METAL PROMOTED REACTIONS. I. REACTIONS

OF 1,2,3-THIADIAZOLE. II. OXIDATION

OF OXIMES BY COPPER SALTS

By

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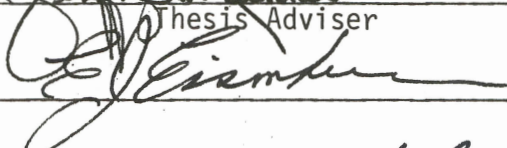for the Degree of
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ACKNOWLEDGMENTS

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REACTIONS OF 1,2,3-THIADIAZOLE

CHAPTER I

INTRODUCTION AND HISTORICAL BACKGROUND

Reactions of 1,2,3-Thiadiazole

Until very recently, the chemistry of 1,2,3-thiadiazole has been a
relatively unexplored area. The first synthesis of a 1,2,3-thiadiazole,
5-anilino-1,2,3-thiadiazole,[1] was reported in 1895. In addition to this
early work, Wolff[2] and Staudinger[3] also reported synthesizing 1,2,3-
thiadiazole compounds. However, these early workers directed their
investigations primarily to their synthetic preparation and the
chemistry of this system was not examined. These early synthetic
routes, and a novel procedure found by Hurd and Mori[4] in 1955, are the
only methods available for the formation of 1,2,3-thiadiazoles. The
latter preparation will be discussed later in the text.

1,2,3-Thiadiazoles (1) are usually regarded as five-membered
aromatic heterocycles. Bond length data obtained from microwave spec-
troscopy[5] indicate, however, that structure 1 with the N(2)-N(3) and

1a; $R^1 = C_6H_5$, $R_2 = H$

1
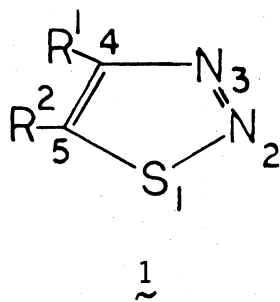
C(4)-C(5) double bonds represents the major resonance contributor. The N(2)-N(3) bond (bond length 1.290 Å) is in fact the shortest bond thus far observed in any heterocyclic aromatic ring. By comparison the N-N bond in pyridazine is 1.330 Å.

As mentioned earlier, several methods exist for the preparation of 1,2,3-thiadiazoles. The method of choice is that of Hurd and Mori,[4] which involves the reaction of an arylhydrazone, containing an methylene group, with thionyl chloride. The synthetic yields are generally excellent. The synthesis is rationalized[4] below (Eq. 1).

$$Y = \underline{e.g.}, \ SO_2\!-\!\!\bigcirc\!\!-\!CH_3, \ -C\!-\!OCH_2CH_3 \ (2)$$
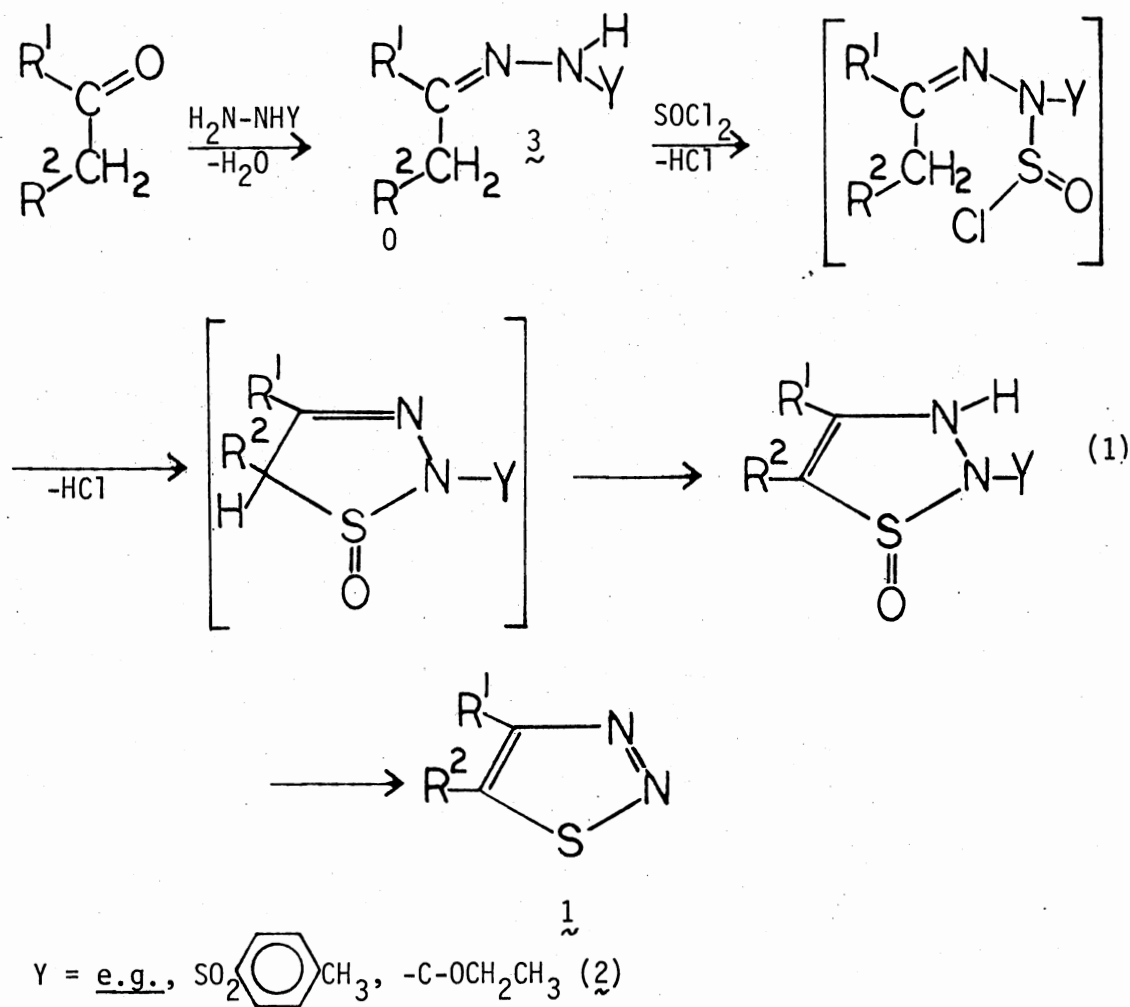
1,2,3-Thiadiazole systems have the potential of eliminating nitrogen from the ring, thereby, forming a reactive intermediate. Thermal or photochemical extrusion of nitrogen is possible. Meir and Buhl[6] have reported that at 230°, 1,2,3-thiadiazole loses nitrogen gas, forming an intermediate which rearranges to thioketene. The structure of the intermediate has not been elucidated but it is postulated to be one of the three following possibilities:[7] a 1,3-dipolar ion 4, a diradical species 5 or a thioketocarbene 6. Coupling of the intermediate species yields several products.[6] The intermediate may dimerize to a 1,4-dithiinene 7 or dimerize and extrude a sulfur atom to yield a thiophene 8. If the intermediate couples with a thioketene, a 1,4-dithiafulvene 9 is produced.
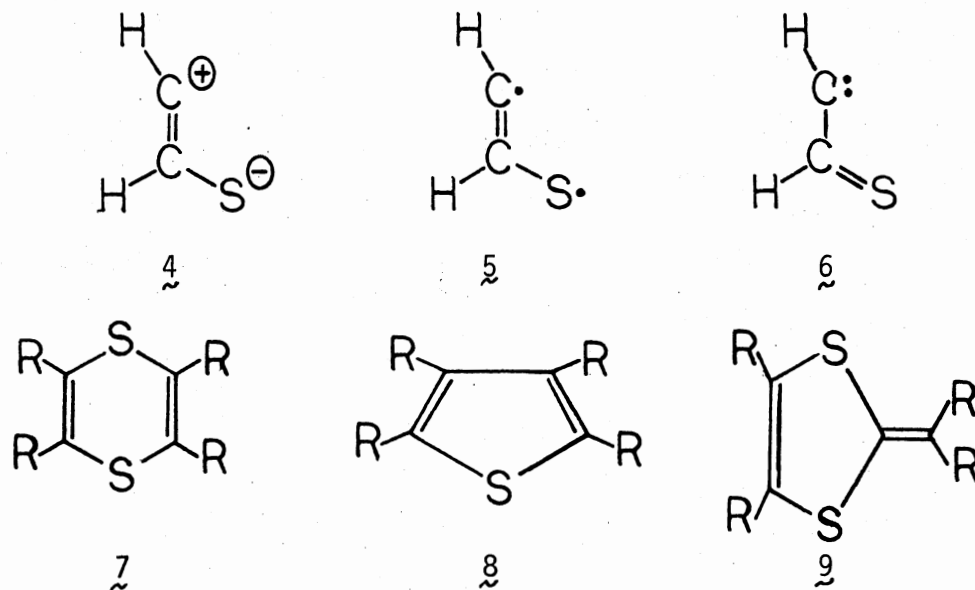
Photolysis of 1,2,3-thiadiazole is believed to also generate one of the three intermediates 4-6.[7] In addition to compounds 7, 8, and 9, compounds 10 and 11 have been obtained from the ultraviolet irradiation of substituted 1,2,3-thiadiazoles.[7]

10   11
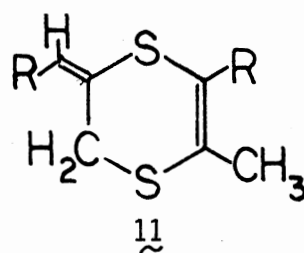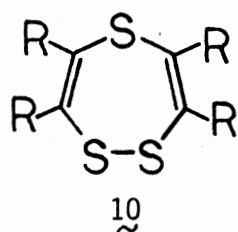
One other possible reaction product is thiirene 12. However, on
the basis of Huckel's aromaticity rule, such a molecule would be ex-
pected to be "antiaromatic" and consequently unstable. The inter-
mediacy of the parent thiirene 12 (R=H) has been observed upon the
photolysis of 1,2,3-thiadiazole in inert matrices.[8] CNDO/2 calcula-
tions regarding the relative stability of thiirene 12 (R=H) and the
thioketocarbene 6 (R=H) indicate that the open chain isomer 6 (R=H)
possesses slightly higher energy and hence thiirene 12 (R=H) is
slightly more stable.[9]

12
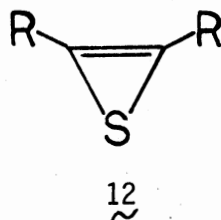
Another interesting reaction of 1,2,3-thiadiazoles proceeding with
the loss of nitrogen involves the formation of an alkynyl thioether.[10]
Like furan, thiophene and thiazole, 1,2,3-thiadiazole 1 (R^2=H) can be
metallated with n-butyl lithium at the five position. However, the
metallated molecule readily loses nitrogen to yield an unusual nucleo-
phile, the alkynyl thiolate 13 (Eq. 2). The acyclic lithium salt 13 is
stable only at temperatures below -65°. Addition of a reactive alkyl-
ating agent at these temperatures yields a stable arylalkynyl thioether
14, which upon hydrolysis produces an arylacetic acid. Consequently,

$$(2)$$

X=Cl,Br,I
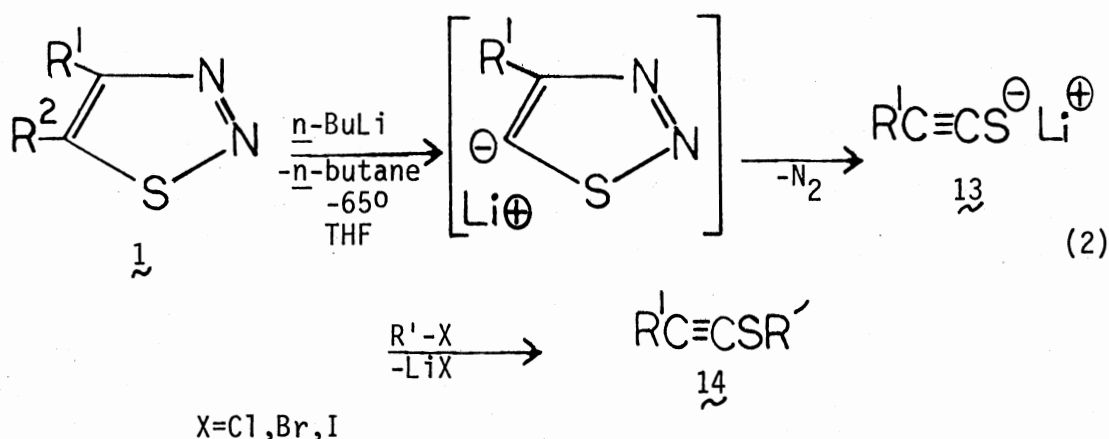
a direct synthetic application of the cleavage reaction of 1,2,3-thia-
diazoles 1 consists of the preparation of arylacetic acids from ketones.

If 4-aryl-1,2,3-thiadiazoles 1 are dissolved in an alcoholic
solution of potassium hydroxide and the resulting mixture is heated to
40°, 1,4-dithiafulvenes 9 are obtained. The formation of 9 can be
rationalized[11] as shown in Eq. 3. As indicated in Eq. 3, 4-aryl-
1,2,3-thiadiazoles afford predominantly cis isomers 9a rather than trans
isomers 9b, presumably for steric reasons.

Oxidation of 1,2,3-thiadiazoles by peracid occurs at the two
position as demonstrated by the conversion of cycloalkenyl-1,2,3-
thiadiazoles (15) to cycloalkenyl-1,2,3-thiadiazole-2-oxides[12] (16)
with one equivalent of peracetic acid (Eq. 4).

Upon the addition of more peracetic acid, 1,2,3-thiadiazole-1,1,2-
trioxides (17) are formed. These experiments suggest that the electron
density is greatest at the nitrogen in the two position. Consequently,
of the several resonance structures 15a-15d that can be drawn, re-
sonance structure 15b may be slightly favored. A similar situation
apparently exists in thiophene.[13]

$$ \text{Ar–thiadiazole} \xrightarrow[\text{EtOH}]{\text{KOH}} Ar C \equiv C S^{\ominus} K^{\oplus} \xrightarrow{\text{EtOH}} \underset{H}{\overset{Ar}{C}} = C = S $$

$$ ArC \equiv CS^{\ominus} \quad \longrightarrow \quad \text{(dithiolylidene)} \xrightarrow{\text{EtOH}} \text{9a} \tag{3} $$

9a

9b

$$ 15 \;+\; \underset{CH_3}{HOOC} \;=\!=\; 16 \tag{4} $$

17
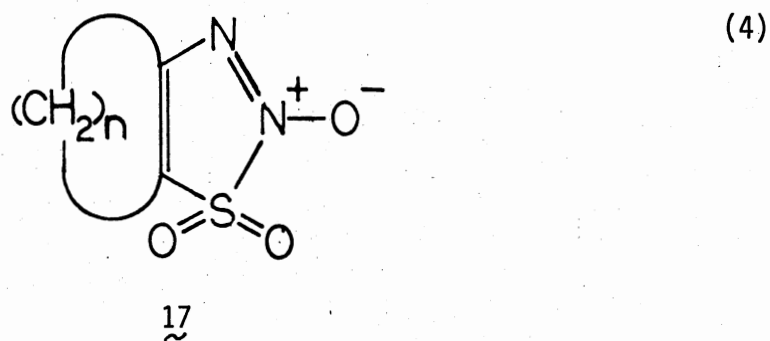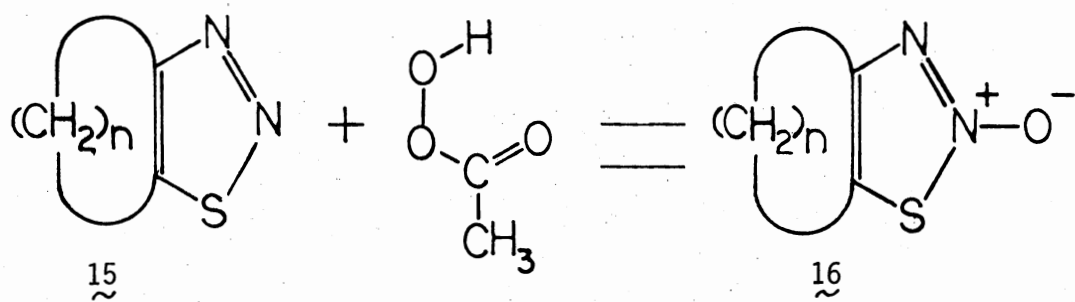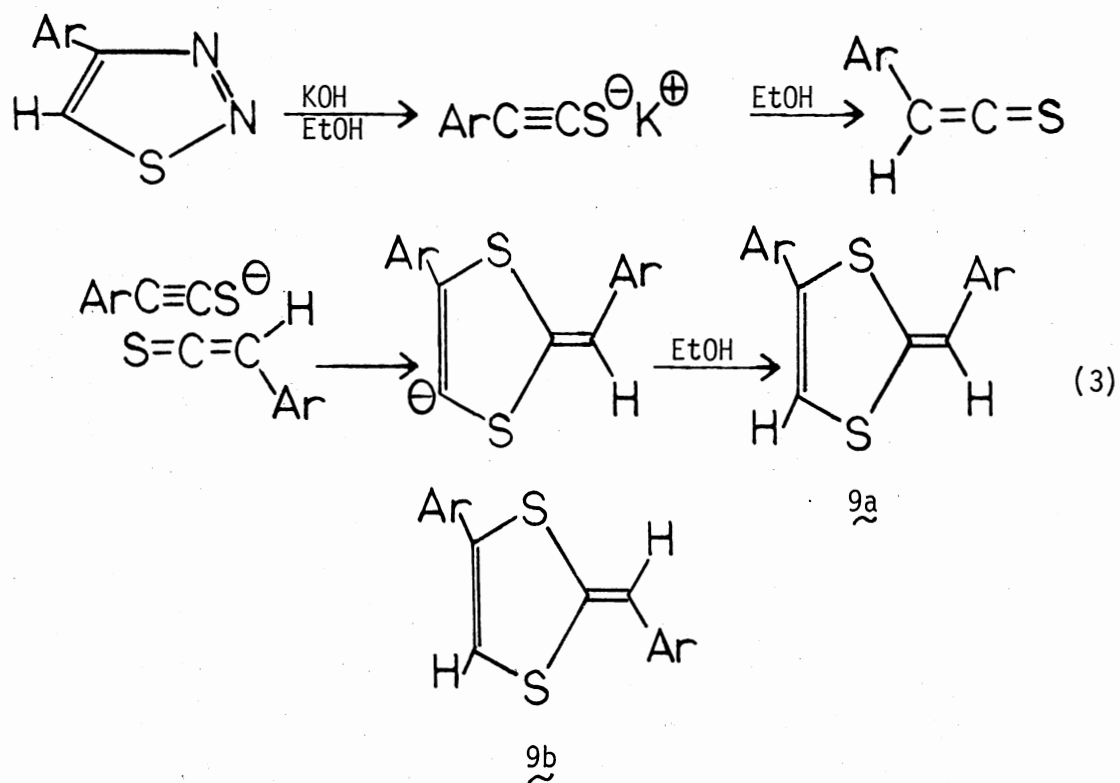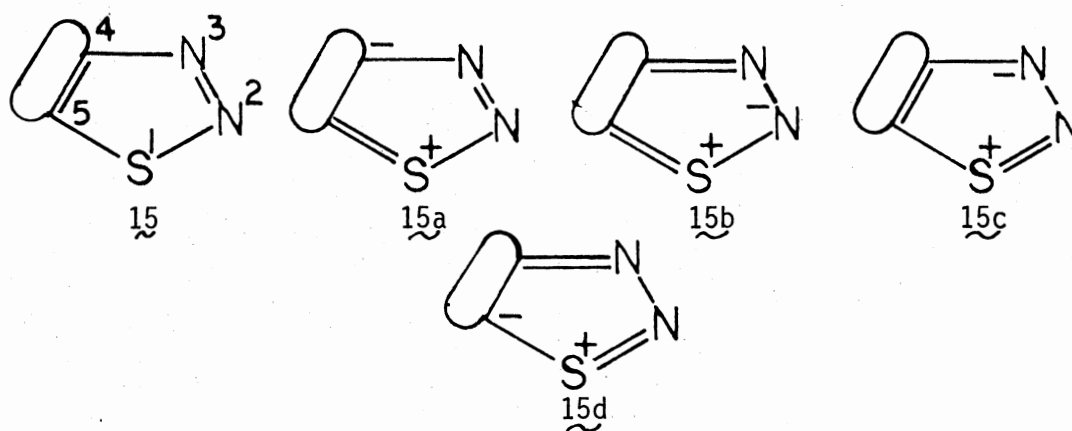
Transition Metal Complexes of
1,2,3-Thiadiazole

Sigma donation is an important mode of transition metal co-
ordination. In order for complexation, via sigma donation, to be
possible, the potential ligand must possess an electronically rich site
or sites. Such a site is usually a non-bonded pair of electrons or a
loosely bound pair of electrons as in the pi system of an olefin or an
aromatic molecule. The Effective Atomic Number Rule[14] (EAN Rule) is
a generalization stating that transition metals in zero or low oxidation
states, form complexes in such a way as to achieve an effective atomic
number equal to that of the next rare gas. Structural predictions of
transition metal complexes are made by using the EAN Rule.

Structural predictions of 1,2,3-thiadiazole complexes may be diffi-
cult since the potential ligand possesses several electronically rich
sites. Complexation of transition metals, with ligands similar to 1,2,3-
thiadiazole has been observed. For example, complexation between Group
6B metal carbonyls and thiazolidine-2-one (18) occurs at the sulfur atom

to yield complex 19.[15] Five carbonyl groups donating ten electrons
(two electrons each) and a non-bonding pair on sulfur, afford the Group
6B metal a closed shell in complex 19.
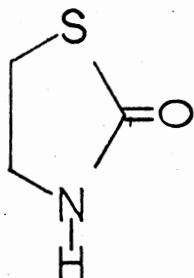
18
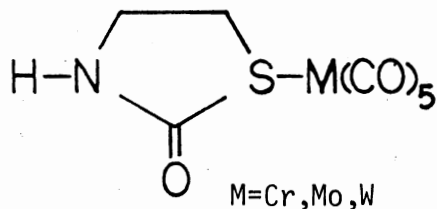
M=Cr,Mo,W

19

Another ligand containing sulfur which complexes to Group 6B
metals is thiophene.[16] Like 1,2,3-thiadiazole, thiophene possesses
two pi bonds. Complex 20 involves both sulfur and the two pi bonds so
that thiophene is a six-electron donor to the transition metal. Iron
(a Group 5 metal), in contrast to the Group 6B metals, does not form
a stable complex with thiophene, but rather extrudes sulfur from the
ring to yield ferrole[17] (21).
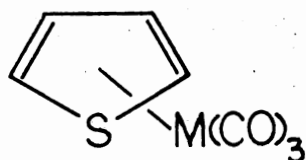
20   M=Cr,Mo,W
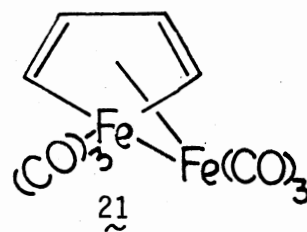
21

Azo compounds, which possess N-N double bonds (c.f., 1,2,3-thia-
diazoles) are an interesting class of ligands owing to their ability to
form a variety of complexes with transition metals. Four types of
complexes have been identified in which the N-N sigma bond remains in-
tact in the coordination.[18] These types of coordination involve one or

both nitrogen lone electron pairs (i and ii, respectively), coordination to the N-N pi bond (iii) and coordination with both lone pairs and the pi bond simultaneously (iv). Complexes of type iii have been prepared[19], but are rare.

i   ii   iii   iv
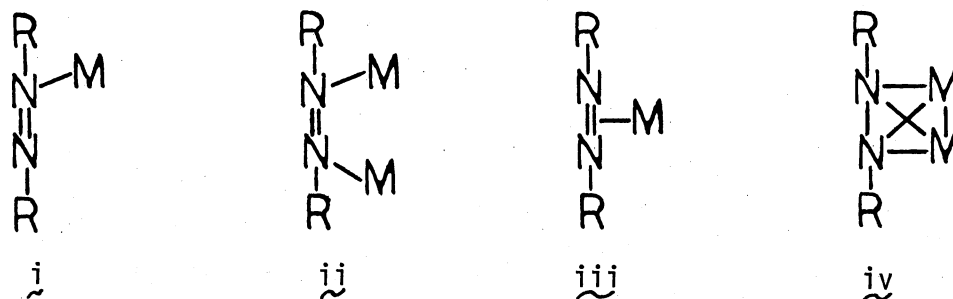
Complex types i and ii have been prepared from a variety of azo compounds and Group 6B metal carbonyls. For example, 2,3-diazabicyclo-[2.2.1] hept-2-ene (DBH) (22) upon treatment with tetrahydrofuran chromium pentacarbonyl affords high yields of 23[20a] (Eq. 5). However,

(5)
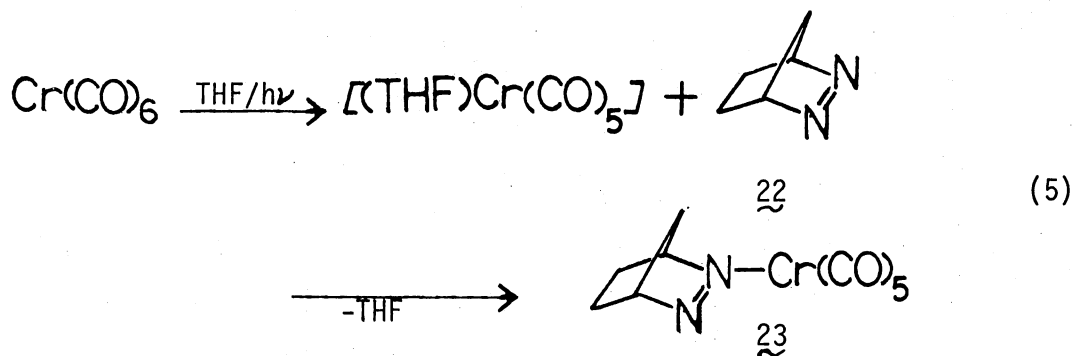
heating complex 23 to approximately 80° yields the complex 24[20a] (Eq. 6).

Iron carbonyls are also known to form azo complexes of structure type i and ii. For example, irradiation of iron pentacarbonyl and DBH (22) yields complex 25[21] in which the azo group donates two electrons (Eq. 7). Complex 25 reacts with further iron carbonyl fragments giving a stable product 26 of structure type iv in which the azo function

donates a total of six electrons to the transition metal.

$$3 \text{ Moles } \underset{\sim}{23} \xrightarrow{80^{o}}$$

$$+ Cr(CO)_6 + 3CO \qquad (6)$$

$$\underset{\sim}{24}$$

$$DBH \ (\underset{\sim}{22}) \xrightarrow[h\nu]{Fe(CO)_5} \underset{\underset{\sim}{25}}{}$$

$$\xrightarrow[-2CO]{Fe(CO)_4} \underset{\underset{\sim}{26}}{} \qquad (7)$$
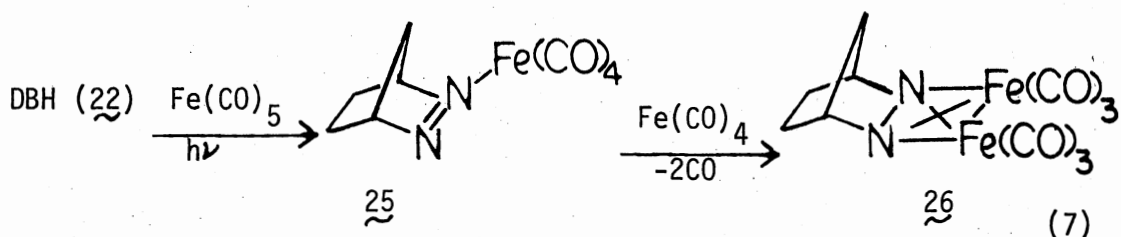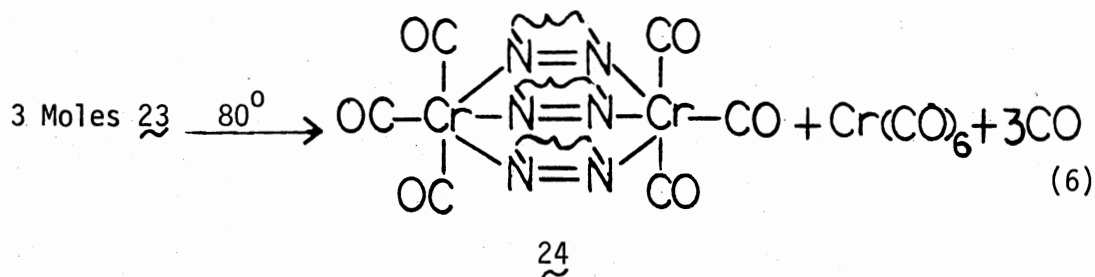
In view of the preceding discussion, 1,2,3-thiadiazole is an interesting potential ligand for complexation with transition metals since it possesses non-bonding pairs of electrons on sulfur, non-bonding electron pairs on the nitrogens, an azo pi bond, an olefinic bond between the carbons and a delocalized pi system over the entire molecule.

Schrauzer and Kisch[9] have reported a reaction of 1,2,3-thiadiazole with iron carbonyl. Diiron nonacarbonyl under thermal conditions, or iron pentacarbonyl under photochemical decomposition, extrudes nitrogen from the 1,2,3-thiadiazole ring yielding the stable thioketocarbene iron carbonyl complex $\underset{\sim}{27}$ (Eq. 8). The complexed organic fragment donates six electrons to the two iron moieties.

The reaction has been studied utilizing an unsymmetrical disubstituted 1,2,3-thiadiazole ($\underset{\sim}{1}$).[22] The results suggest the intermediacy of a symmetrical complex of thiirene; for example, $\underset{\sim}{28}$ or $\underset{\sim}{29}$, which yields

two isomeric products $\underset{\sim}{30}$ and $\underset{\sim}{31}$ (Eq. 9).
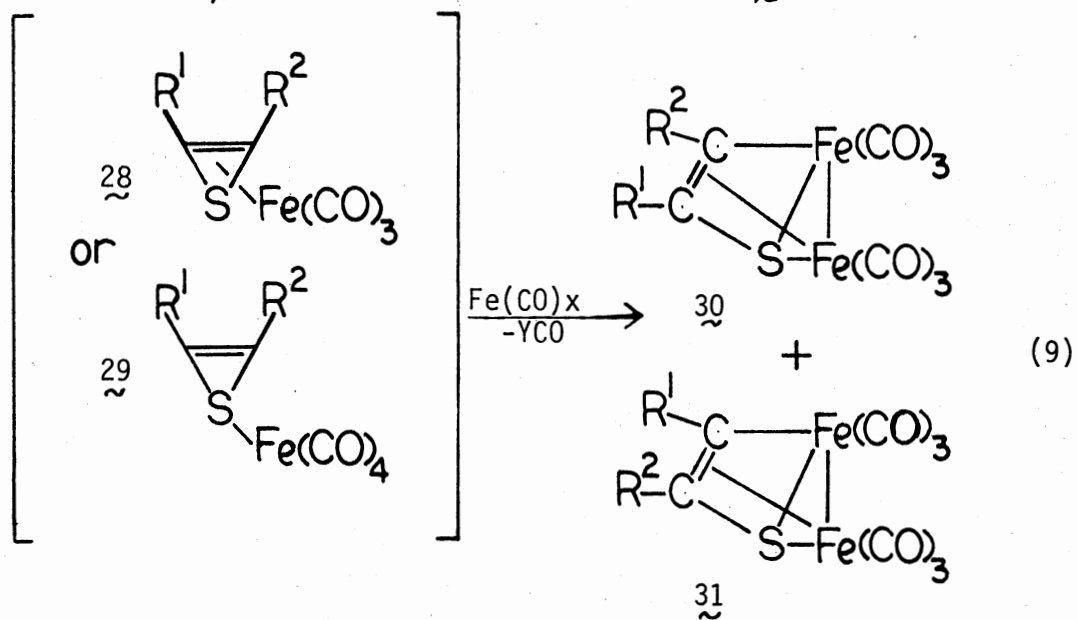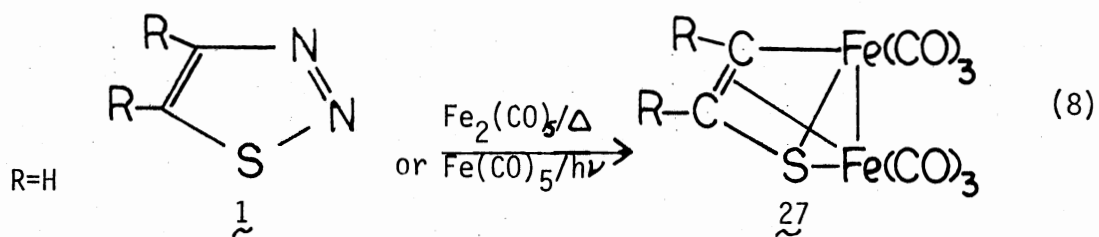
CHAPTER II

STATEMENT OF THE PROBLEM

Group 4A Thioalkynes from 1,2,3-Thiadiazole

As mentioned in the Introduction and Historical Background (p. 5), the synthetic utility of the reaction of the lithium arylalkynyl thiolate with alkylating agents[10] suffers from the fact that the alkylating agent must be added immediately at temperatures below -65°, since at temperatures above -65°, the thiolate couples to yield 1,4-dithiaful-venes. A possible method for trapping and storing the reactive species for later synthetic use would be to allow the thiolate to react with Group 4A metal halides (e.g., a silyl halide) to yield Group 4A alkynylthiols, e.g., the silyl species $\underset{\sim}{32}$ (Eq. 10). The resulting compounds hopefully would be relatively stable and yet undergo facile alkylation at sulfur to give 1-alkynyl thioethers ($\underset{\sim}{14}$).

$$\underset{\sim}{13} + \text{Cl}-\overset{\overset{R^1}{|}}{\underset{\underset{R^3}{|}}{\text{Si}}}-R^2 \longrightarrow RC\equiv CS\overset{\overset{R^1}{|}}{\underset{\underset{R^3}{|}}{\text{Si}}}-R^2 \xrightarrow{R'-X} \underset{\underset{\underset{\sim}{14}}{}}{RC\equiv CSR'} \quad (10)$$

$$\underset{\sim}{32} \qquad X=Cl,Br,I$$
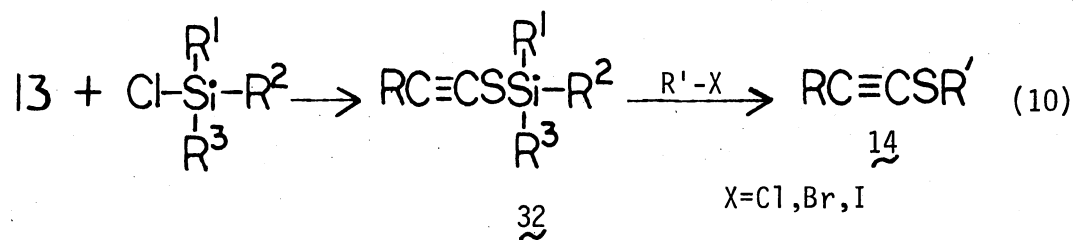
If the Group 4A alkynylthiol prove to be unstable, stability could perhaps be enhanced by complexation of the triple bond with dicobalt octacarbonyl to yield complex $\underset{\sim}{33}$. Dicobalt octacarbonyl is known to react with acetylenes and yield complexes which are stable towards a

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variety of electrophilic reagents.[23] Therefore, perhaps both Group 4A

metal halides and the transition metal species, dicobalt octacarbonyl,

$$RC\!\!-\!\!CSSiR_3$$
$$(CO)_3Co\!\!-\!\!Co(CO)_3$$

33
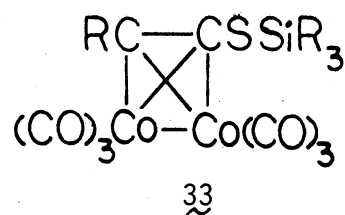
could yield stable compounds which are in effect "masked" or protected

alkynyl thiolates. Regeneration of the thiolates should proceed readily

upon addition of aqueous ferric chloride.[23,24]

The methods described above for trapping and storing alkynyl

thiolates were examined to determine the feasibility and possible

synthetic usefulness.

Transition Metal Complexes Derived

from 1,2,3-Thiadiazoles

Another interesting reaction involving transition metal complexes

would be with the alkynyl thiolate precursor, 1,2,3-thiadiazole. There

are a number of electronically rich sites in the molecule, as stated

in the Introduction and Historical Background (p. 11). Schrauzer and

Kisch[9] have examined the reaction of 1,2,3-thiadiazole with iron

carbonyls. Nitrogen was extruded from the ring and thioketocarbene-

iron complexes were formed. This reaction is particularly interesting

in view of the fact that of the several possible complexes which could

have been formed by analogy to the reactions of other heterocycles,

only the one thiocarbene complex involving the extrusion of nitrogen

was observed. Transition-metal promoted extrusions of small labile

molecules have, of course, been documented previously.[25] Surprisingly,
the reaction of 1,2,3-thiadiazoles with transition metal species other
than iron carbonyls has not been reported. In view of the variety of
interesting complexes which possibly could be prepared and the infor-
mation which could be obtained regarding preferred sites for coordination
and comparative reaction modes for different transition metal species,
it was deemed of interest to examine the reaction of a 1,2,3-thiadiazole
with several transition metal species, esp. Group 6B metal carbonyls.

The products obtained from complexation of 1,2,3-thiadiazoles and
iron carbonyls suggest that a thiirene complex (28 or 29) was an
intermediate[22] (p. 11). However, the complex was apparently unstable
and was not isolated. Other transition metals (e.g., Cr, Mo and Co)
might also extrude nitrogen but, perhaps in contrast to iron, form
stable complexes of thiirene (12). This would prove useful in trapping
the elusive thiirene to study the chemical and physical properties of
the molecule in various media rather than being confined to studying
the species in inert matrices[8] at low temperatures. Also, the complex
might prove to be sufficiently stable to permit the storage of thiirene
(12) until it is needed in synthesis. The ability of transition metals
to stabilize and to effectively store highly reactive organic species
for eventual synthetic use has been demonstrated previously.[26a,b]

Another possible reaction of transition metals with 1,2,3-thiadia-
zole would be the extrusion of sulfur from the ring with replacement or
insertion by the metal into the ring to give compound 34. Precedent
for this type of reaction is found in the reaction of iron carbonyls
with thiophene[17] (see page 9). Also, nitrogen could be extruded from
complex 34 to give the highly strained complex 35. This would be in-

teresting since the complex 35 is one valence bond description of an acetylene complex.[27a,b] Consequently, a direct synthetic application of the complex formation from 1,2,3-thiadiazole (1) consists of the preparation of acetylenes from ketones (see p. 3).
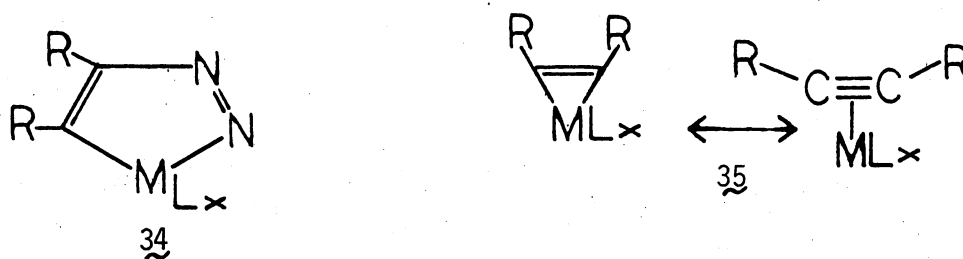
Another interesting and possible reaction of 1 with transition metals would involve the 1,2,3-thiadiazole (1) pi system and produce compound 36. This type of reaction would be interesting in that 1,2,3-thiadiazoles could be potential ligands in the metallocene 37. Also, the coordination of the pi system in 36 and 37 would represent other examples of the rare azo complex type iii (p. 10). The transition
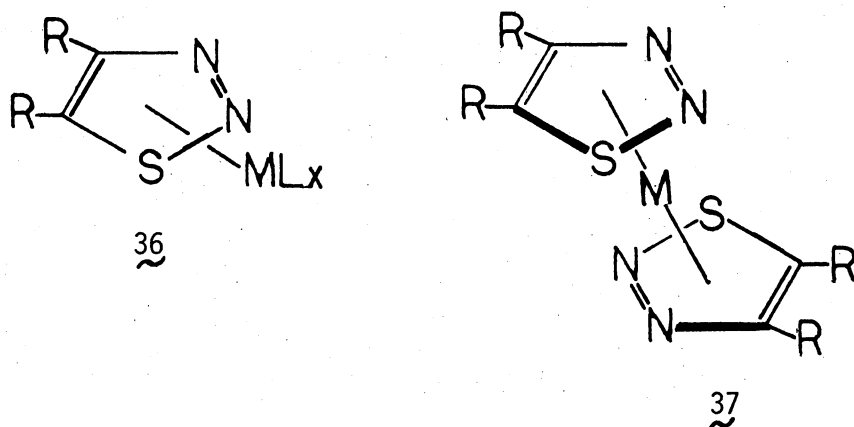
metal would be complexed to the N-N pi bond as well as to sulfur and the C-C pi bond. Additionally, complexation by the transition metals to 1,2,3-thiadiazole could occur at the olefinic bond to give 38, at either of sulfur's lone electron pairs to give 39, or at the electron

pairs on either nitrogen to give 40 or 41.

$$\underset{\sim}{38}$$

$$\underset{\sim}{39} \quad MLx$$

$$\underset{\sim}{40}$$

$$\underset{\sim}{41} \quad \begin{array}{ll} a: & M = Cr \\ b: & M = Mo \end{array}$$
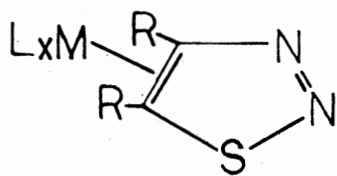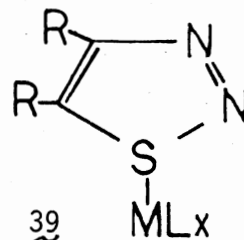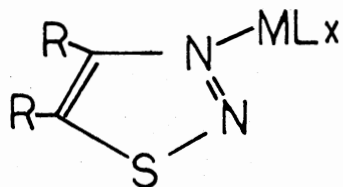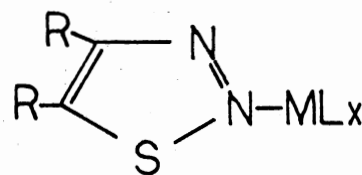
In view of the foregoing discussion, the reactions of 1,2,3-
thiadiazoles with Group 6B metal carbonyl species were to be examined.

CHAPTER III

RESULTS AND DISCUSSION

Group 4A Thioalkynes from 1,2,3-Thiadiazoles

As indicated in the Introduction and Historical Background, aryl-
alkynyl thiolates (13) are very reactive species. These species tend
to readily couple to form 1,4-dithiafulvenes (9) at low temperatures
(see p. 6). For synthetic utility, the addition of the thiolate 13 to
alkyl halides and acyl halides, offers a valuable method of introducing
thioacetylenes into molecules. This functionality is of considerable
interest in natural product chemistry, since it potentially can serve
as a valuable precursor to other types of compounds. If a stable
alkynyl thiolate 13 could be generated and be easily stored but at the
same time remain sufficiently reactive for synthetic use, then time
and effort for its preparation in the laboratory could be saved. One
possible method of trapping and "stabilizing" the thiolate 13 would
entail their reaction with silyl halides. Silyl halides are known to
react with nucleophiles such as thiolates. Also silicon groups may
tend to stabilize the thiolate through $(p \rightarrow d) \pi$ bonding.[28] Silicon
would be ideal because silyl groups presumably would be easily cleaved
from sulfur with the addition of alkylating agents (e.g., methyl iodide).
Nucleophiles tend to attack the silicon effecting S-Si cleavage.[28]

The preparation of silyl alkynylthiol 32 has not been reported;

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consequently, the preparation of these compounds would afford a new class of compounds which hopefully would exhibit interesting chemistry.

As mentioned earlier (p. 5), arylalkynylthiolates (13) can be generated from 4-aryl-1,2,3-thiadiazole (1). 4-Phenyl-1,2,3-thiadiazole (1a) was used to generate the reactive 1-phenylethynyl thiolate (13) since 1a was easily prepared from common reagents.

t-Butyldimethylsilyl chloride (42) was used as the silylating agent since it was commercially available and contained bulky alkyl substituents. Since the first step of the undesirable coupling of the thiolate species to afford 1,4-dithiafulvenes appears to be rearrangement to the thioketene (p. 6), bulky alkyl groups may inhibit the rearrangement because of steric hindrance. Therefore, hopefully, the bulky silyl group would bond to sulfur and stabilize the thiolate species in the form of the silylalkynylthiol 43.
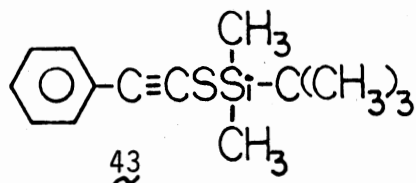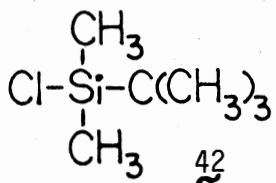
t-Butyldimethylsilyl chloride (42) was added at low temperature to the alkynylthiolate (13) solution, and the resulting solution was allowed to come to room temperature. An IR spectrum of the solution indicated that an acetylene was present in the solution (absorption at 2160 cm^{-1}). However, after two hours of continued stirring, the IR spectrum no longer possessed an absorption band corresponding to the acetylene. After work up, several compounds were isolated, 1,4-dithiafulvene (44) and three possible silylated substituted 1,4-dithiafulvenes (45-47). Compound 43 was not detected by mass spectrometry or IR

spectrometry. The identity of the reaction products was established

by NMR spectroscopy and mass spectrometry. The NMR spectrum of 44 also

44

45

46

47
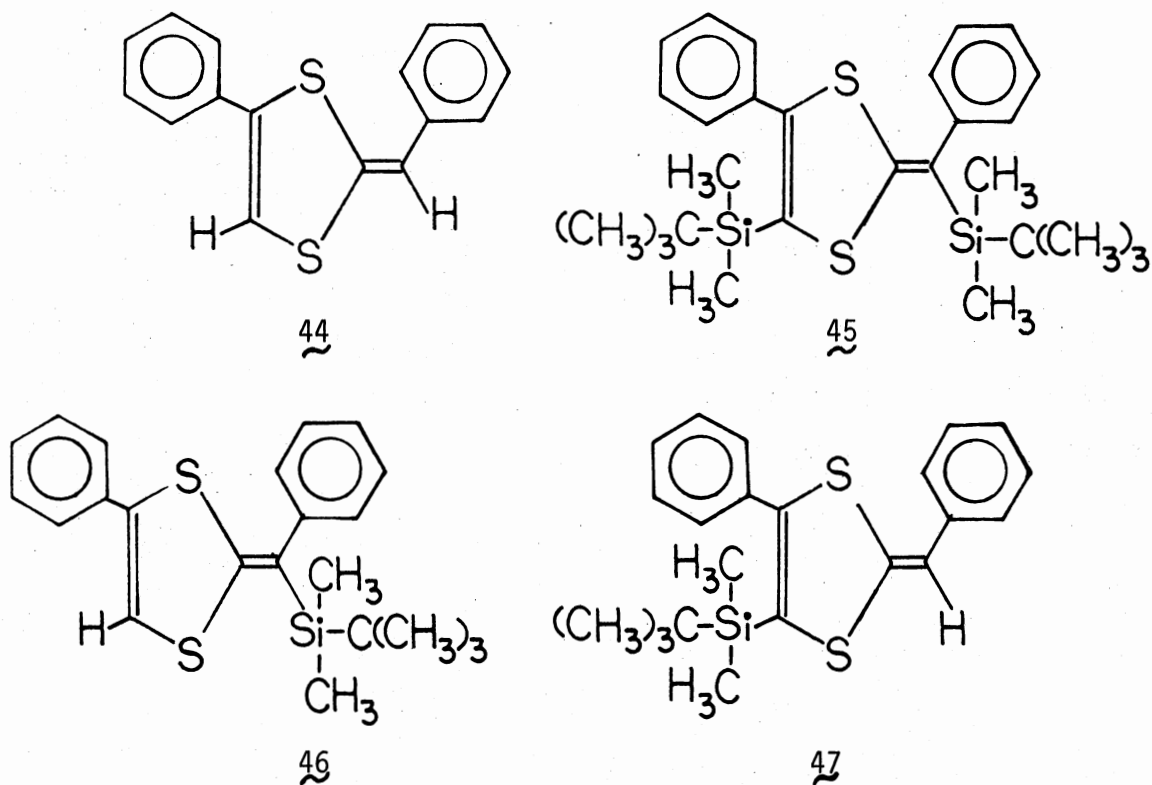
indicated that the compound was the cis isomer. The melting point of

44 agreed with that reported in the literature. Compound 44 was formed

from the hydrolysis of 45. The stereochemistry of the bis-silyl 1,4-

dithiafulvene is believed to be in the cis configuration as shown in

45. It was reported[11] that the cis configuration of 9a was the kinetic

product. Therefore, if 45 was in the trans configuration, the trans

product 44 would be the expected product. However, this is not the

case. The silylated 1,4-dithiafulvenes have not been previously re-

ported. From the compounds 44-47 which were isloated, it appeared

that, if indeed, the silylalkynylthiol 43 was initially formed as

suggested by IR examination of the reaction mixture, the compound

unfortunately readily couples to form 1,4-dithiafulvenes.

During the course of this investigation a relatively stable silyl-
alkynylthiol 48 was reported by British workers.[29] Remarkably, 48 was
reported to be stable when heated although temperatures were not cited
in the report. Apparently, the substituent bonded to the C-C triple
bond must be large to afford stability by preventing facile coupling
of the silylalkynylthiol 48.

$$H_3C-\underset{\underset{H_3C}{|}}{\overset{\overset{H_3C}{|}}{C}}-C\equiv CSSi(CH_3)_3$$
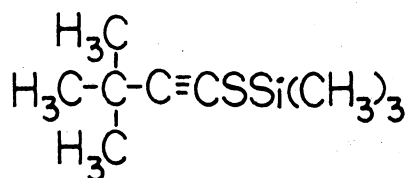
48

A possible method for stabilizing the reactive silylalkynylthiol
32 would involve complexation of the C-C triple bond with transition
metals. Complexation of alkyne 13a was attempted by addition of di-
cobalt octacarbonyl to a solution believed to contain 13a (prepared as
mentioned above) at 25°. The reaction mixture was stirred for one day,
and worked up. Two materials were isolated. Spectroscopic data in-
dicate that one material was tetracobalt dodecacarbonyl.[30] The other
material failed to melt at a temperature less than 300° and was in-
soluble in pentane, benzene, THF and dichloromethane. It was only
partially soluble in ether. Spectroscopic data have been accumulated,
but assignments of the absorption bands have not been made due to the
complexity of the mass and NMR spectra. The IR spectrum indicated the
presence of a cobalt carbonyl moiety (2050 cm^{-1}). The mass spectrum
contained peaks beyond the limit of the instrument (650 m/e) indicating
a high molecular weight compound. The chemical and physical properties

of the material indicate a polymeric compound. Apparently, if the acetylene dicobalt hexcarbonyl complex did initially form, the complex was not stable under these conditions. It is possible a transition-metal promoted polymerization could occur; either from the silylalkynyl-thiol 43 or the silylated 1,4-dithiafulvene (45).

The work indicated that under the conditions used in the reaction (e.g., Group 4A element, the substituents of the Group 4A element, solvent and temperature) the silylalkynylthiol 43 was unstable and could not be easily isolated. Also, the attempted stabilization of 43 with dicobalt octacarbonyl did not afford a stable silylalkynylthiol complex 33. In view of the pronounced instability of the majority of the silyl-alkynylthiols 32 reported,[29] the project was terminated.

Transition Metal Complexes Derived
from 1,2,3-Thiadiazoles

In view of the number of electronically rich sites present in 1,2,3-thiadiazoles (1), complexation by transition metals could afford a number of interesting complexes (see p. 15). Complexation of 1,2,3-thiadiazole with Group 6B metals was obtained by two different methods. The first method involves the initial formation of trisacetonitrile chromium or molybdenum tricarbonyl.[31] 4-Phenyl-1,2,3-thiadiazole was added to the acetonitrile complex to give a possible dimer, which will be discussed later, and 4-phenyl-1,2,3-thiadiazole chromium or moly-bdenum pentacarbonyl (41a or b). The second method involves the initial formation of THF chromium or molybdenum pentacarbonyl.[32] After the addition of 1a, the product which is isolated is, again, 4-phenyl-1,2,3-thiadiazole chromium or molybdenum pentacarbonyl (41a or b).

Spectroscopic evidence suggests that the pentacarbonyl complexes prepared by the two different methods are, indeed, the same. The IR spectrum gave metal carbonyl absorption bands characteristic of sulfur or azo complexes of Group 6B metal.[15,20a] The mass spectra indicates that the compounds are indeed pentacarbonyl complexes.

The dissociation of the complexes imposed serious problems in the structural elucidation and purification of the complexes. Column chromatography with deactivated, acid-washed alumina afforded the best method of purification thus far examined. The initial purification method involved the recrystallization of the chromium pentacarbonyl several times at -70°. The resulting bright yellow complex melted at $73-75^{\circ}$. The melting point appeared to be unusually low; the free ligand, 4-phenyl-1,2,3-thiadiazole melts at $77-79^{\circ}$.[10] The IR spectrum of the material showed strong $C \equiv O$ stretches characteristic of a pentacarbonyl complex; however, an absorption band at 1225 cm^{-1},[33] assignable to a mode of the free ligand, was also observed. The presence of the free, uncomplexed thiadiazole was also suggested by NMR examination of the material. In order to determine the efficiency of the recrystallization techniques, the complex was recrystallized three times in pentane. After each recrystallization an IR spectrum was obtained, and each time the intensity of the 1225 cm^{-1} band was compared to that of the 1950 cm^{-1} band. After each recrystallization, the 1225 cm^{-1} band became more intense by approximately 20% and only 81% of the sample was recovered. This phenomenon was observed for degassed acetone, benzene, diethyl ether, THF, carbon disulfide and Skelly B. The greatest increase in the 1225 cm^{-1} band, 35%, came from recrystallization from either ether or THF; whereas, the use of acetonitrile gave

no detectable dissociation. These observations clearly indicate that the complex easily dissociates to give the free ligand in solution and as a consequence, recrystallization is not an efficient purification method for these species. It was also observed that the 4-phenyl-1,2,3-thiadiazole molybdenum complex (41b) dissociates more readily than the chromium pentacarbonyl complex. The reason for this observation is not understood, but similar observations regarding the relative ease of dissociation have been reported with other azo complexes of Group 6B metals.[20b] The dissociation of the complexes imposed problems in the structural assignments. Examination of the complexes in solution for extended periods of time could not be made. For example, the ^{13}C NMR spectra took several hours to obtain and within that time, the complexes had dissociated. The resulting spectra were identical to that obtained from uncomplexed 4-phenyl-1,2,3-thiadiazole. Another example of the dissociation problem was encountered when crystals were being grown for X-ray crystallographic analysis. Since the crystals are slowly grown in solution, the complex dissociated, liberating free 4-phenyl-1,2,3-thiadiazole (1a) which co-crystallized with the remaining complex. This resulted in impure complexes.

Purification and crystal formation were attempted by sublimation; unfortunately, the complexes did not sublime. Attempts to sublime the complexes at room temperature for several hours resulted in complex dissociation. Since dissociation is a major problem, analytically pure samples have not as yet been prepared. As a consequence, elemental analysis has not yet been obtained.

Although the complexes are slightly contaminated by 4-phenyl-1,2,3-thiadiazole (1a), several observations can be drawn from the spectro-

scopic data. First, the mass and NMR spectra suggest that, unlike iron carbonyls, carbonyl species of chromium and molybdenum do not extrude nitrogen or sulfur from the thiadiazole. This observation may be a reflection of the facile dissociation of the complex, i.e., a reflection of the fact that 4-phenyl-1,2,3-thiadiazole (1a) is a poor ligand for Group 6B metals. The metal may not complex strong enough to the azo function to extrude nitrogen from the ring. The same argument may explain the failure to observe extrusion of sulfur from the ring.

Second, the complex definitely does not involve pi complexation to the thiadiazole ring as a whole. This is evident from the IR and mass spectra. If the EAN rule is obeyed, and assuming the pi system of the ligand donates six electrons, then the Group 6B metal can only have three carbonyl groups. However, the IR and mass spectra clearly shows the presence of a metal pentacarbonyl moiety. A possible explanation for the formation of the pentacarbonyl complex is, that as the metal approaches the complex the most electronically rich site which the metal encounteres is a non-bonding pair on either nitrogen or sulfur. In addition, the phenyl group may inhibit complexation of the metal at the olefinic function in the ring.

Last, complexation does not occur at the phenyl group in the thia-diazole. Spectral evidence again provides the basis for this claim. Were complexation to occur at the phenyl group, the IR spectrum would show a tricarbonyl pattern for the complex, but as stated above this was not observed. Additionally, the NMR spectrum would exhibit an up-field chemical shift for the absorptions of the phenyl protons relative to those of the free ligand. The failure to observe complexation with the phenyl group is perhaps due to the fact that 1,2,3-thiadiazole is a

strong electron withdrawing group and as a consequence the electron density in the phenyl ring is sufficiently diminished to prevent facile complexation.

In view of the previous discussion, presumably, as seen in other heterocyclic complexes, one of the heteroatoms in the thiadiazole ring is the electronically rich site for coordination. As to which heteroatom only one supportive argument can be made. As stated earlier (p. 6) the oxidation of thiadiazole by peracid occurs at the two position,[12] suggesting that the electron density is highest at this position. If that assumption is correct then, the most stable complex might involve complexation at the two position.

When comparing the product formation in the reaction of $\underset{\sim}{1a}$ with iron carbonyls or Group 6B metal carbonyls, clearly, extrapolation of the behavior of one metal to another cannot be made when examining heterocyclic ligands.

In addition to the pentacarbonyl complexes, the complexes referred to as dimers A and B in the experimental methods were also isolated from the reactions of trisacetonitrile chromium or molybdenum tricarbonyl and $\underset{\sim}{1a}$. These dimers, as were the pentacarbonyl complexes, were difficult to purify. Recrystallization with several different degassed solvents was attempted, but in each case rapid decomposition of the complex occurred. The best solvent system was a 1:10:4 mixture of acetonitrile, dichloromethane and pentane, respectively. Acetonitrile was added to stabilize the complex; without this solvent, the dichloromethane and pentane solution gave rapid decomposition of the complex. In degassed acetonitrile alone, the complex is stable for several hours. The material was chromatographed over deactivated,

acid-washed alumina to yield mainly the pentacarbonyl complex suggesting

possibly, that the complex may be a dimer. Spectroscopic evidence also

suggests the material to be a dimeric complex. The IR (CH$_3$CN) spectrum

for the chromium complex gives a strong absorption band at 1840 cm^{-1}.

The frequency for this band is too low to be due to a terminal carbon

monoxide ligand. Also, the frequency is too high to be due to an

organic carbonyl absorption such as a ketone or an ester. Presumably,

the absorption is due to a bridging carbonyl group[34] (49). The NMR

spectrum shows an absorption for the thiadiazole ring proton with the

same chemical shift as the pentacarbonyl complexes. The mass spectrum

of the chromium complex, however, does not show a parent ion which

corresponds to the molecular weight of the presumed dimer. A peak is

present corresponding to the parent ion of 4-phenyl-1,2,3-thiadiazole

$$LxM \overset{\overset{\displaystyle O}{\|}}{\underset{49}{\triangle}} MLx$$
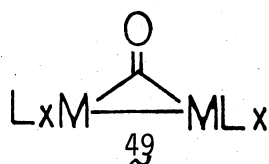
chromium pentacarbonyl (41a); the peak is also the highest m/e in the

spectrum. Therefore, two conclusions can be drawn. First, the sample

may contain a small amount of the pentacarbonyl complex, or second,

the injection of the complex into the ionization chamber instantaneously

cleaves the "dimer" to yield the pentacarbonyl complex which would then

give the corresponding pentacarbonyl complex spectrum. Also, the addi-

tion of carbon monoxide to the molybdenum "dimer" (50a) rapidly yields

the pentacarbonyl complex in high yield; the amount of 4-phenyl-1,2,3-

thiadiazole was less than 12% of the total yield. This suggests a

dimer is adding carbon monoxide, cleaving and forming two equivalents

of the pentacarbonyl thiadiazole complex 41b (Eq. 11). If carbon

monoxide is bubbled into a solution of the presumed dimer in acetonitrile
for an extended period of time, the prominent product is molybdenum
hexacarbonyl. However, if triphenylphosphine is added to a solution of
the "dimer" 50a, the formation of the triphenylphosphine molybdenum

$$50 \quad \begin{array}{l} a: \quad M = Mo \\ b: \quad M = Cr \end{array}$$
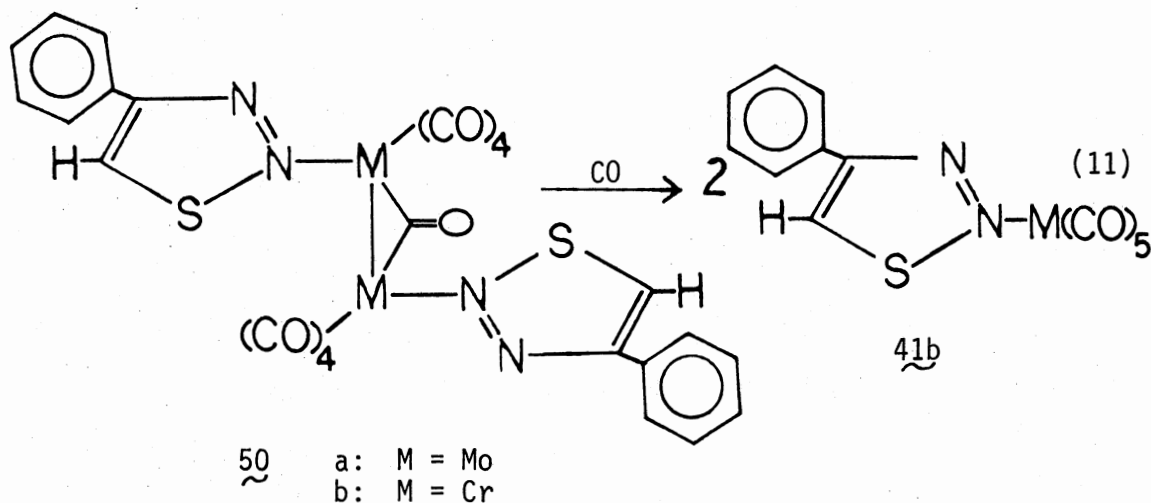
complex is not observed. The results of the last experiment may be
explained by steric factors. Before metal induced reactions can occur,
the metal must first coordinate to an electronically rich site on the
reactant. However, in the case of the dimer, the coordinated ligands
may "protect" the metal so that the bulky triphenylphosphine cannot
initially coordinate to metal, hence no reaction can take place under
the conditions used in the experiment.

If, indeed, the complex 50 is dimeric, this would be another
example of Group 6B metal carbonyl complexes in which a labile group
(i.e., S or N_2) was not extruded from the ring. The metal must be co-
ordinated to an electronically rich site in the ring, presumably a
heteroatom. The only suggestive evidence as to which heteroatom is
coordinated to the metal is that which was presented earlier. The
oxidation of 1,2,3-thiadiazoles by peracid[12] suggests the electron

density is the greatest at the two position in the ring.

Another transition metal system which may complex to 4-phenyl-1,2,3-thiadiazole (1a) is cyclopentadienyldicarbonyl iron dimer 51.

51
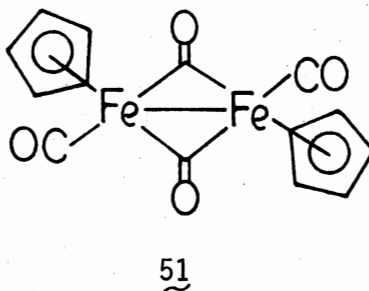
This transition metal system is similar to the iron carbonyl species which Schrauzer and Kisch[9] used to extrude nitrogen from the 1,2,3-thiadiazole ring. By analogy, the complex 51 may promote the extrusion of nitrogen. The reaction was performed at 90° in toluene. Schrauzer and Kisch[9] also used elevated temperatures to effect their reactions. After work up, two products were isolated. Spectroscopic data has been accumulated but definitive interpretation of the data has been difficult. The IR spectra clearly indicate the presence of transition metal carbonyls in both products. The IR spectra also indicate that both products possess terminal and bridging carbonyls. The NMR spectra for both complexes indicate two regions of absorption, one in the aromatic region (the proton on the thiadiazole ring 1a may have shifted upfield after complexation) and the other in the region corresponding to the absorption of metallocyclopendienyl protons. The integrated spectra indicate the presence of two cyclopentadienyl, two phenyl and two vinyl groups. Consequently, two equivalents of the 1,2,3-thiadiazole (1a) have reacted with one equivalent of complex 51. The mass spectra, however, point to complexes similar to that prepared by Schrauzer and Kisch,[9] in which one equivalent of 1,2,3-thiadiazole complexes to one

equivalent of diiron nonacarbonyl with the extrusion of nitrogen from the thiadiazole. The mass spectra indicate empirical formulas suggesting, by analogy to Schrauzer and Kisch's complex, thioketocarbene complexes. If the complexes are indeed thioketocarbene complexes, two isomers would be possible. The mass spectra for both complexes are similar. The reaction of 1a with diiron nonacarbonyl apparently proceeds through a symmetrical intermediate 28 or 29, which ultimately upon isolation of the final products, yielded two positional isomers.[22] By analogy a similar symmetrical intermediate (e.g., 52) could also be formed in the complexation with complex 51. Loss of carbon monoxide

52
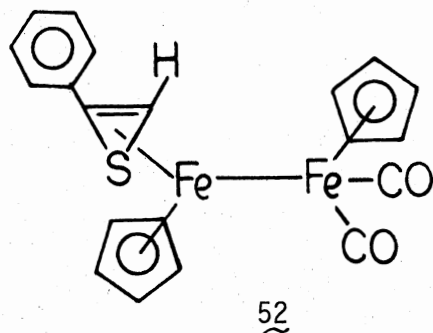
from intermediate 52 could give the thioketocarbene complexes 53 and 54. However, the IR and NMR analysis did not confirm structural assignments for complexes 53 and 54. A better description for the complexes may be 55 and 56.

53

54
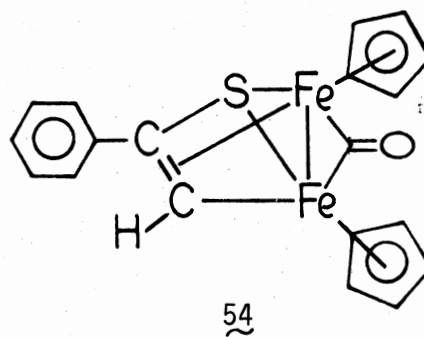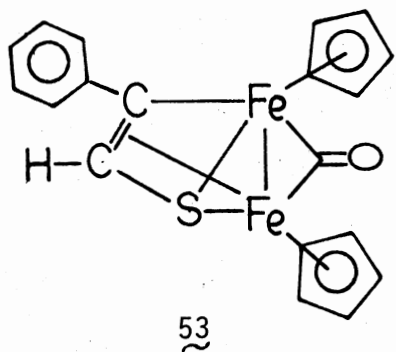
The complexes may have formed from the dimerization of thiirene $\underline{12}$ in complex $\underline{52}$. The complexes $\underline{55}$ or $\underline{56}$ would show the observed NMR and IR spectra, yet could instantaneously cleave in the mass spectrometer to give the observed spectra of complexes $\underline{53}$ or $\underline{54}$.
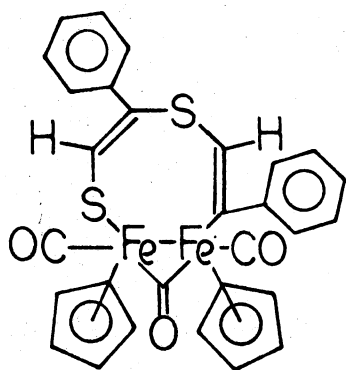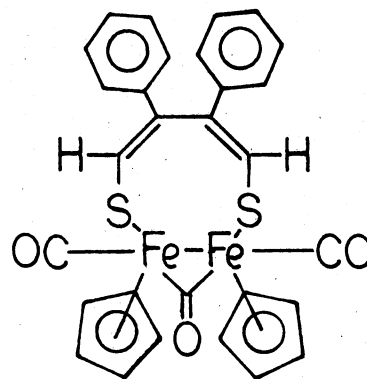
$$\underset{\sim}{55} \qquad\qquad\qquad \underset{\sim}{56}$$

Clearly, detailed structural assignment must await crystallographic analysis. Although the structures are unknown, the fact does remain that nitrogen was extruded from the $\underline{1a}$ ring. This mode of coordination to 1,2,3-thiadiazole fragments represents another example of the various types of complexes which can occur with 1,2,3-thiadiazoles. Also, it was interesting that a complex of the type $\underline{iv}$ was not isolated. Type $\underline{iv}$ azo complexes, as mentioned earlier[21] (p. 10), are commonly formed from iron carbonyls and azo compounds $\underline{57}$.
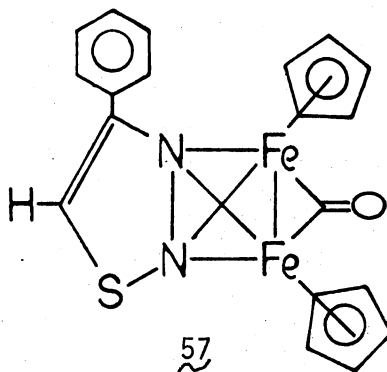
$$\underset{\sim}{57}$$

Another ligand similar to 1,2,3-thiadiazole was the by-product from the silylalkynylthiol work. It was of interest to determine what kind of complex could occur with 1,4-dithiafulvenes 44, and diiron nona-carbonyl. The reaction initially performed in ether at room temperature, failed to yield a complex. The reaction performed in n-hexane at elevated temperatures, however, was more rewarding. After work up of the reaction, spectroscopic evidence suggested that a complex was indeed formed. An IR spectrum of the purified complex indicated that the complex was an iron tetracarbonyl. An NMR spectrum revealed that fragmentation of 44 had not occurred. Presumably, coordination of the iron is at one of the sulfur atoms, since ostensibly they are the most electronically rich sites in the dithiafulvene 58. This complex is interesting since it is somewhat similar to thiophene. However, un-like thiophene, iron moieties did not extrude sulfur from the ring.[17] Therefore, extrapolation of the reactions involving one heterocyclic complex to another can not be made and clearly, more research is needed in the field of transition metal complexation to heterocyclic compounds.
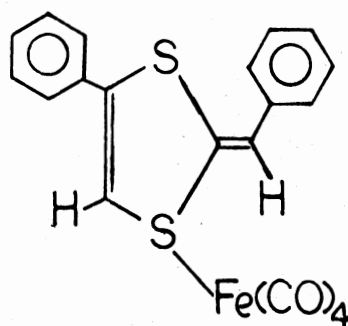
58

CHAPTER IV

EXPERIMENTAL

4-Phenyl-1,2,3-Thiadiazole Reactions

Melting points were obtained from a Thomas-Hoover capillary melting point apparatus and were uncorrected. Proton magnetic resonance spectra were taken on a Varian XL-100 high resolution NMR spectrometer and a Varian A60 NMR spectrometer with tetramethylsilane (TMS) used as an internal standard. Infrared spectra were recorded on a Beckmann-8A Spectrophotometer. Low resolution mass spectra were obtained on a CEC 21-100B Double Focusing Mass Spectrometer.

Solvents were dried immediately before use. Acetonitrile and tetrahydrofuran (THF) were distilled under N_2 from phosphorus pentaoxide and sodium/benzophenone, respectively.

Carbethoxyhydrazine (2)

Carbethoxyhydrazine (2) was prepared by the method of Diels.[35] Diethyl carbonate (205 ml, 1.69 mol) was added to 88.0 g of 85% aqueous hydrazine hydrate to yield carbethoxyhydrazine (130 g, 73.9%) mp, 43-44° (lit.[35] mp, 44-45°).

Acetophenonecarbethoxyhydrazone (3)

Acetophenonecarbethoxyhydrazone (3) was prepared by the procedure of Raap and Micetich.[10] A mixture of acetophenone (24.0 ml, 0.21 mol),

carbethoxyhydrazine (2) (21.2 g, 0.20 mol), acetic acid (0.5 ml) and methanol (75 ml) yielded pale yellow acetophenonecarbethoxyhydrazone (3) (19.3 g, 43.4%) mp, 115.5-116.5° (CH_3OH-H_2O) (lit.[10] mp, 117-119°); NMR (DCCl$_3$): δ 7.72 (m, 2, o-C_6H_5), 7.28 (m, 3, m + p-C_6H_5), 4.32 (q, 2, J= 7Hz, CH_2CH_3), 2.20 (s, 3, CH_3) and 1.35 (t, 3, J = 7Hz, CH_2CH_3).

4-Phenyl-1,2,3-Thiadiazole (1a)

4-Phenyl-1,2,3-thiadiazole (1a) was prepared by the procedure of Raap and Micetich.[10] Acetophenonecarbethoxyhydrazone (3) (18.9 g, 0.10 mmol; rigorously dried by heating to 40° at 0.025 mm) was added slowly to ice-cooled thionyl chloride (50 ml) giving a vigorous evolution of gas. The resulting red-brown solution was heated at 60° for one hour. The solution was allowed to cool to room temperature and was concentrated in vacuo to give a red-brown mass. Recrystallization three times from acetonitrile gave 4-phenyl-1,2,3-thiadiazole (1a) (8.40 g, 52%) mp, 77-78° (lit.[10] mp, 78-79°); IR (CH_3CN): 695vs, 890vs, 1225vs (ring breathing) and 1270 cm^{-1} w; NMR (acetone-d$_6$): δ 9.22 (s, 1, CH=C), 8.12 (m, 2, o-C_6H_5) and 7.49 (m, 3, m + p-C_6H_5); mass spectrum (8 eV) (rel. intensity, composition): 162(9.4, $C_8H_6N_2S$), 135(9.4), 134(100, C_8H_6S), 108(9.4, C_6H_3S), 102(7.8, C_8H_5), 90(25, C_7H_6) and 89(19, C_7H_5).

4-Phenyl-1,2,3-Thiadiazole Chromium Pentacarbonyl (41a)

A. Preparation of Trisacetonitrile Chromium Tricarbonyl.[31] Chromium hexacarbonyl (Alfa Inorganics) (2.02 g, 9.17 mmol) in 48 ml of acetonitrile was magnetically stirred under argon in a 100 ml round bottom

flask fitted with a West condensor. The solution was heated at 82° for 8½ hr yielding a bright yellow solution of <u>trisacetonitrile</u> chromium tricarbonyl. The complex was not isolated.

B. <u>Thermal Preparation of 4-Phenyl-1,2,3-Thiadiazole Chromium Pentacarbonyl (41a)</u>. A solution of 4-phenyl-1,2,3-thiadiazole (1a) in 8 ml of acetonitrile was added by syringe to the <u>trisacetonitrile</u> chromium tricarbonyl solution prepared in A. The resulting dark red mixture was stirred for 30 min and then concentrated at 25 mm and approximately 40° to yield a bright red solid residue. The crude material was dissolved in 3 ml of benzene and chromatographed over Stage 5 deactivated, acid-washed alumina. The complex was eluted with Skelly B. The chromatography was repeated to yield yellow-orange 4-phenyl-1,2,3-thiadiazole chromium pentacarbonyl (41a) (0.60 g, 28%) mp, 110-112° (dec); IR (CH_3CN): 1905sh (C ≡ O stretch), 1945vs (C ≡ O stretch) and 2050 cm^{-1} w (C ≡ O stretch); NMR (acetone-d_6): δ 9.31 (s, 1, <u>CH</u>=C), 8.01 (m, 2, <u>o</u>-C_6H_5), 7.48 (m, 3, <u>m</u> + <u>p</u>-C_6H_5); mass spectrum (8 eV), <u>m/e</u> (rel. intensity, composition): 354(2.12, $C_{13}H_6N_2O_5SCr$), 326(1.06, $C_{12}H_6N_2O_4SCr$), 298(1.06, $C_{11}H_6N_2O_3SCr$), 270(1.06, $C_{10}H_6N_2SCr$), 242(2.12, $C_9H_6N_2OSCr$), 220(10.1, $Cr(CO)_6$), 214(4.2, $C_8H_6N_2SCr$), 162(10.64, $C_8H_6N_2S$), 134(100, C_8H_6S) and 102(35.11, C_8H_6). Facile decomposition of the complex in a variety of degassed solvents (<u>i.e.</u>, pentane, diethyl ether, THF, benzene, carbon disulfide) posed serious problems in the attempts to purify the complexes. Chromatography proved the best method in purification. However, the samples were not analytically pure and as a result elemental analysis was not obtained. The complex after purification still contains approximately 10% thiadiazole determined quantitatively by IR (CH_3CN).

C. Tetrahydrofuran Chromium Pentacarbonyl.[32]   In a photolysis
vessel, a solution of chromium hexacarbonyl (2.01 g, 9.13 mmol) in
325 ml of tetrahydrofuran (THF) was cooled to 0^0. The solution was
mixed by continuous bubbling of argon through a frit in the bottom of
the apparatus. Irradiation of the degassed solution with a 450 watt
Hanovia lamp with a Kimax filter for 2½ hr gave a clear yellow solution
of THF chromium pentacarbonyl. The complex was not isolated due to its
instability.

D. Indirect Photolytic Preparation of 4-Phenyl-1,2,3-Thiadiazole
Chromium Pentacarbonyl 41a. The THF chromium pentacarbonyl solution
prepared in C was poured into a solution of 4-phenyl-1,2,3-thiadiazole
(1a) (1.28 g, 7.89 mmol) in 20 ml THF by U-tube under argon. The re-
sulting dark red solution was magnetically stirred for 30 min and then
concentrated (in vacuo; 25 mm, 25^0) to yield a red solid, wt 2.58 g.
The solid was extracted with approximately 60 ml of pentane. Chroma-
tographing of the pentane-soluble material two times over Stage 5
deactivated, acid-washed alumina with elution by Skelly B gave yellow-
orange 4-phenyl-1,2,3-thiadiazole chromium pentacarbonyl 41a (0.67 g,
24%) mp, 110-112^0; IR (CH$_3$CN): 1905sh (C $\equiv$ O stretch), 1945vs (C $\equiv$ O
stretch) and 2050 cm^{-1} w (C $\equiv$ O stretch); NMR (acetone-d$_6$): δ 9.31 (s,
1, CH=C), 8.01 (m, 2, o-C$_6$H$_5$) and 7.48 (m, 3, p + m-C$_6$H$_5$); mass
spectrum (12 eV) m/e (rel. intensity, composition): 354(2.65, C$_{13}$H$_6$N$_2$O$_5$
SCr), 326(0.89, C$_{12}$H$_6$N$_2$O$_4$SCr), 298(0.89, C$_{11}$H$_6$N$_2$O$_3$SCr), 270(1.76, C$_{10}$
H$_6$N$_2$O$_2$SCr), 242(4.42, C$_9$H$_6$N$_2$OSCr), 220(15.21, C$_6$O$_6$Cr), 214(8.84, C$_8$H$_6$N$_2$
SCr), 162(20.35, C$_8$H$_6$N$_2$S), 134(100, C$_8$H$_6$S) and 102(75.22, C$_6$H$_6$).

4-Phenyl-1,2,3-Thiadiazole Molybdenum

Pentacarbonyl (41b)

A. Preparation of Trisacetonitrile Molybdenum Pentacarbonyl.[31]
A solution of molybdenum hexacarbonyl (1.99 g, 7.56 mmol) in 60 ml of
acetonitrile was heated at 83° while magnetically stirred under argon
for 21 hr. The dark yellow-green solution of trisacetonitrile moly-
bdenum tricarbonyl was cooled to room temperature. IR (CH_3CN): 1795s
(C ≡ O stretch) and 1910vs (C ≡ O stretch); (Lit.[36] values, 1790vs and
1910vs).

B. Thermal Preparation of 4-Phenyl-1,2,3-Thiadiazole Molybdenum
Pentacarbonyl (41b). A solution of 4-phenyl-1,2,3-thiadiazole (1a)
(0.81 g, 5.05 mmol) in 8 ml of acetonitrile was added by syringe to
the triacetonitrile molybdenum tricarbonyl solution prepared in A.
The resulting dark red solution was stirred for 2 hr and then was
concentrated in vacuo (21 mm, 40°) to give a bright red solid, wt 3.14
g. Molybdenum hexacarbonyl was removed by sublimation (0.1 mm, 25°),
and the remaining solid was chromatographed over Stage 5 deactivated,
acid-washed alumina with Skelly B. Nitrogen was blown into the
collection flask to immediately evaporate the solvent and to give
orange-brown, 4-phenyl-1,2,3-thiadiazole molybdenum pentacarbonyl (41b)
(0.47 g, 16%) mp, $90-94^o$ (dec); IR (CH_3CN): 1900vs (C ≡ O stretch)
and 1950s cm^{-1} (C ≡ O stretch); NMR (acetone-d_6): δ 9.39 (s, 1, CH=C
complexed), 9.22 (s, 1, CH=C, uncomplexed), 8.22 (m, 2, o-C_6H_5), 7.70
(m, 3, m + p-C_6H_5). Facile decomposition of the complex in a variety
of degassed solvents (e.g., pentane, diethyl ether, THF, benzene,
carbon disulfide) caused serious problems in the attempts to purify

the complexes. Chromatography proved the best method of purification. However, the samples were not analytically pure, and as a result elemental analysis was not obtained. The complex still contains approximately 20% thiadiazole determined quantitatively by IR (CH_3CN) in purification.

C. <u>Tetrahydrofuran Molybdenum Pentacarbonyl</u>.[32] In a photolysis vessel, a solution of molybdenum hexacarbonyl (2.50 g, 9.48 mmol) in approximately 325 ml of tetrahydrofuran (THF) was cooled to 0°. The solution was mixed and degassed by continuous bubbling of argon through the frit in the bottom of the vessel. Irradiation with a 450 watt Hanovia lamp with a Kimax filter for 2 1/5 hr gave a yellow-green solution of THF molybdenum pentacarbonyl. The complex was not isolated.

D. <u>Indirect Photolytic Preparation of 4-Phenyl-1,2,3-Thiadiazole</u> <u>Molybdenum Pentacarbonyl (41b)</u>. A solution of 4-phenyl-1,2,3-thiadiazole (1a) (1.08 g, 6.64 mmol) in 9 ml THF was added by syringe to the THF molybdenum pentacarbonyl solution prepared in C. The resulting red-orange solution was stirred for 20 min and concentrated <u>in vacuo</u> (21 mm, 25°) to yield a dark red solid, wt 3.19 g. The material was chromatographed over Stage 5 deactivated, acid-washed alumina with Skelly B. Nitrogen was blown into the collecting flask to evaporate the solvent and prevent decomposition of the orange-brown complex. Chromium hexacarbonyl was removed by sublimation (0.05 mm, 25°) to yield orange-brown 4-phenyl-1,2,3-thiadiazole molybdenum pentacarbonyl (41b) (1.19 g, 45%) mp, $90-93^{\circ}$ (dec); IR (CH_3CN): 1905vs (C $\equiv$ O stretch) and 1950 cm^{-1} s (C $\equiv$ O stretch). This complex was not analytically pure again due to problems in recrystallization.

"Dimer A" (50a) in the Formation of 4-Phenyl-1,2,3-Thiadiazole Molybdenum Pentacarbonyl

The procedure for the preparation of the "dimer A" (50a) was identical to the procedure for 4-phenyl-1,2,3-thiadiazole molybdenum pentacarbonyl (41b) with the exception of one modification. A solution of 4-phenyl-1,2,3-thiadiazole (1a) in 8 ml of acetonitrile was added to a solution of trisacetonitrile molybdenum tricarbonyl prepared from molybdenum hexacarbonyl (2.07 g, 8.77 mmol) and 50 ml acetonitrile. The resulting dark red solution was concentrated in vacuo (22 mm, 45°) to give a dark red solid, wt 2.63 g. The material was crystallized from 1:10:4 mixture of acetonitrile (to stabilize the complex), methylene chloride, and n-hexane to give a dark red crystalline solid (50a) (0.41 g, 10%, based on 4-phenyl-1,2,3-thiadiazole) mp, 86-88° (dec); IR (CH_3CN): 1840vs (C ≡ O stretch), 1910s (C ≡ O stretch), 1945sh (C ≡ O stretch) and 2020 cm^{-1} w (C ≡ O stretch); NMR (CS_2): δ 9.02 (s, 1, CH=C), 9.12 (m, 2, o-C_6H_5) and 7.49 (m, 3, m + p-C_6H_5). Also the NMR spectrum shows a band at δ 9.22 (s, 1, CH=C) for approximately 15% 4-phenyl-1,2,3-thiadiazole (1a).

"Dimer B" (50b) in the Formation of 4-Phenyl-1,2,3-Thiadiazole Chromium Pentacarbonyl

The procedure used was identical to that used in the preparation of "dimer A" (50a). Chromium hexacarbonyl (2.00 g, 9.09 mmol) and 4-phenyl-1,2,3-thiadiazole (1a) (0.98 g, 6.07 mmol) gave the dark red "dimer B" (50b) (0.48 g, 11.6% based on initial amount of 4-phenyl-1,2,3-thiadiazole) mp, 82-86° (dec); IR (CH_3CN): 1845vs (C ≡ O stretch), 1920s (C ≡ O stretch), 1945sh (C ≡ O stretch) and 2070 cm^{-1} w (C ≡ O

stretch). Also an absorption occurs at 1225 cm^{-1} w corresponding to approximately 8% 4-phenyl-1,2,3-thiadiazole.

Reaction of "Dimer A" (50a) with Carbon Monoxide

A magnetically stirred solution of "dimer A" (50a) (0.10 g, 0.13 mmol) in 20 ml of acetonitrile was heated to 83°, and carbon monoxide was bubbled into the bright red solution for 90 min to yield a yellow solution. After being cooled to room temperature, the solution was concentrated in vacuo (25 mm, 40°) to give a yellow solid. Chromatography of the material over Stage 5 deactivated, acid-washed alumina with Skelly B gave impure orange-brown 4-phenyl-1,2,3-thiadiazole molybdenum pentacarbonyl (41b) (0.10 g, 95% based on initial dimer) mp, 88-90°; IR (CH$_3$CN): 1905v (C ≡ O stretch) and 1950 cm^{-1} vs (C ≡ O stretch); NMR (acetone-d$_6$): δ 9.41 (s, 1, CH=C, complexed) 9.22, less than 8% of 4-phenyl-1,2,3-thiadiazole (s, 1, CH=C, uncomplexed), 8.25 (m, 2, o-C$_6$H$_5$) and 7.70 (m, 3, m + p-C$_6$H$_5$).

Reaction of "Dimer A" (50a) with Triphenylphosphine

To the red solution of "dimer A" (50a) (0.10 g, 0.13 mmol) in 15 ml of acetonitrile was added triphenylphosphine (0.07 g, 0.26 mmol) under argon. The magnetically stirred solution was maintained at room temperature for 6¼ hr and then heated at 55° for 2 hr. After being cooled to -15°, the solution was filtered to give triphenylphosphine (0.05 g, 73% recovered) mp, 78-80° (lit.[37] mp, 78-79°) mmp, 77-79°. The red filtrate was concentrated in vacuo (23 mm, 40°) to

yield impure "dimer A" (50a) (0.09 g, 89% recovery) mp, 84-87°; IR

(CH$_3$CN): 1855vs (C $\equiv$ O stretch), 1915vs (C $\equiv$ O stretch), 1950sh (C $\equiv$ O

stretch), 1980vs (C $\equiv$ O stretch) and 2020 cm^{-1} w (C $\equiv$ O stretch). The

spectra was not calibrated and this resulted in a shift of each peak

by 5 cm^{-1}. The band at 1980 cm^{-1} is presumably molybdenum hexacarbonyl.

Reaction of "Dimer B" (50b) with

Carbon Monoxide

Into the yellow solution of "dimer B" (50b) (0.09 g, 0.13 mmol)

in 15 ml acetonitrile was bubbled carbon monoxide at approximately ten

bubbles per minute for 35 min. The resulting yellow-green solution was

concentrated in vacuo (20 mm, 40°) to give a yellow solid, wt 0.10 g

mp, 71-73°. Chromatography of the material over Stage 5 deactivated,

acid-washed alumina with Skelly B gave yellow-orange 4-phenyl-1,2,3-

thiadiazole chromium pentacarbonyl (41a) (0.08 g, 88%) mp, 110-113°;

IR (CH$_3$CN): 1905sh (C $\equiv$ O stretch), 1950vs (C $\equiv$ O stretch) and 2070

cm^{-1} w (C $\equiv$ O stretch).

Preparation of 2,6-di(t-Butyldimethylsilyl)-

3,6-Diphenyl-1,4-Dithiafulvene (45)

A solution of 4-phenyl-1,2,3-thiadiazole (1a) (1.16 g, 7.14 mmol)

in 34 ml of THF was magnetically stirred and cooled to -70° under argon.

n-Butyl lithium (2.65 ml, 6.49 mmol) was added slowly to the solution

by syringe so that the temperature did not exceed -65°. The solution

was stirred at -70° with the steady evolution of gas. After gas

evolution had subsided (ca. 30 min), a solution of t-butyldimethylsilyl

chloride (42) (0.98 g, 6.39 mmol) in 8 ml THF was added by syringe to

the vortex of the stirred solution. After coming to 25° over a period

of 1 hr, the IR (THF) spectrum indicated an absorption at 2160 cm^{-1}

(C ≡ C stretch). The resulting solution was concentrated leaving a

yellow solid, wt 2.04 g. The solid was extracted with pentane to give

a yellow solid, wt 1.02 g. Recrystallization from pentane gave 2,6-

di(t-butyldimethylsilyl)-3,6-diphenyl-1,3-dithiafulvene (45) (1.00 g,

28%) mp, 187-188°; IR (CS_2): 685w, 730s, 1110vs, 1370vs, 2860vs (C - H

stretch) and 2930 cm^{-1} (C - H stretch); NMR (CS_2): δ 1.20-0.5 (m, 15,

-CH$_3$ + C(CH$_3$)$_3$), 6.75 (s, 1, CH=C) and 7.34 (m, 10, C_6H_5).

The pentane insoluble material from above was extracted with

diethyl ether to give a yellow solid. Recrystallization from ether-

pentane gave 3,6-diphenyl-1,4-dithiafulvene (44) (0.76 g, 40%) mp,

123-126° (lit.[11] mp, 126-128°); IR (CS_2): 695s, 745s, 815s, 1260s,

2960s, (C - H stretch) and 3070 cm^{-1} vs (C - H stretch); NMR (CS_2):

δ 6.39 (d, 2, J=5H$_2$, CH=C) and 7.23 (m, 10, 2C_6H_5).

Attempted Preparation of Silylalkynylthiol
Cobalt Hexacarbonyl (33)

A magnetically stirred solution of 4-phenyl-1,2,3-thiadiazole (1a)

(0.98 g, 6.05 mmol) in 28 ml THF was cooled to -70° under argon. A

pentane solution of n-butyl lithium (2.4 ml, 5.88 mmol) was added by

syringe to the solution at a rate such that the temperature did not

exceed -65°. The resulting bright yellow solution was stirred at -70°

for 45 min during which time the evolution of gas was observed. A

solution of t-butyldimethylsilyl chloride (42) (0.95 g, 6.22 mmol) in

8 ml THF was added by syringe to the solution, cooling was discontinued,

and after the reaction mixture had come to room temperature, dicolbalt

octacarbonyl (3.00 g contaminated with cobalt carbonate) was slowly

added with the evolution of gas to yield a black solution. The solution
was stirred for 22 hr and then concentrated in vacuo (22 mm, 25$^{\mathrm{o}}$) to
yield a black gummy residue. The residue was extracted with pentane,
and the pentane-soluble material, wt 1.33, sublimed (0.15 mm, 25$^{\mathrm{o}}$)
to give tetracobalt dodecacarbonyl[30], (0.38 g): IR (CS_2): 1860s
(C = O stretch) and 2050 cm^{-1} s (C = O stretch): NMR (CS_2) gave no
peaks; mass spectrum (12 eV) m/e (rel. intensity, composition): 572
(5, $C_{12}O_{12}Co_4$), 544(3, $C_{11}O_{11}Co_4$), 516(3, $C_{10}O_{10}Co_4$), 488(2, $C_9O_9Co_4$),
460(2, $C_8O_8CO_4$), 432(3, $C_7O_7CO_4$), 404(2, $C_6O_6Co_4$), 376(2, $C_5O_5Co_4$),
320(2, $C_3O_3Co_4$), 264(10, $C_1O_1Co_4$), 236(80, Co_4) and 118(100, Co_2).

The pentane insoluble material was extracted with ether to
yield a black solid (1.08 g). The compound did not melt below 300$^{\mathrm{o}}$;
IR (CS_2): 800s, 1080s, 1260s and 2030 cm^{-1} vs; NMR (CS_2); δ 0.15 (m),
0.58 (s), 0.95 (m), 1.38 (s) and 7.30 (m). Mass spectrum (8 eV)
gave a complex spectrum with peaks corresponding to m/e greater than
instrument capability which is 650 m/e.

3,6-Diphenyl-1,4-Dithiafulvene Iron
Tetracarbonyl (58)

Diiron nonacarbonyl (0.12 g, 0.32 mmol) was added under argon to a
magnetically stirred solution of 3,6-diphenyl-1,4-dithiafulvene (0.09 g,
0.31 mmol) in 17 ml of n-hexane. The resulting dark red-brown
solution was heated at 69$^{\mathrm{o}}$ for 38 hr, cooled to room temperature and
concentrated in vacuo (27 mm, 40$^{\mathrm{o}}$) to give a red oil. The oil was
chromatographed over Stage 2 deactivated, acid-washed alumina with
Skelly B to yield 3,6-diphenyl-1,4-dithiafulvene iron tetracarbonyl
(58) (0.6 g, 73%); IR (CS_2): 1990s (C ≡ O stretch), 2030s (C ≡ O

stretch) and 2060 cm^{-1} s (C $\equiv$ O stretch); NMR (CS$_2$): δ 6.35 (m, 2, $\underline{CH}$=C), 7.23 (m, 10, $\underline{C_6H_5}$).

2-Phenylthioketocarbenedicycopenta-
dienylmonocarbonyl Diiron ($\underset{\sim}{53}$-$\underset{\sim}{54}$)

To a solution of 4-phenyl-1,2,3-thiadiazole ($\underset{\sim}{1a}$) (0.17 g, 1.04 mmol) in 15 ml toluene was added cyclopentadienyldicarbonyl iron dimer ($\underset{\sim}{51}$) (0.33 g, 0.95 mmol). The red-brown solution was magnetically stirred and heated at 90° for 13 hr under argon. After being cooled to room temperature, the solution was concentrated $\underline{in}$ $\underline{vacuo}$ (25 mm, 60°) to give a red-brown solid, wt 0.39 g. The material was chromatographed over Stage 2 deactivated, acid-washed alumina. Elution with Skelly B gave recovered dimer (0.22 g, 64% recovery) mp, 192 (dec) (lit.^{38} mp, 194° dec); IR (CH$_2$Cl$_2$): 1770s (C $\equiv$ O stretch), 1953s (C $\equiv$ O stretch) and 1995 cm^{-1} s (C $\equiv$ O stretch); NMR (CCl$_4$) δ 5.25 (s, 10, $\underline{C_5H_5}$). Elution with benzene gave two broad bands. The pink band was collected to give brown 2-phenylthioketocarbenedicyclopentadienyl-monocarbonyl diiron ($\underset{\sim}{52}$ or $\underset{\sim}{53}$) (0.01 g, 3.1% based on starting 4-phenyl-1,2,3-thiadiazole) mp, 151-153° (dec); IR (CH$_2$Cl$_2$): 1600vs, 1805vs (C $\equiv$ O stretch) and 1970 cm^{-1} vs (C $\equiv$ O stretch); NMR (CCl$_4$): δ 4.61 (s, 5, $\underline{C_5H_5}$), 4.80 (s, 5, $\underline{C_5H_5}$), 6.98 (m, 5, $\underline{C_6H_5}$) and 7.33 (m, 5, $\underline{C_6H_5}$); mass spectrum $\underline{m/e}$ (rel. intensity, composition): 404(5.84, C$_{19}$H$_{16}$OSFe$_2$), 376(16.57, C$_{18}$H$_{16}$SFe$_2$), 274(25.97), 186(100, C$_{10}$H$_{10}$Fe), 121(94.15, C$_5$H$_5$Fe) and 102(99.05, C$_8$H$_6$).

Elution of the remaining blue-gray band and concentration of effluent gave black 1-phenylthioketocarbenemonocarbonyl diiron ($\underset{\sim}{52}$ or $\underset{\sim}{53}$) (0.01 g, 2.1% based on starting thiadiazole) mp, 93-95°; IR (CH$_2$Cl$_2$):

1595vs, 1805s (C $\equiv$ O stretch), 1915sh (C $\equiv$ O stretch), 1990s (C $\equiv$ O stretch) and 2030 cm^{-1} s (C $\equiv$ O stretch); NMR (CCl$_4$): δ 4.61 (s, 5, C$_5$H$_5$), 4.80 (s, 5, C$_5$H$_5$) and 7.21 (m, 10, 2C$_6$H$_5$); mass spectrum m/e (rel. intensity, composition): 404(10.95, C$_{19}$H$_{16}$OSFe$_2$), 274(54.43, ?), 263(63.13, ?), 186(100, C$_{10}$H$_{10}$Fe), 121(76.0, C$_5$H$_5$Fe) and 102(76.10, C$_8$H$_6$).

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METAL PROMOTED REACTIONS. PART II.

OXIDATION OF OXIMES BY

COPPER SALTS

CHAPTER I

INTRODUCTION AND HISTORICAL BACKGROUND

Oxidation of Oximes by Copper Salts

Oxidation is defined as a loss of electrons while reduction is a gain of electrons. A useful generalization in organic chemistry is that oxidation involves the removal of hydrogen to form multiple bonds or to form new bonds between carbon and a more electronegative element.[1] Oxidation of organic compounds, such as acetylenes,[2,3] aldehydes,[4,5] alcohols[6,7] and amines[8,9] by copper salts has been well documented. Copper is known to exist in the 0, 1+, 2+ and 3+ oxidation states, although Cu^{+3} is least encountered due to its extremely large oxidation potential.[10] In general most oxidations by copper involve a cupric-cuprous couple.[10]

Brackmann[11] and co-workers reported a series of unusual reactions in which methanolic solutions of aldehydes, ammonia, sodium methoxide, cupric chloride and oxygen yielded nitriles. The proposed reaction sequence (Eq. 1-6) involves an imine radical intermediate (1).

$$RCH = 0 + NH_3 \rightleftharpoons RCH + NH + H_2O \qquad (1)$$

$$RCH = NH + \overset{\ominus}{O}CH_3 \rightleftharpoons RCH = N\ominus + HOCH_3 \qquad (2)$$

$$RCH = N\ominus + Cu^{+2} \longrightarrow RCH = N\cdot \ (1) + Cu^+ \qquad (3)$$

$$RCH = N\cdot \ (1) + O_2 \longrightarrow RCH = N-O-O \qquad (4)$$

$$RCH = N-O-O\cdot \longrightarrow RC = N + HO-O\cdot \qquad (5)$$

$$HOO\cdot + Cu^{+1} \longrightarrow HOO- + Cu^{+2} \qquad (6)$$

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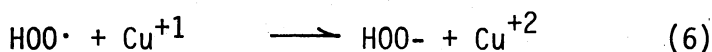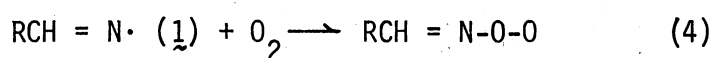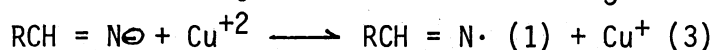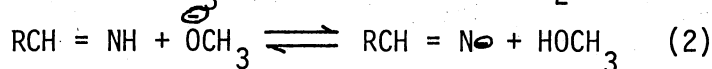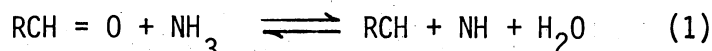
Although the best yields of nitrile are obtained with catalytic amounts of cupric chloride and excess molecular oxygen, the reaction also proceeds with stoichiometric amounts of cupric chloride in the absence of oxygen. Better yields are also obtained if the aldehyde lacks a hydrogen on the α-carbon to prevent a competing aldol condensation.

Another reaction involves the oxidation of benzoin (2) by cuprous chloride and oxygen in pyridine (Eq. 7) to give a high yield of benzoic acid[12,13](4). The intermediacy of benzil (3) was proposed. The oxidation of benzoin (2) with cupric chloride afforded only benzil (3). In addition to benzoin, hydrobenzoin[12] (5), (Eq. 8) and α-methylbenzoin[12] (7), (Eq. 9) undergo C-C bond cleavage.
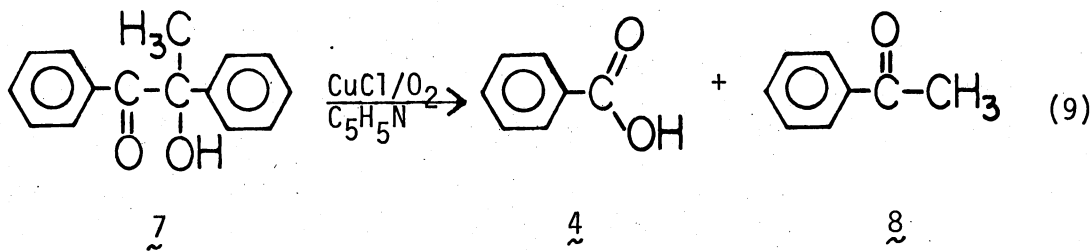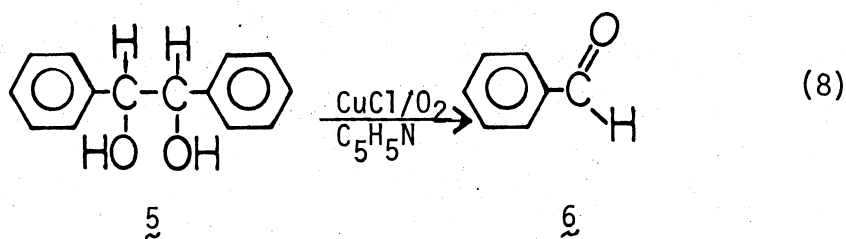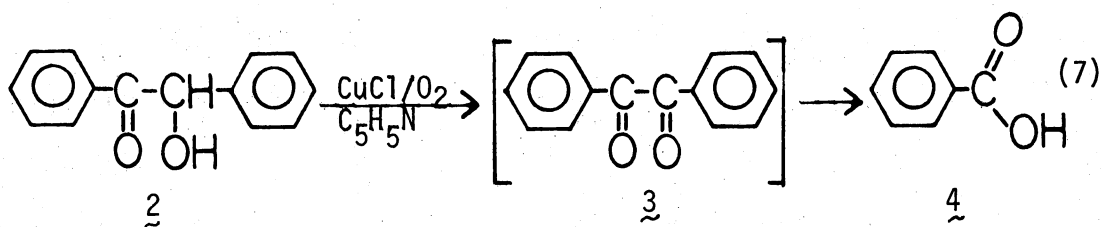
Another interesting C-C bond cleavage reaction was reported involving the oxidative C-C double bond cleavage of enamines by copper salts to yield either an aldehyde or ketone and an amide.[14] Aldehyde enamines are known to be stable to molecular oxygen; however, in the

presence of cuprous chloride, they rapidly react with oxygen and suffer cleavage. For example, when the morpholine enamine of cyclohexanecar-boxaldehyde (9) is oxidized with catalytic amount of cuprous chloride and oxygen (Eq. 10), cyclohexanone (10) and 11 are formed in quantitative yield.

$$\text{9} \xrightarrow[\text{CHCl}_3]{\text{CuCl/O}_2} \text{10} + \text{11} \quad (10)$$
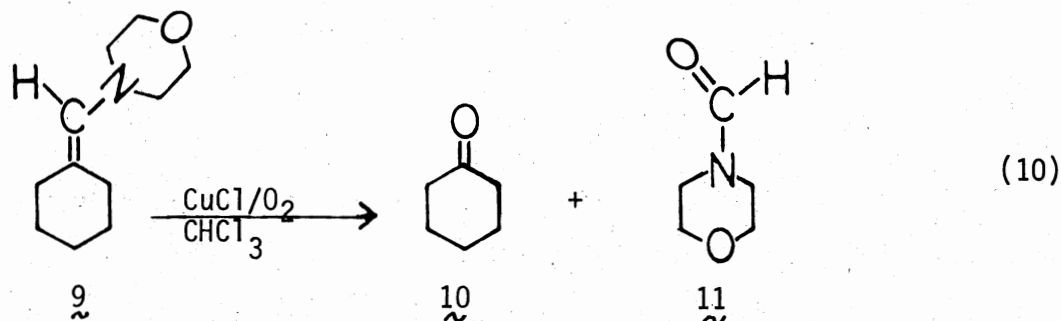
Sterically hindered enamines prepared from ⍺-alkylated ketones can also be cleaved in a similar manner. When 12 is oxygenated at 0° in the presence of a catalytic amount of cuprous chloride, acetone and N,N-dimethylisbutylamide (13) are formed in an 80% yield (Eq. 11).

$$\text{12} \xrightarrow[\text{CHCl}_3]{\text{CuCl/O}_2} + \text{13} \quad (11)$$
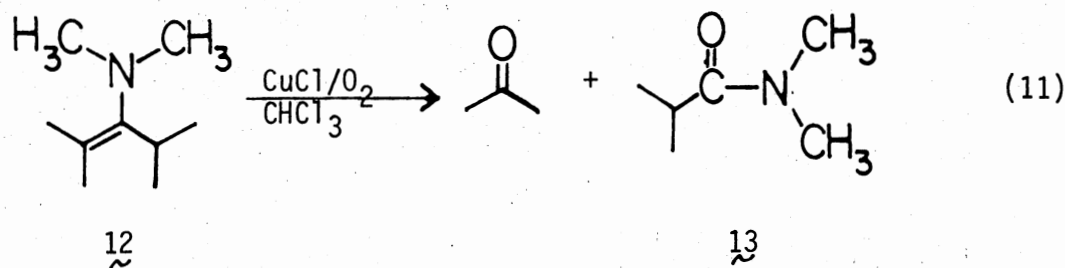
The rate of oxidation was reported to be dependent upon the amount of the copper salt as well as on the counter anion associated with the copper species. Cupric acetate, cuprous acetate, cupric nitrate and cupric sulfate were ineffective as oxygenation catalysts, whereas cuprous cyanide, and the chloride and bromides of both copper oxidation states were effective.

Most interesting are the reports by Huber[15] and Foote[16] of a similar
oxidative cleavage of enamines to aldehydes or ketones and amides using
dye-sensitized photo-oxygenation. Singlet oxygen is believed to be the
active species in this photo cleavage. The copper catalyzed reaction
on the other hand, proceeds readily even in the dark, and undoubtedly
singlet oxygen does not play a role.

Copper salts also effect C-C bond cleavage of aromatic rings.
For example, catechol (14) in the presence of cuprous chloride, oxygen
and methanol in pyridine gave high yields of the monomethyl ester of
cis,cis-muconic acid (15)[17] (Eq. 12); neither muconic acid itself nor
its dimethyl ester was isolated. In the absence of methanol, the
reaction gave only trace amounts of cis,cis-muconic acid (16). The
addition of 1.5 molar equivalents of methanol gave the best yield,
72%; as the metal catalyst, cuprous chloride showed the highest
activity, while cupric chloride showed no activity.
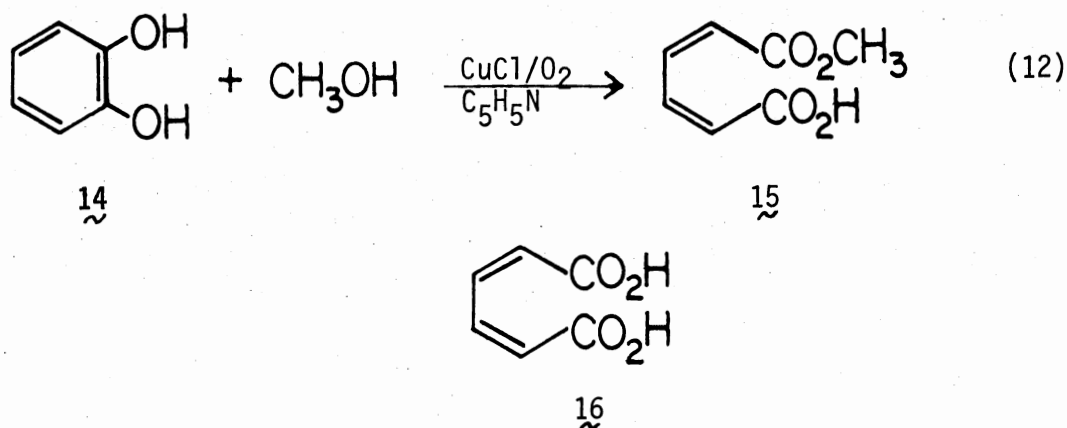
The oxidative reaction of catechol (14) by copper salts mimics the
reaction of the biological enzyme pyrocatechase, which contains copper
ion. In the biological reaction, cis,cis-muconic acid (16) is formed.
Several intermediates, based on $^{18}O_2$ incorporation, have been sug-

gested.[18,19] For example, the cyclic peroxide 17 was proposed; however,

the formation of the monomethyl ester could not be rationalized from

intermediate 17. As a consequence, the species 18 was regarded as a

more satisfying alternative. Intermediate 18, which could have been

formed from an electrophilic attack by oxygen on the aromatic ring,[20]

could generate anhydride 19. Subsequent methanolysis of the anhydride

would afford the monomethyl ester 15, the observed product[17] (Eq. 13).
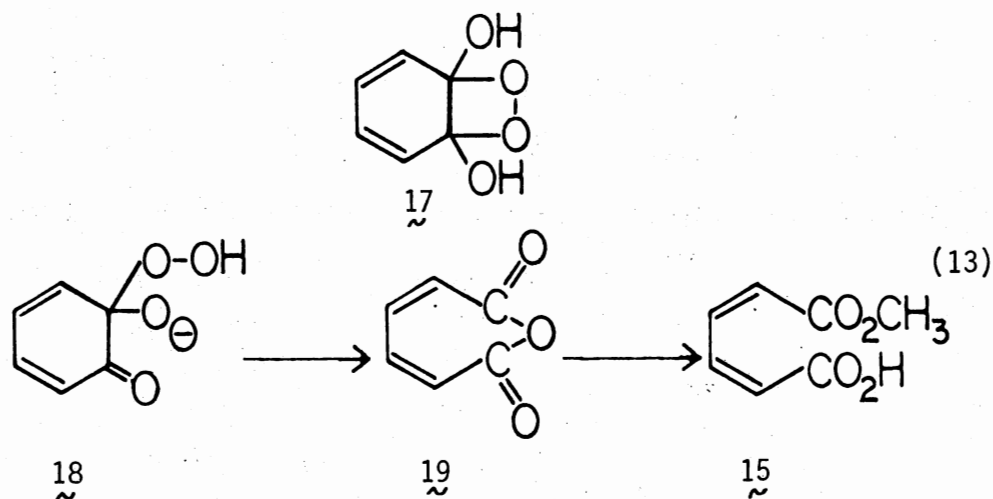
Another oxidative ring cleavage involved the oxidation of o-phenyl-

enediamine (20) with cuprous chloride (a catalytic amount) and oxygen

in pyridine.[21] At room temperature, cis,cis-mucononitrile (21) was

isolated[21] in high yield (Eq. 14).
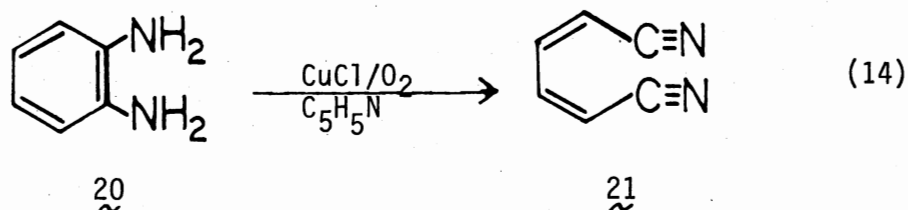
A functionality similar to the vicinal enediamine functionality in

o-phenylenediame is found in α-dihydrazone derivatives of α-diketones

(22). In contrast, however, the reaction of dihydrazones with cuprous chloride and oxygen in pyridine, afforded C-C bond formation,[22] not cleavage. Acetylenes were isolated in high yield (Eq. 15). Although the oxidation of α-dihydrazones to acetylenes is known to occur with strong oxidizing agents such as mercuric oxide,[23] silver trifluoroacetate[24] and lead tetraacetate,[25] this oxidative method using cuprous chloride and oxygen is advantageous since it occurs under mild conditions and requires an inexpensive reagent.

$$R-\underset{\underset{\underset{H_2N}{\diagup}}{\overset{\|}{N}}}{C}-\underset{\underset{\underset{NH_2}{\diagdown}}{\overset{\|}{N}}}{C}-R \quad \xrightarrow[C_5H_5N]{CuCl/O_2} \quad RC\equiv CR + 2N_2 + 2H_2O \qquad (15)$$

$$\underset{22}{}$$
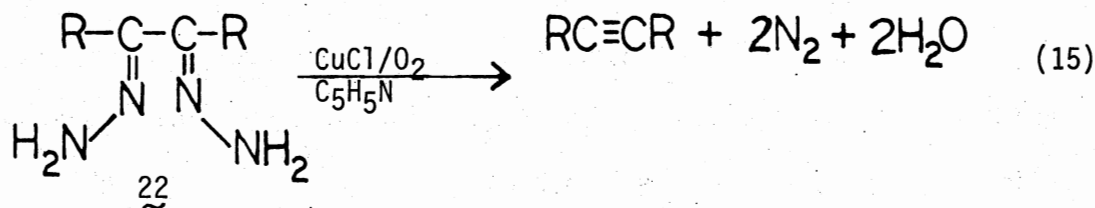
Oximes (23), like the enamines and hydrazones, are organic derivatives of ketones and aldehydes. They undergo a variety of specific reactions, such as hydrolysis to carbonyls,[26] reduction to amines[27] or hydroxylamines,[28] Beckmann rearrangement[29] to amides and the oxidation to nitro compounds.[30] An oxime, like an enamine or a hydrazone, can in part be represented by a resonance structure 23b in which electrons are donated by a heteroatom to carbon. The order of the
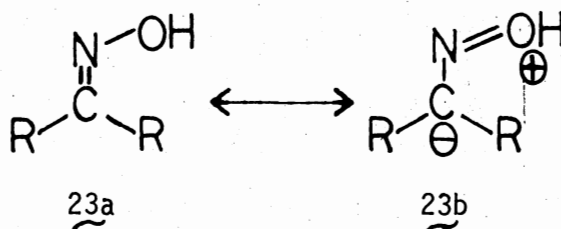
degree of delocalization of electrons is: enamine > hydrazone > oxime.[31] This delocalization phenomenon is apparently important in the

oxidation promoted by transition metal salts, with the degree of de-localization affecting the types of products which are formed. For example, as stated earlier, cuprous chloride oxidation of enamines afforded aldehydes or ketones and amides[14] (Eq. 10-11). However, oxidation of the monohydrazones of α-diketones 24 with cuprous chloride gave diazo compounds 25[22] (Eq. 16). Monohydrazones can

$$R-\underset{\underset{O}{\|}}{C}-\underset{\underset{N_{\diagdown NH_2}}{\|}}{C}-R \qquad\qquad R-\underset{\underset{O}{\|}}{C}-\underset{\underset{N_2}{\|}}{C}-R \qquad (16)$$

$$\underset{24}{\qquad\qquad} \qquad\qquad \underset{25}{\qquad\qquad}$$
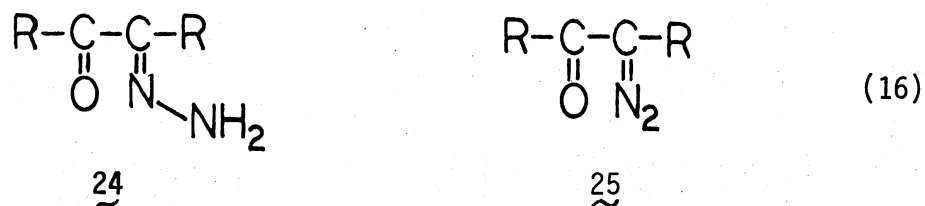
of course, also be oxidized to diazo compounds with mercuric oxide.[32] Oximes, by analogy, would be expected to be susceptible to oxidation by transition metal salts.

The Beckmann rearrangement of an oxime to an amide occurs with re-agents such as phosphorus pentachloride,[33] concentrated sulfuric acid,[34] acetyl chloride,[35] and the Beckmann mixture.[36] Transition metal salts have been reported[37] to facilitate amide formation from oximes. For example, benzaldoxime (26) on being heated in benzene with cuprous chloride rearranged to benzamide (27) (Eq. 17) in high yield. However,

$$\qquad\qquad\qquad (17)$$

$$\underset{26}{\qquad\qquad} \qquad\qquad \underset{27}{\qquad\qquad}$$
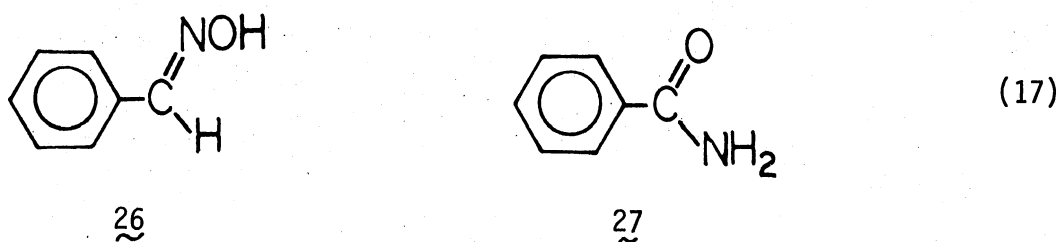
the reaction was not general. When benzophenone oxime (28) was heated in toluene with cuprous chloride, benzophenone (29) was isolated in high

yield (Eq. 18). Detailed experimental for the reaction was not given.
With slight modification such as changes in solvents, temperature and
of the addition of co-solvents and/or co-reactants, this reaction may
prove a valuable method of mild deoximation. Deoximation by hydrolysis

(18)

                    28   29
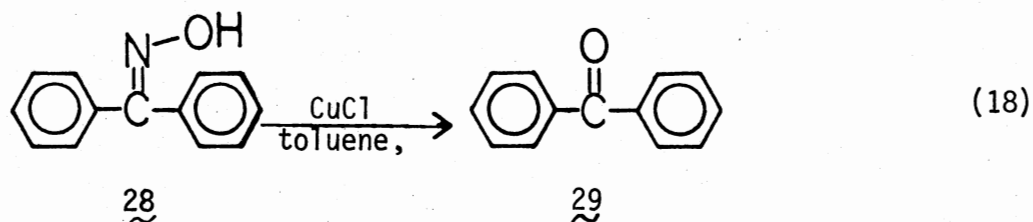
of oximes has been known to give aldehydes or ketones in poor yield due
to steric hindrance and/or side reactions. As a consequence, other
methods of deoximation have been investigated. Deoximation was reported
with potassium permangante,[38] potassium dichromate,[38] ozone,[39] ceric
ion,[40] chromous acetate,[41] and lead tetraacetate.[42]

Ketoximes and lead tetraacetate were reported[43] to give α-acyl-
oxynitroso compounds. For example, cyclohexanone oxime (30) and lead
tetraacetate at 5° gave an unstable blue oil. Treatment of the oil
with dilute sulfuric acid gave cyclohexanone (10) and acetic acid. The
intermediate blue oil was postulated to be α-acyloxynitroso species
31 (Eq. 19).

        30   31   (19)
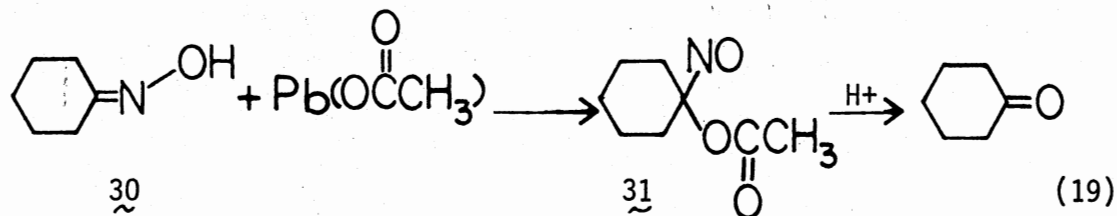
The use of oximes as precursors to ketones containing acid-or-base-
sensitive groups was often impractical in view of the side reactions
which often occurred employing conventional hydrolysis methods. As a

consequence, another deoximation method using transition metal salts, was developed by Corey and Richman.[41] The reductive deoximation reaction using chromous acetate was highly effective even in the presence of epoxides, esters, ketals and himithioketals. The reaction involved first, the conversion of oxime to its O-acetate derivative (an acetoxime) and second, treatment of the derivative with two equivalents of chromous acetate in a 9:1 ratio of THF and water to give the carbonyl. It was suggested that chromous acetate causes a reductive cleavage of the acetoxime N-O bond to yield an imine, which under the reaction conditions undergoes rapid hydrolysis to the ketone.[41]

Deoximation of acetoximes of conjugated enones and aryl alkyl ketones occurs more readily than for the corresponding non-conjugated acetoxime. This order of reactivity is opposite to that for the acid-catalyzed hydrolysis of oximes. The free oxime also undergoes deoximation with chromous acetate, but the reaction is slower and requires higher temperatures. Unfortunately, O-acetate aldoximes did not react.

Tervalent titanium salts also cause deoximation under mild conditions.[44] The addition of two equivalents of titanium (III) chloride to acetophenone oxime (32) in dioxane gave acetophenone (8) at room temperature within one hour (Eq. 20). An imine 33 was the suggested intermediate. The reaction proceeded readily with oximes,
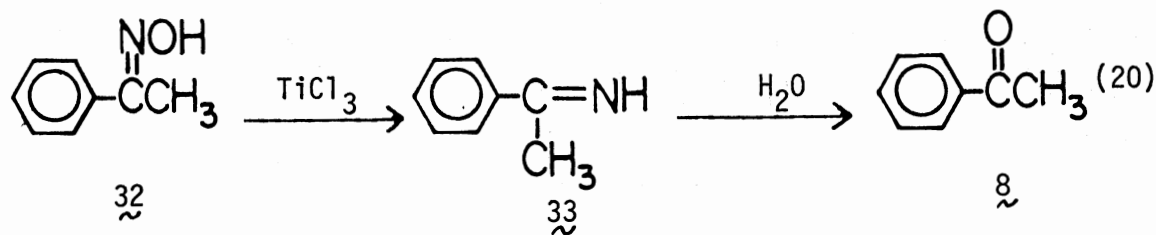
thus prior acetylation was unnecessary. Also the reaction occurs at room temperature and can be followed by a color change. Lastly, unlike chromous acetate, deoximation by titanium chloride occurs with aldoximes.

CHAPTER II

STATEMENT OF THE PROBLEM

Reactions of organic compounds with copper salts appear through-
out the literature. However many of the reactions are not general,
and predictions considering product formation are not easily made.
The reactions of benzoin,[12,13] catechol[17] or o-phenylenediamine[21]
involving C-C bond cleavage may all involve similar, if not common,
intermediates. Species 34, derived from treatment of benzoin with
base, is similar to the possible intermediate 35 and 36 from catechol
and o-phenylenediamine respectively. In each case apparently the
electron density at the α-carbon is high, as documented for enolate
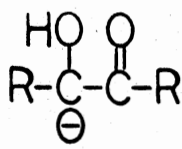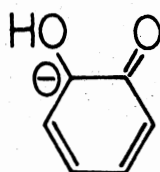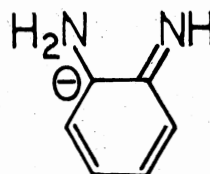
34	35	36

anions.[45] This same phenomenon is evident in enamines. A major re-
sonance contributor to the ground state of enamine 37 is structure 38.[46]

37	38

59
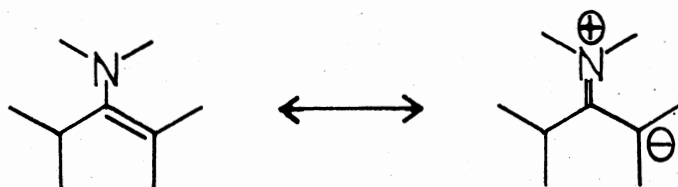
Electrophilic oxygen is then able to attack the α-carbanion[47] which then causes the C-C bond cleavage, and carbonyl formation. However, the role of the copper ion is not understood. The copper ion presumably is involved in electron transfer at some point in the reaction, or the copper ion may coordinate to the organic carbanion stabilizing a favorable resonance contributor, such as 38, which would then allow oxygen to attack the complex and yield the C-C bond cleavage products.[10]

In the reductive deoximation reactions, the metal presumably transfers an electron to the carbon-nitrogen bond in the oxime. The deoximation method using chromous acetate involved initial acylation of the oxime (39).[41] Presumably, this would remove electron density from nitrogen making addition of an electron from the metal to the C=N bond easier. The resulting radical anion 40 would be protonated by water to yield the radical 41 (Eq. 21).

$$\text{(21)}$$
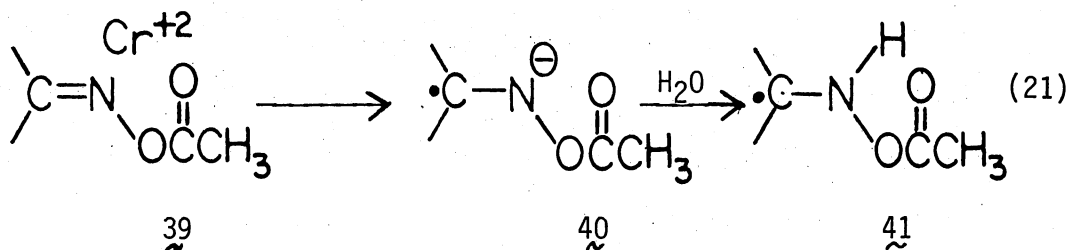
A second equivalent of chromous ion could donate an electron to the radical to yield anion 42. B-Elimination of acetate ion would give the imine 43 which is hydrolyzed to the ketone (Eq. 22). The negative charge is on the carbon in anion 42. This may prove an interesting intermediate in the presence of molecular oxygen.

In view of the preceding discussion, the treatment of oximes with copper salts and molecular oxygen might constitute a mild oxidative

(22)

41   42   43
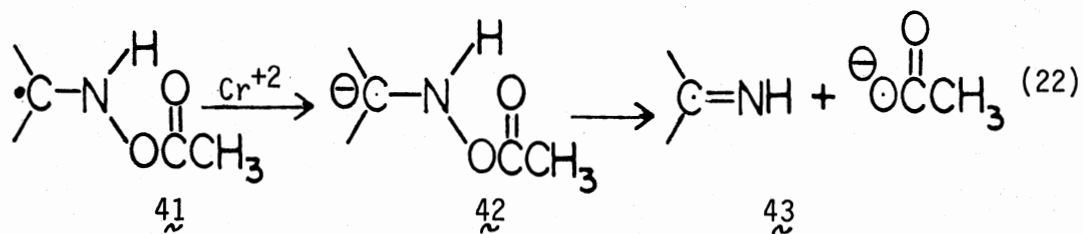
deoximation method. The main factor seems to be the existance and

stability of a carbanion. Since the negative charge is on the carbonyl

carbon, see structure 44, and not on the α-carbon (e.g., as with

enamines), treatment with molecular oxygen could yield the peroxide

anion 45 which might give the cyclic, strained peroxide 46.[48] Cleavage

of the O-O bond and C-N bond, (c.f., the cleavage of dioxetanes),[49]

(23)

44   45   46
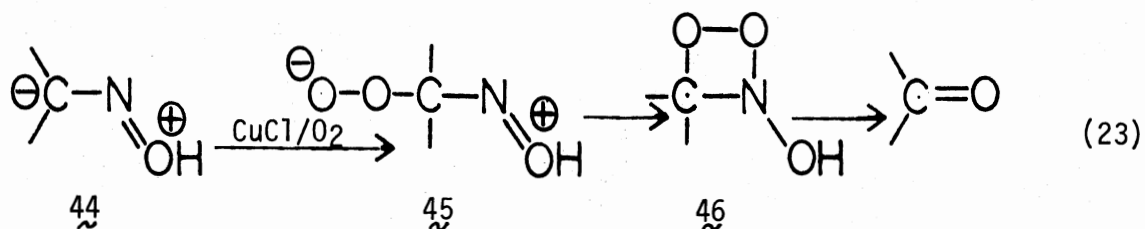
could afford the aldehydic or ketonic species (Eq. 23). In order to

increase electron density on the carbon and thus to facilitate formation

of the peroxide anion, the oxime could be treated with a mild base such

as pyridine to give anion 47.

47
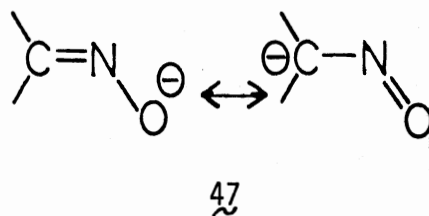
In addition to deoximation, other reaction pathways involving oximes

and copper salts are possible. For example, the oxime may yield N-

substituted amides via Lewis acid-catalyzed Beckmann rearrangement.[37]

In fact, oximes may undergo deoximation by Lewis acid catalyzed[26]

hydrolysis. Another possible reaction pathway involving oximes, copper salts and oxygen could yield the corresponding nitro compounds. This reaction is known to occur with oximes and peracids.[30] Also, if copper accepts an electron from the non-bonded electron pair on nitrogen, several other products could possibly be formed. For example, if the radical cation 48 is generated, nitrogen may show radical behavior and 48 may couple to yield azine dioxide 49 (Eq. 24).[50]

$$\underset{48}{\overset{\displaystyle \Large\substack{\backslash\\[-2pt]}}{}} \qquad (24)$$

48   49
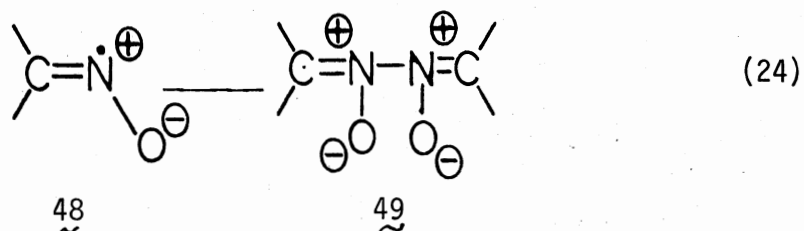
The investigation will involve a series of reactions of ketoximes, copper salts and molecular oxygen to determine the amount of ketone which may be generated.

CHAPTER III

RESULTS AND DISCUSSION

Despite the numerous copper promoted reactions which have been cited in the literature, the role of the copper ion is not clear and more importantly, the mechanisms for these reactions are generally not understood. Since the ionization potential associated with the cuprous-cupric couple is small (<u>i.e.</u>, the copper ions can easily accept or donate electrons), copper ions associated with oxygen could make ideal oxidizing agents.[10] Also, copper salts are generally inexpensive and easily obtained.

Oximes were used as the reactant in this study for several reasons. First, by analogy to the oxidation of enamines[14] and hydrazones[22] by copper salts, it was anticipated that under similar conditions, oximes may also be oxidized in a specific manner. Copper ions may be versatile reagents in oxidative reactions and extrapolation from one oxidative reaction (<u>e.g.</u>, the reaction of enamines) to another (<u>e.g.</u>, that of oximes) may be possible. Second, oximes are valuable precursors in the preparation of ketones and aldehydes. However, synthetically useful oximes often contain functionalities such as epoxides, esters, ketals and himithioacetal which can undergo undesirable side reactions using conventional deoximation procedures. The use of ionic copper species might afford a novel, mild deoximation procedure. Last, oximes are easily prepared and are stable compounds.

This study examined several ketoximes to determine if copper catalyzed deoximation could be effected, and if so, could it be generalized to variously substituted ketoximes. Benzophenone oxime (28) was chosen to represent diaryl ketones, acetophenone oxime (32) to represent arylalkyl ketones, and cyclohexanone oxime (30) to represent dialkyl ketones. Also, the possible mild deoximation of cyclohexanone oxime (30) by copper ions would prove a valuable method in introducing ketonic functionality (e.g., via the Barton Reaction[50]) into steriods and other natural products. Benzoin oxime (50) was also examined since earlier reports stated that benzoin afforded C-C bond cleavage to yield benzoic acid in quantitative yields[12,13] (see page 50), so the oxime might then also exhibit C-C bond cleavage.

A catalytic amount, 7.5% (mole %) with respect to the oxime, of cuprous or cupric ion was added to each oxime in the presence of molecular oxygen. Pyridine (one equivalent) was added to each solution to hopefully serve as a base for generation of the oximate anion. The results were encouraging in that deoximation did indeed occur. No attempts were made to optimize the yield of ketone. However, by changing a variable or variables in the reaction conditions, a high yield of ketone could perhaps be obtained. The results of the investigation are shown in Table I.

The possibility did exist that each oxime was simply undergoing Lewis acid catalyzed hydrolysis[26] rather than oxidative deoximation. Therefore, the experiments were repeated with exclusion of oxygen. The chloroform was degassed with nitrogen prior to addition of the oxime or copper salt, and then nitrogen, rather than oxygen, was bubbled into the oxime solution. Indeed, the yields of ketone were less in each

TABLE I

REACTIONS OF OXIMES WITH CUPROUS AND CUPRIC IONS[a]

Oxime	Ion	Atmosphere	% Ketone[b]( )[c]	% Oxime Reacted
Cyclohexanone	Cu^{+1}	O_2	24 (35%)	69
Cyclohexanone	Cu^{+2}	O_2	13 (42%)	32
Cyclohexanone	Cu^{+1}	N_2	11 (21%)	53
Cyclohexanone[d]	Cu^{+1}	O_2	27 (27%)	99
Cyclohexanone[e]	Cu^{+1}	O_2	51 (77%)	64
Acetophenone	Cu^{+1}	O_2	15 (38%)	40
Acetophenone	Cu^{+2}	O_2	2 (22%)	9
Acetophenone	Cu^{+1}	N_2	2 (17%)	12
Benzophenone	Cu^{+1}	O_2	68 (68%)	100
Benzophenone	Cu^{+2}	O_2	62 (62%)	100
Benzophenone	Cu^{+1}	N_2	17 (63%)	27
Benzoin	$Cu^{+1} or Cu^{+2}$	O_2	0 (0%)	0

a) All reactions were conducted in $CHCl_3$ with 7.5% (mole %) of the anhydrous copper chloride species at room temperature. Reaction time was 14 hrs.
b) Based on 100% oxime reacted.
c) Based on oxime which had reacted.
d) One equivalent of CuCl and 23½ hr reaction time.
e) Reaction performed at 0° for 24 hr with 1 eq of CuCl.

case which suggests that oxygen is needed in the reaction. Although ketones are formed in the nitrogen reactions, this may be due to traces of oxygen or water in the solvent. Alternatively, it was possible that the ketone arises from a hydrolytic as well as from an oxidative pathway. The solvent was not dried before use but was simply degassed with argon. The exclusion of water from the reaction mixture may be very important. It has been reported that cuprous ion in the presence of water and oxygen can generate the hydrogen peroxide anion.[10] If the hydrogen peroxide anion is the oxidizing agent, then the role of the copper is only as an indirect oxidizing agent. The hydrogen peroxide anion could presumably attack the oxime to yield ketone. Anhydrous salts were used; the oximes were dried in vacuo before use; pyridine was dried and the oxygen was passed through a drying tube to exclude moisture from the reaction. The only material not vigorously dried was the solvent.

Another important observation involves the comparative yields of ketone formation from reactions utilizing cupric or cuprous ion as the catalyst. The data indicates that in most cases, cuprous ion may be the better deoximating catalyst. In each case, except with benzoin oxime, the cuprous ion generates a higher yield of ketone. In fact, in some cases the yield of ketone from reactions with cupric ion is comparable to the yield of the nitrogen reaction. The yields obtained with cupric ion may be lower since the reactions with this ion were generally heterogeneous, whereas the reactions with cuprous ion were homogeneous. Another reaction solvent could perhaps give better yields of ketones with cupric ion. However, this point was not examined.

Another important consideration concerning the role of the copper

catalyst is the quanitity of the copper ion. The quantity of the cata-
lyst may effect the yields of ketone. In fact, copper ion may be a re-
agent and not a catalyst. This might have explained why the ketone
yields were low. The cuprous ion in concentration of 7.5% donates elec-
trons to 7.5% of the oxime and the remaining ketone was formed during
work up. To examine this possibility, the reaction with cyclohexanone
oxime was repeated with equivalent of cuprous ion. However, only 27%
of the ketone was formed as compared to 24% with a catalytic amount of
copper although more oxime did react with excess copper. Therefore,
cuprous ion is indeed a catalyst and not a reagent for deoximation
under these conditions.

Strong acids and bases are known to effect hydrolysis of oximes
to ketones. Since the work up procedure was performed by washing the
reaction mixture with dilute aqueous acid, the hydrolysis of unchanged
oxime was a possibility, although unlikely since the concentration of
the acid was only 2%. However, the possibility of hydrolysis was
examined. A given amount of acetophenone oxime was added to the re-
action vessel containing the other reagents, but instead of adding
oxygen, the solution was immediately worked up. After work up, 91% of
the material was recovered, and GLC chromatography indicated that hy-
drolysis had not occurred. The melting point also confirmed the oxime.
The IR spectra of the reaction mixtures involving copper ion and oxygen
indicate that carbonyl formation occurred before work up. Therefore,
hydrolysis of acetophenone oxime to ketone was probably minimal. How-
ever, cyclohexanone oxime was partially soluble in the aqueous acid
layer.

The high yields of by-products formed from competing pathways also

posed serious problems in the copper-catalyzed oxidation reactions since
the ketone was the desired product. Consequently, the formed ketone
was usually a minor product in the reaction. In addition, the yields
of ketone formation in a nitrogen atmosphere were low yet the amount
of oxime which reacted was quite high (e.g., 53% for cyclohexanone
oxime). A possible explanation was that a portion of the oxime was
lost during acid work up. To examine this possibility, sodium bi-
carbonate and ether was added to the aqueous acid solution of the
acetophenone oxime reaction after the chloroform layer was removed.
The ethreal solution was removed and concentrated. NMR analysis in-
dicated that less than 5% of acetophenone oxime was present. Therefore,
two possibilities exist. First, the oxime could react with a copper
species in some manner and the resulting product or products could
remain in the chloroform layer. Gas chromatography of the chloroform
solution, however, failed to indicate the presence of any material
other than the ketone and unchanged oxime. It is a possibility that
the by-products were too polar and were strongly absorbed onto the
column. The NMR and IR absorptions for the by-product might coincide
with those absorptions (chemical shifts or frequencies) exhibited by
the oxime. Second, the by-products may be very soluble in either
aqueous acid or basic solutions and therefore would not be found in
the chloroform solution after work up.

In the reactions involving cyclohexanone oxime and oxygen, gas
chromatography of the chloroform solution revealed the presence of a
material in addition to cyclohexanone and the unchanged oxime. The
identity of this material has not as yet been established.

In the reported oxidation of enamines by cuprous chloride and

molecular oxygen,[14] the reaction temperature was kept at 0°. An explanation was not given for this requirement, although the low temperature presumably may be necessary to avoid undesirable side reactions. The oxidation of cyclohexanone oxime was repeated at 0°, with the hope of reducing the amount of by-products. After careful work up, the GLC analysis indicated that very little oxime and ketone had been recovered. Sodium bicarbonate and ether were added to the aqueous acid solution and after the removal and concentration of the ethreal solution, GLC analysis indicated that 69% of oxime had reacted, and 51% of ketone had been formed. Therefore, only 18% remained unknown. These results suggest that higher yields of ketones from other oximes could perhaps be obtained at 0° using this solvent system. This possibility, however, was not examined. The GLC analysis also indicated the presence of a third material which had an identical retention time to the unidentified material obtained from the reactions of cyclohexanone oxime at room temperature. This may accound for the last 18% of the unknown material. As a control to determine the source of this unknown material, cyclohexanone in chloroform was treated with cuprous chloride and molecular oxygen in the presence of one equivalent of pyridine. After work up, GLC examination of the products suggested the generation of the unknown material. By comparison of retention times, the unknown material was shown not to be cyclohexane, cyclohexene, 1,2-cyclohexadione or benzene. One other possibility for the volatile compound is 1,2-cyclohexenone. However, this possibility has not been examined.

The NMR spectra of the reaction products from the oxidative reactions with both acetophenone oxime and cyclohexanone oxime showed identical absorptions at δ3.55, 0.92 and 0.82. The same reactions

performed in a nitrogen atmosphere did not show these absorptions.
This was a curious development in that possibly a common function
existed for both oximes or a side reaction was occurring which did not
involve the oxime. The evidence also suggested that the unknown mater-
ial in the reaction of cyclohexanone oxime was not the impurity observed
by NMR since a similar material was not found by GLC analysis of the
reaction products from the oxidation of acetophenone oxime. In order to
determine the source of the impurity, the reaction was repeated except,
the oxime was omitted. After the usual work up, the NMR spectrum did
indicate the presence of the impurity. The actual source of the im-
purity has not been determined. However, the important issue is that
the product did not arise from the oxime.

In the initial investigations, pyridine was excluded from the
reaction mixture and the IR spectrum of the reaction mixture indicated
that deoximation did not proceed. When a catalytic amount of pyridine
was used, IR analysis suggested that the reaction did proceed slightly.
However, with one or slightly more than one equivalent, the reaction
proceeded fairly well. The explanation for this observation may be that
in the neutral oxime the carbon of the oxime function may not be
sufficiently electronically rich for facile oxidation. Yet if a mild
base is present, the oxime proton is abstracted (pK_a = 10)[32] to give the
oximate anion 47. This then would be favorable to oxidation if any
extrapolation can be drawn from the enamine or hydrazone reactions
involving copper ions and oxygen.

Another possibility is that pyridine was needed to facilitate
electron transfer from copper to the oxime or oxime to the copper. To
explore this possibility, the reaction with acetophenone oxime was

repeated with 2,6-di-t-butylpyridine in place of pyridine. The dialkyl-ated base can not coordinate to the copper ion(s) owing to steric hindrance. The IR spectrum of the reaction mixture did indicate the formation of the ketone. Therefore, pyridine was apparently acting as a base and not assisting in electron transfer by copper in the reaction. Presumably, the basic co-solvent was increasing the concentration of oxime anion 47.

The benzoin oxime failed to react with either cuprous or cupric chloride and pyridine. Several reasons can be offered as to why oxidation did not occur. First, benzoin oxime (Cupron)[51] forms strong complexes with cuprous ion. As a result, the oxime may coordinate to the active site on the metal thereby restricting the oxidative reaction. Second, under the reaction conditions, benzoin oxime was only slightly soluble. Therefore, the reaction was mainly heterogeneous. The oxidation however, could perhaps, proceed under different conditions (e.g., with change in solvent and temperature).

Benzophenone oxime gave high yields of ketone, however, it was re-ported that this compound is somewhat unstable yielding imine, ketone and ammonia.[32]

As stated in the Introduction and Historical Background the reaction of oximes and cuprous chloride in toluene or benzene has been reported to yield substituted amides via Beckmann rearrangement. However, in the course of the present investigation, amide formation was not detected by GLC analysis or NMR spectroscopy.

Discussion of Future Work

As mentioned earlier, no attempts were made to optimize the reaction yields. Therefore, several conditions or factors need to be examined.

Solvent

Different solvent systems need to be examined. As mentioned earlier (p. 52) catechol (14) would not oxidize to the cis,cis-muconic acid until methanol was added.[17] A similar situation may exist in this investigation. The addition of a co-solvent may optimize the yields. Also it is important to use a solvent system so the solution is homogeneous. As was mentioned, several reactions were heterogeneous. Also a solvent system is needed which would be inert to the reaction conditions.

Temperature

The temperature is clearly important in the oxidative reaction. Thermal energy must be supplied to the mixture in order to achieve the activation energy. However, this also increases the chances of competing pathways to yield by-products. Therefore, a series of reactions should be studied to determine at which temperature the yields are optimized.

Anions

The anions associated with the copper cations may also be important. Several reports concerning oxidation of other organic compounds suggest that only certain copper salts afford reaction.[14,17] This may be due to the complex which is formed during reaction. Electron transfer may

only occur with specific complexes containing specific anions. Cuprous and cupric salts containing the counter ions: bromide, cyanide, nitrate and sulfate should be examined since these are fairly inexpensive and easily obtained.

By-Products

Last, the by-products which are formed need to be examined. Although some may be involved with the oxidation with oxygen, from the nitrogen reaction it appears as though side reactions were occurring which did not involve oxygen. The identity of these products is necessary to understand the side reactions and possibly limit these reactions from occurring.

Summary

In summary, this work represents the fulfillment of a prediction concerning the chemical behavior of copper ion and oxygen. Also, it was possible to extrapolate from the metal catalyzed oxidation of enamines to that of oximes. This study represents another example in which copper ions can interact with organic compounds. Also it was found that deoximation with inexpensive, easily obtainable copper ions can be realized. The major interest now in the project is to optimize the yield of the ketone and identify the other products. Lastly, the question as to whether this is another example of a transition metal and molecular oxygen mimicing singlet oxygen arises.[14] The reaction of singlet oxygen with oxime anions (47) is suggested.

CHAPTER IV

EXPERIMENTAL

Oxidations of Oximes by Copper Salts

Melting points were obtained from a Thomas-Hoover capillary melting point apparatus and were uncorrected. Proton magnetic resonance spectra were taken on a Varian A-60 NMR spectrometer with tetramethysilane (TMS) used as an internal standard. Infrared spectra were recorded on a Beckmann-8A spectrophotometer and GLC chromatograms were recorded on a Varian Aerograph series 2700 with a column of the dimensions, 5' X ¼". The column material was 15% OV-101 on Chrom G with HP 100/120 mesh support. Peak areas were determined by triangulation with = 10% error. In order to correlate peak areas with grams of sample, the areas were corrected by a response factor determined by the method submitted by Schupp.[52] The peak areas were then compared to peak areas of known concentration of authentic material. Samples were diluted in 1 ml of chloroform and 1 ul of solution was injected into the instrument. Retention times of the samples were also compared to known, authentic material.

In order to exclude water from the oxidation reactions, all reagents were dried. Pyridine was distilled from potassium hydroxide. All oximes were dried _in vacuo_ (0.05 mm, 25°) and chloroform was degassed with argon before each experiment. Benzoin oxime (50) was

obtained commercially (Fisher Scientific Company) and used without purification, mp, 149-151°, (lit.[51] mp, 150.5-151.0^o).

Anhydrous Cuprous Chloride

Cuprous chloride was prepared by the procedure of Fieser and Williamson.[53] Sodium chloride (10 g, 0.17 mol) was added to a boiling solution of cupric sulfate pentahydrate (CuSO$_4$ · 5H$_2$O) (30.0 g, 0.12 mol) in 100 ml of water. A solution of sodium bisulfate (7.0 g, 0.07 mol) and sodium hydroxide (4.5 g, 0.11 mol) in 50 ml of water was added slowly to the hot cupric sulfate solution. The resulting solution was cooled in ice water to yield white cuprous chloride. The solution was decanted, and the solid was washed two times with 30 ml of 95% of ethanol and once with 30 ml of anhydrous ether. The anhydrous cuprous chloride was dried in vacuo (0.03 mm, ca. 80°), wt 16.6 g, 70% (based on cupric sulfate).

Anhydrous Cupric Chloride

Cupric chloride (Baker's Analyzed Reagent) was commercially obtained. In order to remove water of hydration, cupric chloride (30.0 g, 0.18 mol) was dried in vacuo (0.05 mm, ca. 80°) to yield brown cupric chloride (24.0 g, 0.18 mol).

Benzophenone Oxime (28)

Compound 28 was prepared by the procedure of Lackman.[54] Powdered sodium hydroxide (110 g, 2.76 mol) was slowly added to a solution of benzophenone (100 g, 0.55 mol), hydroxylamine hydrochloride (60 g, 0.85 mol), 200 ml of 95% ethanol and 40 ml of water. The solution was

then refluxed for 10 min and after cooling to room temperature, was poured slowly into a solution of 300 ml of concentrated hydrochloric acid in 2ℓ of water. The resulting white precipitate was collected by filtration and found to be benzophenone oxime (28) (86.7 g, 80% based on benzophenone); mp, 140-141° (lit.[54] mp, 141-142°); IR (CS_2) spectrum show the absorptions: 3565s (O-H stretch), 3250vs (O-H stretch), 3060vs (C-H stretch), 1300s (C=N bend), 1150s (C-H in-plane bend), 1000vs, 905vs (C-H in-plane bend), 765vs (C-H out-of-plane bend) and 690 cm^{-1} s (C-H out-of-plane bend). In comparing the spectrum to that of the ketone the IR (CS_2) spectrum showed: 3300w (overtone), 3060vs (C-H stretch), 1660vs (C=O stretch), 1300vs (C=O bending), 1270vs (C-H in-plane bend), 1150s (C-H in-plane bend), 910vs (C-H in-plane bend), 760s (C-H out-of-plane bend) and 700 cm^{-1} vs (C-H out-of-plane bend).

Cyclohexanone Oxime (30)

Compound 30 was prepared by a modification of the procedure of Baeyer.[55] A mixture of cyclohexanone (26.8 g, 0.27 mol), 100 ml of 5M aqueous hydroxylamine hydrochloride, 100 ml of 5M aqueous sodium acetate and 170 ml of 95% ethanol was refluxed for 3 hr. The resulting solution was cooled to room temperature and concentrated. The resulting white precipitate, cyclohexanone oxime (30), was collected by filtration, wt 14.2 g. The filtrate was extracted with 75 ml of ether, and the ethereal solution was concentrated to yield 5.6 g of cyclohexanone oxime (30). The combined cyclohexanone oxime weighed 19.8 g (64% based on starting cyclohexanone); mp, 86-88° (lit.[55] mp, 88°). The IR (CS_2) spectrum showed the following absorptions: 3590s (O-H stretch), 3240vs (O-H stretch), 2920vs (C-H stretch), 1660w (C=N stretch),

1315s (C-H bend), 1220w (C-H bend), 945s, 890s (C-H bend) and 700s (C-H bend). In comparison the IR (CS$_2$) spectrum for cyclohexanone showed: 3420v (O-H stretch), 2900vs (C-H stretch), 1710vs (C=O stretch), 1300vs (C-H bend), 1215 (C-H bend), 1115vs (C=O bend), 900vs (C-H bend) and 745vs (C-H bend).

Acetophenone Oxime (32)

Compound 32 was prepared by the procedure of Janny.[56] Powdered sodium hydroxide (111 g, 2.77 mol) was slowly added to a solution of acetophenone (64 ml, 0.55 mol), hydroxylamine hydrochloride (60 g, 0.87 mol), 190 ml of methanol and 50 ml of water. The reaction became vigorous and the reaction flask was placed in ice water. After the addition was complete, the solution was refluxed for 15 min and allowed to cool to room temperature. A white precipitate was collected by filtration, wt 94.2 g. The solid was recrystallized from 60 ml of methanol to yield acetophenone oxime (32). (51.2 g, 68.9% based on acetophenone; mp, 58-60°), (lit.[56] mp, 60°); IR (CS$_2$): 3590vs (O-H stretch), 3250vs (O-H stretch), 2900s (C-H stretch), 1630w (C=N stretch), 1355s (sym CH$_3$ bend), 1280 (C-H in-plane bend), 1000vs (C-H in-plane bend), 910 cm^{-1} (C-H in-plane bend), 750vs (C-H out-of-plane bend) and 690 cm^{-1} vs (C-H out-of-plane bend). In comparison, the IR (CS$_2$) spectrum for acetophenone showed absorptions: 3360s (overtones), 3060vs (C-H stretch), 1680vs (C=O stretch), 1350vs (C-H in-plane bend), 1250vs (C=O bend), 1080vs (C-H in-plane bend), 950vs, 750vs (C-H out-of-plane bend) and 690 cm^{-1} vs (C-H out-of-plane bend).

Copper Catalyzed Oxidation of Oximes

The general procedure for the oxidation is illustrated below.
Deviations from this procedure are indicated.

Reaction of Acetophenone Oxime (32),
Cuprous Chloride and Oxygen

Anhydrous cuprous chloride (0.03 g, 7.5%, 0.3 mmol) was added to a
solution of acetophenone oxime (32) (0.52 g, 3.82 mmol) and pyridine
(2 ml, 24.9 mmol) in ca. 30 ml of degassed chloroform. Molecular oxygen
(ca. 20 bubbles per min) was bubbled into the solution for 14 hr at room
temperature. The resulting dark green solution was washed twice with
50 ml of 2% hydrochloric acid and once with 50 ml of saturated sodium
chloride solution. The organic layer was removed and concentrated to
afford a yellow oil, wt 0.52 g. GLC analysis indicated the presence of
0.31 g (60% recovered) of unchanged oxime and 0.07 g (40% based on
oxime reacted) of acetophenone. Retention times of the ketone and
oximes were 83 sec and 222 sec, respectively, at a column T^o = 140° and
flow rate 55 ml/min. The response factor was calculated for the ketone
and oxime to be 0.98 and 0.84, respectively; NMR (CS_2): δ 7.40 (m, 2,
o-C_6H_5 both ketone and oxime), 7.21 (m, 3, m + p-C_6H_5, both ketone and
oxime; also 34% of the aromatic protons are undefined), 3.48 (t, im-
purity), 2.42 (s, 3, CH_3, ketone), 2.13 (s, 3, CH_3, oxime), 0.88 (s,
impurity) and 0.80 (s, impurity); IR (CS_2): 3580s (N-H stretch, oxime),
2940s (C-H stretch both oxime and ketone), 1690s (C=O stretch, ketone),
1265vs (ketone), 990s (oxime), 915s (ketone), 760vs (both ketone and
oxime) and 690vs (both ketone and oxime).

Reaction of Acetophenone Oxime (32)
with Cupric Chloride and Oxygen

The generalized procedure described above was followed, except cupric chloride (0.04 g, 0.31 mmol) replaced cuprous chloride. The reaction time was 13 hr, and after the usual work up, a yellow oil, wt 0.55 g, was obtained. GLC chromatography indicated the presence of 0.48 g (91% recovered) of unchanged oxime and 0.01 g (23% based on re-acted oxime) of acetophenone. The retention times for the ketone and oxime at a column $T^o = 140^o$ and flow rate of 55 ml/min were 82 sec and 221 sec, respectively. The response factors were determined to be 1.05 and 0.76 for the ketone and oxime, respectively; NMR (CS_2): δ 9.85 (s, 1, O-H, oxime), 7.46 (m, 2, o-C_6H_5, oxime), 7.26 (m, 3, m + p-C_6H_5) and 2.20 (s, 3, CH_3, oxime); IR (CS_2): 3580s (oxime), 3220vs (oxime), 2920s (C-H stretch), 1680w (both oxime and ketone), 1360s (both oxime and ketone), 1280vs (both ketone and oxime), 1000vs (oxime), 920vs (oxime), 755vs (both oxime and ketone) and 690 cm^{-1} vs (both oxime and ketone).

Reaction of Acetophenone Oxime (32)
with Cuprous Chloride and Nitrogen

The generalized oxidation procedure was followed with the exception that nitrogen was used instead of oxygen. The usual work up afforded a solid mass, wt 0.52 g. The GLC chromatography indicated a weight of 0.43 g (82% recovered) of unchanged oxime and 0.01 g (10% based on reacted oxime) of acetophenone. The retention time at a column $T^o = 140^o$ and a flow rate of 55 ml/min for the ketone and oxime was 82 sec and 221 sec, respectively. The response factor was calculated as 0.91

and 1.05 for the ketone and oxime, respectively; NMR (CS_2): δ 7.38 (m, 2, o-C_6H_5, oxime), 7.20 (m, 3, m + p-C_6H_5, oxime) and 2.11 (s, 3, CH_3, oxime); IR (CS_2): 3580s (O-H stretch, oxime), 1324vs (O-H stretch, oxime), 920vs (oxime), 755vs (both oxime and ketone) and 690 cm^{-1} vs (both oxime and ketone).

Reaction of Cyclohexanone Oxime (30) with Cuprous Chloride and Oxygen

The usual oxidation procedure was followed except cyclohexanone oxime (30) (0.52 g, 4.57 mmol) was used. After the usual work up, GLC analysis of the yellow-green residue, wt 0.40 g, indicated 0.16 g (31% recovered) of unchanged oxime and 0.11 g (34% based on reacted oxime) of cyclohexanone. The retention times were 63 sec and 147 sec for the ketone and oxime, respectively, with a column $T^o = 120^o$ and flow rate of 45 ml/min. The response factors were calculated to be 0.91 and 1.05 for the ketone and oxime, respectively. Also, the presence of a third unidentified material was indicated by the chromatography, retention time 57 sec. Spectroscopic data gave NMR (CS_2): δ 3.54 (t, impurity), 2.25 (m, 4, 2,6-CH_2, oxime), 2.09 (shoulder, 2,6-CH_2, ketone), 1.75 (shoulder, 3,4,5-CH_2, ketone), 1.59 (s, 6, 3,4,5,-CH_2, oxime), 0.91 (s, impurity) and 0.82 (s, impurity); IR (CS_2): 3250w (oxime), 2920vs (both oxime and ketone), 1710vs (ketone), 1310w (both oxime and ketone), 1100w (ketone) and 750 cm^{-1} vs (ketone).

Reaction of Cyclohexanone Oxime (30) with Cupric Chloride and Oxygen

The generalized oxidation procedure was followed except cyclo-

hexanone oxime ($\underset{\sim}{30}$) (0.51 g, 4.53 mmol) and cupric chloride (0.05 g, 0.48 mmol) were used. After the usual work up, GLC analysis of the yellow-green oil, wt 0.47, afforded a weight of 0.35 g (68% recovered) of unchanged oxime and 0.06 g (43% based on reacted oxime) of cyclo-hexanone. Retention times for the ketone and oxime at a column T^O = 120° and a flow rate of 45 ml/min were 63 sec and 145 sec, respectively. The response factors were calculated to be 0.91 and 1.05 for the ketone and oxime, respectively. The chromatogram indicated a third peak, retention time 57 sec. Spectroscopic data gave NMR (CS_2): δ 3.55 (t, impurity), 2.30 (shoulder, 2,6-$\underline{CH}_2$, oxime) 2.19 (d, 2,6-$\underline{CH}_2$, ketone), 1.71 (m, 3,4,5-$\underline{CH}_2$, ketone), 1.68 (s, 3,4,5-$\underline{CH}_2$, oxime), 0.92 (s, impurity) and 0.82 (s, impurity); IR (CS_2): 3240s (oxime), 2900vs (both ketone and oxime), 1710vs (ketone), 1310w (oxime), 1215vs (ketone), 990s (oxime), 920s (oxime) and 750 cm^{-1} vs (ketone).

Reaction of Cyclohexanone Oxime ($\underset{\sim}{30}$)
with Cuprous Chloride and Nitrogen

The generalized procedure was used except that nitrogen and cyclo-hexanone oxime (0.30 g, 2.61 mmol) in 15 ml of chloroform was used instead of oxygen and acetophenone oxime. After the usual work up, a yellow mixture was obtained, wt 0.18 g. GLC analysis indicated a weight of 0.14 g (47% recovered) of unchanged oxime and 0.04 g (29% based on reacted oxime) of cyclohexanone. The response factors were calculated to be 1.00 and 0.92 for the ketone and oxime, respectively. The retention times for the ketone and oxime were 65 sec and 144 sec, respectively, at a column T^O = 120° and a flow rate of 45 ml/min. NMR (CS_2) examination indicated: δ 2.30 (m, 2,6-$\underline{CH}_2$, oxime), 2.22 (shoulder,

2,6-C$\underline{H}_2$, ketone), 1.71 (shoulder, 3,4,5-C$\underline{H}_2$, ketone) and 1.68 (s, 3,4,5-C$\underline{H}_2$, oxime). The spectrum did not show the presence of the usual impurity (see ahead); IR(CS_2): 3240s (oxime), 2920vs (both oxime and ketone), 1710s (ketone), 1310w (both ketone and oxime), 1215vs (ketone), 1100s (oxime) and 745 cm^{-1} vs (ketone).

Reaction of Cyclohexanone Oxime (30) with
One Equivalent Cuprous Chloride and Oxygen

The usual oxidative procedure was followed except one equivalent of cuprous chloride (0.49 g, 4.91 mmol) and cyclohexanone oxime (30) (0.54 g, 4.81 mmol) were used, and the reaction time was 23½ hr. The work up involved washing the reaction mixture 3 times with 50 ml of 10% hydrochloric acid and once with 50 ml of saturated sodium chloride solution. After the organic layer was removed and concentrated, a yellow oil, wt 0.51 g, was obtained. GLC analysis indicated a weight of 0.002 g (1% recovered) of unchanged oxime and 0.13 g (27% based on reacted oxime) of cyclohexanone. The retention times for the ketone and oxime at a column T^o = 120° and flow rate of 45 ml/min were 63 and 129 sec, respectively. A third unidentified compound peak was also indicated on the chromatography, retention time 57 sec. The response factors for the ketone and oxime were 0.99 and 0.96, respectively; NMR (CS_2): δ 7.30 (s, C$\underline{H}$Cl$_3$), 3.54 (t, impurity), 2.54 (sh, oxime), 2.20 (d, ketone), 1.72 (d, ketone), 1.54 (sh, oxime), 0.92 (s, impurity), 0.82 (s, impurity); IR (CS_2): 3240vs (oxime), 2900vs (both oxime and ketone), 1710vs (ketone), 1210vs (ketone), 1100w (oxime) and 750 cm^{-1} vs (ketone).

Reaction of Benzophenone Oxime (28)
with Cuprous Chloride and Oxygen

The generalized procedure was followed except that benzophenone oxime (28) (1.45 g, 7.38 mmol) was used. The usual work afforded a yellow oil, wt 0.99 g. GLC analysis indicated that all the oxime had reacted and 0.92 g (68.4% based on reacted oxime) of benzophenone had been formed. The retention time for the ketone at a column $T^o = 190^o$ and flow rate of 70 ml/min was 198 sec and had a calculated response factor of 1.08; NMR (CS_2): δ 7.75 (m, 2, $\underline{o}$-C_6H_5, ketone), 7.51 (s, 2, $\underline{o}$-C_6H_5, ketone), 7.38 (m, 6, $\underline{m}$ + $\underline{p}$-C_6H_5, ketone); IR (CS_2): 3200w (H_2O), 3060vs (ketone), 1665s (ketone), 1260vs (ketone), 1170s (ketone) 1050vs (ketone), 755vs (ketone) and 695 cm^{-1} (ketone).

Reaction of Benzophenone Oxime with
Cupric Chloride and Oxygen

The generalized procedure was followed except, benzophenone oxime (1.45 g, 7.38 mmol) and cupric chloride (0.06 g, 0.48 mmol) were used instead of acetophenone oxime and cuprous chloride. After the usual work up, GLC analysis indicated that the yellow oil, 1.01 g, did not contain any benzophenone oxime and possessed 0.83 g (62% based on re-acted oxime) of benzophenone. Retention time and response factors for the ketone at a column $T^o = 190^o$ and flow rate 70 ml/min was 198 sec and 1.08, respectively. Spectroscopic data gave NMR (CS_2): δ 7.77 (m, 2, $\underline{o}$-C_6H_5, ketone), 7.50 (s, 2, $\underline{o}$-C_6H_5, ketone) and 7.40 (m, 6, $\underline{m}$ + $\underline{p}$-C_6H_5, ketone; IR (CS_2): 3220w (possibly H_2O), 3060vs (ketone), 1055vs (ketone), 910vs (ketone), 755vs (ketone and 695 cm^{-1} vs (ketone).

Reaction of Benzophenone Oxime (28) with
Cuprous Chloride and Nitrogen

The generalized oxidative procedure was followed except benzo-
phenone oxime (50) (0.52 g, 2.63 mmol), in 15 ml of chloroform, and
nitrogen were used. The usual work up afforded a white solid, wt 0.51 g;
mp, 130-136° (lit.[54] mp, 140-141° for the oxime). GLC analysis in-
dicated a weight of 0.38 (73% recovered) of unchanged oxime and 0.08 g
(62% based on reacted oxime) of benzophenone had been formed. The
retention times for the ketone and oxime at a column $T^0 = 190^0$ and a
flow rate of 70 ml/min were 204 sec and 342 sec, respectively; NMR
(CS_2): δ 7.67 (m, ketone), 7.40 (s, oxime) and 7.25 (m, ketone); IR
(CS_2): 3050w (both ketone and oxime), 1660s (both ketone and oxime),
1280vs (ketone), 910w (both ketone and oxime), 755vs (both ketone and
oxime) and 695 cm^{-1} vs (both ketone and oxime).

Reaction of Benzoin Oxime (50) with
Cuprous Chloride and Oxygen

The general oxidation procedure was followed except benzoin oxime
(50) 1.68 g, 7.38 mmol) was used instead of acetophenone oxime. The
work up washing three times with 12% HCl and once with saturated sodium
chloride, afforded a white residue, wt 1.62, mp 148-150°; (lit.[51] mp,
150-151° for the oxime). GLC analysis indicated only the oxime, 1.50 g.
The retention time at a column $T^0 = 190^0$ flow rate of 70 ml/min was 410
sec. The response factor was calculated as 0.87; NMR (acetone-d_6):
δ7.20 (s, oxime) and 5.62 (s, oxime); IR (acetone): 3280vs (oxime),
2900vs (oxime), 950s (oxime) and 700vs cm^{-1} (oxime).

NMR (CS_2): δ 3.55 (t, impurity), 2.40 (m, oxime), 2.25 (d, ketone), 1.76 (m, ketone), 1.50 (s, oxime), 0.92 (s, impurity) and 0.82 (s, impurity).

Reaction of Cyclohexanone (10) with Cuprous Chloride and Oxygen

The generalized procedure was followed except cyclohexanone (10) (0.50 g, 5.11 mmol) was used for 28 hr instead of acetophenone oxime for 14 hr. The usual work up afforded a green oil wt 0.42 g. GLC analysis indicated that 0.27 g (53% recovered) also another peak was indicated from the chromatogram corresponding to 25% of the area of cyclohexanone. The retention time at a column $T^o = 90^o$ and a flow rate of 40 ml/min was 60 sec and 126 sec for the unknown material and cyclohexanone, respectively. A response factor was calculated to be 1.04 for the ketone; IR (CS_2): 2900vs (ketone), 1700vs (ketone), 1310vs (ketone), 1215vs (ketone), 1115vs (ketone), 1050s (ketone), 900w (ketone) and 745 cm^{-1} vs (ketone).

Reaction of Cuprous Chloride, Chloroform Pyridine and Oxygen

The general procedure was followed except the oxime was excluded from the reaction. After work up, residue was diluted with carbon disulfide and an NMR (CS_2) gave: δ 3.50 (t), 1.50 (t), 0.92 (s) and 0.81 (s). The material was an impurity found in the NMR spectra of the residues of cyclohexanone oxime and acetophenone oxime reactions with oxygen.

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