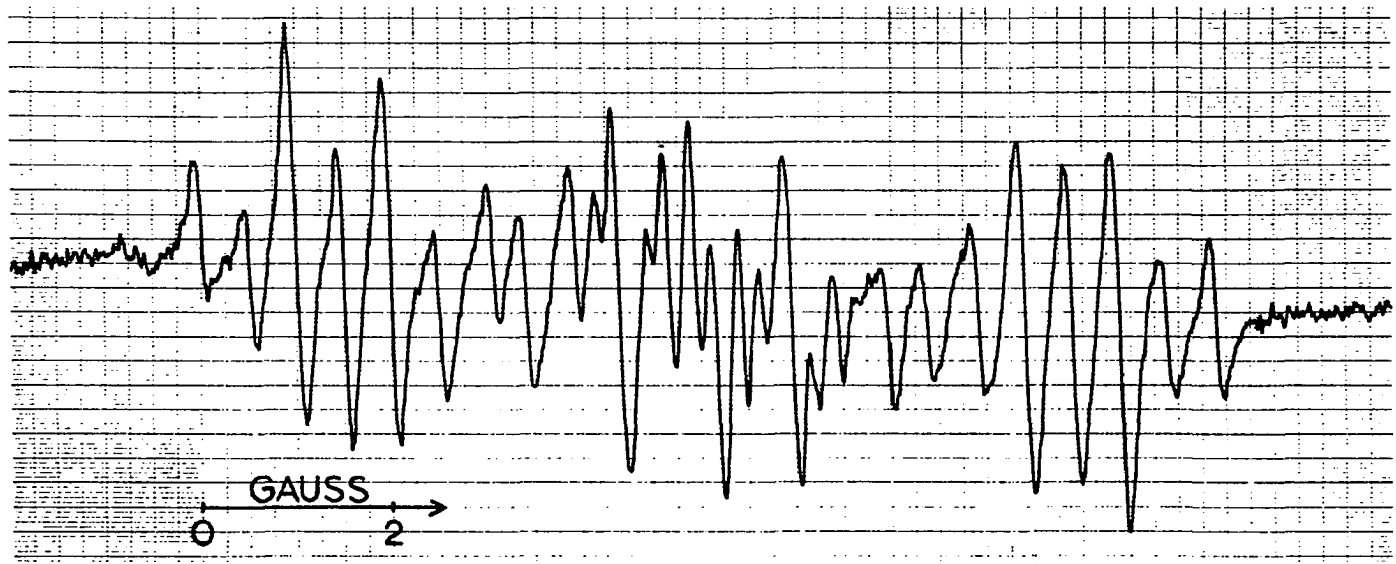


Table I. Splitting constants (gauss) of semidiones related to isatin

R	X	$a^H(4 \text{ and/or } 6)$	$a^H(5 \text{ and/or } 7)$	Other splittings	
	NH	3.17, 3.73	0.92, 1.00	$a^N=1.06, a_{NH}^H=0.19$	
	N ⁻	3.40, 4.23	0.99, 0.99	$a^N = 0.53$	
	NCH ₃	3.02, 3.65	1.00, 1.00	$a^N=0.92, a_{NCH_3}^H=0.61$	
5-CH ₃	NH	3.15, 3.67	0.98	$a^N=0.96, a_{CH_3}^H=0.98$ $a_{NH}^H = 0.19$	
5-CH ₃	N ⁻	3.48, 4.18	1.02	$a^N=0.47, a_{CH_3}^H=1.02$	
5,7-Cl, Cl	NH	3.2, 4.0		$a^N=1.1, a_{NH}^H<0.3$	
5,7-Cl, Cl	N ⁻	3.4, 4.4		$a^N = 0.6$	
	N-OH	2.91, 3.74	0.70, 0.70	$a^N=0.35, a_{OH}^H=0.33$	
	N-O ⁻	2.74, 3.67	1.02, 0.64	$a^N = 0.17$	
	O	3.04, 3.44	0.91, 0.91		
5-CH ₃	O	3.04, 3.42	0.91	$a_{CH_3}^H = 0.91$	
	S	2.43, 2.86	0.82, 0.70		
	CH ₂	2.83, 2.95	0.73, 0.56	$a_{CH_2}^H = 2.63$	
	C(CH ₃) ₂	2.75, 2.87	0.81, 0.47	$a_{CH_3}^H = 0.33$	
	C=O ^a	0.95, 0.95	0.95, 0.95		

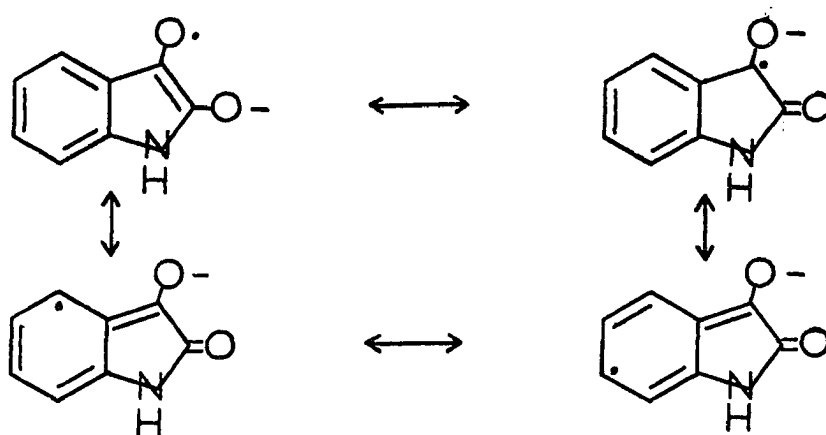
^aReference 20.

1.00 gauss (1H), 0.92 gauss (1H) and 0.19 gauss (1H) and a nitrogen hyperfine splitting of 1.06 gauss. This spectrum has a large amount of overlap of lines due to the near equivalence of the hyperfine interaction of two protons and the nitrogen nucleus. However, the hyperfine splittings can be measured with reasonable accuracy with the aid of a spectrum simulator. The computed spectrum gives a good match with the experimental spectrum, and all the hyperfine splittings are probably accurate to ± 0.03 gauss. The smallest two splittings are probably accurate to ± 0.02 gauss.

The isatin radical dianion hyperfine splitting constants can be measured quite accurately since there is no particular overlap problem. An excellent match of the experimental and computed spectra is obtained with proton hyperfine splitting constants of 4.23 gauss (1H), 3.40 gauss (1H) and 0.99 gauss (2H) and a nitrogen splitting of 0.53 gauss. The decrease of the nitrogen splitting and increase of the aromatic ring proton splittings in the dianion radical relative to the anion radical indicates the repulsive effect of a high heteroatom charge density on the unpaired electron density. A similar, though much smaller, repulsion effect has been observed in the phthalimide anion and dianion radicals (22).

The assignment of the proton hyperfine splittings to specific protons in the isatin radicals can be made by theory

and analogy. The largest proton splittings are expected to be due to the protons ortho and para to the semidione moiety.



This is predicted by simple resonance structures and by molecular orbital calculations (to be discussed). This would also be in accord with the hyperfine splittings of 1-phenylpropane-1,2-semidione which shows proton splittings of 1.84 gauss, 1.59 gauss and 0.53 gauss for the para, ortho and meta protons, respectively (18). One would also predict that the two 1 gauss splittings are due to the meta protons and that the 0.19 gauss proton splitting is from the N-H proton. The validity of these expectations has been demonstrated by the study of several substituted isatins.

When a proton is replaced by a deuterium atom, the hyperfine splitting of the deuterium is about $1/6.5$ of that of the proton (28). A deuterium atom substituted for the 0.19 gauss proton of the isatin radical anion is expected to have too small a splitting to be resolved. However, the 0.19

gauss proton splitting is also small enough to be unresolved in a poor spectrum. Therefore, the N-deuterated isatin radical anion must be prepared by a few different methods and care must be taken to achieve good resolution to insure that the spectra obtained are actually N-D spectra and not poorly resolved N-H spectra.

N-deuteroisatin was prepared which had 87% N-deuterium incorporation according to an NMR experiment in DMSO-d₆. This material was reduced to the radical anion electrolytically in both acetonitrile containing 4% D₂O and DMSO containing 10% D₂O. No 0.19 gauss proton splittings were observed. The N-D spectrum was also obtained by dissociation of isatide in DMSO-d₆ containing potassium t-butoxide. The N-D spectrum, Figure 4, compared well with the computed spectrum based on hyperfine splitting constants of 3.73 gauss (1H), 3.17 gauss (1H), 0.92 gauss (1H), 1.00 gauss (1H) and 1.06 gauss (1N).

Substitution of a methyl group for the N-proton did not affect the hyperfine splitting constants within experimental error. The N-methylisatin radical anion was prepared by reduction of N-methyl isatin with propiophenone enolate in DMSO containing potassium t-butoxide. The experimental spectrum, Figure 5, gave a good match with the computed spectrum with hyperfine splitting constants of 3.65 gauss

Figure 4. First-derivative ESR spectrum of N-deuteroisatin radical anion (top) in DMSO-d₆; calculated spectrum for Lorentzian line width (bottom) 0.20 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

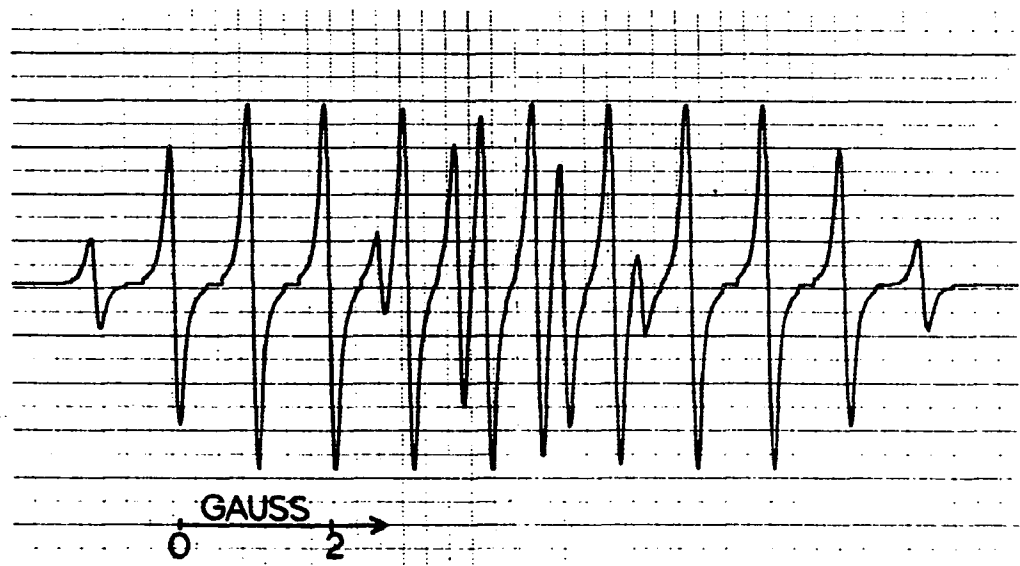
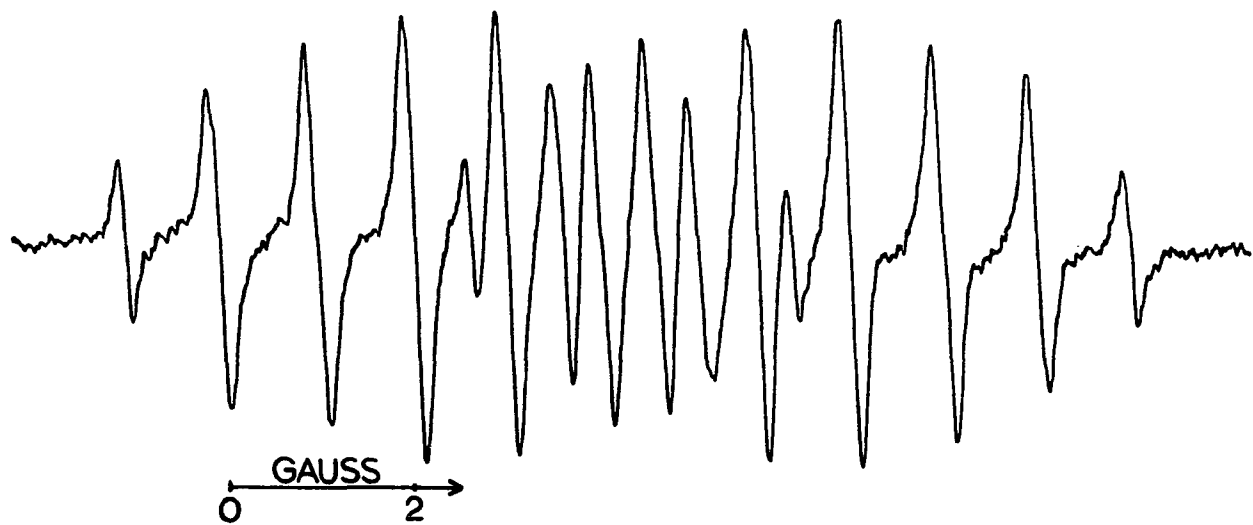
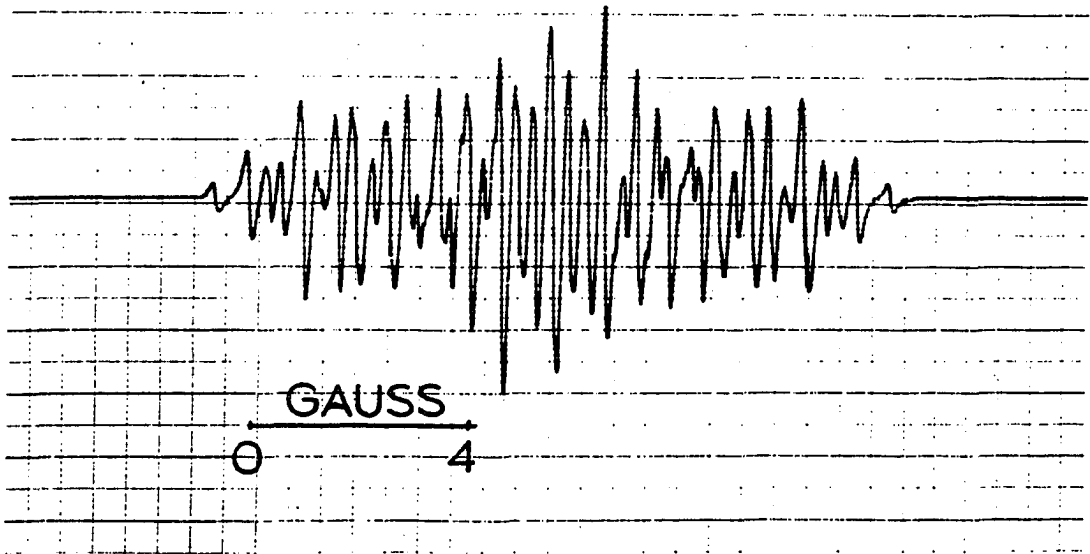
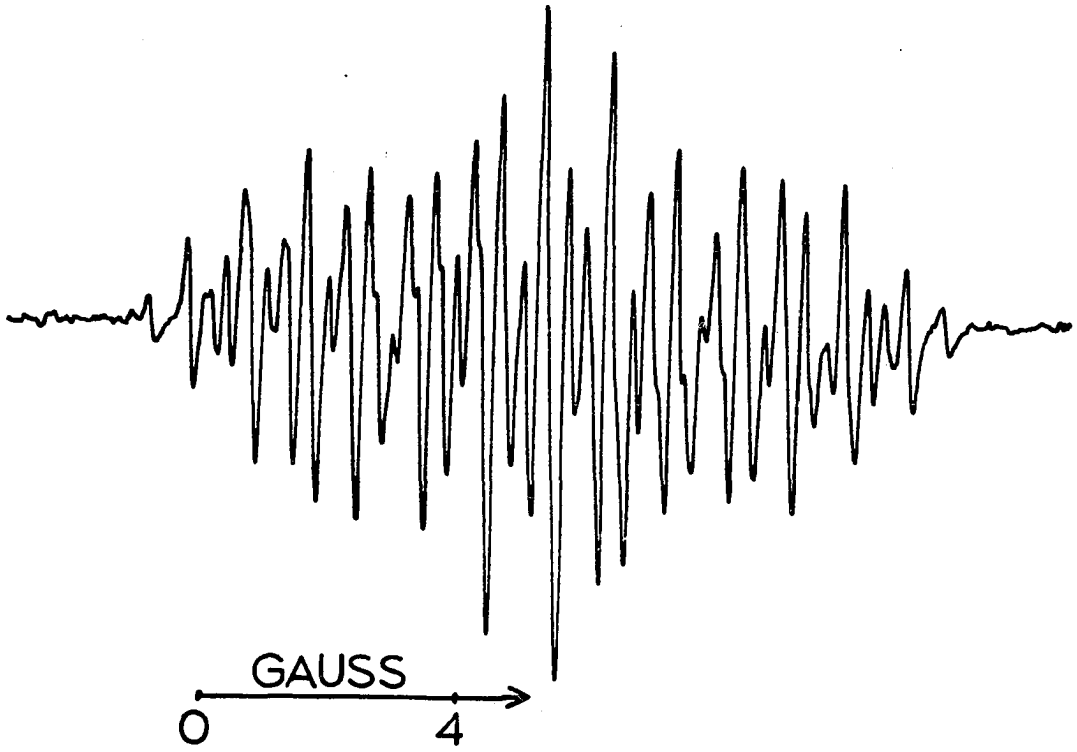
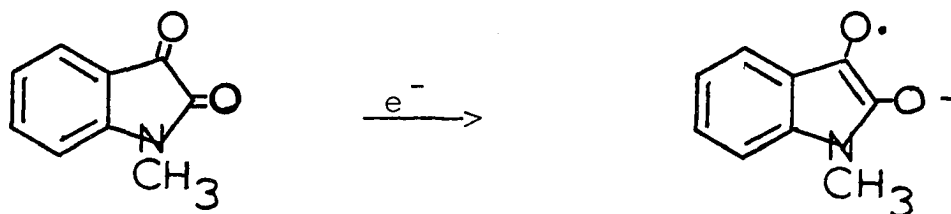


Figure 5. First-derivative ESR spectrum of N-methylisatin radical anion (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) of 0.20 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

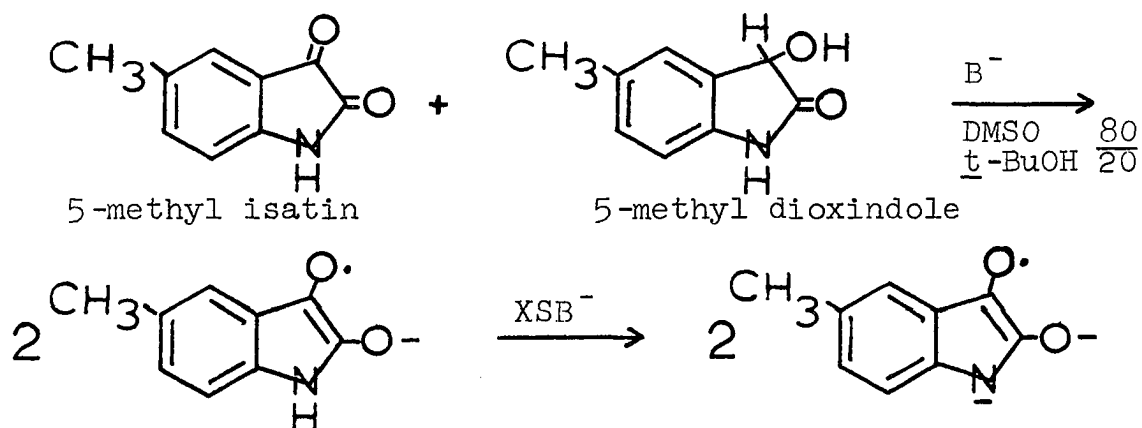




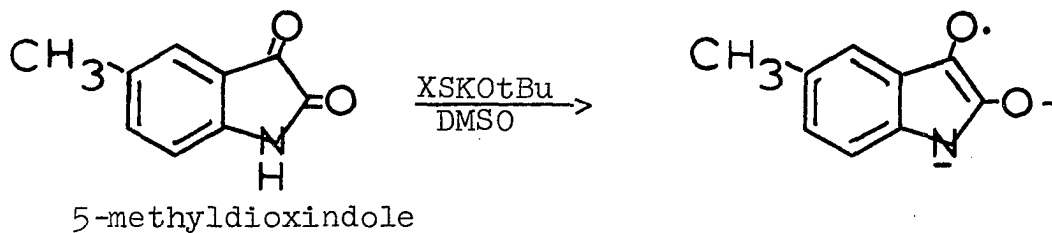
N-methylisatin

(1H), 3.02 gauss (1H), 1.00 gauss (2H), 0.92 gauss (1N) and 0.61 gauss (3H). The aromatic proton and the nitrogen splittings are probably accurate to only ± 0.10 gauss because of near equivalence of splittings.

Proof that the 1.0 gauss hyperfine splittings were due to the meta protons in the isatin radical anion and dianion was obtained by the study of some substituted semidiones. The red 5-methylindole-2,3-semidione was prepared by disproportionation of 5-methyldioxindole and 5-methylisatin in DMSO-t-butyl alcohol 80:20 in the presence of an equivalent amount of potassium t-butoxide. A slight excess of potassium



t-butoxide produced a mixture of radical dianion and radical anion, even in the protic medium. The ESR spectrum of the 5-methyl isatin radical anion, Figure 6, exhibited hyperfine splitting constants of 3.67 gauss (1H), 3.15 gauss (1H), 0.98 gauss (4H), 0.96 gauss (1N) and 0.19 gauss (1H). Comparison with the spectrum of the unsubstituted semidione showed that a 1.0 gauss hyperfine splitting in the parent semidione had been replaced by the methyl splitting. The ESR spectrum of the dianion radical, Figure 7, was obtained by the reaction of 5-methyldioxindole with excess potassium t-butoxide in DMSO. This spectrum indicated hyperfine



splittings of 4.18 gauss (1H), 3.48 gauss (1H), 1.02 gauss (4H) and 0.47 gauss (1N). Again, the meta methyl substitution had replaced one of the 1.0 gauss proton hyperfine splittings with a three proton 1.0 gauss methyl splitting.

Similar results were obtained from the study of the 5,7-dichloro derivatives. The 5,7-dichloroindole-2,3-semidione was prepared by the reaction of 5,7-dichloroisatin and 5,7-dichlorodioxindole with less than an equivalent of potassium

Figure 6. First-derivative ESR spectrum of 5-methylisatin radical anion (top) in DMSO-t-butyl alcohol 80:20; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

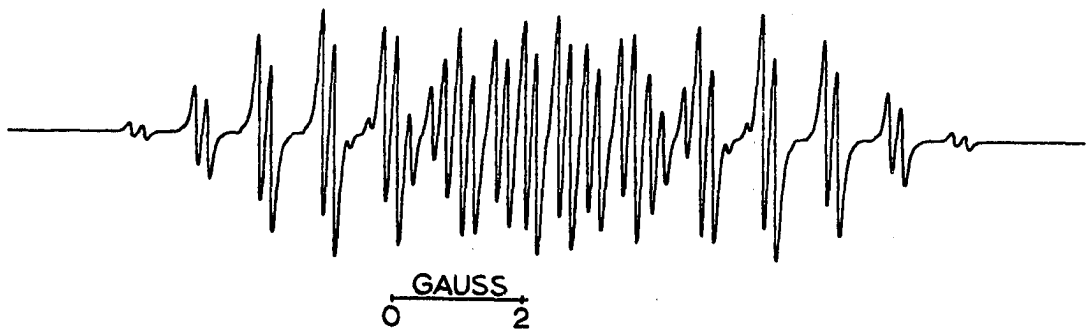
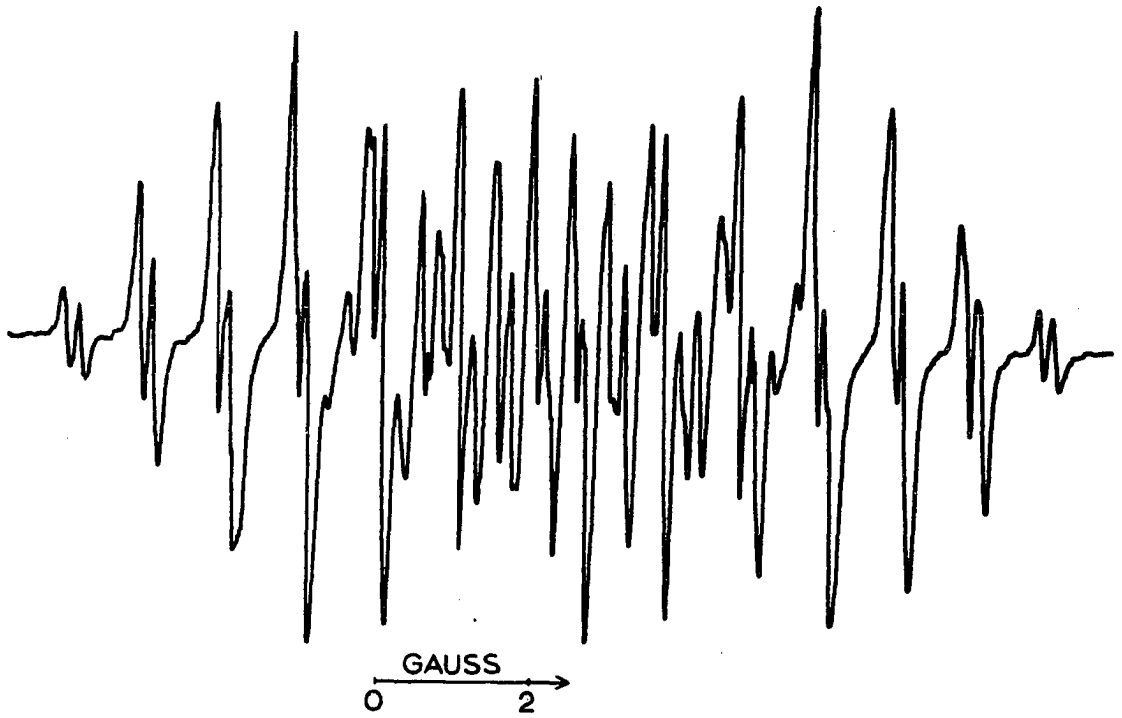
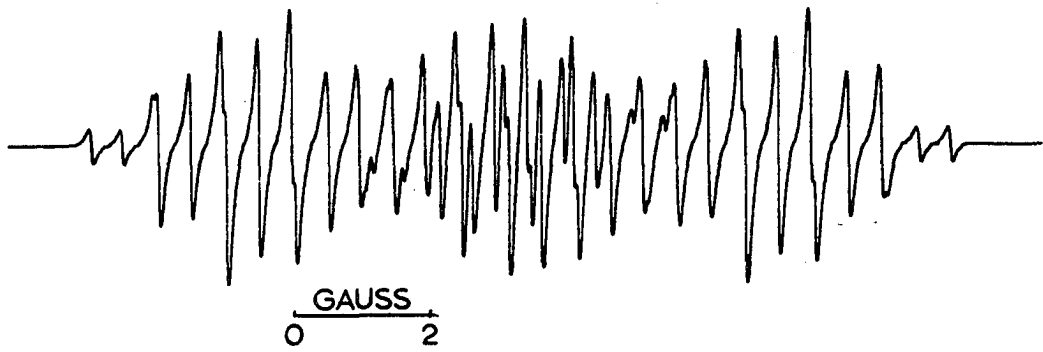
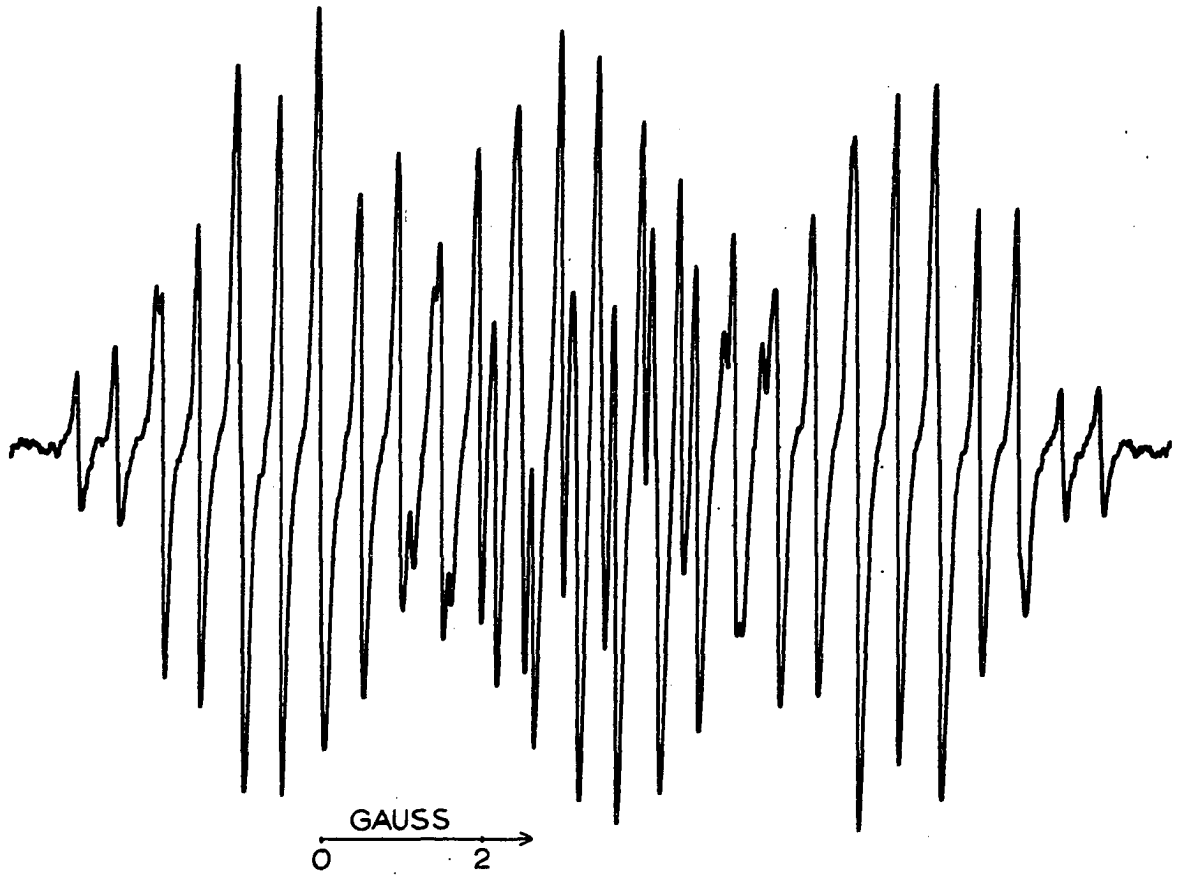
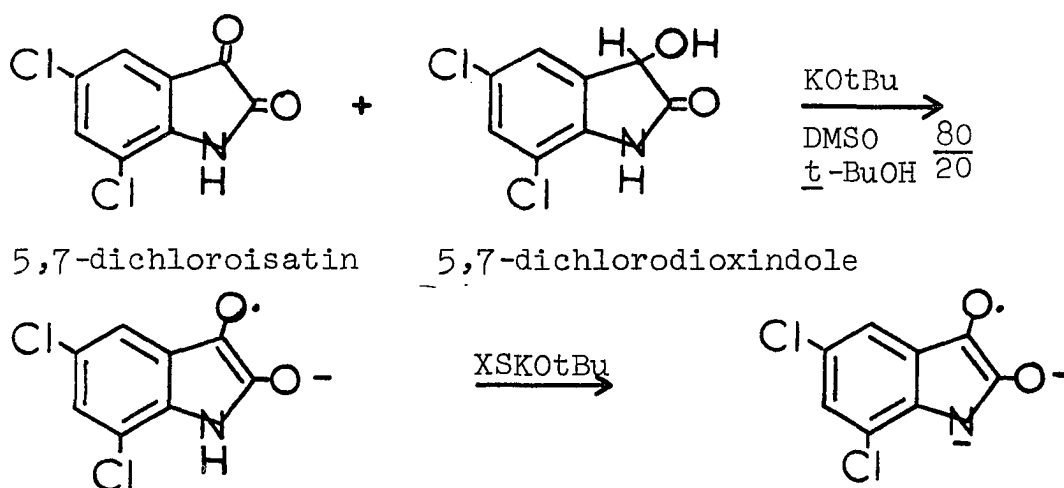


Figure 7. First-derivative ESR spectrum of 5-methylisatin dianion radical (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

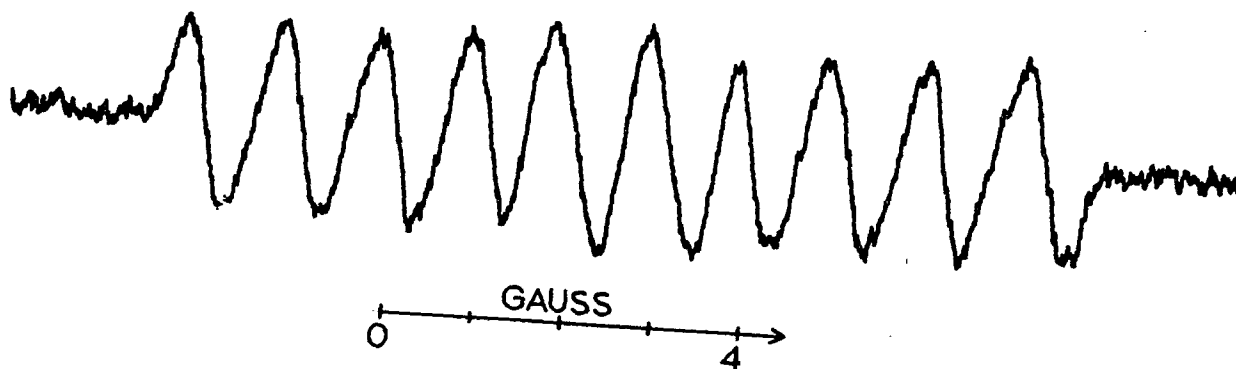
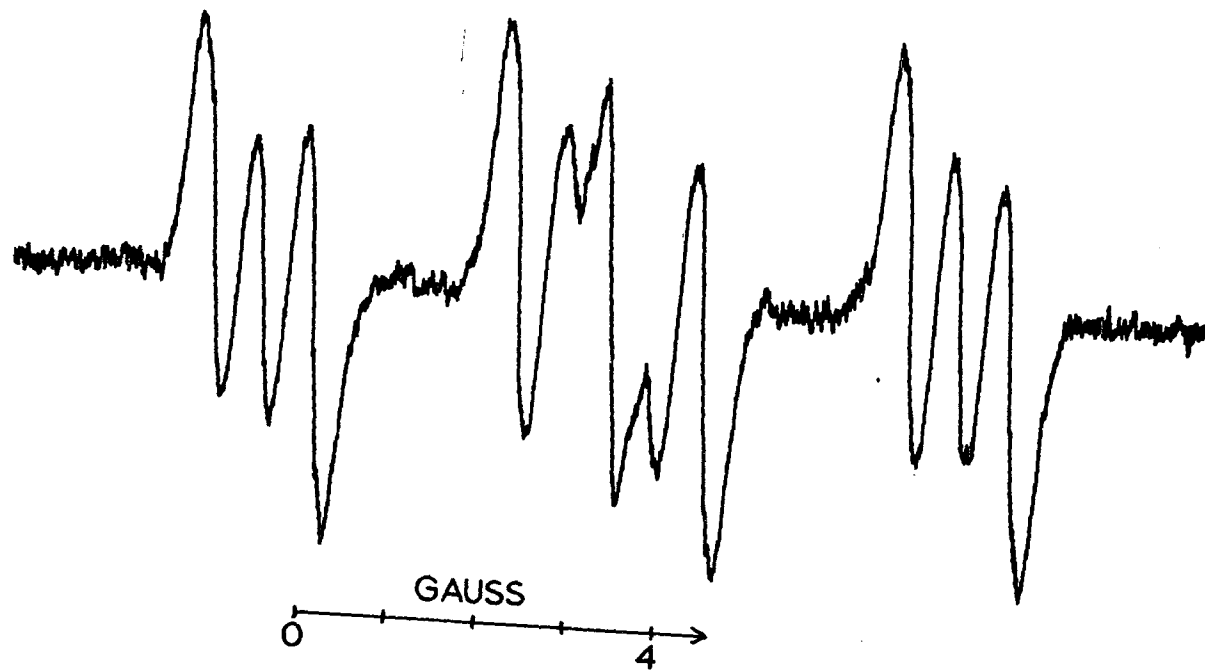


t-butoxide in DMSO-t-butyl alcohol 80:20. This radical anion was very easily deprotonated to the dianion radical even in the presence of t-butyl alcohol. The ESR spectrum of the radical anion, Figure 8, exhibited hyperfine



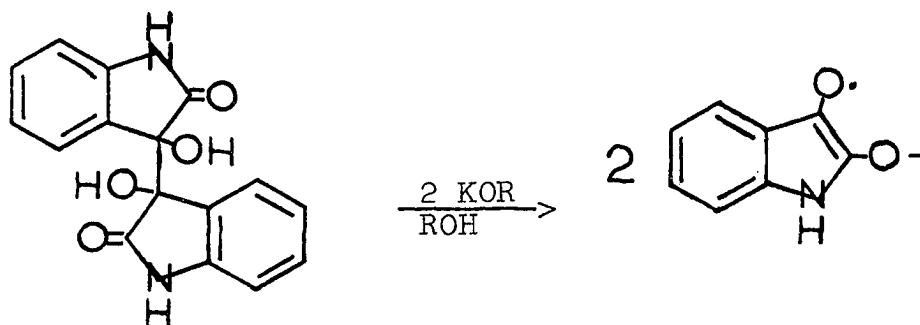
splittings of 4.0 gauss (1H), 3.2 gauss (1H) and 1.1 gauss (1N). The line broadening caused by the hyperfine interaction of the chlorine atoms, which possess a nuclear spin, was sufficient to obscure the N-proton hyperfine splitting within the 0.4 gauss linewidth. The dianion radical of 5,7-dichloroisatin was prepared in both DMSO and DMSO-t-butyl alcohol 80:20 by both reduction of the isatin with propiophenone enolate and by oxidation of the dioxindole. The ESR spectrum, Figure 8, indicated hyperfine splittings of 4.4 gauss (1H), 3.4 gauss (1H) and 0.6 gauss (1N). Again, the linewidth broadening effect of the chlorine atoms was evident from the 0.3 gauss linewidth. The larger proton

Figure 8. First-derivative ESR spectrum of 5,7-dichloroisatin dianion radical (top) in DMSO-t-butyl alcohol 80:20; first-derivative ESR spectrum of 5,7-dichloroisatin radical anion (bottom) in DMSO-t-butyl alcohol 80:20.



splittings in the isatin semidione anions and dianions are obviously due to the ortho and para protons since these splittings remained in the meta substituted derivatives. An inductive effect of the chlorine substitution was evident from the increase in proton hyperfine splittings in the dichloro derivatives. This effect was less important in the radical dianion than in the radical anion, as expected.

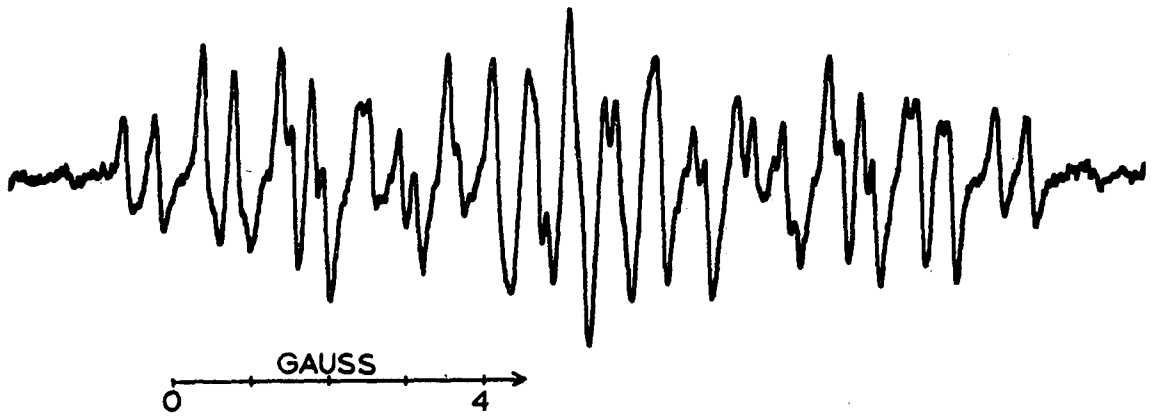
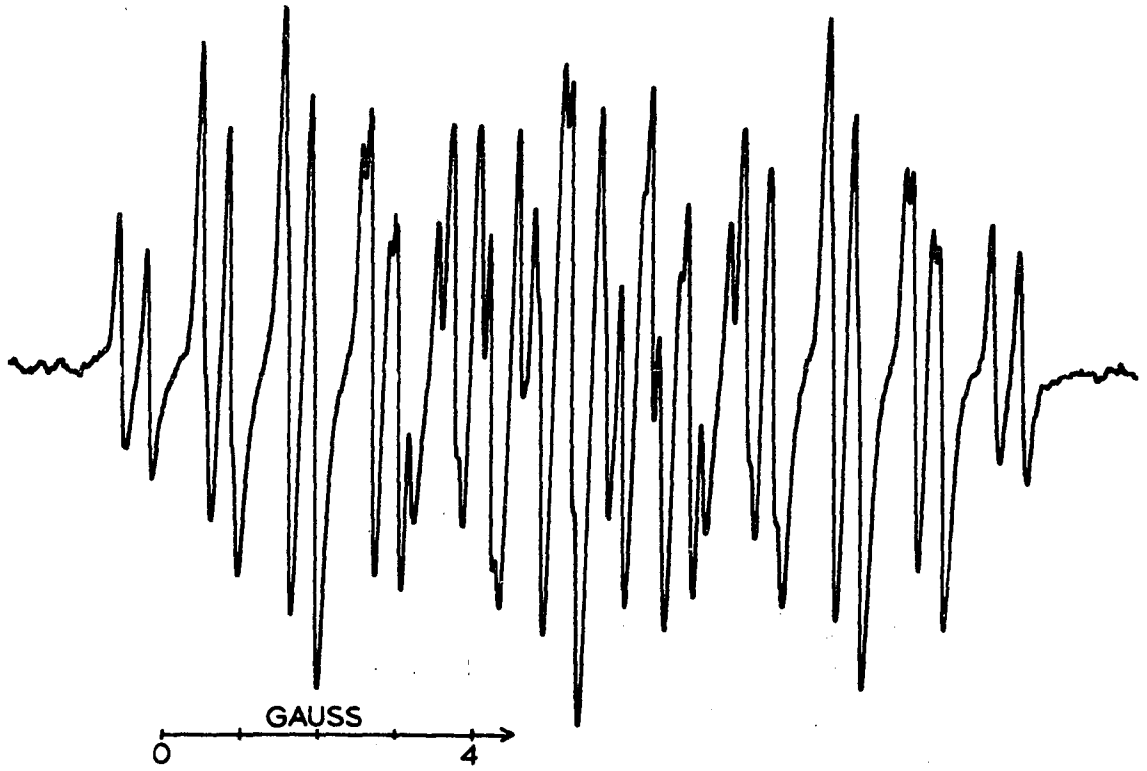
The isatin radical anion was stable in the absence of oxygen in all the solvents studied. The hyperfine splittings showed only a small solvent effect. When the solvent was varied from DMSO to ethanol to water, the N-H proton hyperfine splitting increased from 0.19 gauss to 0.36 gauss to 0.40 gauss. There were slight changes of the other splittings. The semidione was generated in ethanol and water by the reaction of isatide with the potassium salt of the conjugate base of the solvent. The ESR spectrum in



isatide

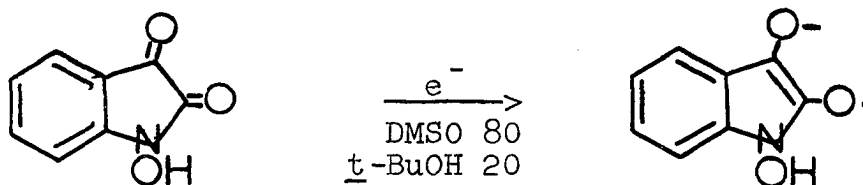
ethanol, Figure 9, exhibited hyperfine splittings of 3.74 gauss (1H), 3.21 gauss (1H), 1.11 gauss (1N or 2H), 1.04

Figure 9. First-derivative ESR spectrum of isatin radical anion (top) in ethanol; first-derivative ESR spectrum of isatin radical anion (bottom) in water.



gauss (2H or 1N) and 0.36 gauss (1H). The ESR spectrum in water, Figure 9, indicated hyperfine splittings of 3.77 gauss (1H), 3.24 gauss (1H), 1.10 gauss (1N or 2H), 1.00 gauss (2H or 1N) and 0.40 gauss (1H).

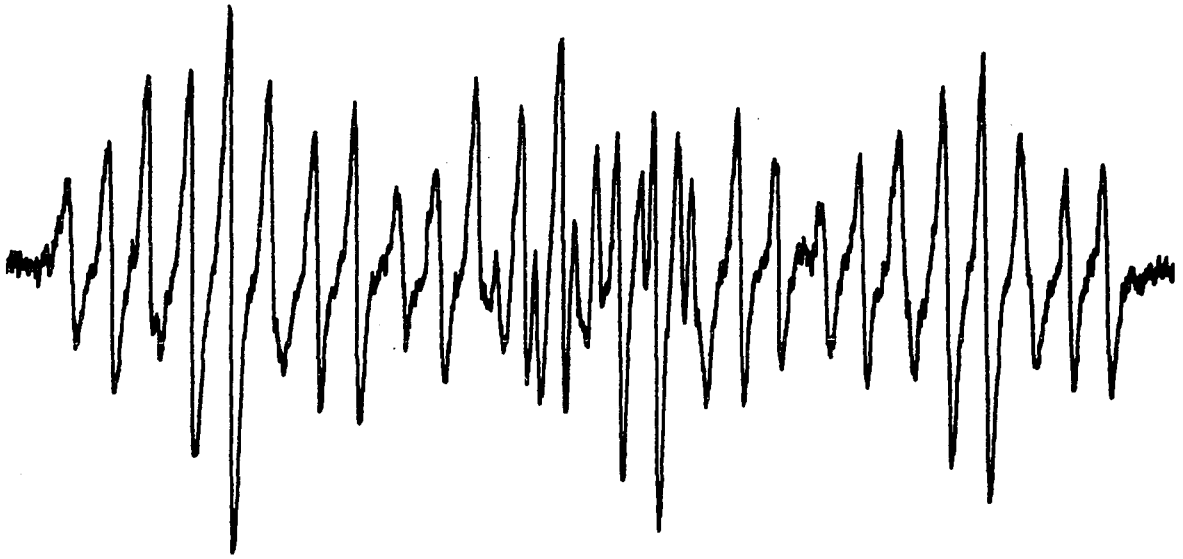
The N-hydroxyindole-2,3-semidione was prepared by the reduction of N-hydroxyisatin with or without propiophenone enolate in DMSO-t-butyl alcohol 80:20 in the presence of potassium t-butoxide. The ESR spectrum, Figure 10, exhibited hyperfine splittings of 3.74 gauss (1H), 2.91 gauss (1H), 0.70 gauss (2H), 0.33 gauss (1H) and 0.35 gauss (1N). The nitrogen splitting was about one-third of that in the unsubstituted isatin. The reaction of N-hydroxyisatin with



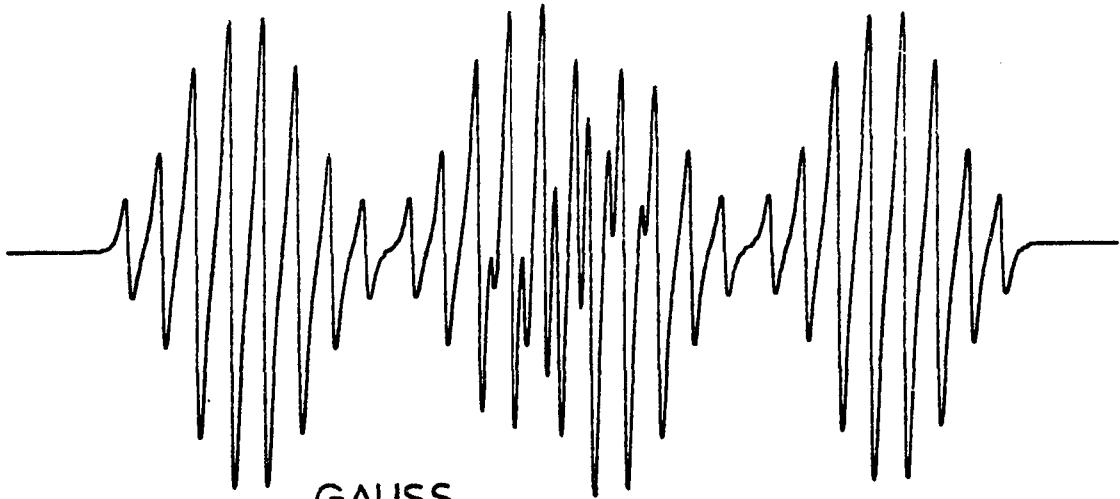
N-hydroxyisatin

propiophenone enolate in DMSO resulted in reduction and deprotonation and yielded the dianion radical. The spectrum of the dianion radical, Figure 11, indicated hyperfine splittings of 3.67 gauss (1H), 2.74 gauss (1H), 0.64 gauss (1H), 1.02 gauss (1H) and 0.17 gauss (1N). Comparison of

Figure 10. First-derivative ESR spectrum of N-hydroxyisatin radical anion (top) in DMSO-t-butyl alcohol 80:20; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

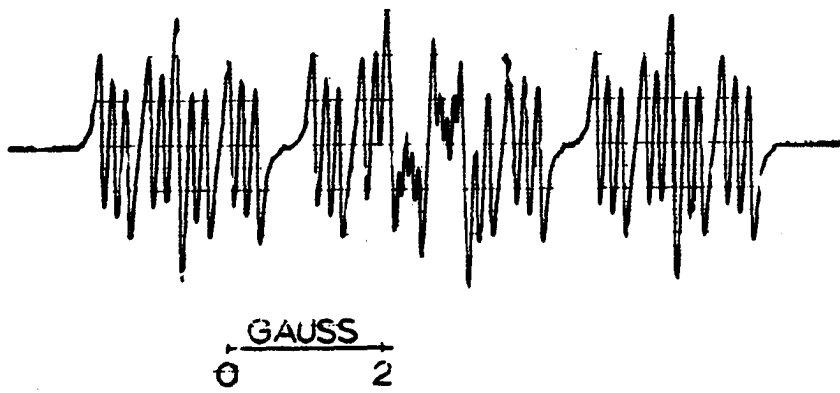
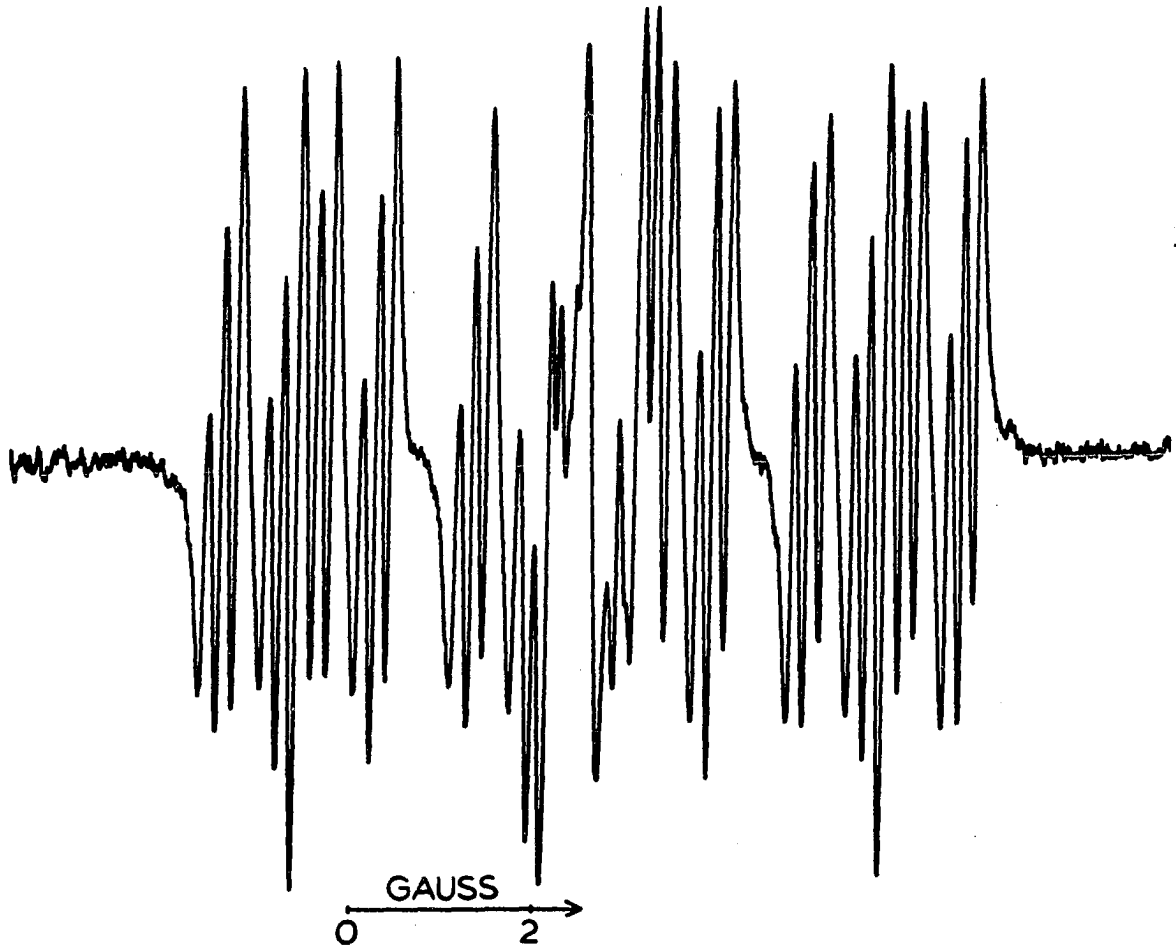


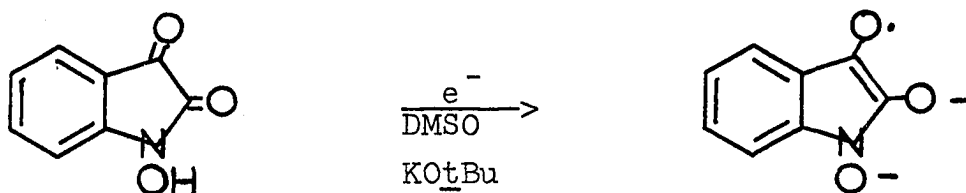
GAUSS
0 2



GAUSS
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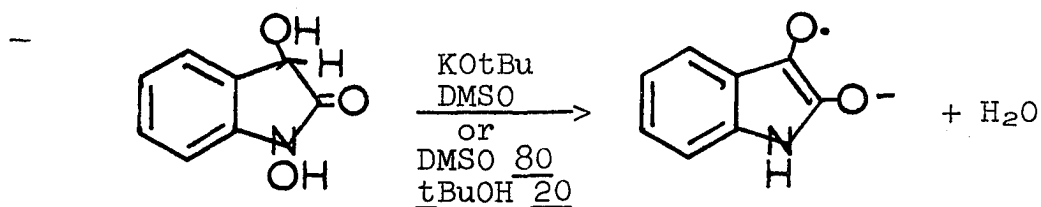
Figure 11. First-derivative ESR spectrum of N-hydroxyisatin dianion radical (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.





N-hydroxyisatin

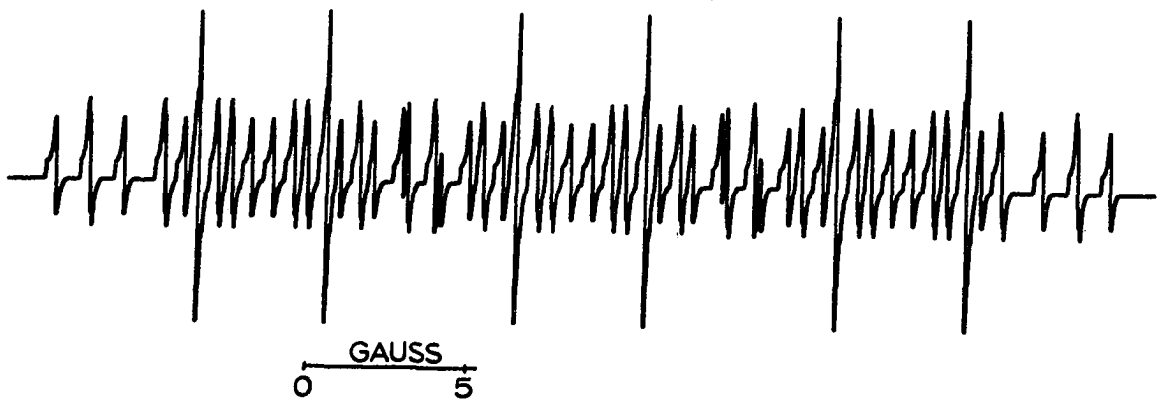
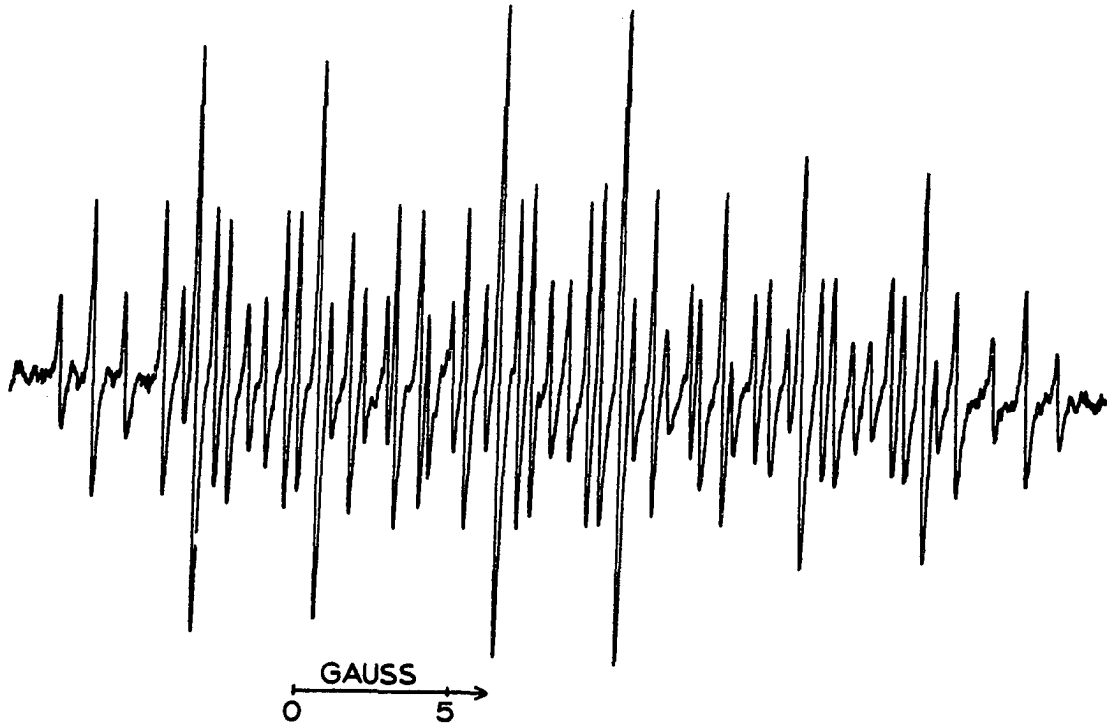
the ESR spectra of the dianion radical and the anion radical indicated a repulsive effect of the negative charge of the oxygen atom on the unpaired spin density on the nitrogen atom. Since the negative charge was one bond removed from the indole π system the effect on the aromatic proton splittings was small. One would have expected N-hydroxydioxindole to oxidize to the same semidiones obtained by reduction of N-hydroxyisatin. This did not occur. Instead a 1,3-elimination of H_2O occurred, producing the radical anion of isatin. This reaction was first observed by Dr. P. Bruni in these laboratories.



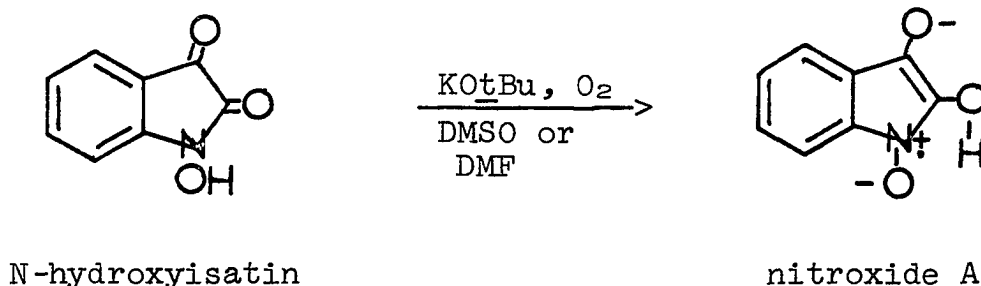
N-hydroxydioxindole

Although the reaction of N-hydroxyisatin with the reducing agent, propiophenone enolate, in basic DMSO produced the semidione dianion, the omission of the reducing agent resulted in quite a different reaction. When N-hydroxyisatin was treated with potassium t-butoxide in DMSO in the presence or absence of oxygen a radical was produced which was apparently a nitroxide. The ESR spectrum, Figure 12, exhibited hyperfine splitting constants of 3.98 gauss (1H), 3.35 gauss (2H), 1.05 gauss (2H) and 9.85 gauss (1N). The radical was, unlike the isatin and N-hydroxyisatin semidiones, very stable in the presence of oxygen. Oxygen did not seem to be necessary for the formation of this radical in DMSO, since it could be prepared by treatment of N-hydroxyisatin with potassium t-butoxide in a well deoxygenated solution. However, the strongest signal of the radical was obtained by omitting the deoxygenation procedure. Oxygen may have been participating in the radical formation or it may have been preventing a side reaction. The radical could not be produced in protic conditions. Addition of small amounts of water to the basic DMSO solution of the radical quenched the ESR signal. The radical could not be produced in DMSO-t-butyl alcohol 80:20 as the semidione was produced instead. No signals were obtained in methanol or t-butyl alcohol. The radical could be produced in DMF however, by the reaction of N-hydroxyisatin with potassium t-butoxide and air. The ESR

Figure 12. First-derivative ESR spectrum of nitroxide
A (top) in DMSO; calculated spectrum for
Lorentzian line width (bottom) 0.15 gauss
and splitting constants from text performed
by JEOLCO JNM-RA-1 spectrum accumulator.



spectrum in DMSO was identical to the spectrum obtained by reacting impure commercial isatin with potassium t-butoxide in DMSO. The radical was surely a nitroxide since it was stable to oxygen and had nitrogen and aromatic proton hyperfine splitting constants typical of an aromatic nitroxide. The nitroxide probably had the structure A indicated. The hyperfine splitting constants of the nitroxides derived from



N-hydroxyisatin have been listed in Table II along with pertinent examples from the literature (44, 45, 46, 47).

The deuterated nitroxide A-d was prepared by treatment of N-hydroxyisatin with potassium t-butoxide and air in DMSO- d_6 . The ESR spectrum, Figure 13, indicated hyperfine splitting constants of 3.98 gauss (1H), 3.35 gauss (1H), 1.05 gauss (2H), 9.85 gauss (1N) and 0.52 gauss (1D). Evidently one of the 3.35 gauss protons in nitroxide A was an exchangeable aliphatic proton.

Table II. Splitting constants (gauss) of nitroxides derived from isatin and related nitroxides

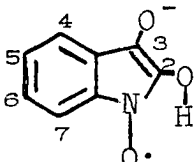
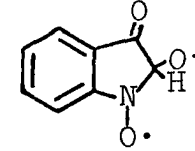
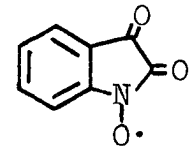
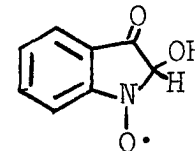
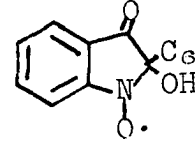
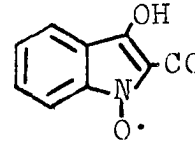
Nitroxide	a^N	a^H and position	Solvent	Reference
	9.85	3.98 (5 or 7) 3.35 (5 or 7) 3.35 (O-H) 1.05 (4 and 6)	DMSO or DMF	
	8.6	11.5 (2) 3.2 (5 and 7) 1.1 (4 and 6)	DMF or HMPA	
	6.23	2.56 (5 or 7) 2.32 (5 or 7) 0.80 (4 or 6) 0.59 (4 or 6)	DMSO	
	9.66	3.38 (5 and 7) 1.08 (4 and 6) 12.48 (2)	$\frac{\text{CH}_3\text{OH}}{\text{H}_2\text{O}} \frac{1}{3}$	45
	10.00	3.24 (5 and 7) 1.08 (4 and 6)	$\frac{\text{CH}_3\text{OH}}{\text{H}_2\text{O}} \frac{1}{3}$	45
	8.96	2.90 (5 and 7) 1.00 (4 and 6) 0.52 (OH)	Mesitylene	45

Table II continued.

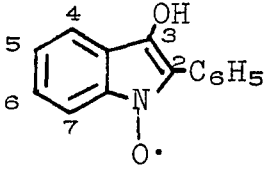
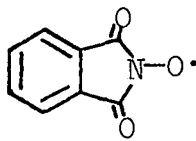
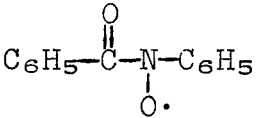
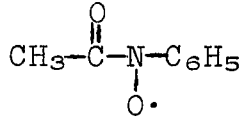
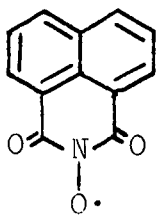
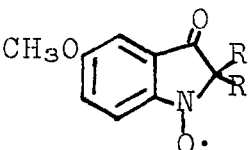
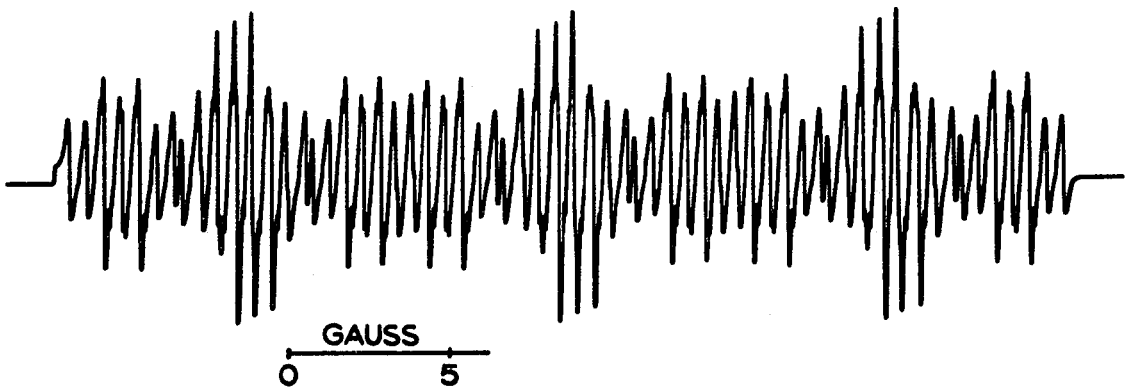
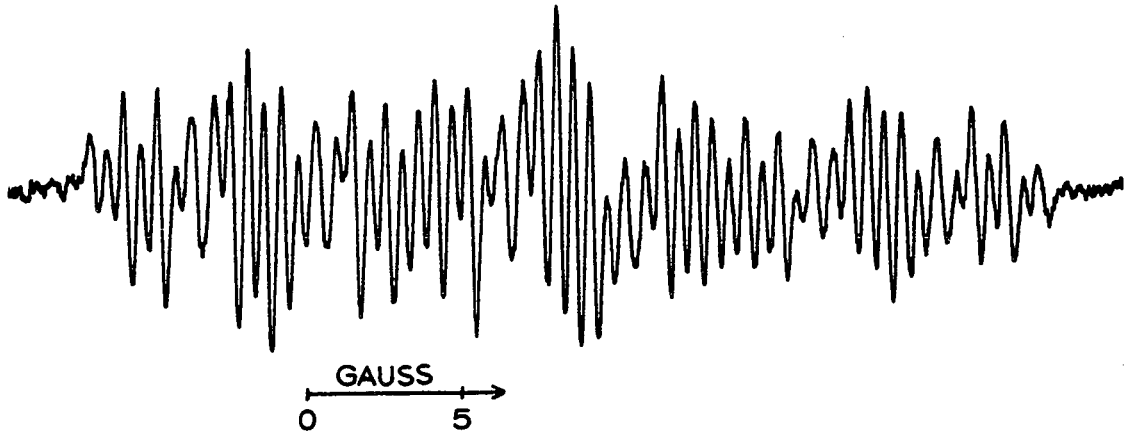
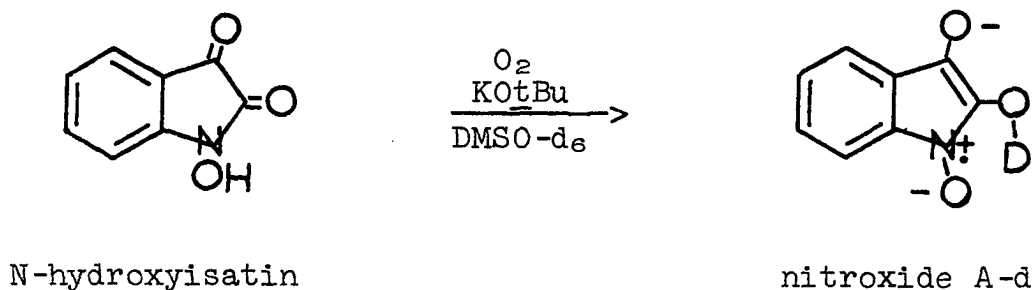
Nitroxide	a^N	a^H and position	Solvent Reference
	9.24	2.97 (5 and 7) 1.05 (4 and 6) 0.48 (OH)	Mesitylene 45
	4.23		46
	7.55	1.54 (ortho and para) 0.64 (two meta)	47
	7.18	1.47 (ortho and para) 0.62 (two meta) 0.23 (CH ₃)	47
	4.2		48
	10.00		48

Figure 13. First-derivative ESR spectrum of deuterated nitroxide A (top) in DMSO-d₆; calculated spectrum for Lorentzian line width (bottom) 0.25 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.





The reaction of N-hydroxyisatin with potassium t-butoxide and oxygen in HMPA produced a different nitroxide, which had structure B. The ESR spectrum of this radical,

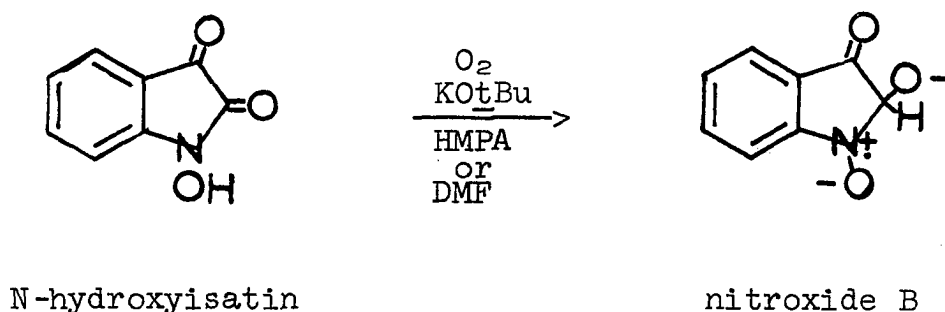
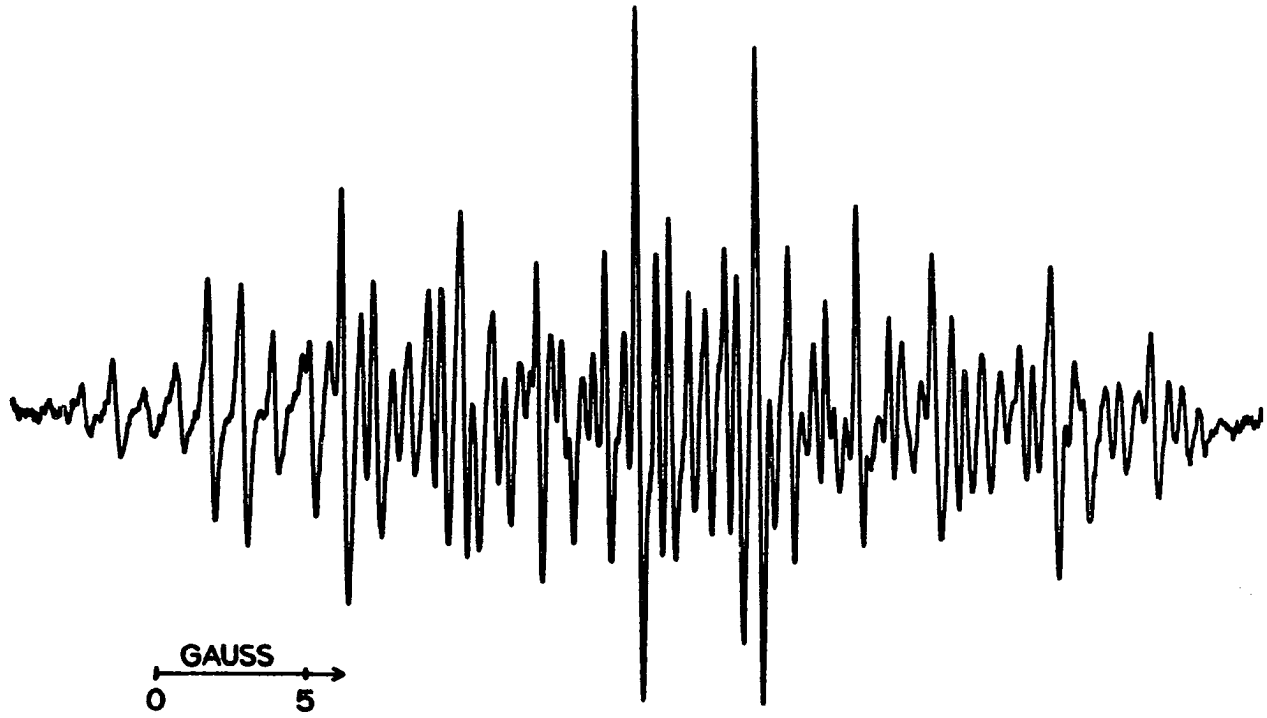


Figure 14, exhibited hyperfine splittings of 11.5 gauss (1H), 3.2 gauss (2H), 1.1 gauss (2H) and 8.6 gauss (1N).

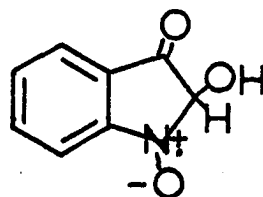
The radical formed very slowly and was resolvable only after a few hours. When N-hydroxyisatin was reacted with potassium t-butoxide and oxygen in DMF, the ESR spectrum indicated the presence of both nitroxide A and nitroxide B as shown in Figure 14.

The structure indicated for nitroxide B is reasonably certain. Nitroxide B is the deprotonated form of the

Figure 14. First-derivative ESR spectrum of the mixture of nitroxide A and nitroxide B (top) in DMF; first-derivative ESR spectrum of nitroxide B (bottom) in HMPA.



2-hydroxy-3-ketoindoline nitroxide shown below and in Table II. This previously reported (44) nitroxide has splitting

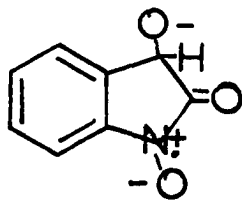


2-hydroxy-3-ketoindoline nitroxide

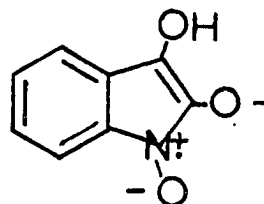
constants quite similar to those of nitroxide B. When the Heller-McConnell relation (48) is applied to the previously reported nitroxide an 11.0 ± 1.6 gauss splitting is predicted for the aliphatic C-H proton at the 2 position (44). The ketone structures of both the previously reported nitroxide and nitroxide B are therefore in agreement with the well-tested (14, 49) Heller-McConnell relation.

The structure indicated for nitroxide A is less certain. The ketonic structure isomeric with that of nitroxide B might be suggested and the preference for either ketonic isomer might depend on the solvent, with the 3-ketone preferred in HMPA, the 2-ketone structure in DMSO and both in DMF. The 3.35 gauss aliphatic proton splitting is reasonable for the 2-ketone structure. The solvent trend is in accord with an equilibrium governed by the dielectric properties of the solvent. The dielectric constants of DMSO, DMF and HMPA are 48.9, 36.7 and 29.6, respectively (50). However, the nitrogen hyperfine splitting of 9.85 gauss is very

unlikely for a 2-ketone structure. All previously reported 2-keto nitroxides have nitrogen hyperfine splittings of about



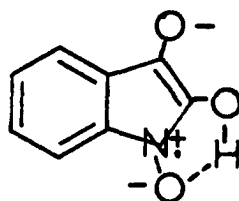
unlikely 2-ketone



unlikely 3-protonated
ene-diol

6-8 gauss (46, 47). The 2,2'-diketonitroxides have nitrogen splittings of about 4 gauss (45, 47), showing the delocalizing influence of the α -carbonyl group. The 3-protonated ene-diol structure is excluded by the work of Lunazzi which indicates a small hydroxyl proton splitting of 0.5 gauss in similar radicals (44).

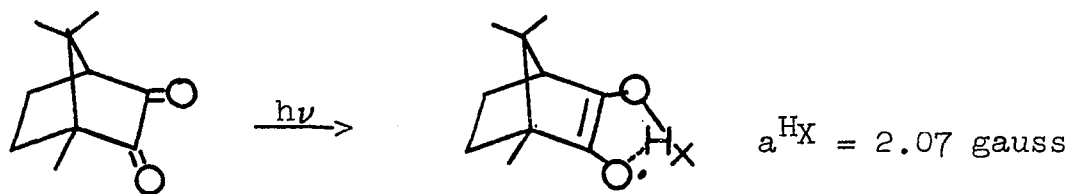
The 2-protonated ene-diol is the probable structure of nitroxide A. The exchangeable proton in nitroxide A might be



nitroxide A

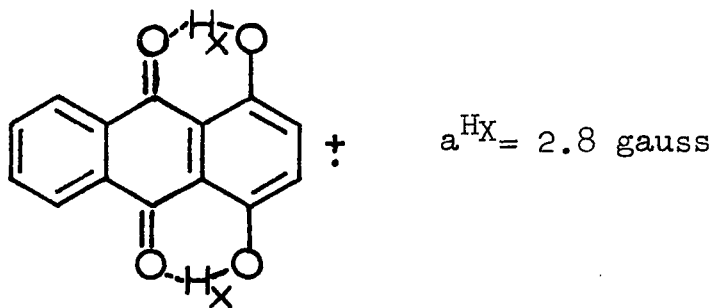
expected to show a solvent effect on the hyperfine splitting if it is a hydroxyl proton. No difference was observed between the spectra in DMSO and DMF. However, intramolecular

hydrogen bonding could prevent any solvent effect. The 3.35 gauss splitting for the hydroxyl proton is not extraordinarily high for such a hydrogen bonded structure. The protonated semidione obtained by photoreduction of camphorquinone in isopropyl alcohol shows a hyperfine splitting of 2.07 gauss for a similarly hydrogen bonded hydroxyl proton (2).



camphorquinone

Dr. F. Neugebauer of these laboratories has shown that some hydrogen-bridged anthracene tetraquinones have large bridged proton splittings.

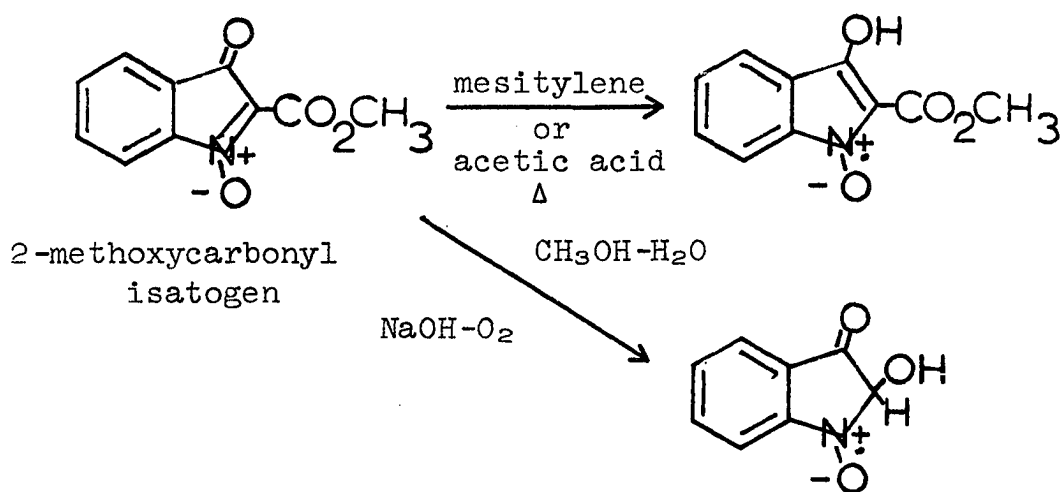


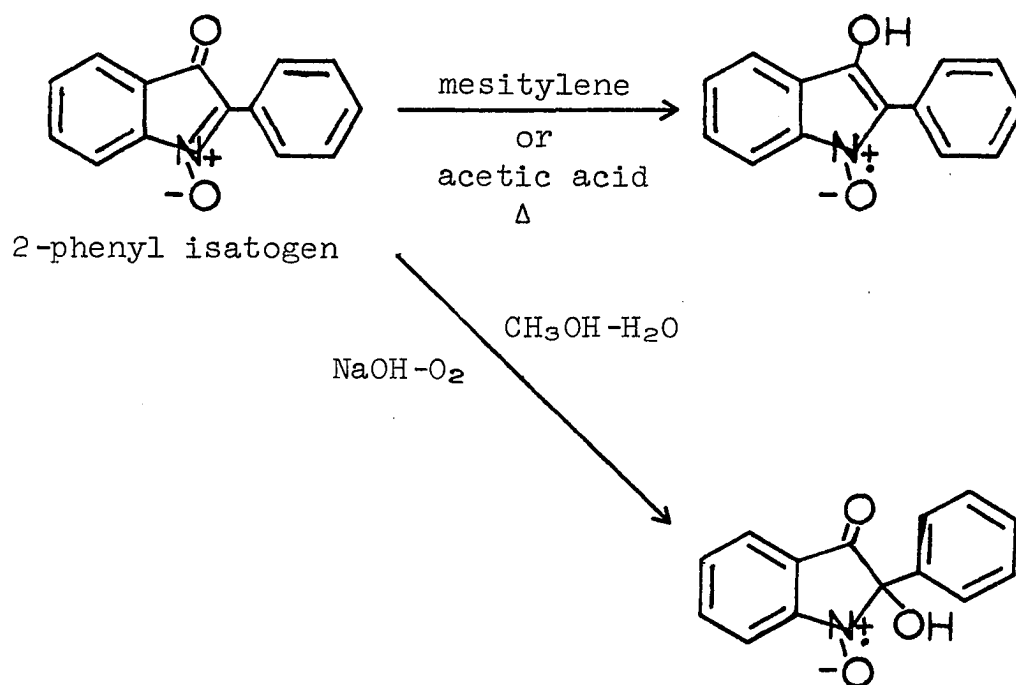
anthracene tetraquinone radical cation

The preceding discussion of the structure of nitroxides A and B has been based entirely on the ESR spectra of the radicals. From a consideration of the chemistry involved, it is not obvious how such nitroxides can be produced from N-hydroxyisatin by the reaction with base and oxygen. The

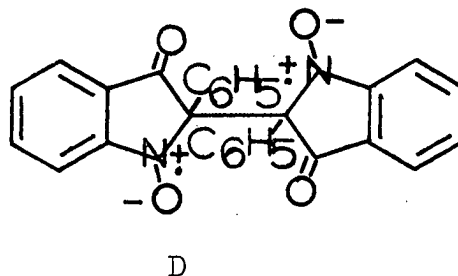
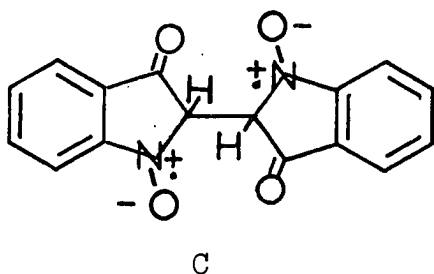
nitroxide formation involves a one electron oxidation of the hydroxylamine function of the N-hydroxyisatin, which is quite reasonable. However, the introduction of the hydroxyketone or the isomeric ene-diol function, as in B and A, respectively, involves a two electron reduction of the diketone moiety. Therefore, the whole process is a one electron reduction in the presence of oxygen. It is also not obvious why species such as A or B, once formed, resist oxidation to the diketone nitroxide.

Nitroxides of the indole-3-one type have been previously prepared by the thermal decomposition of 2-methoxycarbonyl isatogen and 2-phenyl isatogen (44). These radicals have been included in Table II. The nitroxides were hydrogen atom abstraction products in acetic acid or mesitylene and hydroxyl radical abstraction products in basic aqueous methanol. The 2-methoxycarbonyl isatogen was known to decarboxylate in the basic conditions.

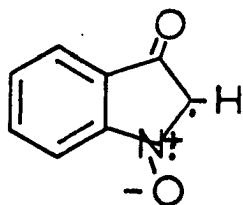




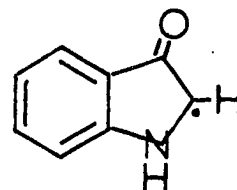
The nitroxide structures assigned by Lunazzi (44), although consistent with the ESR spectra and mechanistically accountable, are not absolutely proven. One wonders about the structures assigned to the products in basic solution, one of which is the previously mentioned protonated form of nitroxide B. The reason for the preference of the keto form is not obvious. Other structures, the nitroxide diradical dimers C and D, are also consistent with the spectra of Lunazzi. However, the leuco-indigoid structure C should



prefer the enol form and should also be rapidly oxidized to the analogous indigoid dinitroxide, just as leuco indigo is rapidly oxidized (51). Therefore, the structural assignment of Lunazzi is probably correct. It should be noted, however, that the intermediate triplet proposed by Lunazzi and discussed below is perfectly analogous to the intermediate proposed for indigo formation, the indoxyl radical.



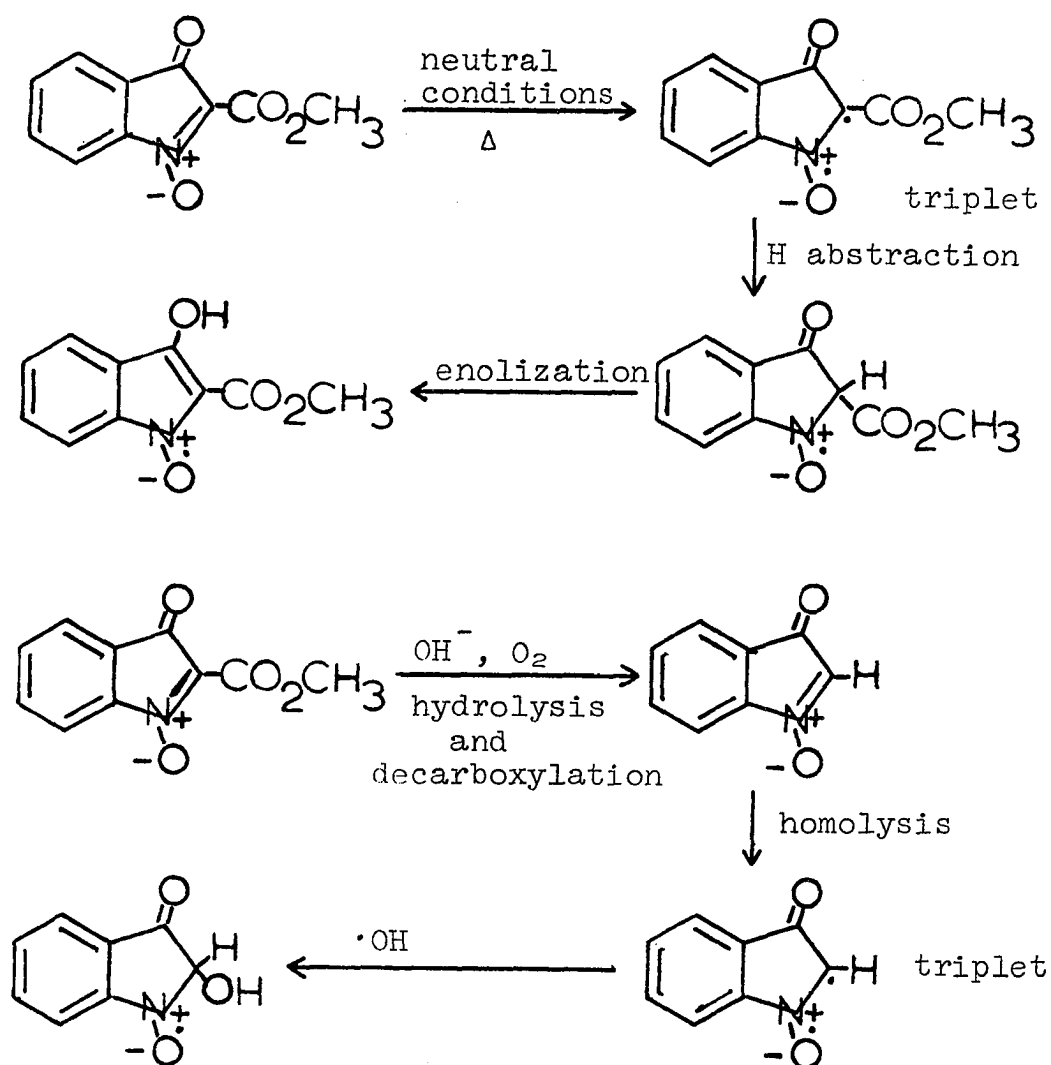
isatogen triplet



indoxyl radical

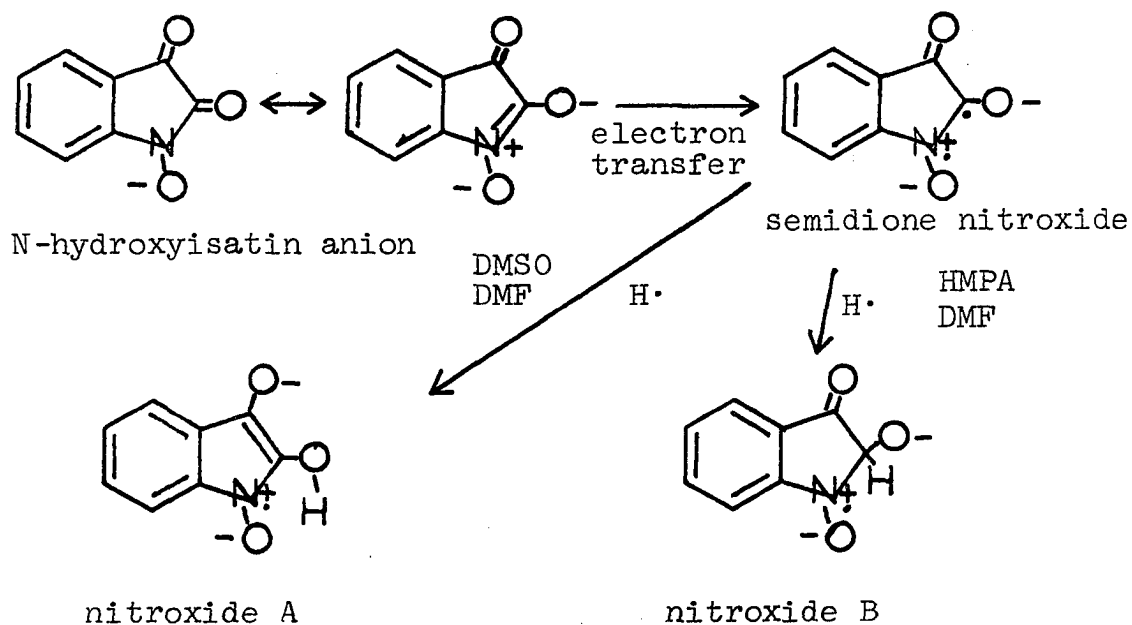
The nitroxide formation from the isatogens was explained by the following mechanism (44). A thermal homolysis of the CN π bond produced a triplet. The triplet abstracted a hydrogen atom from the solvent to yield the nitroxide observed in neutral solution. In the oxygenated basic

solution the triplet abstracted a hydroxyl radical to produce the product nitroxide. No keto-enol equilibria were observed in the temperature range 20°C to 150°C.



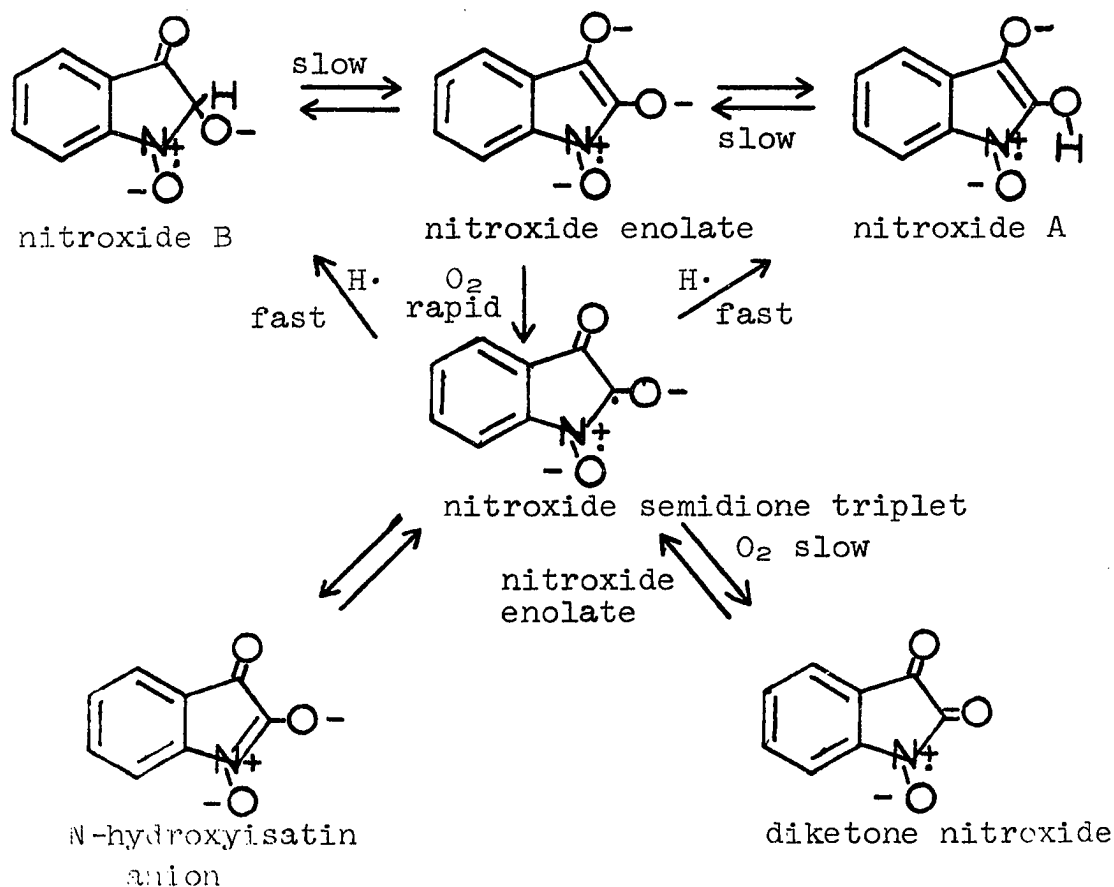
The formation of nitroxides A and B from N-hydroxyisatin in basic solution can be rationalized on the basis of the same mechanism. The anion of N-hydroxyisatin is formally an isatogen. A homolysis of the CN π bond or an intramolecular electron transfer could produce a triplet semidione

nitroxide which could abstract a hydrogen atom to produce A or B. This mechanism does not explain the effect of oxygen.

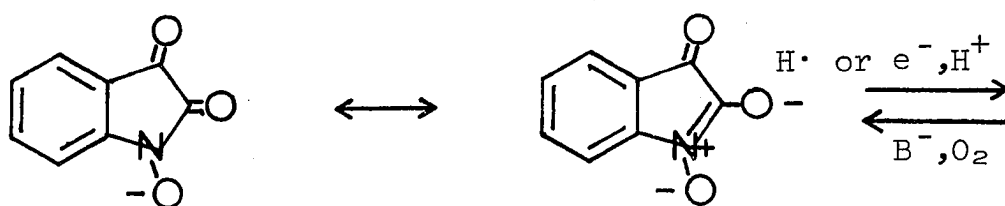


Many other mechanisms can be written to derive a species such as A or B from N-hydroxyisatin. Both reductions, e.g., semidione production from diketones, and oxidations, e.g., semidione production from hydroxyketones, are known to occur in strongly basic solution. The N-hydroxyisatin possesses both a readily reduced dicarbonyl moiety and a readily oxidized hydroxylamine moiety. Nitroxides A and B could be produced by independent reactions at the two functional groups rather than by an intramolecular electron transfer.

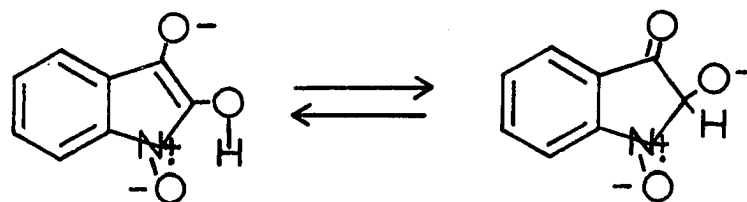
The structures indicated for A and B are reasonable for the ESR spectra. However, it is difficult to imagine that such species could survive in the presence of oxygen and strong base and not be autoxidized to the semidione and ultimately to the diketone nitroxide. A scheme can be devised to account for the apparent lack of oxidation of A and B. One must assume that hydrogen abstraction by the triplet is faster than oxidation and that keto-enol equilibria are slow compared with oxidation of the nitroxide enolate in order to justify this redox cycle. This scheme is strictly speculative.



The triplet intermediate mechanism of Lunazzi is not necessary to explain the reduction of either the isatogens or of the N-hydroxyisatin anion. The reaction may occur by a direct hydrogen abstraction by the isatogen or the N-hydroxyisatin anion. The apparent resistance of nitroxides A and B to oxidation may be simply due to the regeneration of starting material by such an oxidation. This mechanism



N-hydroxyisatin anion



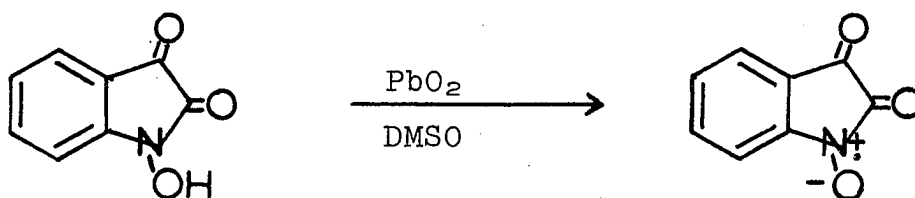
nitroxide A

nitroxide B

assumes that oxidation of the 1-2 bond is preferred to oxidation of the hydroxyketone moiety. Therefore, the triplet is never produced and does not occur to be the precursor to the fully oxidized diketone nitroxide. Perhaps isatogens such as the N-hydroxyisatin anion, are another class of easily reduced singlet compounds which can readily and reversibly accept hydrogen from a donor. Previous examples

of such compounds are chloranil (52), tetracyanoethylene (53) and tetracyanoquinodimethane (54).

A third nitroxide could be prepared from N-hydroxyisatin. This was the diketone nitroxide. This compound was prepared by the reaction of N-hydroxyisatin with lead peroxide in neutral DMSO or dioxane. The radical was not stable in DMSO

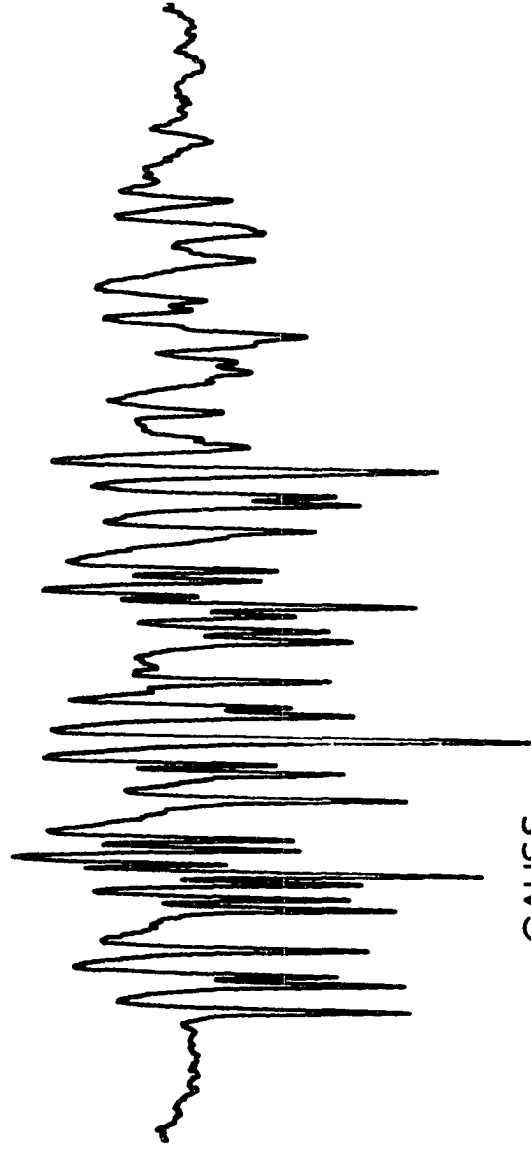


and decayed with a half-life of 460 ± 10 seconds. The ESR signal had much better resolution in DMSO than in dioxane even though the radical was decaying in DMSO. The ESR spectrum, Figure 15, exhibited hyperfine splittings of 2.56 gauss (1H), 2.32 gauss (1H), 0.80 gauss (1H), 0.59 gauss (1H) and 6.23 gauss (1N). The nitrogen splitting is in the range expected of an α -carbonyl nitroxide, as indicated by Table II.

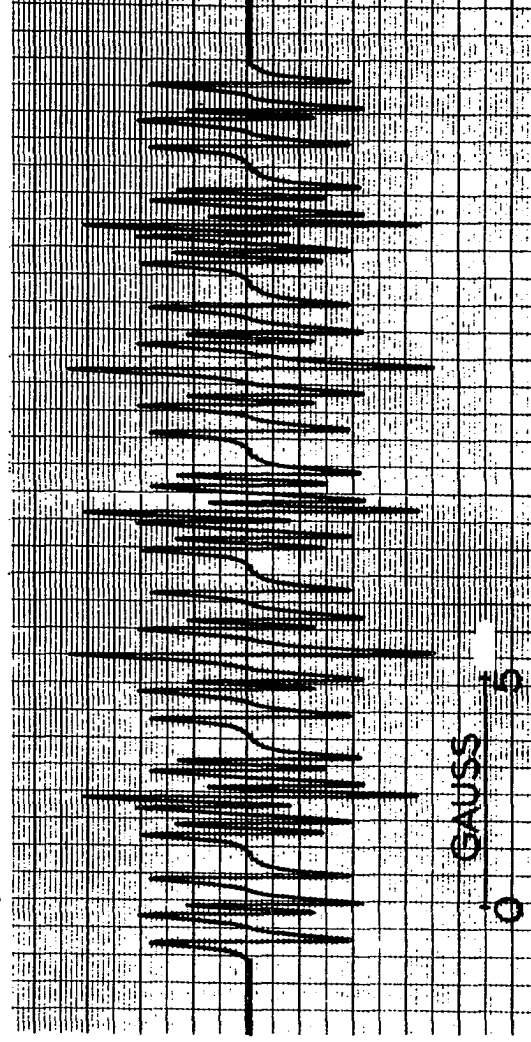
B. Thiophene, Benzofuran and Indane Semidiones

The study of the semidiones of the isatins led naturally to the corresponding oxygen and sulfur heterocycles. The preparation of these semidiones was simplified by the absence of the acid-base equilibria which had complicated the isatin ESR

Figure 15. First-derivative ESR spectrum of 2,3-dioxo-2,3-dihydroindole nitroxide (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.20 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

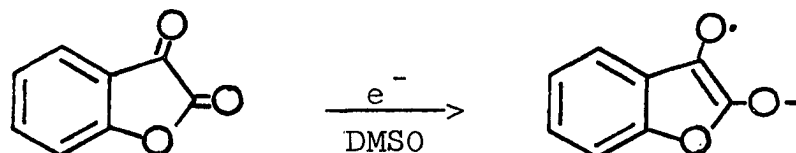


GAUSS
0 5



GAUSS
0 5

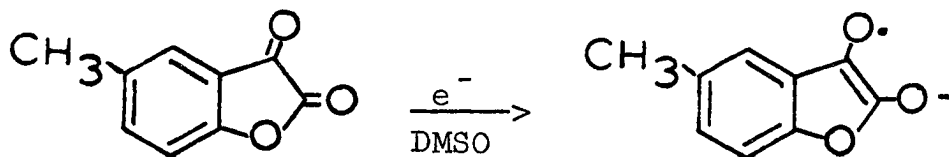
work. The lactone of 2-hydroxyphenylglyoxylic acid, coumaran-2,3-dione, was reduced to the coumaran-2,3-semidione by the reaction with propiophenone enolate and potassium *t*-butoxide in DMSO. The ESR spectrum, Figure 16, exhibited hyperfine splitting constants of 3.44 gauss (1H), 3.04 gauss



coumaran-2,3-dione

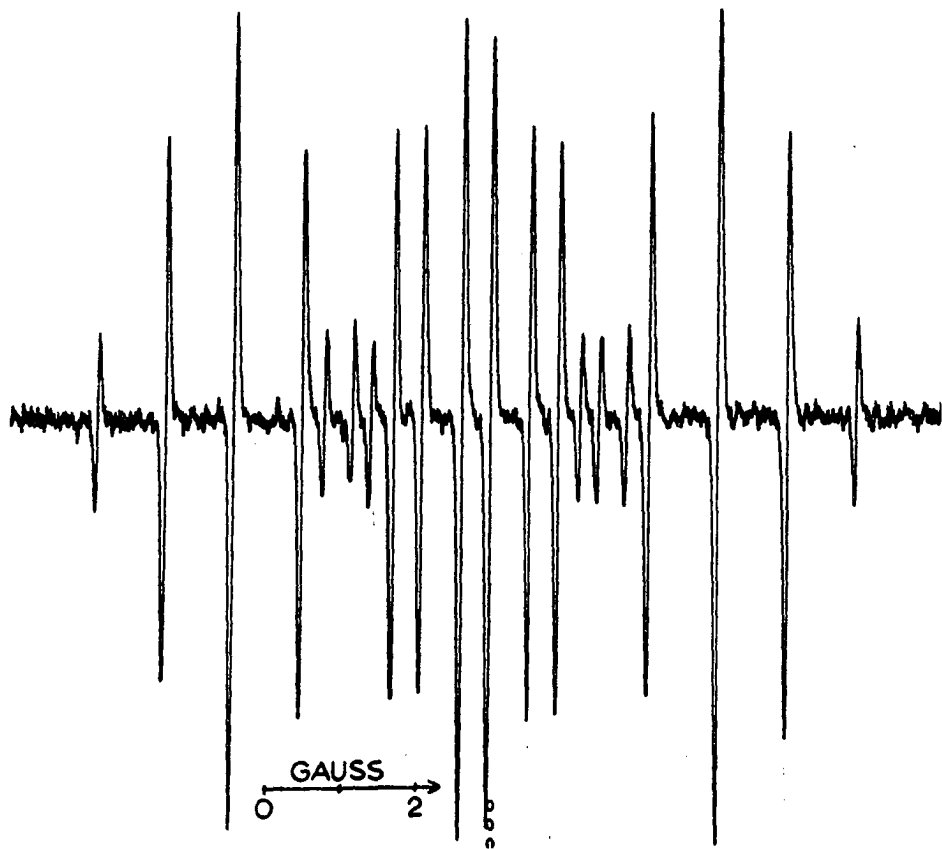
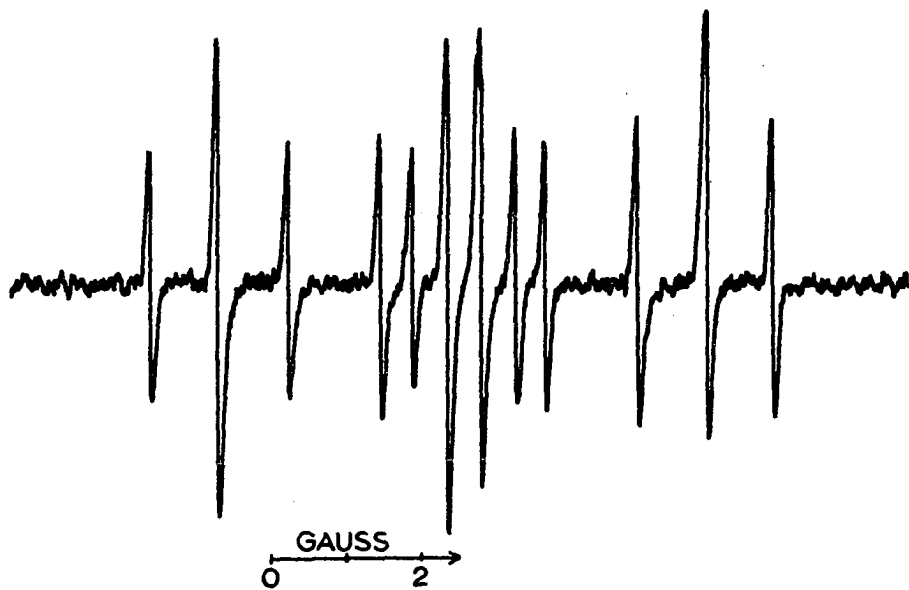
(1H), and 0.91 gauss (2H).

The assignment of the 0.91 gauss splittings to the positions meta to the semidione moiety was obvious from the isatin results and was proven by the preparation of the 5-methyl derivative. The 5-methylcoumaran-2,3-semidione was prepared by the reduction of the dicarbonyl compound with propiophenone and potassium *t*-butoxide in DMSO. The ESR spectrum, Figure 16, indicated proton hyperfine splittings of 3.42 gauss (1H), 3.04 gauss (1H) and 0.91 gauss (4H).

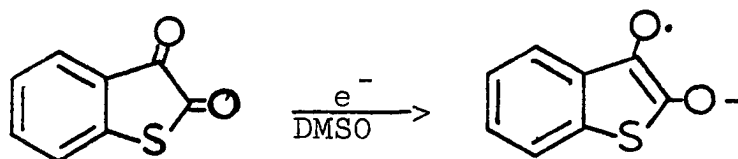


5-methylcoumaran-2,3-dione

Figure 16. First-derivative ESR spectrum of coumaran-2,3-semidione (top) in DMSO; first-derivative ESR spectrum of 5-methylcoumaran-2,3-semidione (bottom) in DMSO.



The sulfur analog of isatin, thianaphthenequinone, was also reduced to the semidione with propiophenone and potassium t-butoxide in DMSO. The ESR spectrum, Figure 17, indicated proton hyperfine splitting constants of 2.86 gauss (1H), 2.43 gauss (1H), 0.82 gauss (1H) and 0.70 gauss (1H).

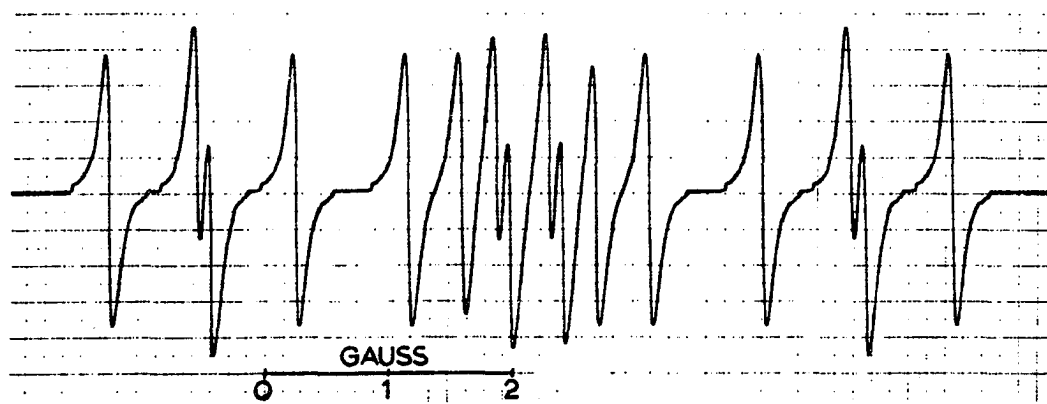
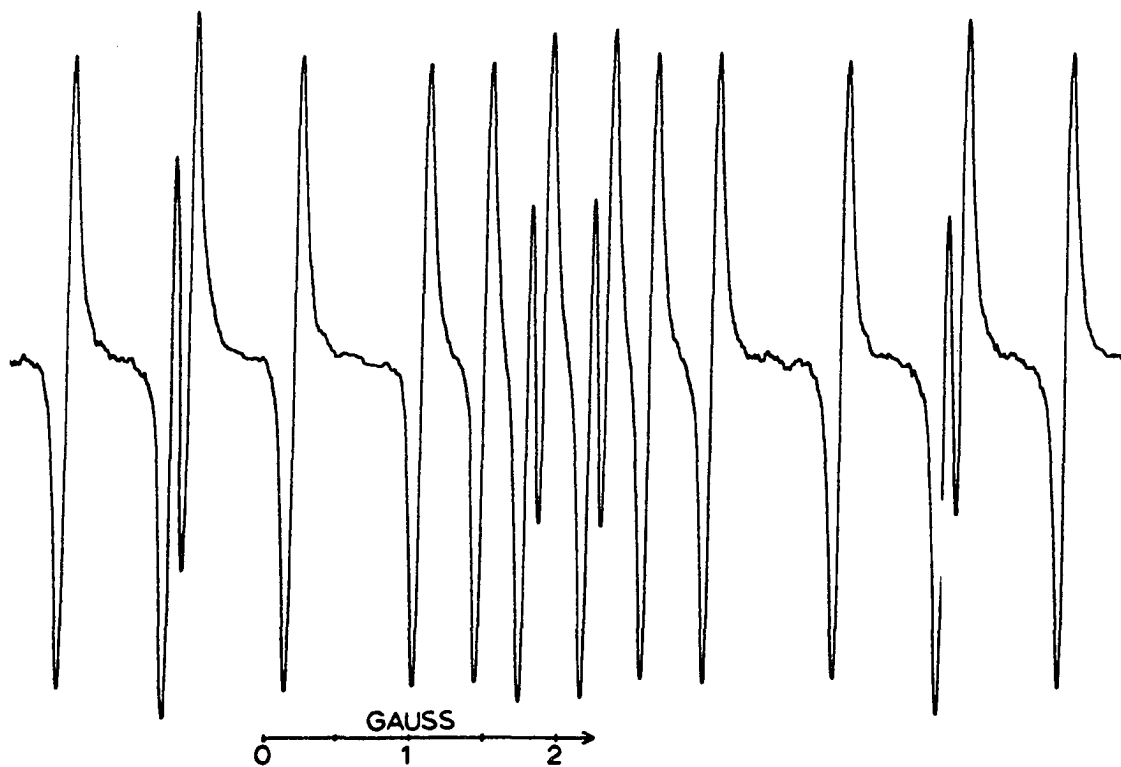


thianaphthenequinone

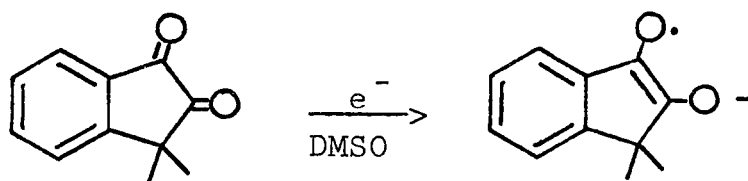
The isatin dianion radical is isoelectronic with the coumaran-2,3-semidione and the latter is a congener of thianaphthene semiquinone. In this series one expects the repulsion of spin density by the heteroatoms to be in the order $N^- > O > S$ since this is the order of heteroatom charge density. The aromatic proton hyperfine splittings, indicated in Table I, reflect this effect and their magnitudes follow the order $N^- > O > S$. Similar trends have been observed in comparison of the oxygen, sulfur and selenium congeners in the benzoxadiazole (25) and dibenzofuran (26) series.

The carbon analog to the isatin series was the 1,2-indanedione. The parent radical, indane-1,2-semidione, has been previously prepared by Dr. F. Neugebauer in these laboratories and its hyperfine splitting constants have been

Figure 17. First-derivative ESR spectrum of thianaphthene - semiquinone (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.



included in Table I. The 3,3-dimethylindane-1,2-semidione was prepared by reduction of the diketone with propiophenone and potassium *t*-butoxide in DMSO. The ESR spectrum, Figure 18, exhibited hyperfine splitting constants of 2.87 gauss (1H), 2.75 gauss (1H), 0.81 gauss (1H), 0.47 gauss (1H) and 0.33 gauss (6H).

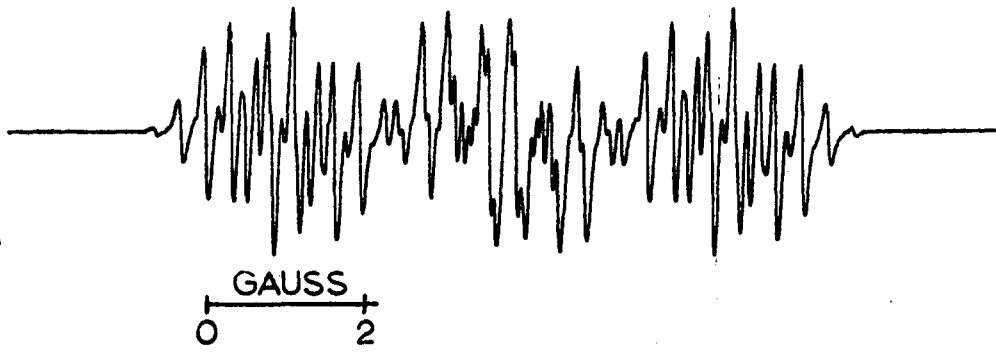
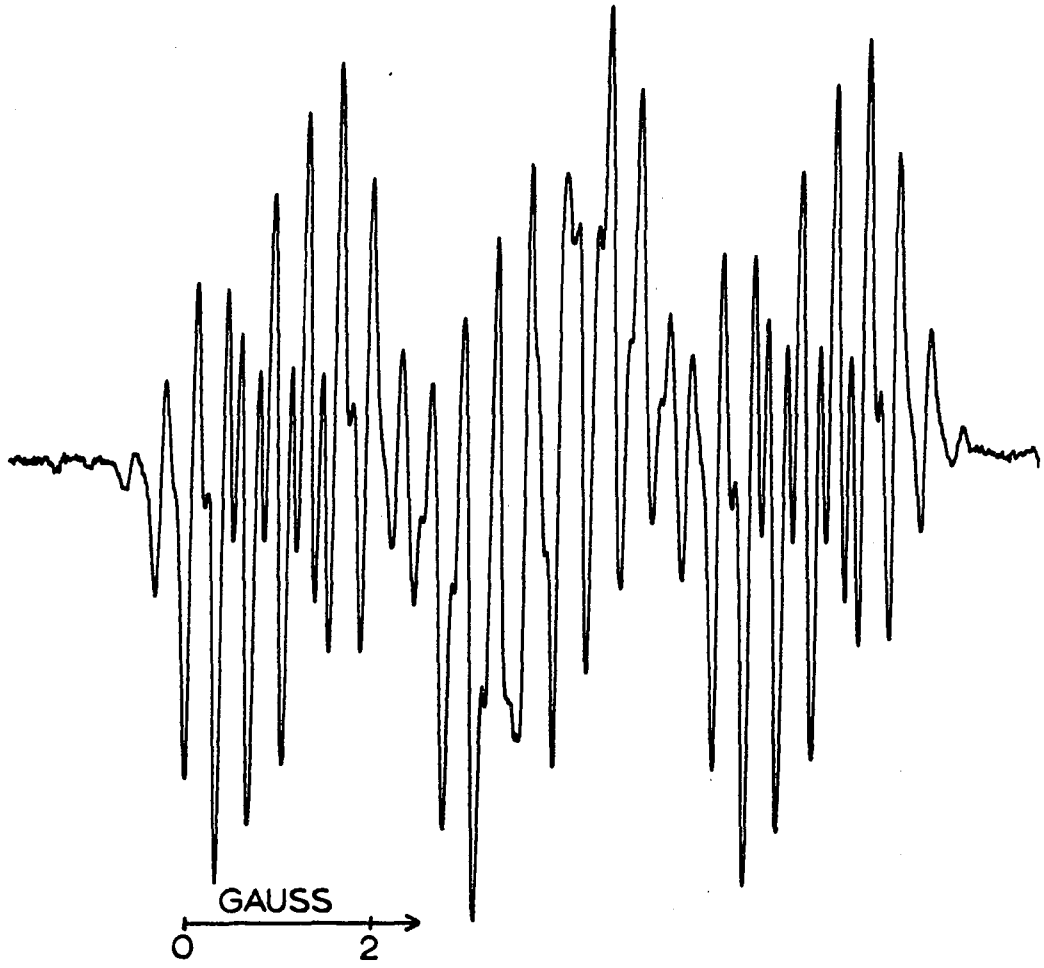


3,3-dimethylindane-1,2-dione

The hyperfine splittings of the ortho and para protons in trans-1-phenylpropane-1,2-semidione (18) are about 1 gauss smaller than in the 1,2-indanesemidiones. Apparently the spin delocalization into the aromatic system is about 40% greater for the indanesemidiones. The π orbitals of the phenyl ring of the 1-phenyl-1,2-propanesemidione may be rotating out of the plane of the π orbitals of the semidione moiety. The aromatic π system in the 1,2-indanesemidione is rigidly held in conjugation with the semidione moiety. This conjugation of the indanedione is also reflected in the low reduction potential, as discussed in another section.

However, the spin density differences may be caused by the

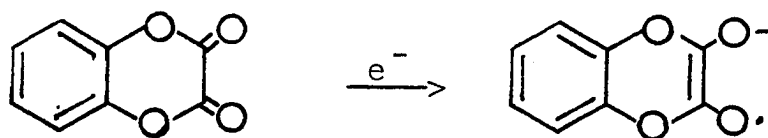
Figure 18. First-derivative ESR spectrum of 3,3-dimethylindane-1,2-semidione (top) in DMSO; calculated spectrum for Lorentzian line width (bottom) 0.15 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.



difference in carbonyl bond angles in the two systems.

C. Semidiones of the Benzoxalate Series

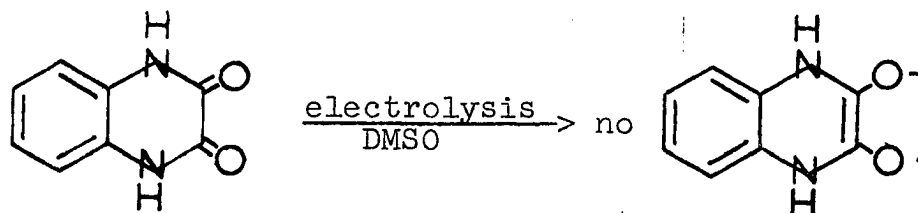
The radical anion of 1,2-benzoxalate has been reported (6). The ESR spectrum had shown that very little delocalization into the aromatic ring occurred, as indicated by the 0.18 gauss aromatic proton splitting constants. Since



1,2-benzoxalate

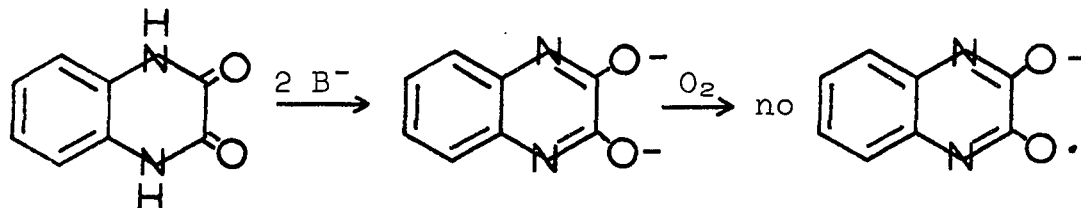
changing the heteroatoms had a profound influence on the spin distribution in the isatin series and in other types of heterocyclic radical anions (25, 26) it was of interest to examine the effect in this series. Therefore, the corresponding nitrogen and sulfur compounds were studied.

The attempted reduction of 2,3-dioxotetrahydroquinoxaline (quinoxaline-2,3-diol) to the semidione was not successful. Both electrolytic and chemical techniques were used. An attempt to oxidize the compound to the dehydro-semidione by

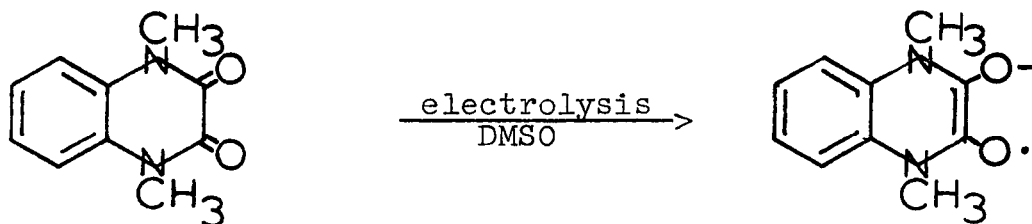


2,3-dioxotetrahydroquinoxaline

treating the compound with potassium t-butoxide and a trace of oxygen in DMSO also failed. However, the N,N-dimethyl



derivative was reducible to the semidione. Electrolytic reduction of 1,4-dimethyl 2,3-dioxotetrahydroquinoxaline in DMSO produced the semidione. The ESR spectrum, Figure 19, showed hyperfine splitting constants of 1.44 gauss (6H), 2.48 gauss (2N) and 0.30 gauss (4H). The aromatic proton hyperfine splittings were quite small as in the 1,2-benzoxalate anion (6).



The sulfur analog prepared was 6-methyl-2,3-dioxo-1,4-benzdithiane. This compound was reduced to the semidione with potassium t-butoxide and propiophenone in DMSO. The ESR spectrum, Figure 20, had only one line of 0.18 gauss linewidth. Expansion of the line on a 1.00 gauss spectrum range indicated possible poorly resolved splittings of about

Figure 19. First-derivative ESR spectrum of 1,4-dimethyl-2,3-dioxo-tetrahydroquinoxaline radical anion (top) produced electrolytically in DMSO; calculated spectrum for Lorentzian line width (bottom) of 0.20 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

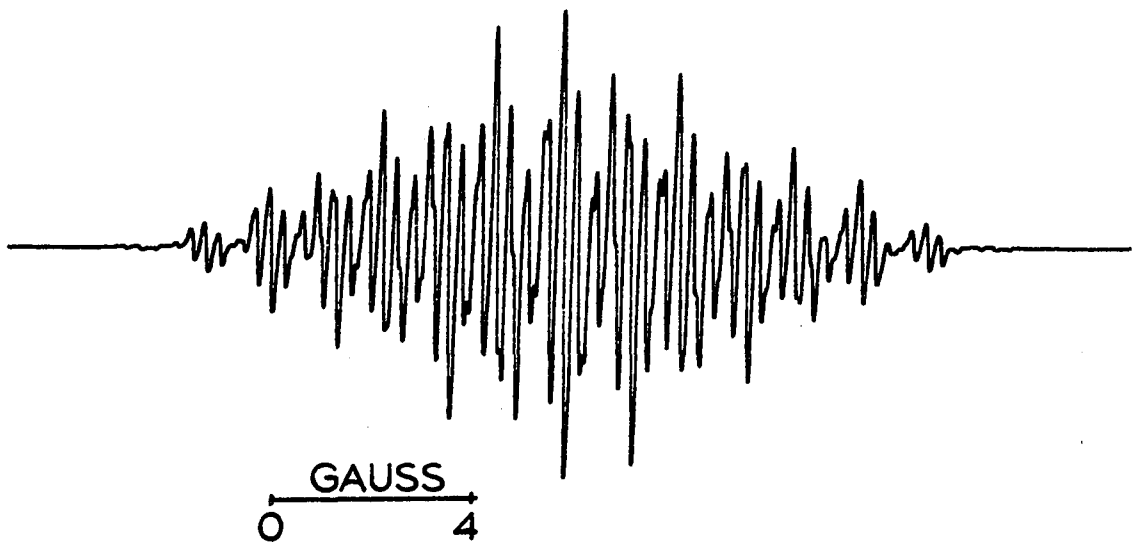
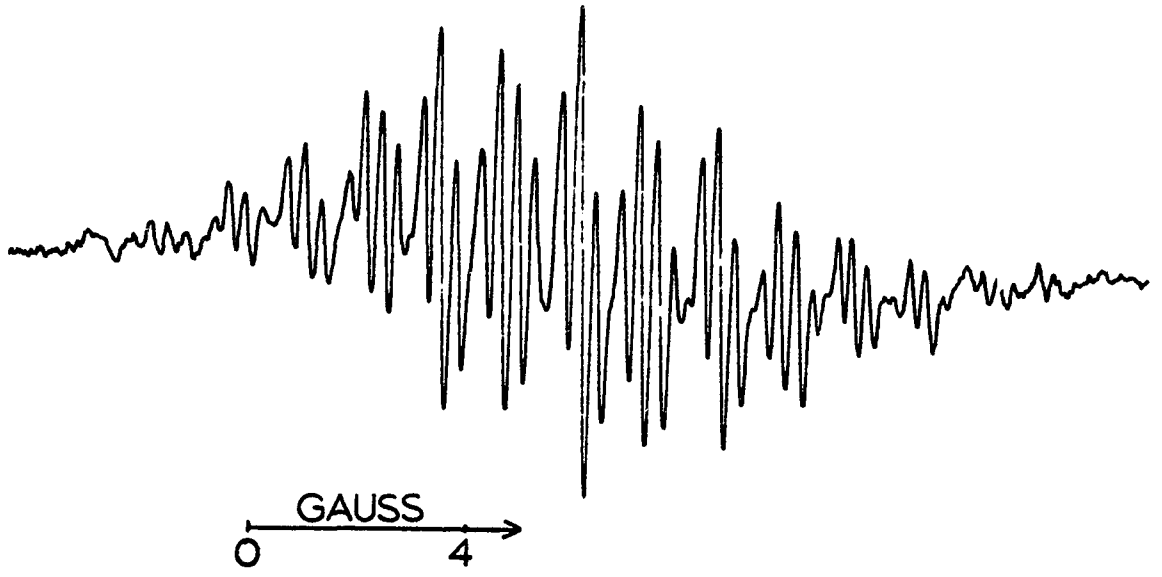
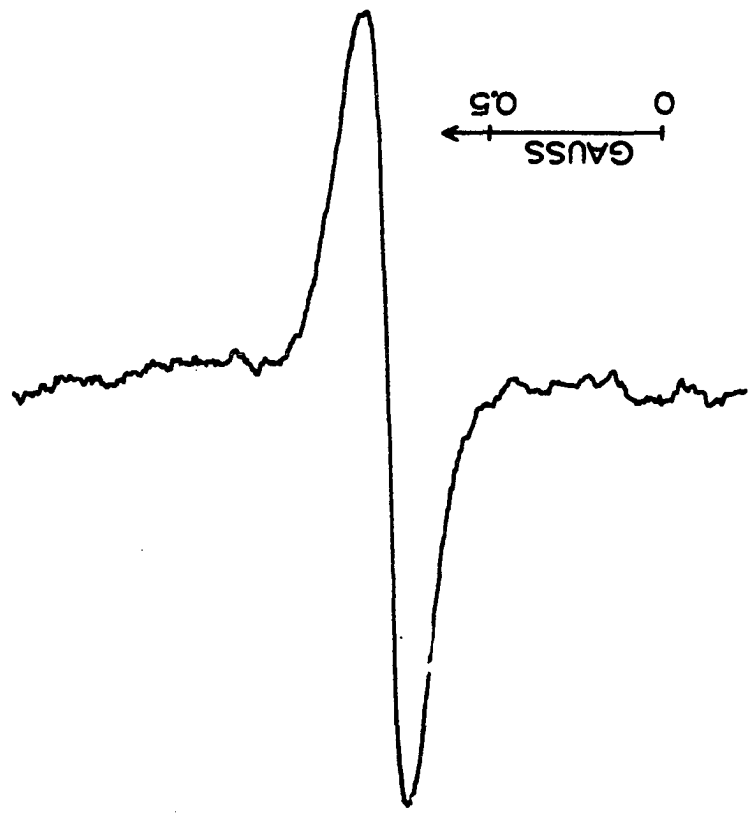
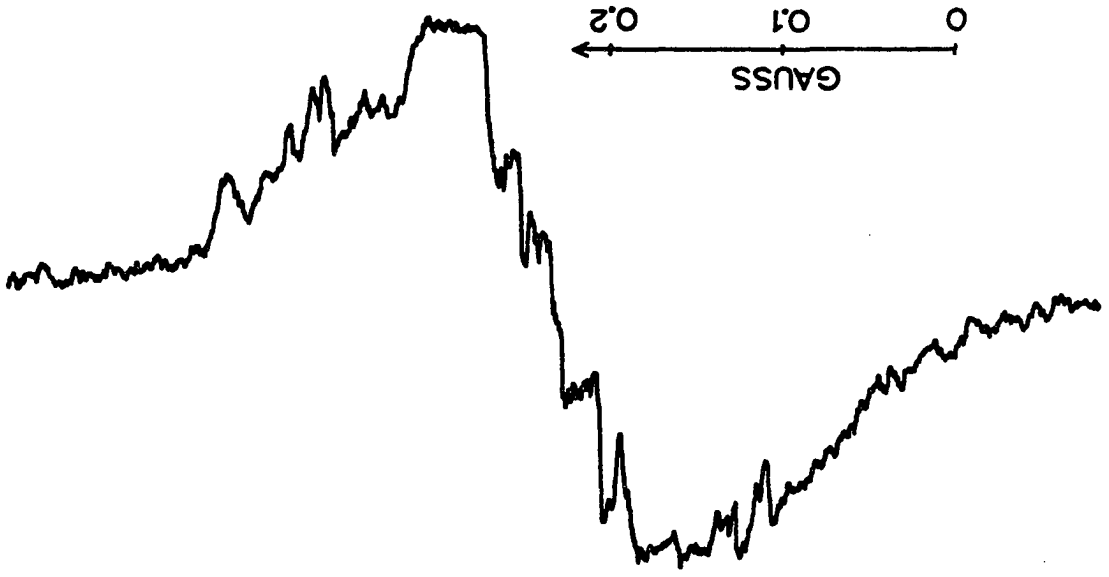
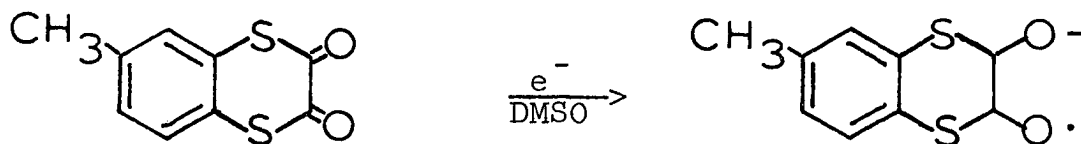


Figure 20. First-derivative ESR spectrum of 6-methyl-2,3-dioxo-1,4-benzdithiane radical anion (top) in DMSO; expanded spectrum showing possible proton splittings (bottom).



0.03 gauss. On the basis of the linewidth the average splitting of the six protons was about 0.03 gauss or less. The splitting constants of the radicals related to 1,2-benzoxalate have been listed in Table III.



6-methyl-2,3-dioxo-
1,4-benzdithiane

The trend in aromatic proton hyperfine splittings in this series of "antiaromatic" semidiones is similar to that in the "aromatic" semidiones related to isatin. The order of aromatic proton splittings for both series of compounds is $N > O > S$, with the greater difference between oxygen and sulfur.

Table III. Splitting constants (gauss) of semidiones related to 1,2-benzoxalate.

R	X	a^H (5,6,7,8)	Other splittings
	O ^a	0.18 (4H)	
	N-CH ₃	0.30 (4H)	$a^N = 2.48$; $a_{NCH_3}^H = 1.44$
6-CH ₃	S	≤ 0.03	$a_{CH_3}^H \leq 0.03$

^aReference (6).

The similarity of the trend in the two series may be due to the capacity of sulfur for unpaired spin density because of its low total electron density (low electronegativity) (25). McLachlan SCF spin density calculations (55) do not corroborate this suggestion. The calculations for the isatin series, Table IV, predict little dependence of either the proton splittings or the heteroatom spin density on the heteroatom variation. The calculations for the benzoxalate series, Table V, predict the trend $S > N > 0$ for the heteroatom spin densities and predict little dependence of the proton splittings on the heteroatom.

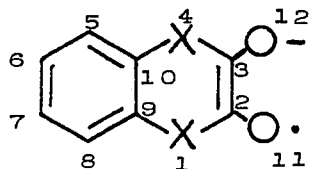
Table IV. Comparison of experimental^a and calculated^c spin densities for the isatin series of semidiones

position	X = NH ^b		X = O ^b		X = S	
	calc. ρ	exp. ρ	calc. ρ	exp. ρ	calc. ρ	exp. ρ
1	-0.012		-0.008		-0.032	
2	0.315		0.324		0.334	
3	0.389		0.382		0.375	
4	0.077	0.155	0.079	0.143	0.072	0.101
5	-0.038	0.038	-0.038	0.038	-0.039	0.029
6	0.071	0.132	0.067	0.127	0.074	0.119
7	-0.047	0.042	-0.045	0.038	-0.051	0.034
8	0.096		0.091		0.101	
9	-0.055		-0.056		-0.048	
10	0.090		0.089		0.100	
11	0.116		0.117		0.113	

$$^a |\text{exp. } \rho_C| = |a^H| / Q_{CH}^H, Q_{CH}^H = -24.$$

^bThe assumption is made that $a^H(4) > a^H(6)$

$$^c \alpha_O^{C=O} = \alpha_C + 1.8 \beta_{CC}, \alpha_N = \alpha_C + 1.5 \beta_{CC}, \alpha_O^{C-O} = \alpha_C + 2.0 \beta_{CC}, \alpha_S = \alpha_C + 1.0 \beta_{CC}, \beta_{C-N} = \beta_{C-O} = 0.8 \beta_{CC}, \beta_{C=O} = \beta_{CC}, \beta_{C-S} = 0.566 \beta_{CC}.$$

Table V. Comparison of experimental^a and calculated^c spin densities for the benzoxalate series

position	X = NCH ₃		X = O		X = S	
	calc. ρ	exp. ρ	calc. ρ	exp. ρ	calc. ρ	ρ
1	0.078	0.097 ^a	0.034		0.108	
2	0.363		0.421		0.338	
3	0.363		0.421		0.338	
4	0.078	0.097	0.034		0.108	
5	0.013	0.013	0.005	0.008 ^b	0.005	<0.001
6	-0.007	0.013	-0.021	0.008	-0.011	<0.001
7	-0.007	0.013	-0.021	0.008	-0.011	<0.001
8	0.013	0.013	0.005	0.008	0.005	<0.001
9	-0.025		-0.041		-0.022	
10	-0.025		-0.041		-0.022	
11	0.078		0.102		0.076	
12	0.078		0.102		0.076	

^a $|\rho_N| = |a_N|/26$, $|\rho_C| = |a_{CH}^H|/24$, all exp. $|\rho|$ values corrected for $a_{CH_3}^H$.

^b Calculated from the data of reference (6).

^c $\alpha_O^{C=O} = \alpha_C + 1.8 \beta_{CC}$, $\alpha_N = \alpha_C + 1.5 \beta_{CC}$, $\alpha_O^{C-O} = \alpha_C + 2.0 \beta_{CC}$, $\alpha_S = \alpha_C + 1.0 \beta_{CC}$, $\beta_{C-N} = \beta_{C-O} = 0.8 \beta_{CC}$, $\beta_{C=O} = \beta_{CC}$, $\beta_{C-S} = 0.566 \beta_{CC}$.

D. Molecular Orbital Calculations

Previous McLachlan molecular orbital calculations on aromatic radicals containing more than one type of heteroatom have proven to be only in fair agreement with the experimental spin densities, even in the case of symmetrical molecules, such as phthalimides (22, 23). McLachlan calculations have proven superior to simple Hückel calculations in predicting spin densities, especially in systems where low positive spin densities at certain positions enhance the importance of induced negative spin densities at those positions (22, 55, 56). The isatin series is such a system. The problem of selecting the proper parameters for calculations is difficult when there are several different types of atoms in an unsymmetrical system. For some quinones (57) and phthalimides (22) more than one choice of parameters can give a satisfactory agreement between experimental and calculated spin densities. Therefore, an agreement or discrepancy can be fortuitous and not physically significant.

Coulomb integral variations have been found to be slightly more significant than resonance integral variations in affecting calculated spin densities (57). In the present calculations, the coulomb integrals, α_X , for both the carbonyl oxygens and the ring heteroatoms of the isatin and benzoxalate series were varied to achieve the best fit of experimental and calculated densities. The best values of the ring heteroatom coulomb integrals were identical to those which had been

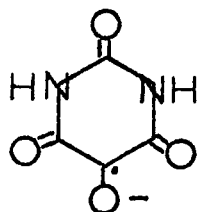
suggested by Streitwieser (56). The best carbonyl oxygen coulomb integral was identical to the value found best by previous workers for ortho-benzosemiquinones (57). These values were: α_O (ring) = $\alpha_C + 2.0 \beta_{CC}$, $\alpha_N = \alpha_C + 1.5 \beta_{CC}$, $\alpha_S = \alpha_C + 1.0 \beta_{CC}$, α_O (carbonyl) = $\alpha_C + 1.8 \beta_{CC}$. The resonance integrals, β_{XY} , were selected from the literature. The values used were β_{CO} (carbonyl) = β_{CC} (56), β_{C-O} (ring) = $0.8 \beta_{CC}$ (57), β_{C-N} (ring) = $0.8 \beta_{CC}$ (56) and β_{C-S} (ring) = $0.566 \beta_{CC}$ (26, 56).

The agreement between calculated and experimental spin densities for the isatin series is reasonable considering the unsymmetrical structure and the limitations of the method. The predicted magnitude of the ortho and para proton splittings is too small (Table IV) and consequently one can not use the calculations to confidently distinguish the ortho and para splittings. The effect of the variation of the near-nodal heteroatom is also under estimated in the calculations. Such an under estimation has also been observed in the phthalimide series in which the heteroatom occupies a nodal position in the highest occupied molecular orbital (22). The alternating nature of the spin density is correctly predicted. In the benzoxalate series, Table V, the calculations incorrectly predict two pairs of aromatic protons instead of four equivalent ones, but the magnitude of the numbers are small and the calculated and experimental spin densities are in fairly good agreement. There is a slight improvement

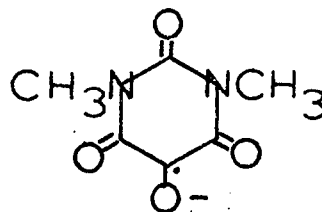
over the previous calculation for the 1,2-benzoxalate semidione (6).

E. Semitriones vs. Semidiones

Previous workers have shown that triketones could rearrange upon reduction in basic solution, with the loss of the central carbonyl group (6, 58, 59). The reduction products reported included the diketone radical anion (6). For example, the reduction of diphenylpropanetrione in basic solution produced the benzil radical anion (6). The reaction was also observed with some diketoesters. The preparation of the triketo radical anions of alloxan and *N,N'*-dimethylalloxan in basic solution has been reported (20) and it was desirable to determine whether decarbonylation had also occurred in this series. Therefore the reduction of

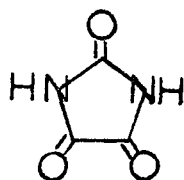


alloxan anion

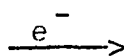


N,N'-dimethylalloxan anion

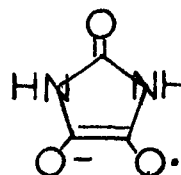
parabanic acid was attempted to answer the question.



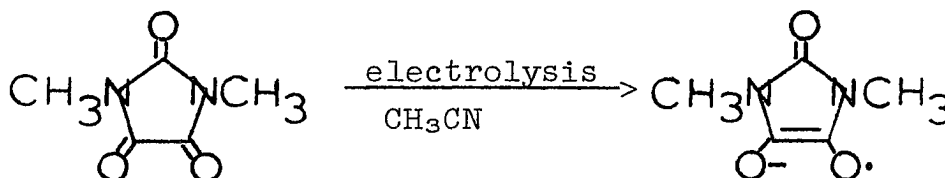
parabanic acid



no



The preparation of the radical anion was not achieved either by reduction in basic solution or by electrolytic reduction. However, the dimethyl semidione was successfully prepared by electrolytic reduction in acetonitrile (21). The ESR spectrum, Figure 21, indicated hyperfine splittings of 1.66

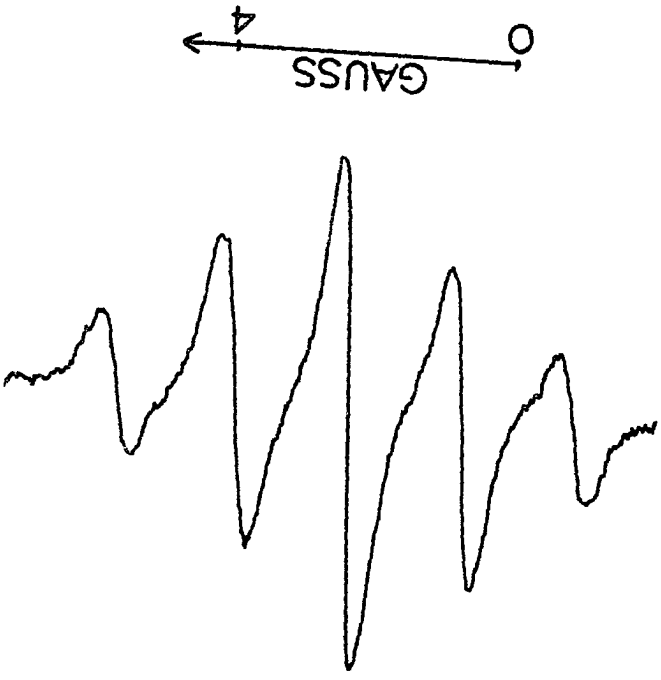
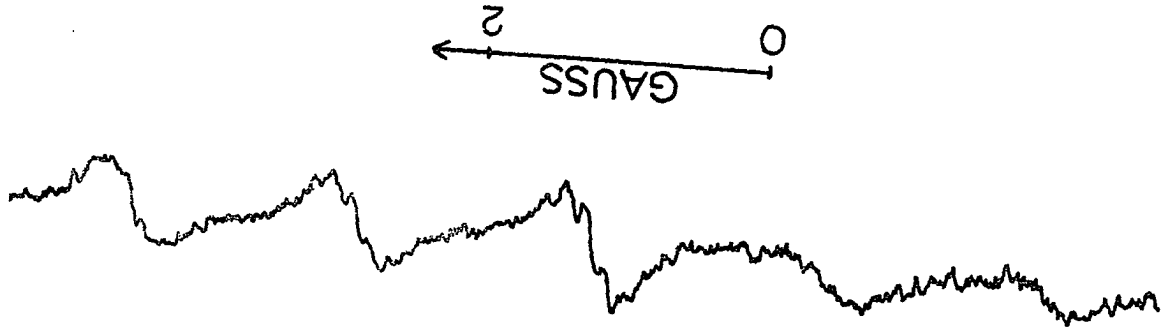


dimethylparabanic acid

gauss (2N) and 0.11 gauss (6H). Not all of the seven line 1:6:15:20:15:6:1 pattern of the six equivalent protons could be discerned and the 0.11 gauss splitting was near the limit of resolution of the ESR signal. However, the larger proton lines and the 0.11 gauss splitting were distinct in the expanded spectrum shown. The reported splittings of the dimethylalloxan anion were 0.50 gauss (2N) and 0.30 gauss (6H) (20). Therefore, no decarbonylation had occurred in the latter system. The reduction potentials of parabanic acid and the dimethyl derivative are similar, as indicated in another section. The failure of parabanic acid to yield the semidione must have been caused by deprotonation.

The methyl-nitrogen hyperfine splitting constant ratio of the dimethylparabanic acid radical anion, $a_{\text{CH}_3}^{\text{H}}/a^{\text{N}}$, has the value 0.066, which is the lowest of any such ratio in

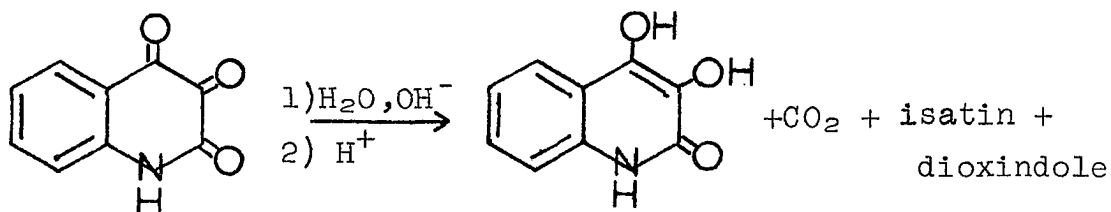
Figure 21. First-derivative ESR spectrum of N,N'-dimethylparabanic acid radical anion produced electrolytically in acetonitrile (top) showing 1:2:3:2:1 pattern of two equivalent nitrogens; expanded spectrum showing proton splittings (bottom).



the literature. The nearest in magnitude is the $a_{\text{CH}_3}^{\text{H}}/a^{\text{N}}$ of 0.35 for the N-methylphthalimide radical anion (22), which is predicted to have a zero spin density at the nitrogen atom according to Hückel calculations and a negative spin density on nitrogen according to McLachlan calculations (22).

Dimethylparabanic acid radical anion is expected to have a similar spin situation at the nitrogen atoms. Hückel and McLachlan calculations are displayed in Table VI. The high a^{N} relative to $a_{\text{CH}_3}^{\text{H}}$ may be a result of the adjacent atom σ - π spin polarization effect on the nitrogen splitting. This possibility is discussed in part IV.

The reaction of 2,3,4-trioxo-1,2,3,4-tetrahydroquinoline (quinisatin) with aqueous base is known to yield the hydroquinone reduction product 2-oxo-3,4-dihydroxy-1,2-dihydroquinoline as well as the rearrangement products isatin and dioxindole (60). More recent work has shown that, depending



2,3,4-trioxo-
1,2,3,4-tetrahydroquinoline

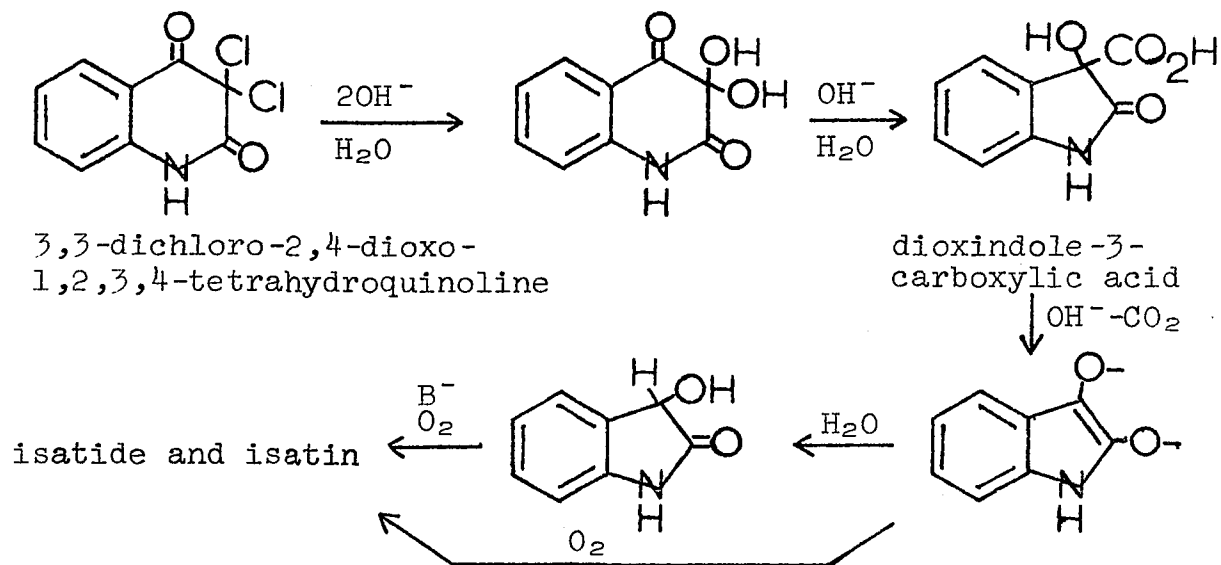
on the amount of alkali and air, the isatide dimer can also be a reaction product (61). The triketone was generated in situ from the 3,3-dichloro-2,4-dioxo-1,2,3,4-tetrahydroquinoline.

Table VI. Calculated spin densities of dimethylparabanic acid radical anion

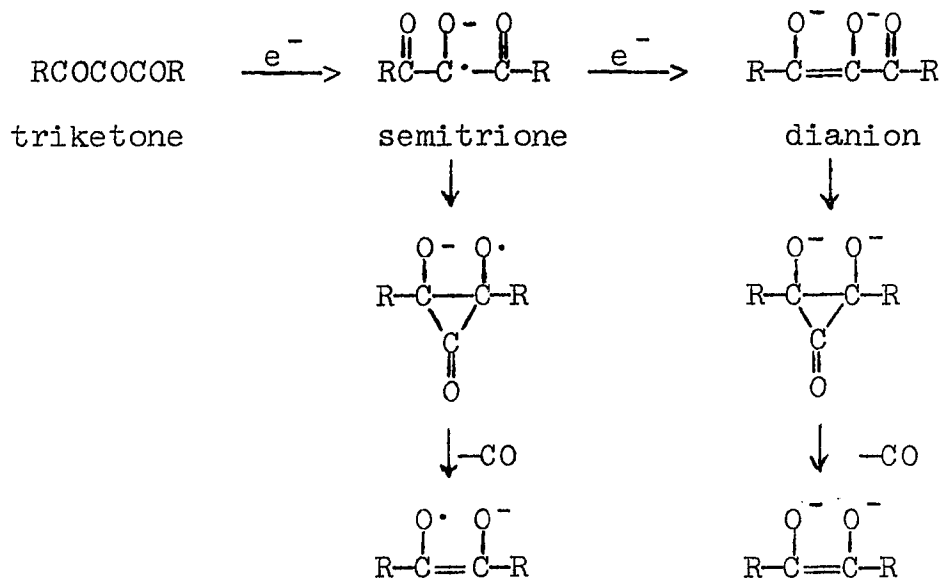
position	calc. ρ -Hückel	calc. ρ -McLachlan
1	0.022	-0.021
2	0.301	0.375
3	0.301	0.375
4	0.022	-0.021
5	0.092	0.105
6	0.114	0.089
7	0.114	0.089
8	0.034	0.011

The mechanism proposed was the benzilic acid rearrangement of the triketone (61). This mechanism had previously been invoked to explain the production of diketone reduction products from the reaction of triketones with base (58). The dioxindole- β -carboxylic acid intermediate was suggested (61).

The possibility that diketone reduction products were produced by an initial reduction to the semitrione radical or the diamagnetic dianion of the triketone has been suggested in a study of acyclic semitriones (6).

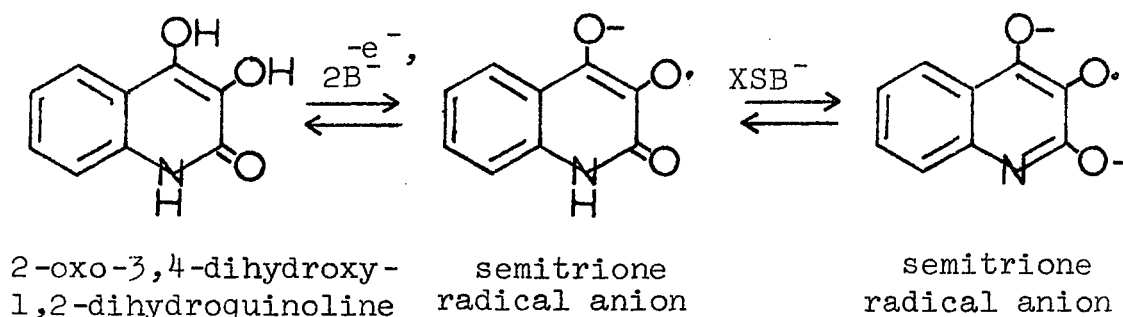


The scheme indicated below was proposed (6).

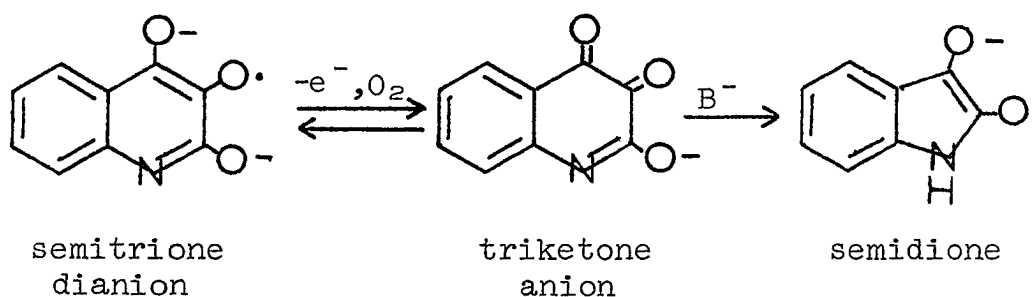


It was of interest in the present study to determine whether the quinisatin \rightarrow dioxindole rearrangement occurred by an initial reduction to the semitrione or dianion or by a

benzilic acid rearrangement of the triketone. Therefore, 2-oxo-3,4-dihydroxy-1,2-dihydroquinoline (quinolinetriol) was prepared and its reaction in basic solution examined by ESR spectroscopy. When this compound was treated with potassium *t*-butoxide in DMSO or DMSO-*t*-butyl alcohol 80:20 in the absence of oxygen the semitrione radicals were produced. The semitrione dianion radical was produced by an excess of base and the semitrione anion radical was produced by an equivalent or less of base. These radicals were stable for at least 16 hours in the absence of oxygen.



When the same compound was treated with potassium *t*-butoxide in DMSO, DMSO-*t*-butyl alcohol or DMSO-ethanol 85:15 in the presence of oxygen the same semitriones were observed by ESR spectroscopy. However, in the presence of oxygen, the radicals were not as stable. Within a few hours the ESR signals of the semitriones were replaced by the signal of the isatin semidione. When a DMSO solution containing 5% water was utilized as the solvent, the semitriones were stable for at least 18 hours, even in the presence of oxygen.



The ESR spectrum of the semitrione dianion radical, Figure 22, exhibited hyperfine splitting constants of 1.82 gauss (1H), 1.59 gauss (1H), 0.67 gauss (1H), 0.61 gauss (1H) and 0.45 gauss (1N). The ESR spectrum of the semitrione anion radical, Figure 23, exhibited hyperfine splitting constants of 1.45 gauss (1H), 1.32 gauss (1H), 0.55 gauss (1H), 0.48 gauss (1H), 0.08 gauss (1H) and 0.66 gauss (1N).

These results indicate that the reaction of 2,3,4-trioxo-1,2,3,4-tetrahydroquinoline with base definitely does not involve a one or two electron reduction prior to the rearrangement. All of the triketone reduction products are present in the experiment described above in the absence of oxygen but no rearrangement occurs. In the presence of oxygen the triketone, or its anion, is also present and the rearrangement does occur. Dioxindole yields the isatin semidione under the same conditions. These results substantiate the benzylic acid rearrangement mechanism suggested by Ziegler (61).

The oxidation of the semitrione to the triketone is apparently quite dependent on the base strength. The hydroxide

Figure 22. First-derivative ESR spectrum of 2,3,4-trioxo-1,2,3,4-tetrahydroquinoline dianion radical (top) in DMSO containing 5% water; calculated spectrum for Lorentzian line width (bottom) of 0.10 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.

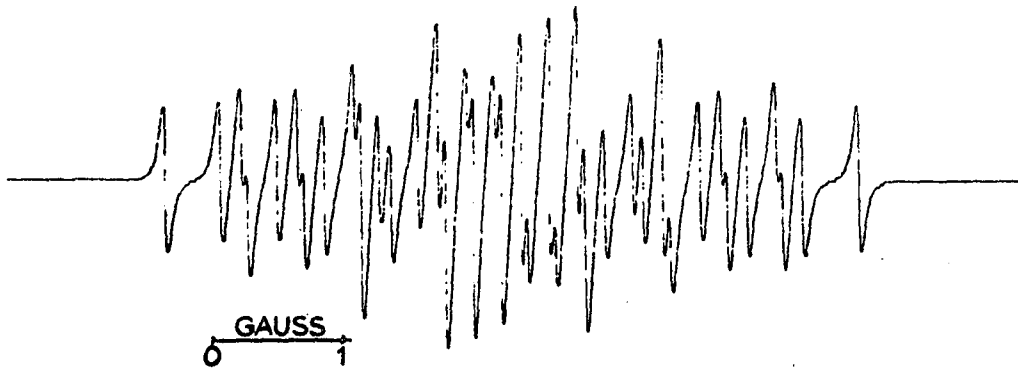
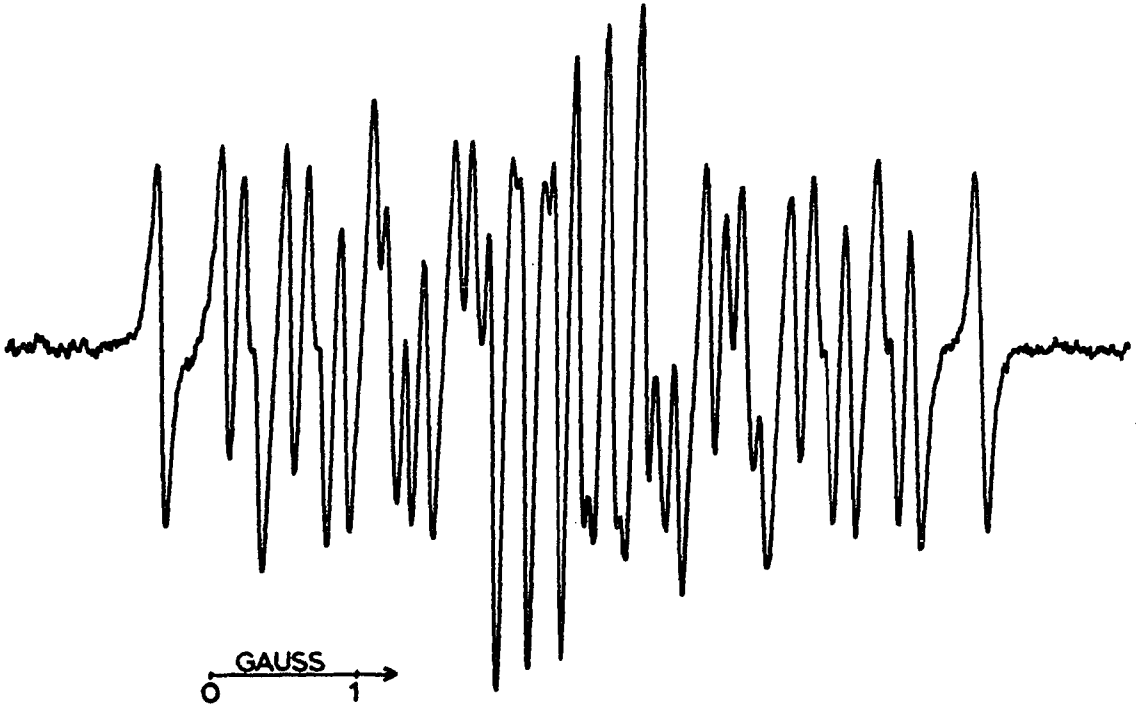
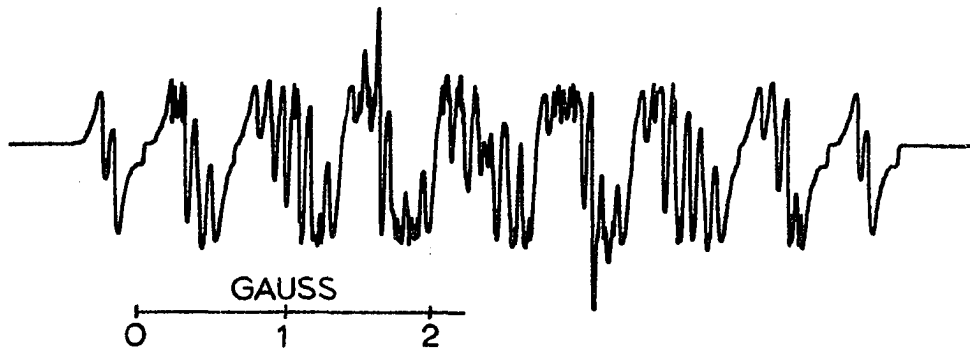
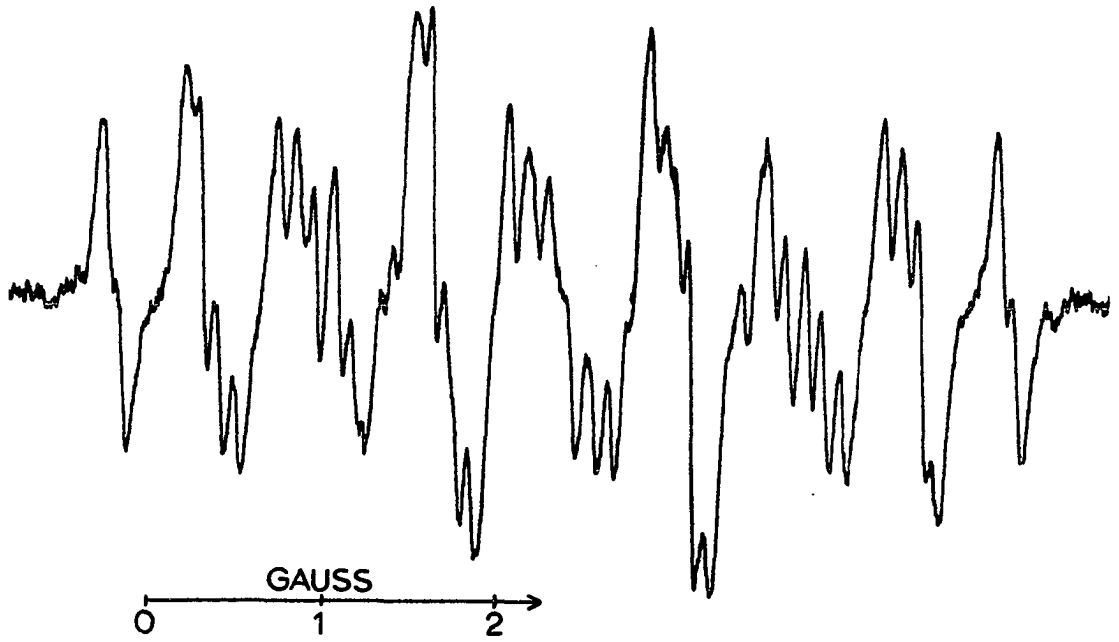
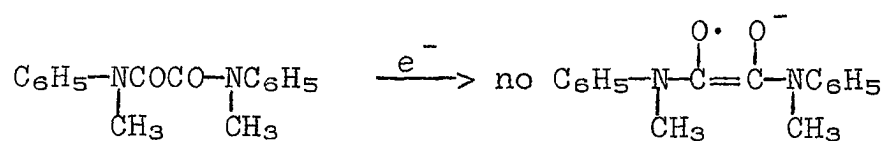


Figure 23. First-derivative ESR spectrum of 2,3,4-trioxo-1,2,3,4-tetrahydroquinoline radical anion (top) in DMSO-t-butyl alcohol 80:20; calculated spectrum for Lorentzian line width (bottom) 0.10 gauss and splitting constants from text performed by JEOLCO JNM-RA-1 spectrum accumulator.



ion present in the DMSO-5% water solution is not sufficient for the oxidation whereas ethoxide and t-butoxide are of sufficient strength.

Several attempts to reduce N,N'-dimethyloxanilide to the semidione were unsuccessful. Electrolysis in DMSO and acetonitrile produced ESR signals, but the signals in the two solvents were different and were not reproducible.



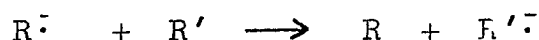
N,N'-dimethyloxanilide

This compound had a high reduction potential (Part III) and the results were not unexpected.

III. POLAROGRAPHY

Polarographic reduction potentials (half-wave potentials) were of interest in the present study for several reasons. The ESR studies utilized the technique of electrolytic reduction in the preparation of certain semidiones. The polarographic reduction potentials were used as an experimental guide to determine voltage requirements for these ESR experiments. The reduction potential was also used to predict the best approach to semidione generation. The common technique of diketone reduction in basic solution failed for compounds having reduction potentials over about 1.2 volts vs. the standard calomel electrode (SCE). The electrolytic method was superior for these compounds.

Electron spin resonance can be used in some mixed systems to qualitatively compare redox potentials. For example, the reduction potential of R' is more positive than that of R in the following reaction. However, the polarographic



reduction potential allows a quantitative comparison of the free energy differences between the oxidized and reduced forms of different compounds. Comparison of reduction potentials of a group of compounds does not necessarily indicate differences in absolute stabilities among either

the compounds or their radical ions. However, structural variations in ionic compounds are generally more important than in neutral compounds in determining energies, particularly when the variations feature changes in factors which affect charge delocalization. These factors include the extent of conjugation of π systems with the reducible moiety and the presence of electron attracting or repelling groups. Consequently, if the reduction potentials of a series of similar neutral compounds are compared, the potentials are expected to reflect the stabilities of the radical anions to a greater extent than the stabilities of the neutral compounds.

The reduction potentials of aldehydes, ketones, diketones, quinones and nitro compounds are strongly pH dependent in aqueous solution (5). The reduction potentials are considerably more positive (easier reduction) in acid conditions than in basic conditions (5). Aqueous solutions are not always suitable for organic polarography due to solubility problems. Furthermore, aprotic conditions are often ideal for ESR studies of electrochemically generated radicals and the polarographic data obtained in the same conditions can be directly compared with the ESR results (6, 9, 10, 11). Consequently the present polarographic work is done in DMSO.

There have been several previous studies of the electrolysis of isatin and related compounds. The polarographic behavior of isatin in water and in 50% aqueous ethanol has been studied (8, 62). Not only did the half-wave potential vary with pH, but also the solution composition varied because of hydrolysis. Several reducible species were present concurrently, resulting in very complicated polarographic waves (8, 62). Cassebaum has studied the aqueous polarographic behavior of many quinoid compounds, including isatin and thianaphthenequinone, in attempts to correlate redox potentials with dehydrogenase activity in amino acid dehydrogenations (7, 63, 64). Schwabe has measured the reduction potential of isatin in 80% ethanol with lithium chloride electrolyte (65). Under these conditions the half-wave potential, $E_{1/2}$, had the value 0.85 volts vs. SCE. This was similar to the value of 0.88 volts obtained in the present work in DMSO, as indicated in Table VII. The preparative electrolytic reduction of isatin and N-alkyl isatins to the dioxindoles and oxindoles in aqueous solution has also been studied (66, 67). The polarographic reduction of parabanic acid has also been performed in buffered aqueous solution (5).

The present polarographic work was done in DMSO with a tetra-n-propylammonium perchlorate supporting electrolyte. All potentials were relative to an aqueous saturated sodium chloride calomel reference electrode having a potential of

Table VII. Polarographic half-wave potentials in DMSO^{a,b,c}

Compound	$E_{1/2}$ volts-1st wave	$E_{1/2}$ volts-2nd wave	n-1st wave
Isatin	-0.88	-1.63	
N-methylisatin	-0.88	-1.83	1.03
5-Methylisatin	-0.91	-1.64	
5,7-Dichloroisatin	-0.65	-1.29	
Coumaran-2,3-dione	-0.65	-1.68	0.85
Thianaphthene-quinone	-0.54	-1.59	0.90
3,3-Dimethylindane-1,2-dione	-0.85	-1.82	0.97
2,3-Dioxotetrahydroquinoxaline	-1.98		
1,4-Dimethyl-2,3-dioxotetrahydroquinoxaline	-1.95	-2.51	
6-Methyl-2,3-dioxo-1,4-benzdithiane	-0.80		
Parabanic acid	-1.35	-2.6	
N,N'-dimethylparabanic acid	-1.29		
N,N'-dimethyloxanilide	-2.16		
Benzil	-1.03	-1.79	

^a0.1 M tetra-n-propylammonium perchlorate electrolyte.

^bExternal sat. NaCl calomel reference electrode.

^cAll potentials are corrected for IR drops.

0.004 volts (less than experimental error) vs. SCE. The results have been recorded in Table VII.

The reversible one-electron nature of the electrochemical reduction of diketones and quinones has long been known (68, 69) and was the best early evidence for the existence of monomeric semidiones and semiquinones (4). This knowledge was used in the present work as a criterion to ensure that conditions were obtained which avoided the overpotentials which could arise from polarization of the reference electrode (70). Nernst equation plots of the polarographic data for the isatin series were made to determine the number of electrons, n , involved in the first reduction wave (71).

The pertinent forms of the Nernst equation are given below for 25°C. The emf, E , of the half-cell reaction, $\text{RCOCOR} \longrightarrow [\text{RCOCOR}]^-$, is the sum of the equilibrium emf, E° , and the

$$E = E^\circ + \frac{0.0591}{n} \log \frac{[\text{ox}]}{[\text{red}]} + \frac{0.0591}{n} \log \left(\frac{D_{\text{red}}}{D_{\text{ox}}} \right)^{1/2}$$

$$E = E^\circ - \frac{0.0591}{n} \log \frac{i}{i_d - i} + \frac{0.0591}{n} \log \left(\frac{D_{\text{red}}}{D_{\text{ox}}} \right)^{1/2}$$

$$E_{1/2} = E^\circ + \frac{0.0591}{n} \log \left(\frac{D_{\text{red}}}{D_{\text{ox}}} \right)^{1/2}$$

concentration and diffusion terms. The limiting current is i_d and the observed current is i . The D_{red} and D_{ox} are diffusion coefficients. It is reasonable to assume that in DMSO the diffusion coefficients of the diketone and semidione are about equal and that the square-root term is near unity. Thus the

diffusion term can be neglected. Therefore, n and $E_{1/2}$ can be obtained from a plot of E vs. $\log i/i_d - i$.

The Nernst plots for N-methylisatin, coumaran-2,3-dione, thianaphthenequinone and 3,3-dimethylindane-1,2-dione indicated $n \cong 1$ (Table VII). The plot for isatin is not a straight line. This may be due to a side reaction of the NH proton at the electrode. The plot for N-methylisatin is presented as an example in Figure 24 and the corresponding data for N-methylisatin are given in Table VIII. The slope of the line in Figure 24 indicates $n = \frac{0.059}{0.057} = 1.0$. The Nernst equation only applies to reversible reactions (71). Tomes has shown that for a one-electron reversible reduction at 20°C the difference between $E_{3/4}$ and $E_{1/4}$ has a value of 0.055 volts (11, 72). The value obtained in the present work is 0.06 volts for N-methylisatin, coumaran-2,3-dione, thianaphthenequinone and 3,3-dimethylindane-1,2-dione. Isatin has a value of 0.07. The ability of the present polarographic conditions to correctly predict the one-electron reversible nature of the reduction supports the reliability of the results.

The results in Table VII indicate that the quinoid behavior of the isatin series increases from N to O to S. The reduction potentials of coumaran-2,3-dione and thianaphthenequinone approach the range of values usually observed for quinoid compounds. Some values of half-wave potentials from the literature are given in Table IX for comparison. It is interesting that

Figure 24. Nernst equation plot for the first wave of the polarographic reduction of N-methylisatin in DMSO. The slope of the line indicates

$$n = \frac{0.059}{0.057} = 1.0.$$

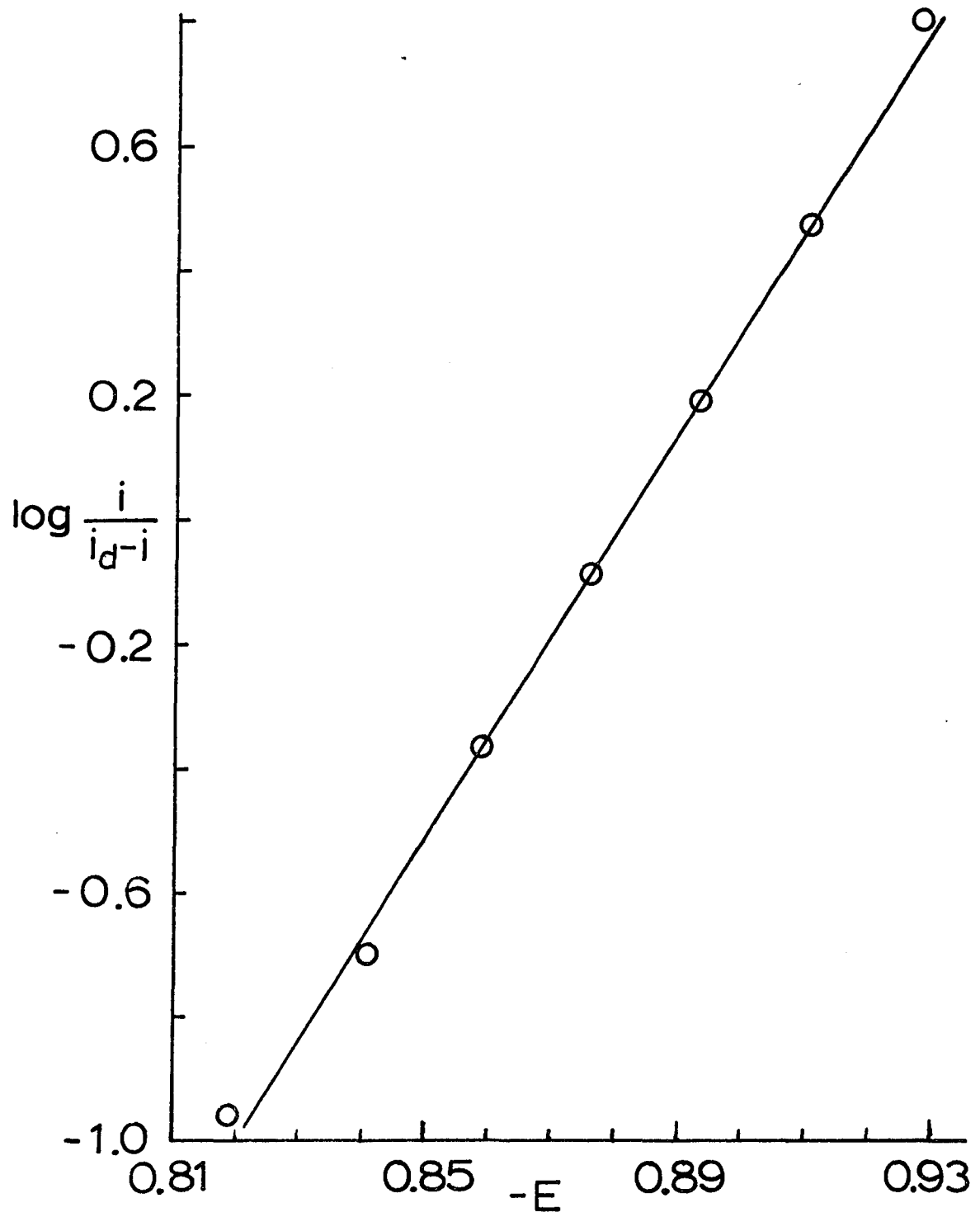


Table VIII. Polarographic data from the first wave of the reduction of N-methylisatin^{a,b}

Point	I μ amps	IR volts	-E volts	-E corr. volts	$\log \frac{I}{I_d - I}$
1	0.225	0.004	0.823	0.819	-0.958
2	0.387	0.007	0.848	0.841	-0.699
3	0.688	0.012	0.871	0.859	-0.362
4	1.02	0.018	0.894	0.876	-0.089
5	1.38	0.025	0.918	0.893	+0.190
6	1.70	0.031	0.941	0.910	+0.474
7	1.96	0.036	0.964	0.928	+0.801

^aR = 18000 ohms.

^bI_d = 2.27 μ amps.

the reduction potential of 3,3-dimethylindane-1,2-semidione is less than that of isatin despite the "aromaticity" of the semidione of isatin. The high reduction potential of benzil compared to 3,3-dimethylindane-1,2-dione is probably caused by rotation of the aromatic π system of the benzil semidione out of the plane of the carbonyl π system. The small aromatic proton hyperfine splittings of the benzil radical anion (6) and the 1-phenylpropane-1,2-semidione (18) also indicate the decreased conjugation relative to the indanediones. An effect of phenyl rotation on the energies and spin densities of semidiones is expected since only one observation of a slow or hindered phenyl rotation has been cited. This is the isopropyl

Table IX. Polarographic half-wave potentials of some diketones and quinones

Compound	$E_{1/2}$ volts vs. SCE	Conditions	Reference
Biacetyl	-0.85	pH 5.6, 50% iso- propanol	73, 5
Bibutyryl	-0.87		73, 5
Biisobutyryl	-0.92		73, 5
Bipivaloyl	-1.31		73, 5
3,3,6,6-Tetramethyl- 1,2-cyclohexane- dione	-0.75		73, 5
3,3,7,7-Tetramethyl- 1,2-cycloheptane- dione	-1.16		73, 5
3,3,18,18-Tetramethyl- cyclooctadecane- dione	-1.25		73, 5
Camphorquinone	-0.80		73, 5
Camphorquinone	-0.99	0.1 M LiCl, 80% ethanol	65, 5
Isatin	-0.85		65, 5
9,10-Phenanthrene- quinone	-0.46		65, 5
Acenaphthenequinone	-0.74		65, 5
o-Benzoquinone	+0.25	pH 5.0 water	5

benzoylformate radical anion (6). The stabilizing effect of electron withdrawing groups on semidiones is evident from the $E_{1/2}$ of 5,7-dichloroisatin. The decrease in reduction potential with an increase in conjugation or with substitution of electron withdrawing groups is a common phenomenon (5).

In a previous study (36) the reduction potentials of some diketones, triketones and ketoesters were measured in DMSO. The reduction potentials of 1,2-cyclohexanedione, 1,2-cyclopentanedione, biacetyl and benzil were found to be 1.89 volts, 2.19 volts, 1.27 volts and 1.16 volts, respectively. The large difference between the reduction potentials of the cyclic and acyclic diketones was attributed to the difference in stability of the cis and trans semidiones.

The low reduction potential of 3,3-dimethylindane-1,2-dione indicates that the cis nature of the semidiones is not the major factor in determining the ease of reduction of the diketones. It is more likely that the high reduction potentials of the aliphatic cyclic diketones are caused by the strain in the semidione ring. As indicated in Table IX, previous workers have found little difference in the reduction potentials of acyclic and cyclic diketones (73). Variable temperature ESR studies by D. Lawson of these laboratories have shown only a 2-3 kcal/mole difference in the energy of cis and trans aliphatic semidiones. A difference in reduction potential of 0.10 volt amounts to 2.3 kcal/mole.

The reduction potentials correlate crudely with the energy of the lowest unoccupied molecular orbital (LUMO) of the dicarbonyl compounds as determined by Hückel calculations. The parameters used are those utilized in the spin density calculations. The plot of the half-wave potential vs. the

molecular orbital energy is given in Figure 25. The data used are shown in Table X. Such correlations have been used in previous ESR work to justify parameters used in molecular orbital calculations (6, 11, 74). In the isatin series the

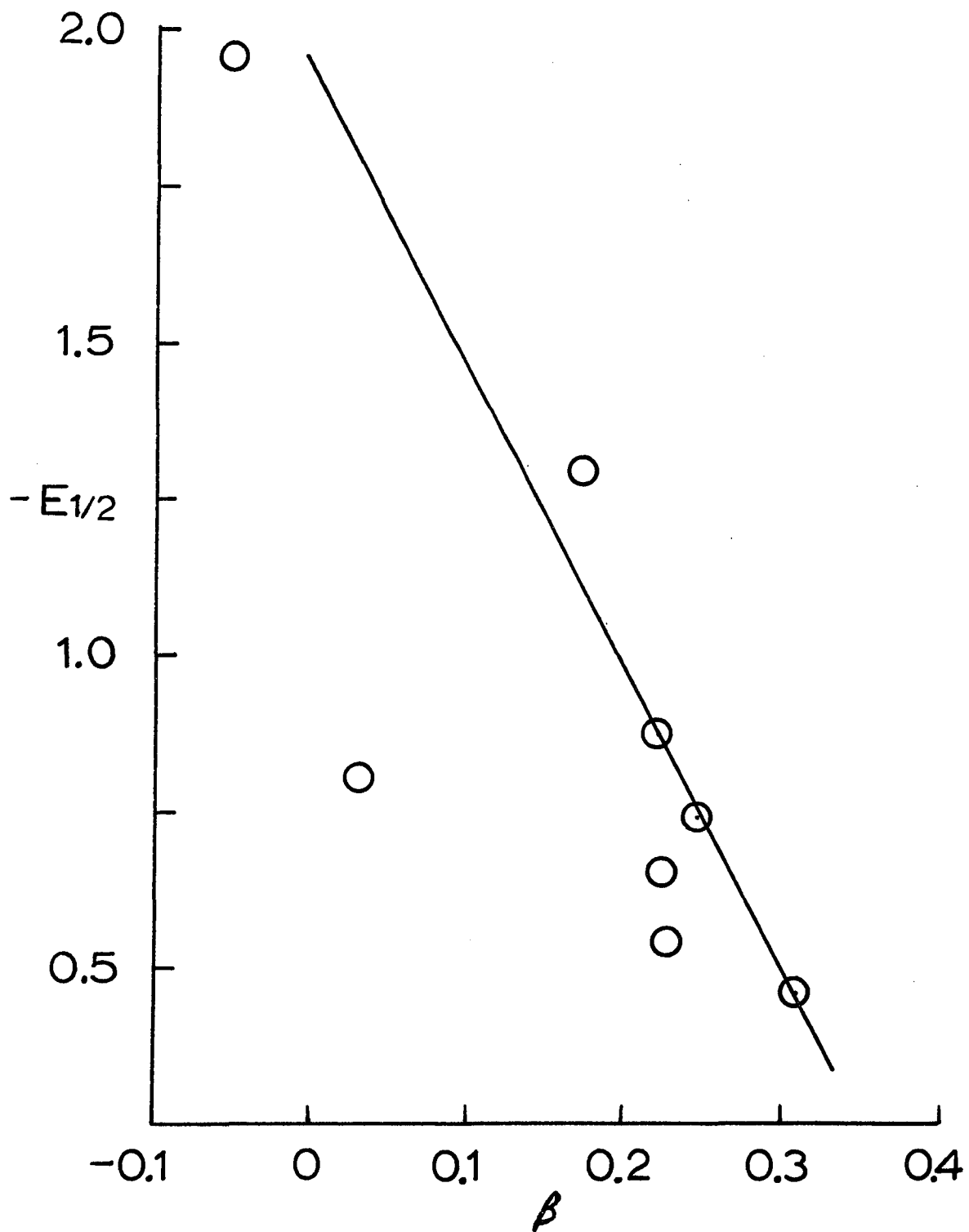
Table X. Energy of the LUMO in units of β_{CC}

Compound	E (β)	$-E_{1/2}$ volts
Isatin	0.221	0.88
Coumaran-2,3-dione	0.223	0.65
Thianaphthenequinone	0.226	0.54
N,N'-dimethylparabanic acid	0.170	1.29
6-Methyl-1,4-benzdithiane	0.033	0.80
2,3-Dioxotetrahydroquinoxaline	-0.051	1.98
9,10-Phenanthrenequinone	0.308	0.46 ^a
Acenaphthenequinone	0.245	0.74 ^a

^aResults from Reference 65 in 80% ethanol. These conditions gave a value of $E_{1/2}$ for isatin similar to that obtained in the present work. See Table IX.

calculation predicts smaller differences than those observed experimentally. The calculated value for the benzdithiane system does not fit too well. The line indicated in Figure 25 fits the equation $E_{1/2} = -1.92 - 4.3\beta$. This is not very consistent with the slope of 2.5 previously reported for one electron reductions (6, 74). Such correlations are expected

Figure 25. Plot of half-wave reduction potentials in DMSO in volts (ordinate) versus the energy of the lowest unoccupied orbital in units of β (abscissa).



to be crude for heteroatom systems and are strictly predicted only for aromatic hydrocarbons (12, 75). A high slope is also obtained in the phthalimide series (11).

IV. THE ADJACENT EFFECT IN NITROGEN HYPERFINE SPLITTING

The "direct effect" and "adjacent effect" contributions to ^{13}C and ^{14}N hyperfine splittings have been briefly discussed in the introductory section. The present section is concerned with the evaluation of the relative magnitude of these effects in α -nitrogen semidiones. This involves the determination of the magnitude of the σ - π spin polarization parameter Q_{CN}^{N} , which relates the nitrogen hyperfine splitting to the magnitude of the spin density on the adjacent carbon atoms. There have been several recent discussions of the magnitude of Q_{CN}^{N} (21, 32, 33) and much of the related data and theory have been reviewed by Bolton (35).

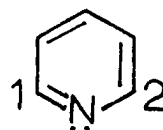
There are some trends of data that support the contention that the adjacent effect is an important contribution to nitrogen hyperfine splitting when the direct effect is small in nitrogen π radicals. The ratio of the proton hyperfine splitting constant to the nitrogen hyperfine splitting constant, $a_{\text{NH}}^{\text{H}}/a^{\text{N}}$, is usually about unity for radicals which have a nitrogen spin density of a magnitude about equal or larger than the sum of adjacent carbon spin densities. The ratio $a_{\text{NH}}^{\text{H}}/a^{\text{N}}$ is much lower than unity for some α -nitrogen semidiones and related radicals. These are radicals in which the nitrogen spin density is relatively low compared with adjacent carbon spin densities. The ratio of the methyl proton hyperfine splitting to the nitrogen splitting, $a_{\text{NCH}_3}^{\text{H}}/a^{\text{N}}$, is

also approximately unity for radicals having a high nitrogen spin density. Like the $a_{\text{NH}}^{\text{H}}/a^{\text{N}}$ ratio, the ratio $a_{\text{NCH}_3}^{\text{H}}/a^{\text{N}}$ is much lower than unity for some α -nitrogen semidiones and related radicals and these are also radicals with a low spin density on nitrogen and a large spin density on adjacent positions. The data are summarized in Table XI. The variation of these ratios suggests that both the NH (or NCH₃) proton splitting and the nitrogen splitting can not be merely proportional to the nitrogen spin density. Either the nitrogen splittings are enhanced in certain compounds (those with $\rho_{\text{N}} \ll \rho_{\text{C}_1} + \rho_{\text{C}_2}$) relative to the proton splittings by the adjacent effect or else the proton (NH and methyl) splittings are diminished for some unknown reasons in these cases. If the adjacent effect is responsible for the variation in ratios, then in favorable cases, its magnitude, i.e., the magnitude of Q_{CN}^{N} , should be susceptible to quantitative evaluation.

The Karplus-Fraenkel equation (29) must have more than one form when applied to nitrogen splittings since more than one type of bonding situation can occur. The equation is as follows for the case of an aza or pyridine-type nitrogen with a nonbonded pair of electrons (35).

$$a^{\text{N}} = Q_{\text{N}}^{\text{N}} \rho_{\text{N}} + Q_{\text{CN}}^{\text{N}} (\rho_{\text{C}_1} + \rho_{\text{C}_2})$$

$$Q_{\text{N}}^{\text{N}} = (P^{\text{N}} + 2 Q_{\text{NC}}^{\text{N}})$$



The parameter P^{N} is the polarization parameter which describes

Table XI. Trends in proton-nitrogen hyperfine splitting ratios

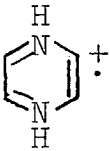
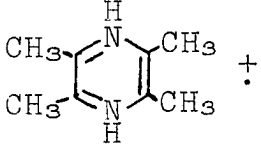
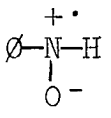
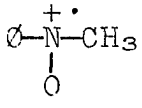
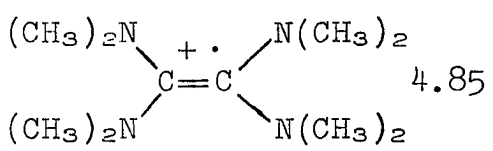
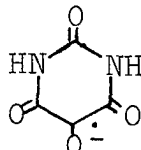
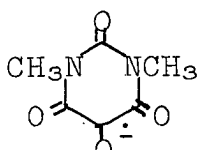
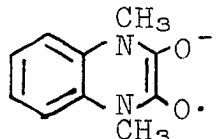
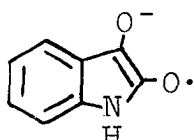
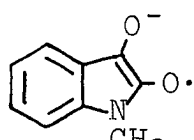
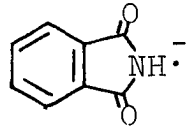
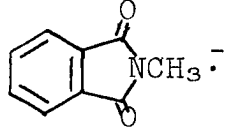
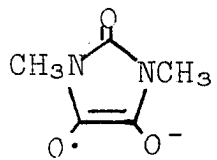
Radical	a^N	a_{NH}^H	$a_{NCH_3}^H$	$\frac{a_{NH}^H}{a^N}$	$\frac{a_{NCH_3}^H}{a^N}$	Reference
$\cdot NH_3$	19.5	25.9		1.33		76
$\cdot N(CH_3)_3$	18.0		26.7		1.48	77
	7.60	8.30		1.09		78
	6.64	6.95		1.05		31
$H_2N-C_6H_4-NH_2^{\cdot+}$	5.29	5.88		1.11		79
$(CH_3)_2NC_6H_4-N(CH_3)_2$	6.99		6.76		0.97	80
	9.9	13.0		1.3		47
	11.0		10.4		0.95	47
		4.85	2.84		0.59	
			3.28		0.68	81

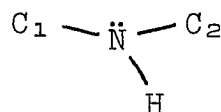
Table XI continued

Radical	a^N	a_{NH}^H	$a_{NCH_3}^H$	$\frac{a_{NH}^H}{a^N}$	$\frac{a_{NCH_3}^H}{a^N}$	Reference
	0.59	0.48		0.81		20
	0.50		0.30		0.60	20
	2.48		1.44		0.58	
	1.06	0.19		0.2		
	1.0		0.61		0.6	
	2.40	0.41		0.17		22
	2.54		0.90		0.35	22
	1.66		0.11		0.066	

the effect of the unpaired spin (in a p or π orbital) on the nonbonded electron pairs (pair of 1s electrons and pair of hybrid ($\sim SP^2$) electrons). The parameter Q_{NC}^N represents the contribution to the nitrogen splitting by the polarization of the nitrogen 2s electrons of the N-C σ bonds by the π spin density on nitrogen, ρ_N . In the case of a trigonally bonded nitrogen with a π lone pair the equation is as follows (35).

$$a^N = Q_N^N \rho_N + Q_{CN}^N (\rho_{C_1} + \rho_{C_2})$$

$$Q_N^N = (S^N + Q_{NH}^N + 2 Q_{NC}^N)$$



The parameter S^N represents the contribution to the nitrogen splitting by the σ - π spin polarization of the nitrogen 1s electrons by the π spin density on nitrogen. The parameters Q_{NH}^N and Q_{NC}^N represent the contribution to the nitrogen splitting by the interaction of the nitrogen 2s electrons in the σ -bonds with the nitrogen π spin density.

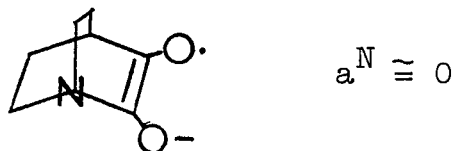
The values of Q_N^N and Q_{CN}^N are expected to vary with changes in the bonding situation. The exact value should depend on the bond angles and lengths, the hybridization of the nitrogen atom and the charge on the radical (33). The value of Q_N^N increases as the amount of 2s character in the orbital containing the unpaired electron increases, so that pyramidal aminium ions have a much larger nitrogen splitting than planar aminium ions (82), as predicted (83). Similarly, the value of

Q_{CN}^N is expected to depend on the degree of 2S character in the nitrogen contribution to the N-C σ bond. Other things being equal, the magnitude of the Q_{CN}^N should vary with nitrogen hybridization according to the series $Q_{CN}^N \text{ sp} > Q_{CN}^N \text{ sp}^2 > Q_{CN}^N \text{ sp}^3 > Q_{CN}^N \text{ pyramidal}$.

The parameter Q_N^N is not expected to be the same for all types of heterocyclic nitrogen π radicals. The value of Q_N^N for an aza nitrogen with a σ lone pair has been estimated to be +24 gauss and Q_N^N for a nitrogen π radical of the N-H type has been estimated to be +28 gauss (35). Considering the variations in the results of a number of workers these values of the parameter Q_N^N probably are reliable to ± 5 gauss when applied to most radicals (31, 33, 34, 35, 79).

There have been many previous estimates of the parameter Q_{CN}^N for nitrogen π radicals (30, 31, 32, 33, 24, 84, 21). The general method of estimation has been the calculation of ρ_{C_1} , ρ_{C_2} and ρ_N by M. O. methods and/or the determination of ρ_{C_1} and ρ_{C_2} from the semi-empirical McConnell relation, $a_{CH}^H = Q_{CH}^H \rho_C$ (27). The estimates of Q_{CN}^N have ranged from -4 gauss to +14 gauss although most of the reported values have been in the range of ± 3 gauss for both the aza and NH types of radicals.

The Q_{CN}^N for a tetrahedral sp^3 nitrogen bonded to a carbon π system is known to be approximately zero (21). The ESR spectrum of the quinuclidine-2,3-semidione exhibits no nitrogen



quinuclidine-2,3-semidione

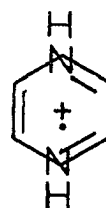
hyperfine splitting, and from the linewidth, an upper limit of 0.10 gauss is placed on the nitrogen splitting (21). In that system ρ_N must be zero since the nitrogen lone pair is in the nodal plane of the π system. For such a compound the Karplus equation reduces to only the adjacent effect. Since the carbonyl carbon atoms have a ρ_C of 0.25 to 0.35 an upper limit of $|Q_{CN}^N| \leq 0.4$ gauss is required (21). The zero Q_{CN}^N for this case of a tetrahedral nitrogen should not be taken as evidence of a zero Q_{CN}^N for other bonding situations, such as in the planar sp^2 nitrogen radicals. As has been mentioned, the value of Q_{CN}^N is expected to decrease as the 2S nature of the nitrogen σ bonding to the π system decreases.

There are two general classes of π radicals which are especially applicable to the problem of reliably determining the value of Q_{CN}^N . The first class includes the symmetrical radicals which have a protonated carbon or a nitrogen at every position in a cyclic aromatic ring. In such radicals, the ρ_C at each carbon atom can be obtained from the McConnell relation and the nitrogen ρ_N can be deduced from symmetry and/or M. O. calculations.

Studies which fit this criterion have yielded the following results. Stone and Maki have estimated Q_{CN}^N to be -2 ± 2 gauss from studies of the pyrazine anion and similar radical anions (30). Atherton, Gerson and Murrell estimated Q_{CN}^N to be -1.5 gauss for the same type of anions (79). Barton and Fraenkel have concluded that $Q_{CN}^N = +2.62$ gauss from studies of the dihydropyrazine radical cation (31).



pyrazine anion

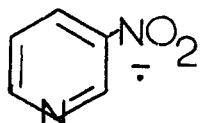


dihydropyrazine cation

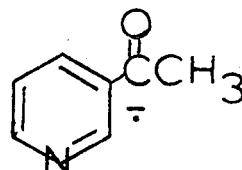
The second general class of π radicals which is expected to be of particular value in determining Q_{CN}^N includes those radicals which have a very low ρ_N and a very high $\rho_{C_1} + \rho_{C_2}$. In such radicals, the nitrogen hyperfine splitting is expected to arise largely from the adjacent effect and the direct effect should be minimal, the reverse of the usual situation.

Only one study of nitrogen π radicals which fit this second criterion has been reported. This was the work of Cottrell and Rieger in which the 3-nitropyridine and 3-acetylpyridine radical anions were prepared (32). In these radicals the ring nitrogen occupied a meta position to the spin label (nitro or acetyl) and had a low ρ_N . The ortho and para

carbons, adjacent to the nitrogen, not only had large ρ_C 's but possessed protons for application of the McConnell relation, $a_{CH}^H = Q_{CH}^H \rho_C$. The value of Q_{CN}^N in this study was found to be -0.8 to -1.8 gauss (32).



3-nitropyridine anion



3-acetylpyridine anion

No previous studies which fit the second criterion ($\rho_N \ll \rho_{C_1} + \rho_{C_2}$) have been reported for nitrogen π radicals in which the nitrogen possesses a π lone pair and is bonded to three other atoms. Some of the α -nitrogen semidiones do fit this criterion of having a large $\rho_{C_1} + \rho_{C_2}$ and a small ρ_N . The phthalimide radical anions possess the same quality but have not been discussed in terms of Q_{CN}^N (22, 23). Both types of radicals suffer from the liability that the adjacent carbon atoms possess no protons for application of the McConnell relation. Therefore, the adjacent carbon spin densities must be estimated by M. O. methods. An estimation of the nitrogen spin density is also required. The hyperfine splitting of the proton or methyl group bonded to the nitrogen is required for such an estimation and a proportionality, i. e., the McConnell relation, must exist between the nitrogen spin density and the hyperfine splitting of the proton or methyl

group. These proportionalities are not proven to be generally applicable, particularly for the methyl group.

The McConnell relation parameter Q_{CH}^H has been shown to be somewhat charge dependent and the parameter is expected to be an absolute constant only for neutral radicals (35). However, the relation is approximately valid and all the estimates of Q_{CH}^H have been in the range of -20 to -30 gauss with most estimates clustered between -22 and -28 gauss (28, 35). Since Q_{CH}^H is not an absolute constant for radical ions, one expects that Q_{NH}^H will not be a constant either. The negative sign of this parameter has been experimentally proven (85) and the magnitude has been found to vary from 22 to 34 gauss (35). The effect of the variation of the polarity of the N-H bond on Q_{NH}^H is not known. Drastic changes in polarity certainly should cause changes in the σ bond spin density on the proton. One expects extreme acidity of the N-H proton to have a diminishing effect on the a^H/a^N ratio. The radical anions presently discussed are probably not extremely acidic.

The application of the McConnell relation to methyl proton splittings also requires a consideration of charge effects. The $Q_{CCH_3}^H$ is predicted to be a constant only for certain neutral radicals and for radical ions estimates of this parameter have ranged from +18 to +38 gauss (35). The values of $Q_{CCH_3}^H$ for radical cations are often about twice the values for radical anions (18) and values for the latter of 18 to 20 gauss are generally applicable (18). The parameter $Q_{NCH_3}^H$ is

therefore also expected to be somewhat variant with charge. Tetramethylhydrazine radical cation requires a $Q_{\text{NCH}_3}^{\text{H}}$ of 27 gauss and Nelsen uses this as an upper limit for radical anions (22).

With all of the possible sources of error in the estimation of Q 's and ρ 's, the use of the radicals discussed in the present work to estimate Q_{CN}^{N} might appear inane. However, the combining of the Karplus and McConnell relations can give an equation for Q_{CN}^{N} in which the most inaccurate Q factors are presented as a ratio in a term of small magnitude when $a^{\text{H}}/a^{\text{N}}$ is low. For the application to N-H radicals the equations are:

$$a^{\text{N}} = Q_{\text{N}}^{\text{N}} \rho_{\text{N}} + Q_{\text{CN}}^{\text{N}} (\rho_{\text{C}_1} + \rho_{\text{C}_2})$$

$$\rho_{\text{N}} = a_{\text{NH}}^{\text{H}} / Q_{\text{NH}}^{\text{H}}$$

$$Q_{\text{CN}}^{\text{N}} = \frac{a^{\text{N}}}{(\rho_{\text{C}_1} + \rho_{\text{C}_2})} - \frac{Q_{\text{N}}^{\text{N}}}{Q_{\text{NH}}^{\text{H}}} \frac{a_{\text{NH}}^{\text{H}}}{(\rho_{\text{C}_1} + \rho_{\text{C}_2})}$$

The similar equation for N-methyl radicals is:

$$Q_{\text{CN}}^{\text{N}} = \frac{a^{\text{N}}}{(\rho_{\text{C}_1} + \rho_{\text{C}_2})} - \frac{Q_{\text{N}}^{\text{N}}}{Q_{\text{NCH}_3}^{\text{H}}} \frac{a_{\text{NCH}_3}^{\text{H}}}{(\rho_{\text{C}_1} + \rho_{\text{C}_2})}$$

Since only the numerators of these equations are experimentally determined, the equations are only of practical significance when a_{NH}^{H} or $a_{\text{NCH}_3}^{\text{H}}$ is very small with respect to a^{N} and when $(\rho_{\text{C}_1} + \rho_{\text{C}_2})$ can be reasonably estimated. These

circumstances have rarely been observed. The utility of the equation also requires that the value of Q_{NH}^{H} or $Q_{\text{NCH}_3}^{\text{H}}$ be of the same order of magnitude as Q_{N}^{N} . In other words, one must assume the adjacent effect to be dominant before one can measure its magnitude by this method. If Q_{NH}^{H} or $Q_{\text{NCH}_3}^{\text{H}}$ is unusually low then the calculation is meaningless. Another limitation is that the signs of a_{NH}^{H} or $a_{\text{NCH}_3}^{\text{H}}$ and a^{N} must be known in order to measure the sign of Q_{CN}^{N} and, if the $a^{\text{H}}/a^{\text{N}}$ ratio is not extremely small, the signs of a^{H} or ρ_{N} and a^{N} must be known to even estimate the magnitude of Q_{CN}^{N} . Fortunately, the sign of ρ_{N} and a^{N} can be theoretically predicted in favorable cases and at least a range of possible Q_{CN}^{N} values can be estimated.

The calculations of Q_{CN}^{N} from a_{NH}^{H} and a^{N} for the isatin and phthalimide (22) radical anions are indicated in Table XII. The ratio $Q_{\text{N}}^{\text{N}}/Q_{\text{NH}}^{\text{H}}$ is assumed equal to -0.94 as suggested by Barton and Fraenkel in a study of dihydropyrazine radical cations in which $\rho_{\text{N}} > (\rho_{\text{C}_1} + \rho_{\text{C}_2})$ (31). The Q_{CN}^{N} values are calculated over a range of $(\rho_{\text{C}_1} + \rho_{\text{C}_2})$ including the sum indicated by the M. O. calculations. The values for isatin radical anion are shown for both the same and opposite signs of a^{N} and a_{NH}^{H} since Hückel calculations predict only a near node at nitrogen in the HOMO. The opposite sign values are correct if the nitrogen spin density is negative as indicated by McLachlan calculations. The values for the phthalimide

radical anion are calculated for only the opposite sign of a^N and a_{NH}^H since Hückel calculations predict an exact node at nitrogen in the HOMO (22).

The calculations of Q_{CN}^N from $a_{NCH_3}^H$ and a^N for the N,N'-dimethylparabanic acid radical anion and the N-methylphthalimide radical anion are indicated in Table XIII.

Table XII. Calculation of Q_{CN}^N from a_{NH}^H and a^N

Radical anion	$\rho_{C_1} + \rho_{C_2}$	Opposite sign a^N and a_{NH}^H $ Q_{CN}^N ^d$	Same sign a^N and a_{NH}^H $ Q_{CN}^N ^d$
Isatin	0.30	2.8	4.0
	0.41 ^b	1.9	2.9
	0.50	1.6	2.4
Phthalimide	0.15	15.0	
	0.24 ^c	9.9	
	0.40	5.6	

^aThe sign of Q_{CN}^N is identical to the sign of a^N , which is probably negative for both the isatin and phthalimide radical anions.

^bCalculated from McLachlan spin density calculations described in Part II D.

^cCalculated value from Reference (22).

^d Q_{CN}^N/Q_{NH}^H is assumed equal to -0.94. See Reference (31).

The Q_{CN}^N are again calculated over a range of $(\rho_{C_1} + \rho_{C_2})$ including the sum suggested by M. O. calculations. The values of Q_{CN}^N for N,N'-dimethylparabanic acid anion are calculated for both the same (the probable situation) and

Table XIII. Calculation of Q_{CN}^N ^a from $a_{NCH_3}^H$ and a^N

Radical Anion	$\rho_{C_1} + \rho_{C_2}$	Same sign of a^N and $a_{NCH_3}^H$		Opposite sign of a^N and $a_{NCH_3}^H$	
		$Q_N^N/Q_{NCH_3}^H = 1$	$Q_N^N/Q_{NCH_3}^N = 2$	$Q_N^N/Q_{NCH_3}^H = 1$	$Q_N^N/Q_{NCH_3}^H = 2$
		$ Q_{CN}^N $	$ Q_{CN}^N $	$ Q_{CN}^N $	$ Q_{CN}^N $
N,N'-dimethyl- parabanic acid	0.25	6.2	5.8	7.1	7.5
	0.40	3.9	3.6	4.4	4.7
	0.50 ^b	3.1	2.9	3.5	3.8
	0.67	2.3	2.2	2.7	2.8
N-methylphthal- imide	0.15	10.7	5.0		
	0.24 ^c	6.7	3.1		
	0.40	4.0	1.9		

^aThe sign of Q_{CN}^N is identical to the sign of a^N , which is probably negative for these radicals.

^bCalculated from McLachlan spin density calculations described in Part II E.

^cCalculated from Reference (22) for the parent phthalimide radical.

opposite signs of a^N and $a_{NCH_3}^H$ because the nitrogen position is not completely nodal in the Hückel HOMO. The values of

Q_{CN}^N for the N-methylphthalimide radical anion are calculated only for a^N and $a_{NCH_3}^H$ of the same sign since nitrogen is at a complete node in the Hückel HOMO (22). The ratios $Q_{CN}^N/Q_{NCH_3}^H$ of both 1 and 2 are used to allow for errors in estimating these parameters and to allow for charge effects. The "normal" value of Q_{CN}^N is $+25 \pm 3$ gauss and the "upper limit" of $Q_{NCH_3}^H$ is +27 gauss as previously discussed.

The N-methylisatin and N,N'-dimethyldioxotetrahydroquinoxaline radicals discussed in this work are not applicable to this analysis since the $a_{NCH_3}^H/a^N$ ratio is too large and a small difference in relatively large numbers is involved. Spin densities must be known quite accurately in such cases.

The errors in the calculated carbonyl carbon spin densities in the phthalimides may be rather large due to the approximate state of the art of MO calculations (22). One is not able to devise such a radical in which the McConnell relation can be used to "directly measure" these spin densities. Semidione carbonyl carbon spin densities are subject to direct "measurement" by the McConnell relation in some cases, e.g., where a proton or methyl group is directly bonded to the carbonyl carbon in acyclic semidiones. In those cases, the values of carbonyl carbon spin densities have been found to range from 0.15 to 0.39 with higher values for cis semidiones than for trans semidiones (4, 18). Molecular orbital calculations are in reasonable agreement with experimental spin densities (4). Therefore, the range

of possible semidione carbonyl carbon spin densities in isatin and N,N'-dimethylparabanic acid radical anions can be predicted with some confidence. The semidione carbonyl carbon is only one of the two adjacent carbons and the other ρ_C is not as accurately predicted, but the semidione carbonyl spin density is the larger of the two. In the case of the N,N'-dimethylparabanic acid anion the small size and symmetry of the radical limits the reasonable estimates of $(\rho_{C_1} + \rho_{C_2})$ to the values indicated in Table XIII.

The present data suggest that the magnitude of Q_{CN}^N is from 2 to 4 gauss for radicals of the type considered. This conclusion is based on the assumption that the low a_{NH}^H/a^N and $a_{NCH_3}^H/a^N$ ratios of the radicals in which $\rho_N \ll \rho_{C_1} + \rho_{C_2}$ are due to the dominance of the adjacent effect over the direct effect in these radicals. To assume otherwise implies that both the N-H proton splittings and the N-methyl proton splittings are reduced rather than the nitrogen splittings enhanced in the present systems and that the adjacent effect is not important for radicals which fit the criterion $\rho_N \ll (\rho_{C_1} + \rho_{C_2})$.

Qualitatively, it is apparent from the literature that nitrogen π radicals which have a large unpaired electron density on nitrogen relative to adjacent positions, i. e., $\rho_N > \rho_{C_1} + \rho_{C_2}$, have a_{NH}^H/a^N and $a_{NCH_3}^H/a^N$ ratios near unity. This is true of both aminium ions (31, 79, 80) and nitroxides (47). The nitrogen π radicals which have a smaller unpaired

electron density on nitrogen than on adjacent positions have lower $a_{\text{NH}}^{\text{H}}/a^{\text{N}}$ and $a_{\text{NCH}_3}^{\text{H}}/a^{\text{N}}$ ratios. These cases include tetrakis(dimethylamino)ethylene cation (81) (possibly), the alloxan semitriones (20), the phthalimides (22, 23) and the radicals prepared in the present study. It seems that the adjacent effect is significant in these radicals.

V. EXPERIMENTAL

A. Polarography

All polarography was done with a Leeds and Northrup Electro-Chemograph Type E chart recording polarograph. A two compartment cell was used with a fine frit separating the two compartments. One compartment contained a solution of the substrate and electrolyte in DMSO. This compartment was fitted with a dropping mercury electrode and a nitrogen inlet and outlet. The other compartment contained a solution of electrolyte in DMSO and was connected by a salt bridge to an aqueous saturated sodium chloride calomel reference electrode.

DMSO was distilled in-vacuo from calcium hydride and stored over molecular sieves. The electrolyte was tetra-n-propylammonium perchlorate (86), the preparation of which is described in another section. The electrolyte concentration was 0.1 M and the substrate concentration was 0.001 M. Each sample was deoxygenated with a flow of prepurified nitrogen for 30 min. before measurements were made.

The AC resistance was measured across the dropping mercury electrode, the cell and solutions, and the reference electrode after the polarogram was obtained for each sample. This resistance was used in correcting measured potentials for IR drops across the apparatus. An Industrial Instruments

Inc. model RC 16B2 conductivity bridge was used for the resistance measurements.

B. Electron Spin Resonance Spectra

Most spectra were obtained with a Varian E-3 spectrometer equipped with a 9.5 GC microwave bridge, a 3 inch magnet and 100 kc field modulation. Some spectra were obtained with a Varian V-4502 spectrometer equipped with a 9 in. magnet with 100 kc field modulation.

Semidiones were prepared in basic solution by methods which have previously been reported (1, 13, 20). A typical reduction of an α -diketone, using propiophenone enolate as the reducing agent, involved the following procedure. In one leg of an ESR U-cell was placed the diketone, propiophenone and the DMSO or DMSO-t-butyl alcohol 80:20 solvent. In the other leg of the U-cell was placed solid potassium t-butoxide and solvent. The solutions were deoxygenated for 30 min. with a stream of prepurified nitrogen. Then the attached quartz Varian ESR solution cell was capped and the apparatus inverted for mixing and measurement. Typical concentrations after mixing were 0.05 M diketone, 0.04 M propiophenone and 0.1 to 0.3 M potassium t-butoxide. The apparatus has been described in detail previously (87). Some semidiones were prepared by treating α -diketones with potassium t-butoxide in DMSO or DMSO-t-butyl alcohol 80:20

without an added reducing agent. These reductions were performed exactly as described above except that propiophenone was omitted. Oxidation of α -hydroxy ketones to semidiones was generally performed by treating the α -hydroxy ketone with potassium t-butoxide with concentrations approximately one-third of those in the diketone reductions. In some cases a trace of air was added in the oxidations. The preparation of the semidione from isatide required a smaller concentration of substrate since conversion to the radical was essentially quantitative. The best resolved ESR signal of the isatin radical anion produced from isatide in DMSO was obtained using 0.001 M isatide and 0.002 M potassium t-butoxide. Any excess alkoxide in the aprotic medium produced the isatin dianion radical.

The production of semidiones by electrolytic reduction in the ESR cavity was done by the same method as described by previous workers (6). In some cases a Ag-AgCl-acetonitrile reference electrode was used and in other cases a standard calomel reference electrode was used. The tetrapropyl ammonium perchlorate supporting electrolyte concentration was 0.2 M and the substrate concentration was 0.003 to 0.03 M.

The nitroxide of N-hydroxyisatin was prepared by treating 0.05 M N-hydroxyisatin with an excess of lead peroxide under neutral conditions in DMSO or dioxane. This method

of producing nitroxides has been described (45).

C. Reagents

Dimethylsulfoxide-DMSO

The DMSO used for both the ESR and polarographic work was purified by the following method. Commercial "anhydrous" DMSO was allowed to stand over calcium hydride for a few days. The DMSO was then vacuum distilled from the calcium hydride onto molecular sieves, b.p. $<60^{\circ}\text{C}$.

N,N-dimethylformamide-DMF

Reagent grade DMF was purified by storage over calcium hydride and vacuum distillation from calcium hydride onto molecular sieves.

Acetonitrile

Reagent grade acetonitrile was purified by distillation from phosphorous pentoxide onto molecular sieves in a nitrogen atmosphere.

Tetra-n-propylammonium perchlorate (86)

A 100 g. sample of tetra-n-propylammonium bromide was dissolved in 250 ml. of distilled water. Then 40 ml. of 70% perchloric acid was added. The product was cooled in ice, collected and washed with water. The product was recrystallized twice from distilled water and dried in a vacuum over silica gel for several days. The yield of crystalline product was 84 g. A silver halide test indicated the absence

of bromide in the product.

Isatin

The commercially available isatin was recrystallized twice from benzene, m.p. 200°C, lit. 200°C (88). The IR and NMR spectra were satisfactory.

Dioxindole

Dioxindole was prepared by reduction of isatin with sodium dithionite in aqueous solution as described by Marschalk (89). A 15.0 g. sample of isatin was converted to 11.1 g. of dioxindole, a 73% yield. The product was purified by recrystallization from water, m.p. 165°C, lit. 167-170°C (90). The mass spectrum showed the expected molecular ion at m/e 149.

Isatide

A 1.000 g. sample of isatin (0.068 moles) was dissolved in 55 ml. of 90% ethanol. A 1.015 g. sample of dioxindole (0.068 moles) was dissolved in 15 ml. of 90% ethanol. Approximately 0.5 ml. of morpholine was added to the isatin solution. Then the solutions were combined and heated on the steam bath for an hour. A yellow microcrystalline product was obtained. The yield of isatide was 1.25 g. or 62.5%, m.p. 225°C, lit. 230-245°C (90, 91).

N-deuteroisatin

A 1.0 g. sample of isatin was recrystallized twice from D₂O. The product was dried and stored in a prepurified

nitrogen atmosphere. Comparison of the NMR spectrum of the deuterated compound in DMSO- d_6 with the spectrum of the protonated compound in DMSO showed that the deuterium incorporation amounted to 87%.

N-Methylisatin

A 15 g. sample of isatin was dissolved in 80 ml. of 10% sodium hydroxide solution. A 36 g. sample of dimethyl sulfate was added and the solution was refluxed for 3 hours. The solution was cooled in ice and the solid product collected. The product was washed with cold water and recrystallized from 25% alcohol. The product was impure since it melted slowly from 115°C to 130°C. Two more recrystallizations did not improve the purity. The purification was achieved by column chromatography on silica gel. The impure product was placed on the column as a concentrated chloroform-methanol solution, then was eluted with benzene. The first compound eluted from the column was the desired product. The N-methylisatin was purified further by recrystallization from benzene, m.p. 131°C, lit. 134°C (92). The IR spectrum ($CHCl_3$) showed strong absorptions at 1740 cm^{-1} (C=O), 1610 cm^{-1} (arom. C=C), 1467 cm^{-1} , 1365 cm^{-1} and 1325 cm^{-1} in addition to absorptions at lower frequencies. A medium strength absorption at 862 cm^{-1} in N-methylisatin was absent in the starting material.

5,7-Dichloroisatin

Commercial 5,7-dichloroisatin was recrystallized from

ethanol, yielding orange needles, m.p. 221-222°C, lit. 221-222°C (93). The IR spectrum (KBr) showed a medium strength absorption at 3100 cm^{-1} (N-H) and strong absorptions at 1765 cm^{-1} (C=O) and 1610 cm^{-1} (arom. C=C).

5,7-Dichlorodioxindole

An 11 g. sample of 5,7-dichloroisatin was dissolved in 900 ml. of boiling 45% alcohol. A 15 g. sample of sodium dithionite was added in portions to the hot solution. The solution was refluxed 30 min. The hot solution was filtered and precipitation of the product occurred immediately upon cooling of the filtrate. The product was recrystallized from 400 ml. of 75% alcohol. The yield of pale yellow product was 6.7 g. or 60%, m.p. 215-230°C. The product became orange in the melting point tube at about 200°C indicating autoxidation of the surface of the solid to the isatin. The IR spectrum (KBr) indicated strong broad absorptions at 3400 cm^{-1} and 3200 cm^{-1} (O-H and N-H), strong absorption at 1720 cm^{-1} (C=O) and medium absorption at 1590 cm^{-1} and 1620 cm^{-1} (arom. C=C). The mass spectrum showed a molecular ion at the expected m/e 217. The p + 2 peak at m/e 219 had an intensity of 60% of the parent ion indicating the presence of two chlorine atoms per molecule.

5-Methyldioxindole

A 0.15 g. sample of 5-methylisatin was dissolved in 25 ml. of 50% ethanol. The solution was heated to boiling and 0.30 g.

of sodium dithionite was added. The solution was refluxed for 15 min. and filtered hot. The volume was reduced to about 10 ml. and the solution cooled. The yield of pale yellow needle crystalline product was 0.1 g. or 67%, m.p. 225-240°C. The crystal surface autoxidized above 175°C. The IR spectrum (KBr) exhibited strong absorptions at 3400 cm^{-1} (O-H), 3150 cm^{-1} (N-H), 1700 cm^{-1} (C=O) and 1630 cm^{-1} with a shoulder at 1600 cm^{-1} (arom. C=C). The mass spectrum indicated the expected molecular ion at m/e 163.

2-Hydroxyphenylglyoxylic acid lactone - Coumaran-2,3-dione

The following synthesis was adapted from Baeyer (94) and from Fries (95). A 14.7 g. sample of isatin (0.1 mole) was dissolved in 150 ml. of 1N sodium hydroxide. A 7.0 g. sample (slightly >0.1 mole) of sodium nitrite was added and the solution was cooled in ice to 0-5°C. A cold 150 ml. solution of 2.5 M sulfuric acid was slowly added. The solution was stirred at 0-5°C for 10 min., then heated to 60°C and allowed to stand for an hour with occasional shaking. The solution was filtered to remove tar, treated twice with activated charcoal and extracted with ether. The ether solution was dried with sodium sulfate, then Skelly B (hexane) was added and the solvent evaporated. Refrigeration of the red-yellow oil produced a yellow-brown solid. The product, 2-hydroxyphenylglyoxylic acid, was used without weighing or purification.

The acid was dissolved in 300 ml. of benzene and 200 ml. of Skelly C (heptane). A 15 g. sample of phosphorous pentoxide was added and the mixture refluxed for 30 min. The solution was filtered and evaporated to about 50 ml. The addition of Skelly B produced a yellow solid. This product was quite hygroscopic and quickly became wet in air. The product was redissolved in benzene-Skelly C and refluxed with 30 g. of phosphorous pentoxide. The solution was filtered, evaporated to 50 ml., diluted with Skelly B and cooled. A yellow crystalline product was obtained. The lactone was re-crystallized from benzene-Skelly B and stored in a desiccator, m.p. 128-130°C, lit. 132°C (95). The mass spectrum showed the expected molecular ion at m/e 148.

5-Methyl-2-hydroxyphenylglyoxylic acid lactone - 5-methyl-coumaran-2,3-dione

This compound was prepared from 5-methylisatin by the method described above for the preparation of coumaran-2,3-dione. A 1.0 g. sample of 5-methylisatin was converted to 0.2 g. of pure product, m.p. 146°C, lit. 149°C (96). The IR spectrum (KBr) exhibited strong absorptions at 1820 cm^{-1} , 1745 cm^{-1} , 1720 cm^{-1} , 1610 cm^{-1} and 1600 cm^{-1} . The mass spectrum indicated the expected molecular ion at m/e 162.

Thianaphthenequinone

A 15.4 g. sample of 2-mercaptobenzoic acid (0.1 mole) and a 10 g. sample of chloroacetic acid (>0.1 mole) were

added to 170 ml. of an aqueous solution containing 30 g. of sodium carbonate. The solution was refluxed for 2 hours, then neutralized carefully with 6N hydrochloric acid to pH 5-7. The solution was filtered through a diatomaceous filter aid and the filtrate neutralized to pH 1-2 with hydrochloric acid. The mixture was cooled and the solid product was collected, washed with water and dried at 110°C. The product, 2-carboxyphenylthioglycolic acid, was obtained in a yield of 19.2 g. or 91%, m.p. 212-214°C, lit. 213°C (97).

A 19.2 g. sample of 2-carboxyphenylthioglycolic acid was refluxed with 36 g. sodium acetate in 200 ml. of acetic anhydride for a few hours. The acetic anhydride was removed by vacuum distillation. The residue was extracted with 300 ml. of hot benzene in several portions. The benzene was evaporated and the product vacuum distilled, b.p. 95°C (5-10 mm Hg). The yield of thioindoxylacetate (3-acetoxythianaphthene), a pale yellow oil, was 15.1 g. or 87%. The NMR spectrum, in CDCl_3 vs. TMS, showed a 3 proton singlet at 2.1 ppm (δ) and a 5 proton multiplet at 7.0-7.7 ppm.

The hydrolysis of thioindoxyl acetate to thioindoxyl was carried out under nitrogen to prevent oxidation to thioindigo. A solution of 4.0 g. sodium hydroxide in 50 ml. of water was deoxygenated with nitrogen for 15 min. Then 4.4 g thioindoxyl acetate was added and the mixture deoxygenated for another

20 min. In the inert atmosphere, the mixture was refluxed for 10 min., acidified with 9 ml. of concentrated hydrochloric acid and cooled in ice for several hours. The thioindoxyl was collected and dried under nitrogen. The yield of thioindoxyl was 3.2 g. The product was used without further purification or analysis.

The synthesis of thianaphthenequinone from thioindoxyl was adapted from the methods of Pummerer (98) and Friedländer (99). A 65 ml. solution of 10% sodium hydroxide was deoxygenated and heated under nitrogen. A 3.2 g. sample of thioindoxyl was added to the hot solution. After complete solution was obtained, the solution was cooled to 5°C. A solution of 2.6 g. nitrosobenzene in 30 ml. of alcohol was added dropwise with stirring and cooling. The red precipitate was collected after a few minutes standing in the cold. The crude 2-anil of thianaphthenequinone was recrystallized from aqueous ethanol. The yield of the anil was 3.2 g., or 63%, m.p. 135°C, lit. 151-152°C (98).

The 3.2 g. of thianaphthenequinone-2 anil was refluxed in 100 ml. of 33% sulfuric acid for 3 hours. The solution was filtered hot, the filtrate cooled to room temperature and extracted with chloroform. The chloroform was evaporated leaving a yellow crystalline solid. The product, thianaphthenequinone, was recrystallized twice from benzene-Skelly B, m.p. 118°C, lit. 121°C (99). The mass spectrum indicated

the expected molecular ion at m/e 164. The $p + 2$ peak showed the presence of one sulfur atom per molecule.

3,3-Dimethyl-1,2-indanedione

The diketone was prepared by the sequence of reactions used by Koelsch (100). However, some of the reactions were not as clean as the description of Koelsch so the work-ups were more complicated. A 100 g. sample of mesityl oxide was added slowly to a cold stirred mixture of 180 g. aluminum chloride and 400 ml. of benzene. The mixture was stirred for three hours then ice and 200 ml. of cold 6N hydrochloric acid were added. A 100 ml. quantity of benzene was added and the mixture stirred until all solids were dissolved. The layers were separated and the benzene layer washed with water. The benzene was evaporated and the product fractionally vacuum distilled. IR was used to monitor fractions. A 45.5 g. yield, 25%, of 4-phenyl-4-methyl-2-pentanone was obtained, b.p. lit. 115°C at 11 mm Hg (100). The IR spectrum (CCl_4) showed absorption at 3100 cm^{-1} (arom. C-H), 1600 cm^{-1} (arom. C=O), 700 cm^{-1} (monosubst. arom.), $1700\text{-}1720\text{ cm}^{-1}$ (C=O) and 1390 cm^{-1} (gem-dimethyl).

The 45.5 g. of 4-phenyl-4-methyl-2-pentanone was added to 2 liters of 5.25% sodium hypochlorite solution (Chlorox) containing 31.5 g. sodium hydroxide. The mixture was rapidly stirred for 18 hours at 60°C . The unreacted oil was separated and resubjected to the reaction with another 2 liters of

hypochlorite and 30 g. of sodium hydroxide for 24 hours at 80°C. Each of the aqueous solutions was acidified and extracted with ether. The ether solution was extracted with sodium bicarbonate solution, which was then acidified and extracted with pentane. The pentane solution was dried, partially evaporated and cooled. A white solid was obtained which was recrystallized from pentane. The β -phenylisovaleric acid was obtained in a yield of 12 g., or 26%, m.p. 58°C, lit. 58-59°C (100).

The 12 g. of β -phenylisovaleric acid was converted to 3,3-dimethylindanone-1 by the method of Koelsch (100). An 8.3 g. yield of product, 77%, was obtained, b.p. 95-100°C at 5 mm. Hg, lit. 110°C at 8 mm Hg (100).

The 8.5 g. of 3,3-dimethylindanone-1 was nitrosated with butyl nitrite, as described by Koelsch (100), yielding 3.1 g. of 3,3-dimethyl-2-nitrosoindanone-1, a yellow oil. This was used in crude form in the next reaction.

The 3.1 g. of crude nitroso compound was refluxed 3 hours in a mixture of 10 ml. acetic acid, 3 ml. of 35% formaldehyde and 2 ml. of concentrated hydrochloric acid. The product mixture was cooled and 50 ml. of water added. The product was extracted into chloroform, washed with aqueous sodium carbonate, dried with sodium sulfate and evaporated. The residue was a red liquid. This product was chromatographed on a 50 g. silica gel column with hexane-benzene 85:15 as

the eluent. Three components were observed. The first was a rapidly eluted yellow oil which was not identified. The second component, slowly eluted, was the desired product. The third component was not eluted from the column. The 0.7 g. of product, 3,3-dimethyl-1,2-indanedione, was recrystallized twice from benzene-Skelly B, m.p. 101-102°C, lit. 106-107°C (100). The mass spectrum indicated the expected molecular ion at m/e 174.

N,N-dimethylparabanic acid

A mixture of 12 g. of sodium carbonate in 1 liter of methylene chloride was cooled in ice and stirred. Simultaneously, a solution of 8.8 g. of 1,3-dimethylurea in 100 ml. of methylene chloride and a solution of 15 g. of oxalyl chloride in 100 ml. of methylene chloride were added over a 3 hour period. The mixture was stirred for several hours. The inorganic solid was filtered off and the methylene chloride evaporated. The yield of N,N-dimethylparabanic acid was 12.5 g. or 88%. Part of the material was recrystallized once from ether and twice from ethanol, m.p. 149°C, lit. 149-150°C (101). The IR spectrum (CHCl_3) showed strong absorptions at 1720-1775 cm^{-1} (C=O), 1450 cm^{-1} , 1380 cm^{-1} and 1085 cm^{-1} . No N-H or O-H was detected. The NMR (CDCl_3) exhibited a singlet absorption at 3.16 ppm (δ) vs. TMS.

2,3-Dioxotetrahydroquinoxaline - Quinoxaline-2,3-diol

The procedure of Newbold and Spring (102) was used. A 10.8 g. sample of o-phenylenediamine produced a yield of 9.4 g. of purified 2,3-dioxotetrahydroquinoxaline, m.p. lit 410°C (102). The IR spectrum (KBr) showed weak to medium absorptions at 3400 cm^{-1} , 3050 cm^{-1} , 2950 cm^{-1} and 2860 cm^{-1} and a strong absorption at 1680-1710 cm^{-1} . Evidently the compound exists mainly in the amide form. The mass spectrum exhibited the expected molecular ion at m/e 162.

1,4-Dimethyl-2,3-dioxotetrahydroquinoxaline

The compound was prepared by the method of Newbold and Spring (102). A 3.2 g. sample of 2,3-dioxotetrahydroquinoxaline was converted to 1 g. of product after two recrystallizations from ethanol, m.p. 252°C, lit. 252-253°C (102). The IR spectrum (KBr) showed no N-H or O-H and exhibited strong absorption at 1670 cm^{-1} (C=O). The mass spectrum showed the expected molecular ion at m/e 190.

6-Methyl-2,3-dioxo-1,4-benzdithiane

Reagent grade acetone was dried over anhydrous magnesium sulfate for 24 hours before use of the solvent. A 10 g. sample of oxalyl chloride was slowly added to a solution of 5 g. of 3,4-dimercaptotoluene in 100 ml. of dry acetone. The solution was allowed to stand for several minutes, then was rotary evaporated to 25 ml. and refrigerated. The yellow crystalline product was collected and recrystallized

from benzene. A 0.9 g. yield of 6-methyl-2,3-dioxo-1,4-benzdithiane was obtained, m.p. 173-175°C. The IR spectrum (KBr) showed strong absorptions at 1660 cm^{-1} (C=O), 1640 cm^{-1} and 1590 cm^{-1} (arom. C=C). The NMR spectrum (CDCl_3) showed a methyl singlet at 2.4 ppm (δ) and an aromatic multiplet at 7.1-7.2 ppm vs. TMS. The NMR integration exhibited the 1:1 methyl:aromatic ratio expected. The mass spectrum displayed the expected molecular ion at m/e 210 and the intensity of the $p + 2$ peak indicated that two sulfur atoms were present per molecule.

N,N'-Dimethyloxanilide

A 12.7 g. sample of oxalyl chloride was added to a cold stirred mixture of 22 g. sodium carbonate in 250 ml. of methylene chloride. Then 21.4 g. of N-methylaniline was slowly added. The mixture was stirred for 3.5 hours. The inorganic salt was filtered off. The solution was washed twice with 10% hydrochloric acid, once with water, dried with sodium sulfate and evaporated. The product was treated with activated charcoal in methylene chloride-ether solution then recrystallized twice from methylene chloride-ether. A 16.3 g. yield of N,N'-dimethyloxanilide, 61%, was obtained, m.p. 109-110°C, lit. 110°C (103). The mass spectrum showed the expected molecular ion at m/e 268.

2-Oxo-3,4-dihydroxy-1,2,3,4-tetrahydroquinoline - (quinoline-triol

The compound was prepared by an adaptation of the method of Baeyer (104). A 16.1 g. sample of 2,4-dihydroxyquinoline was converted to 2,4-dioxo-3-oximino-1,2,3,4-tetrahydroquinoline with a 15.2 g. yield after recrystallization, m.p. 211-212°C, lit. 208°C (104). A 10 g. sample of the oxime was heated with stannous chloride in conc. HCl for an hour. The mixture was cooled in a freezer for a few days. The product was collected and recrystallized from water and ethanol. The 2-oxo-3,4-dihydroxy-1,2,3,4-tetrahydroquinoline was obtained with a yield of 2.3 g., m.p. 288°C, lit. >300°C (104). The melting points and IR spectra of three recrystallizations from ethanol were identical. The IR spectrum (KBr) indicated a strong broad absorption at 3300 cm^{-1} and a strong band at 1670 cm^{-1} to 1580 cm^{-1} with peaks at 1610 cm^{-1} and 1590 cm^{-1} . The fingerprint region showed peaks at 940 cm^{-1} (medium), 755 cm^{-1} (medium), 720 cm^{-1} (weak) and 670 cm^{-1} (weak). The mass spectrum exhibited the expected molecular ion at m/e 177.

Elemental analyses

Some of the compounds synthesized did not melt sharply or the melting points were not found in the literature. The elemental analyses of these compounds were obtained, as indicated in Table XIV.

Table XIV. Elemental analyses^a

Compound	Formula	Elements	Calculated %	Found %	
5-Methyldioxindole	$C_9H_9NO_2$	C	66.24	66.66	66.74
		H	5.56	5.57	5.64
		N	8.58	8.65	8.69
5,7-Dichlorodiox- indole	$C_8H_5Cl_2NO_2$	C	44.06	44.25	44.17
		H	2.31	2.30	2.38
		N	6.42	6.29	6.31
		Cl	32.52	32.39	32.41
2-Oxo-3,4-dihydroxy- 1,2,3,4-tetrahydro- quinoline	$C_9H_7NO_3$	C	61.01	60.95	61.06
		H	3.98	4.02	4.08
		N	7.91	7.78	7.84
6-Methyl-2,3-dioxo- 1,4-benzdithiane	$C_9H_6S_2O_2$	C	51.41	51.67	51.55
		H	2.88	2.88	2.84
		S	30.50	32.38	32.40

^aAnalyses were performed by Spang Microanalytical
Laboratory.

VI. CHEMICALS AND SOURCES

Chemical	Source
Potassium <u>t</u> -butoxide	Alpha Inorganics
Calcium hydride	Metal Hydrides, Inc.
Dimethyl sulfoxide	Matheson Coleman and Bell
Hexadeuterodimethyl sulfoxide	Fluka
<u>t</u> -Butyl alcohol	J. T. Baker
N,N-dimethyl formamide	J. T. Baker
Acetonitrile	J. T. Baker
Hexamethylphosphoramide	Mr. D. Lawson
Molecular sieves	Fischer-type 4A
Deuterium oxide	Eastman
Tetra-n-propylammonium bromide	Eastman
Isatin	Aldrich
5,7-Dichloroisatin	Aldrich
5-Methylisatin	Dr. G. Kaupp
N-hydroxyisatin	Dr. T. Kinstle
N-hydroxydioxindole	Dr. P. Bruni
2-Mercaptobenzoic acid	Eastman
Nitrosobenzene	Aldrich
Mesityl oxide	Aldrich
n-Butyl nitrite	Eastman
3,4-Dimercaptotoluene	Aldrich
Oxalyl chloride	Aldrich
1,3-Dimethylurea	Aldrich

Chemical	Source
Parabanic acid	Dr. S. A. Weiner
Tetramethylalloxantin	Dr. M. C. Young
Indoxyl acetate	Aldrich
Benzil	Dr. S. A. Weiner
2,4-Dihydroxyquinoline	Aldrich

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