STUDIES TOWARD THE SYNTHESIS OF ORGANIC CONDUCTORS

By

Larry Lewis Klein

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ABSTRACT

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OF ORGANIC CONDUCTORS

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With the discovery in 1973 that tetracyanoquinodimethane, TCNQ, and tetrathiafulvalene, TTF, form an electrically conducting complex, there arose a need for compounds analogous to these in order to optimize the conductivity. We report here our attempt to prepare hetero-analogs of these systems.

The first area explored was that of the azine ring systems. Potassium 4-dicyanomethylpyridine 1-dicyanomethylide was prepared from 4-chloropyridine. Various carbon, nitrogen, and sulfur protected malononitriles were prepared and used as nucleophiles with 3,6-dichloropyridazine. The work performed on the pyrimidine ring system led to the synthesis of the ethylene ketal and the ethylene dithioketal of 1,3-diaminoacetone along with N,N'-dialkyl derivatives of the former ketal. Synthesis of the sodium and tetrabutylammonium salts of 3-dicyanomethyl-6-methylthio-1,2,4,5-tetra-

zine was also successful.

Several new 2,5-disubstituted derivatives of the thieno[3,2-b]thiophene ring system were prepared. Synthesis of the corresponding diacid, bis-carbomethoxy, bis-carboethoxy, bis-hydroxymethyl, bis-chloromethyl, bis-cyanomethyl, and bis-(carboethoxy)cyanomethyl are described. Two potential donor molecules were also prepared from condensations of 2,5-thieno[3,2-b]thiophene dicarboxaldehyde with 1,2-benzenedithiol, and 4-methylbenzene-1,2-dithiol followed by oxidation.

Synthetic efforts toward 3,4,7,8-tetrathiopyridazino[4,5-d]pyridazine are described including the preparation of several new tetra-alkylthio derivatives of this ring system. Finally, construction of the skeleton of a bis-benzannulated diaza-azulene was achieved, providing a key step toward the goal of synthesizing a tetracyano diaza-azulene quinone.

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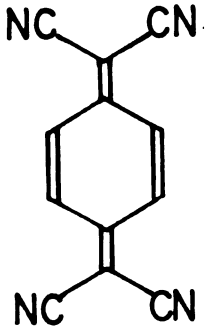
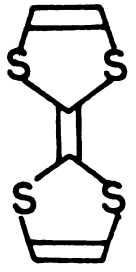
INTRODUCTION

The majority of organic compounds are poor electrical conductors with conductivities of $10^{-10}\ \Omega^{-1}cm^{-1}$ to $10^{-12}\ \Omega^{-1}cm^{-1}$. This is due, in part, to the delocalization of paired electrons in the sigma bonded framework. However, in 1962, a DuPont group reported the synthesis of tetracyanoquinodimethane, TCNQ, 1, and later, several of its non-metallic radical ion salts[1,2]. These crystalline complexes were found to conduct electricity mainly along one axis, thereby behaving as a one-dimensional organic metal. Since that time several comprehensive reviews of this field from the perspective of solid state physics, physical chemistry, and synthetic chemistry have been published[3].

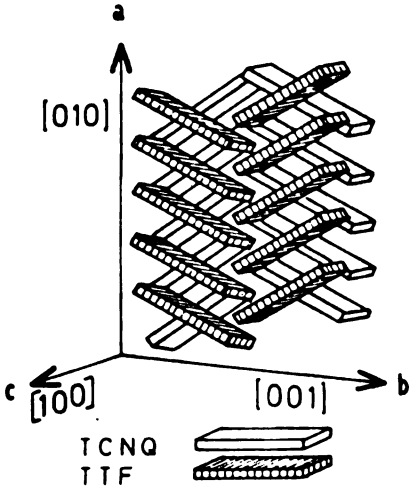
To date, the most studied example of an organic metal is the charge transfer complex between TCNQ and tetrathiafulvalene, TTF, 2. This complex has a room temperature conductivity of $10^{2}\ \Omega^{-1}cm^{-1}$, comparable to graphite, but more exciting and controversial is its conductivity at low temperatures, measured to be $10^{4}\ \Omega^{-1}cm^{-1}$ at $60^{\circ}K$[4]. The TCNQ molecule serves as the electron acceptor while the TTF molecule is the donor. The X-ray structure of this complex shows segregated stacks of TCNQ and of TTF ions, each stack existing in a face-to-face arrangement to maximize interactions[5]. This structure is shown in Figure 1.



TCNQ



TTF



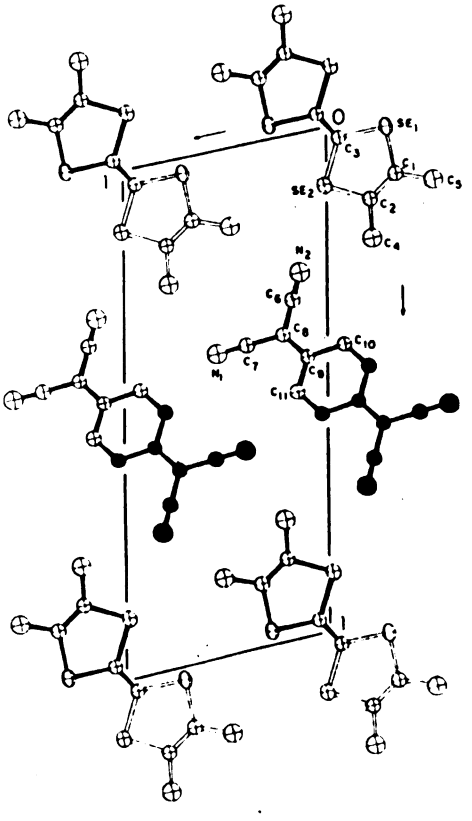


FIGURE: 1 Structure of TCNQ : TTF

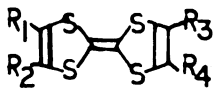
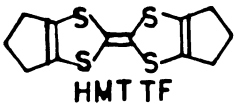
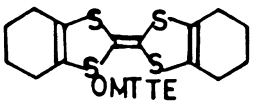
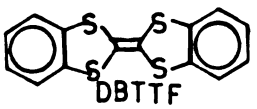
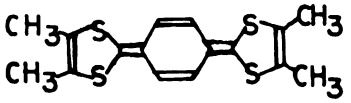
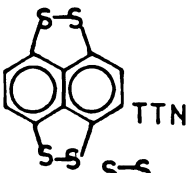
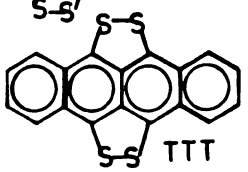
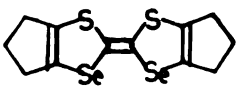
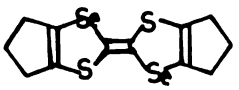
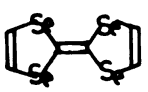
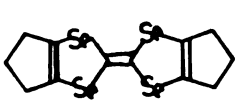
The overlapping electron cloud can be considered as the conducting media. By attaching electrodes along the three crystallographic axes to measure the conductivities, it has been shown that axis "a" (Figure 1) is the conducting axis. The conductivity has also been found to be directly dependent on the distance between the stacked molecules, i.e., decreasing the interplanar distance increases π overlap and thus, the conductivity.

Complete transfer of an electron from the donor species to the acceptor in the complex has been shown to be unnecessary, in fact, those salts with highest conductivity contain the species in mixed valence states[6]. Incomplete charge transfer results in partially filled energy levels that allow an electron flow much as in n or p type semiconductors. This situation can be promoted by regulation of the oxidation and reduction potentials of the interacting species. One report proposes that the difference in these respective values between the donor and the acceptor will be proportional to the conductive properties, thereby suggesting why some donors only form conducting salts with particular acceptors[7]. More information about the properties of organic metals has been obtained by modifying either nucleus in a systematic way. Compilations of the conductivity ranges, however, have shown that these factors do not yet completely explain this phenomena.

The thought behind the design of an organic conductor has evolved through a combination of theory and practice. It is believed by theorists that several characteristics should be incorporated into a possible conductor: 1) the molecule should be planar, with extensive delocalized π electron systems to facilitate stacking of molecules in the solid state; 2) it should have comparatively small size with maximum polarizability; 3) it should be symmetrical so as not to introduce intrinsic structural disorder; 4) it should be nominally divalent, necessary for mixed valence[8].

Listed below in Table 1 are several donor modifications and their TCNQ salt conductivities at room temperature[9]. In I-2, substitution of the TTF molecule with alkyl sidechains causes a twofold increase in the conductivity, and yet, I-4 has a lower value than TTF. Besides sidechain modification, extension of the unsaturated system was also carried out. The benzo analogs of TTF and TTN, I-5 and I-8 respectively, have recently been prepared as has the phenylene compound, I-6. These variations have, in general, not increased the conductivity to any great extent. The third type of modification, heteroatomic exchange, has resulted in significant improvement in conductivity. The most striking example is I-12, whose TCNQ salt has the highest room temperature conductivity measured thus far.

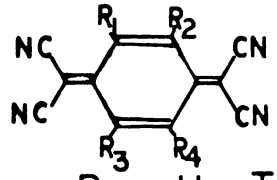
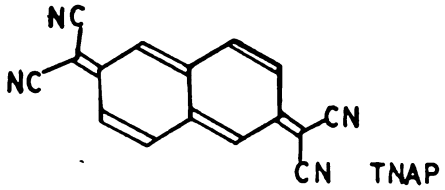
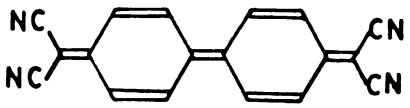
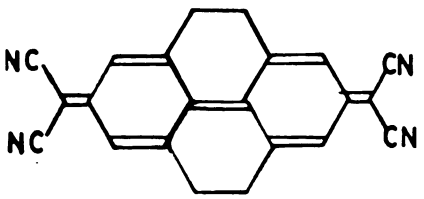
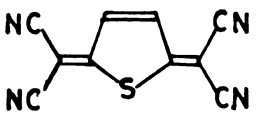
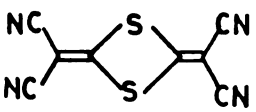
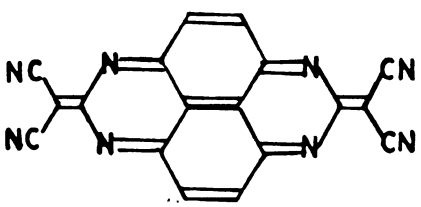
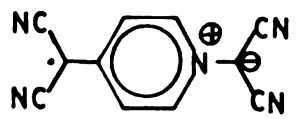
TABLE I

	ENTRY[9]	RATIO: TCNQ	PELLET CONDUCTIVITY($\Omega^{-1}cm^{-1}$) room temperature
			
1	R_{1-4} = H (TTF)	1:1	500
2	R_{1-4} = CH_3 TMTTF	1.1:2	10^{3}
3	 HMTTF	1:1	500
4	 OMTTE	1:1	5×10^{-5}
5	 DBTTF	1:1	10^{-7}
6		1:2	10^{-3}
7	 TTN	1:1	40
8	 TTT	1:1 1:2	1 100
9		1:1	100
10		1:1	2×10^{-6}
11		1:1	800
12		1:1	2,000

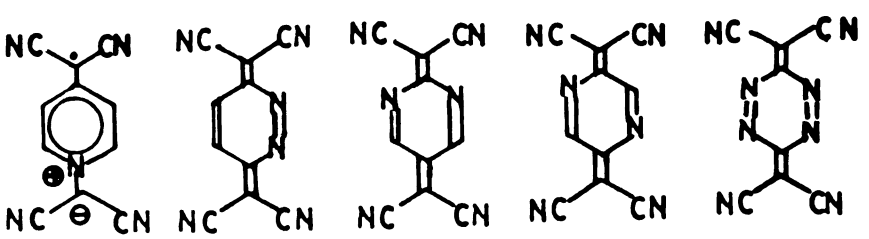
Regarding modification of the acceptor, much less work has been done. The majority of the changes have involved sidechain variations in TCNQ itself. Many derivatives of TCNQ have been synthesized, incorporating OR, SR, F, Cl, Br, I and alkyl substituents onto the ring[10]. Some of these examples with higher conductivities are shown in Table II. The extended systems II-5 and II-6 have been known for some time, with only II-4 leading to stable charge transfer compounds. Heteroatom exchange in these acceptor systems is less common. The mono-sulfur and di-sulfur analogs to TCNQ, II-8 and II-9, have been prepared. However, II-9 forms non-conducting complexes with TTF, and although the radical anion of II-8 has been isolated, it has failed to undergo any charge transfer with this donor. In the case of II-10, the dianion could not be oxidized to a stable radical, although work involving this system is continuing. Compound II-11 was prepared by Bell Laboratories[11] and ourselves. A more detailed description of this work will follow.

In order to understand the process of conduction in organic solids, more derivatives need to be synthesized and studied. In light of the work done thus far, we felt that the most advantageous direction to follow was to apply heteroatomic exchange to both TCNQ and TTF to form new acceptor and donor

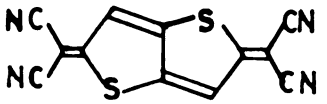
TABLE II

		PELLET CONDUCTIVITY (RT) with TTF	Ref.
1	 $R_{1-4} = H$ TCNQ	$500\ \Omega^{-1}\,cm^{-1}$	10
2	$R_{1-4} = F$ $TCNQF_4$	—	10
3	$R_1 = R_4 = H$, $R_2 = R_3 = F$	2×10^{-5}	12
4	$R_1 = R_4 = H$, $R_2 = R_3 = CH_3$	3	13
5	 TNAP	40	14
6		—	15
7		2×10^{-1} w/TMTTF	16
8		—	17
9		10^{-6}	18
10		—	19
11		10^{-2}	3

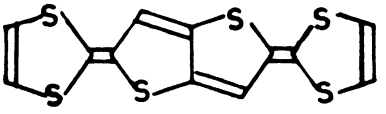
analogs. It has previously been hypothesized that the substitution of nitrogen for carbon in electron acceptors should increase the ion's affinity for electrons[19]. With this in mind, one of our goals was to synthesize the molecules 3-7, of which are all aza-analogs of TCNQ. Although this goal seemed to be a logical step in the search for organic conductors, none of these molecules were previously known, either in the quinoid form shown, the reduced form, or in any derivatized state. The aim of this research was not only to construct these molecules, but in doing so, to forge new synthetic approaches to the particular substitution patterns on these heteroatomic rings.



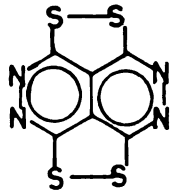
The second part, of this work was devoted to the thienothiophene ring system, 8, which is a sulfur analog of TNAP, and the synthesis of its TTF analog, 9. The third part will describe synthetic work performed on the tetraazanapthalene donor, 10, and the dibenzo-diaza-azulene system, 11.



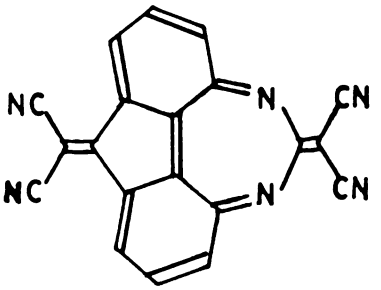
8



9



10



11

RESULTS AND DISCUSSION

I. PYRIDINE NUCLEUS

The pyridine ylide, 3, is peculiar in this group of synthetic targets in that it yields a neutral radical upon oxidation of its conjugate base. In theory, this greatly decreases the coulomb interactions between the electron clouds on face-to-face molecules. The resulting decreased interplanar distance should, in turn, enhance the conductivity. Of course, the final result will be dependent on the mode of stacking in the solid state, where a face-to-face array of like molecules would be necessary.

Of the two synthetic routes to 3 that were envisioned, the first to be studied employed a nucleophilic attack of malononitrile anion upon 4-chloropyridine, 13. The ensuing reaction with tetracyanoethylene oxide as shown in Figure 2, could yield the conjugate acid of the target molecule. In

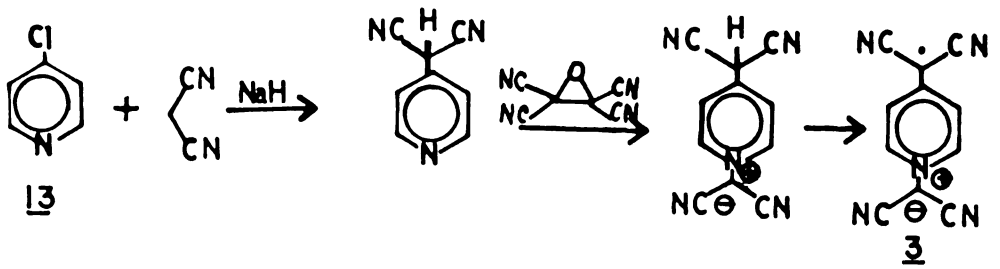


FIGURE 2: First attempted route toward 3.

most cases the pyridine nucleus is far too electron rich to

undergo nucleophilic substitution, and this problem has been countered in two ways. Smith and Evans[20] succeeded in substituting this chlorine with 5-alkyl barbituric acid derivatives in the presence of acetic anhydride(Figure 3). Presumedly, initial acetylation of the pyridine nitrogen activated the ring allowing attack by nucleophiles. The second method of activation is shown by the substitution of

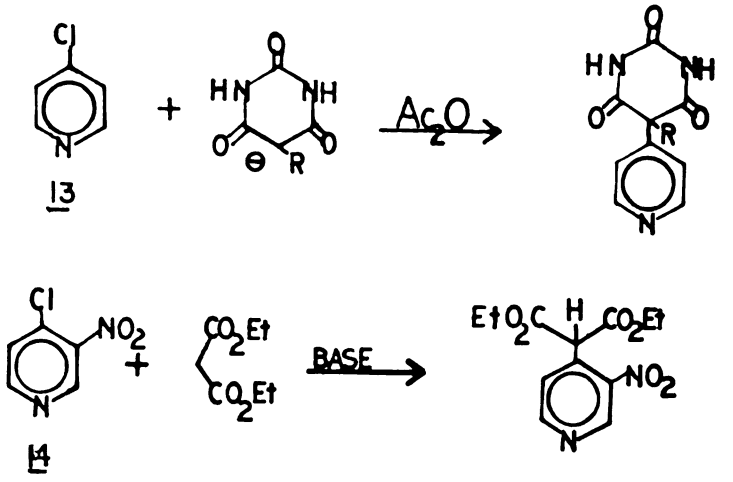
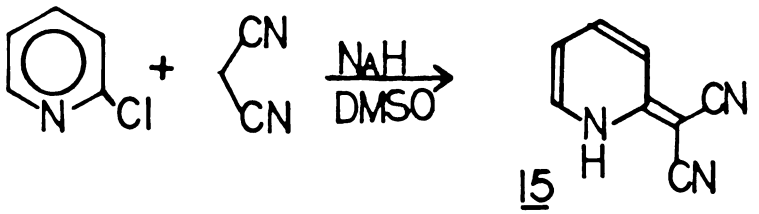


FIGURE 3. Nucleophilic substitutions of 4-chloropyridines.

chlorine in 14 by sodio diethylmalonate(Figure 3)[21]. The ortho nitro group accelerates the attack, possibly via electron transfer. Subsequent removal of this activating group would be necessary, so this method was not studied further.

However, in 1975, Pollack[22] showed that direct reaction of malononitrile anion in dimethyl sulfoxide with 2-chloropyridine yields the compound 15, shown in the fa-

vored tautomeric form(Figure 4). Under these same

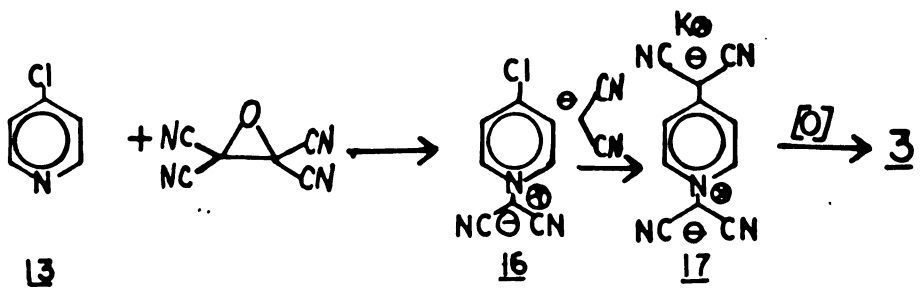


15

FIGURE 4: Reaction of 2-chloropyridine with malononitrile.

conditions, though, reaction with 13 led to a cyano containing water soluble dye. This result was repeatedly attained from the many attempts to react 13 with the malononitrile anion. The autoquaternization of 4-chloropyridine is known to occur slowly at room temperature and is inhibited in basic solution. A possible reason that 15 could be prepared under these conditions is that the site of reactivity, the nitrogen, is blocked. All other efforts toward substitution of the chlorine in 13 with different bases led to the same result.

The second route to 3, (Figure 5) takes advantage of the ylide structure in 16 to activate the ring toward the final substitution. 4-Chloropyridine was prepared



13 16 17

FIGURE 5: Second attempted route toward 3.

by neutralization of its commercially available hydrochloride salt followed by extraction with ether. Evaporation of the ether and addition of dry reaction solvent completed the procedure used in most cases when the free base was needed. Its reaction with tetracyanoethylene oxide yielded a bright yellow crystalline compound, 16. Reaction conditions proved critical as the yields ranged from 10% to 70%.

Reaction of the activated chlorine in 16 with the malononitrile anion led to a high melting (>300°) very insoluble salt. To generate the malononitrile anion, sodium methoxide in methanol or benzene, sodium hydroxide in ethanol, potassium t-butoxide in tetrahydrofuran, and sodium hydride in toluene were used. The product of each process exhibited an infrared spectrum showing the ylide structure, a para substituted pyridine ring, loss of the aromatic chlorine and a multiple cyano peak at 2130cm-1 and 2200cm-1. The PMR in dimethyl sulfoxide shows doublets at δ6.7 and δ7.7 as an AA'BB' pattern. Other variations using hindered amines left tarry oils as products. Attempts to silylate or alkylate this anion went for naught as it was quite unreactive. Only the potassium salt, 17, could be obtained in crystallized form as purple needles by evaporating an acetone solution. An elemental analysis (CHN) of this salt was consistant with its formulation.

Further evidence for this structure was achieved by an alternate synthesis shown in Figure 6. The use of t-butyl-malononitrile

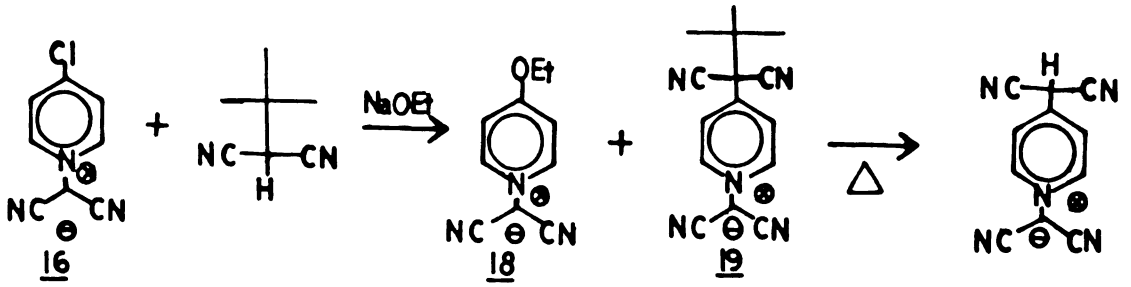


FIGURE 6: Alternate route toward 17.

as a protected malononitrile equivalent has precedence in the work of Wheland and Martin[10]. Since there is no hydrogen α to the cyano groups in the adduct, further reaction of this site in the basic medium is prevented. In the synthesis of polyhalo TCNQ's, these workers found that by using t-butyl malononitrile as a masked dicyano moiety, a displacement of the halide on the electron deficient ring can occur. The t-butyl group is then removed thermally under neutral conditions as isobutylene. Because the ylide structure decreases the electron density of the chloropyridine ring, this process seemed applicable to 16. Milder conditions were first attempted using sodium ethoxide as the base. However, this resulted in a mixture of two products, 18 and 19, the ethoxy compound being the major product. With sodium hydride, 19 was produced in 81% as a bright yellow powder, mp 218°C.

From PMR data, the pyrolytic cleavage of the t-butyl group seems to take place most readily in dimethyl sulfoxide, rather than mesitylene or propionic acid. The reaction can be conveniently monitored by heating a sample of 19 in a PMR tube in deuterated dimethyl sulfoxide. As the intensity of the t-butyl signal decreases, the aromatic proton pattern of two doublets changes. The downfield doublet centered at δ8.45, corresponding to the 3,5-protons in 19, disappears, and a doublet at δ6.7 appears. The signal for the 2,6-protons retains the same chemical shift in both samples. The PMR of the product after warming 10-40 hours at 110°C, shows the same spectrum as that shown by the previously described salt, 17, giving further evidence for its structure.

A final alternate synthesis should be mentioned. It was thought that if the diester, 20, could be made, ammonolysis followed by dehydration could afford the conjugate acid of 3(Figure 7). In the event, reaction of 16 with sodio diethyl

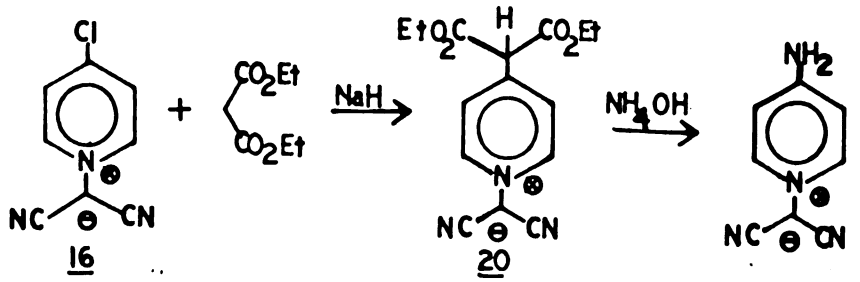


FIGURE 7: Third attempted route toward 3.

malonate in ethanol gave the diester, but ammonolysis caused cleavage of the original nucleophile. The product was shown by PMR, infrared, and mass spectrometry to be 4-amino-N-dicyanomethyl pyridine.

At the same time this study was underway, a group at Bell Laboratories reported (in an ACS meeting abstract) a similar preparation of 17 as shown in Figure 5[11]. Their studies on its oxidation to the radical-ylide, 3, led to the conclusion that this radical species, once created, was not stable and perhaps underwent dimerization or polymerization. The anionic form of this compound has been complexed with TTF (See Table II, entry 11), however the conductivity was low, at 10^{-2} $\Omega^{-1}cm^{-1}$. In its protonated form, 17 has been incorporated into the TCNQ-TTF complex[23], but further work on this compound has not been reported.

II. PYRIDAZINE NUCLEUS

The substitution of two ring carbons in TCNQ by two nitrogens gives rise to three possible isomeric diazine analogs, pyridazine, 4, pyrimidine, 5, and pyrazine, 6(Figure 8). Pyridazine 4, and pyrazine 6, are chemically

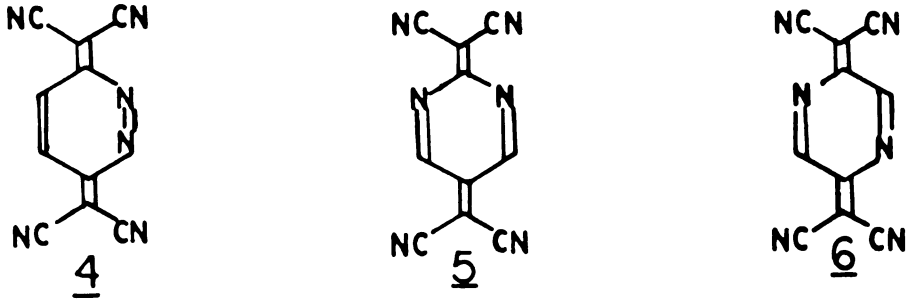


FIGURE 8: Tetracyano-diazinequinone analogs to TCNQ.

similar in that the two functionalized sites have equivalent positions in the respective molecules. Synthetic methods used to prepare one of these isomers, could most probably be repeated for the other. The third isomer, pyrimidine 5, will be discussed separately.

Since the nitrogens are unsubstituted, these molecules could form radical anions, rather than ylides, in much the same way that TCNQ does. As previously mentioned, a heteroatom exchange should retain the same molecular structure and possibly, the same solid state structure as TCNQ. The changes imparted to the electronic system, though, might allow greater π overlap. Also, the lowered degree of symme-

try of these molecules should decrease crystal distortions, known as Peierls transitions, which occur at very low temperatures. Since a conductor-to-insulator transition accompanies this distortion, then by lessening its incidence, one is capable of testing for potential superconductivity at even lower temperatures.

The pyridazine compound 4 is analogous in structure to 3,6-pyridazinedione, 21, (Figure 9) which was previously synthesized in situ

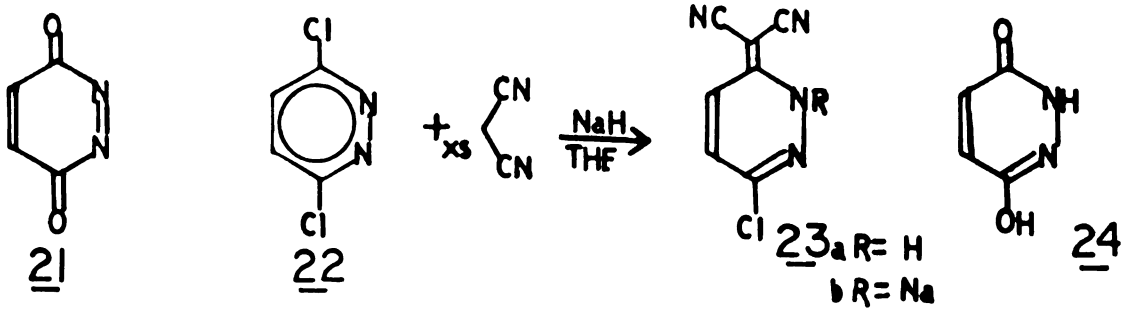


FIGURE 9: Pyridazine quinones.

and shown to be a very reactive dienophile[24]. The failure to isolate 21 may also indicate stability problems for 4. However, the exchange of the oxygen in these quinones for the dicyanomethyl group normally decreases their reactivity[25]. The greater delocalization of electrons and the increase in size of the terminal group in the cyano compounds may serve to restrict both Michael-additions and cycloadditions from occurring.

3,6-Dichloropyridazine, 22, was used as a starting material for this synthesis. The halogens are known to be readily replacable by oxy, thia, aza, and, though less often, by carbon nucleophiles[26]. A direct displacement with malononitrile anion obtained through the use of sodium hydride in tetrahydrofuran, has been attempted but this afforded only 23a[27]. This compound is bright yellow and is known to exist mainly in the tautomeric structure shown in Figure 9. This form is found to be prevalent in most hydroxy azines and was confirmed by X-ray crystallographic studies on 2(H)pyridazine-3-one and maleic hydrazide, 24[28]. Another method of indicating the predominant tautomer is UV spectroscopy, which shows distinctive peaks depending upon the main contributor to the electronic structure. However, this molecule, 23a, shows a PMR spectrum in DMSO whose signals appear at δ7.4(s) and δ10.3(br s), the latter being the tautomeric proton.

Increasing the ratio of base or malononitrile to 22, or using harsher conditions still yields only 23a, probably due to the acidity of the tautomeric proton. Following the substitution of chlorine in 22, the acidity of this proton increases relative to the malononitrile proton. A facile transfer of the tautomeric proton onto malononitrile occurs to give 23b as the product. Substitution of the second chlorine in this anion apparently does not occur.

To solve this problem one must modify the nucleophile by either increasing its reactivity to undergo the second attack or replacing the proton by some protecting group. The former method was applied in the synthesis of the polycyano compound 25(Figure 10). Friedrich[29] found that, although monosubstitution occurs with typical solvent systems, the use of hexamethylphosphoramide activates the nucleophile such that disubstitution will take place. This method was tried on 22 using malononitrile and malonic ester anions as nucleophiles, though in both cases only monosubstituted products were isolated.

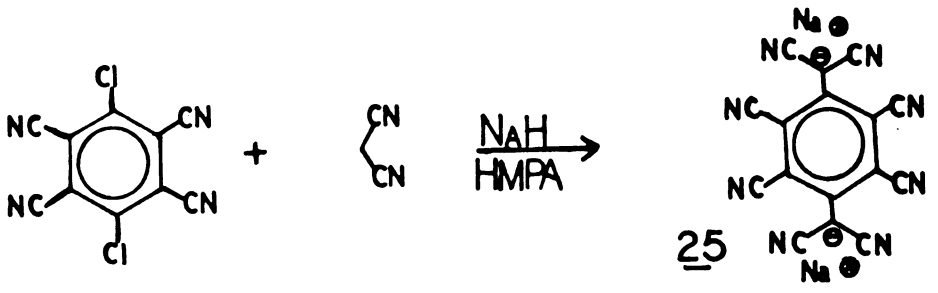


FIGURE 10: Synthesis of 2,3,5,6-tetracyano-TCNQ.

Protection of the dicyanomethyl moiety may be accomplished by substitution of the tautomeric hydrogen in 23a or by initial addition of a protected malononitrile group to 22 itself. In the first case, methylation of 23a with trimethyloxonium fluoroborate led to only an insoluble polymeric

material. However, when sodium hydride was reacted with 23a to form the anion, 23b, this same alkylation gave one product, 26, isolated in 41%(Figure 11). This solid exhibited two signals in its PMR spectrum,

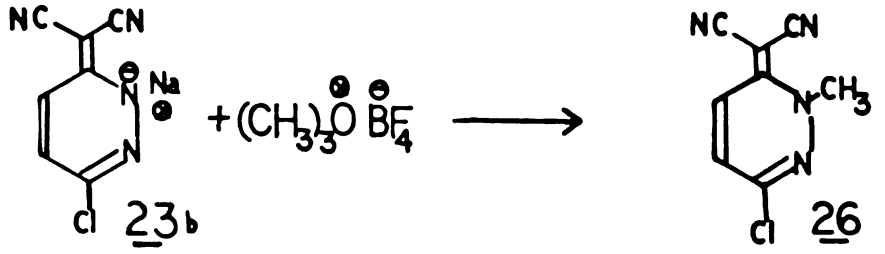


FIGURE 11: Alkylation of dicyanopyridazine, 23a.

a singlet at δ4.15 and an AB quartet centered at δ7.42 in a ratio of three to two. From previous studies of the methylation of tautomeric 3,6-disubstituted pyridazines, it is assumed that the alkylation has taken place on the ring nitrogen[28]. Treatment of this "protected" pyridazine with malononitrile anion at reflux for 2 hours provided a deeply colored mixture of products which was not further characterized.

Protected malononitrile groups have already been described with the use of t-butyl-malononitrile in the production of tetrafluoro TCNQ, 28b(Figure 12)[10]. Upon heating, 28a loses two equivalents of isobutylene to give a dihydro precursor of 28b. This scheme was repeated by reacting two moles of the conjugate base

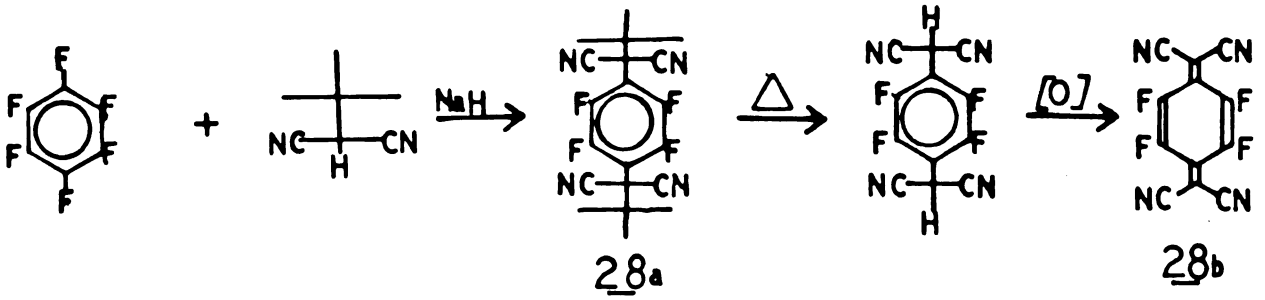


FIGURE 12: Synthesis of tetrafluoro-TCNQ.

of t-butyl-malononitrile with 22. After purification by column chromatography, 31% of 29 was isolated as white flakes(Figure 13). The PMR,

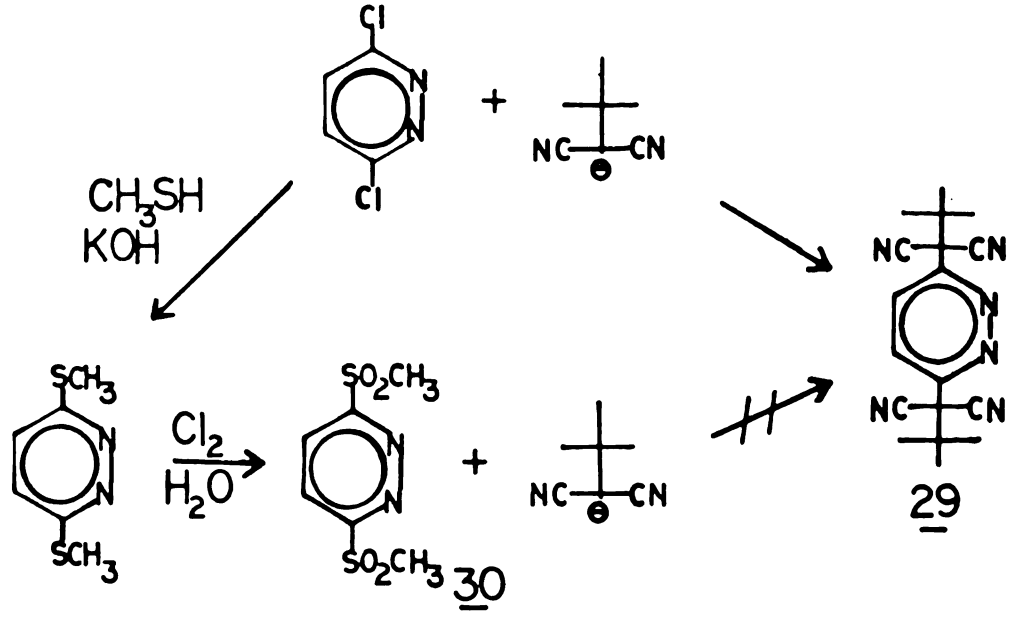


FIGURE 13: Synthesis of tetracyano-pyridazine 29.

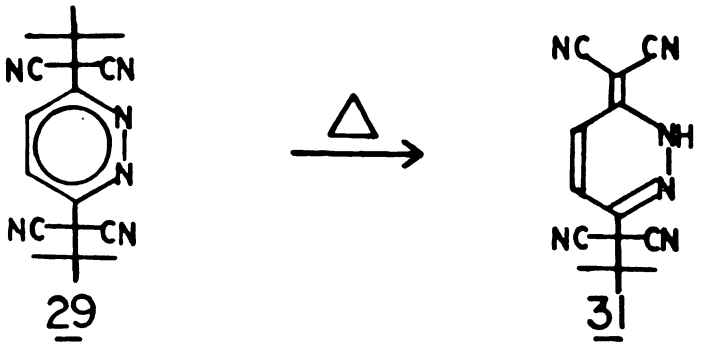
IR and mass spectral values were all those expected for 3,6-bis(t-butyldicyanomethyl)pyridazine.

Attempts to increase the yield by increasing the labil-

ity of the leaving group, i.e. from chlorine to methylsulfonyl as shown, led to 3,6-bis(methylsulfonyl)pyridazine, 30. However, when the same reaction conditions used for 22 were applied to 30, no replacement of methyl sulfonyl groups was observed.

The thermolysis of 29 was effected under varying conditions, but only one major product was isolated in each instance, this being the mono-t-butyl compound, 31. The color of this compound, bright yellow, can be used to detect its presence, and in most cases mild heating induced this color change. A list of reaction solvents and their results are shown here in Table 3. Run 6 was chosen as the best procedure as the yield (61%) was highest. Pyridazine 31 was also shown by TLC to be the main product in the other runs. When 31 was isolated and purified, its infrared spectral data were very similar to the chloro compound, 23a, and its PMR spectrum showed two singlets of ratio nine to two appearing at δ1.12 and δ7.3, respectively in dimethyl sulfoxide. The signal due to the tautomeric proton was not seen.

Resubmitting 31 to the same reaction conditions returned starting material along with a small amount of an orange solid. This compound was isolated by column chromatography and showed a base peak in the mass spectrum of only m/e149. The infrared spectrum exhibited only a very broad



29 31

TABLE III

ENTRY	SOLVENT	T°C	TIME(min)	RESULT
1	ANISOLE	152	300	29, 31
2	MESITYLENE	162	600	31
3	DECALIN	195	30	31
4	TRIGLYME	222	180	31
5	QUINOLINE	237	5	31
6	PHENYL ETHER	259	5	31 60%
7	SULFOLANE	285	20	—
8	$(Bu)_4N^{\oplus}\ Br^{\ominus}$	120	5	31
9	DMSO	120	360	—

signal in the cyano region, and this product appeared to be due to a degradative process. It is possible that the desired product may not be stable under these thermolytic conditions; however if so, there is still only a very small amount of it being formed.

Since the t-butyl group proved to be troublesome to remove, methodology directed toward different protected malononitriles was sought. A solution to this problem would have utility not only for this problem but also for various other α-haloazines such as 32, 33 or 34(Figure 14).

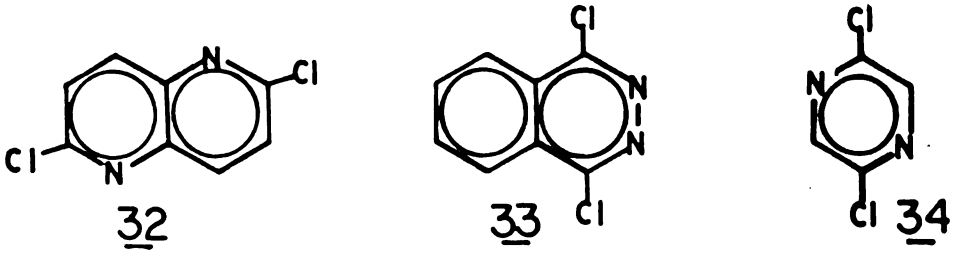


FIGURE 14: Other potential targets of malononitrile anion.

It was thought that by making the attached carbon group more bulky or by stabilizing the alkene which forms on thermolytic cleavage, the reaction would go to completion. To this end, various substituted malononitriles 35a-d were prepared by sodium borohydride or trimethylammonium formate[31] reduction of the condensation products of the corresponding carbonyl compound and malononitrile (Figure 15). However, under the same

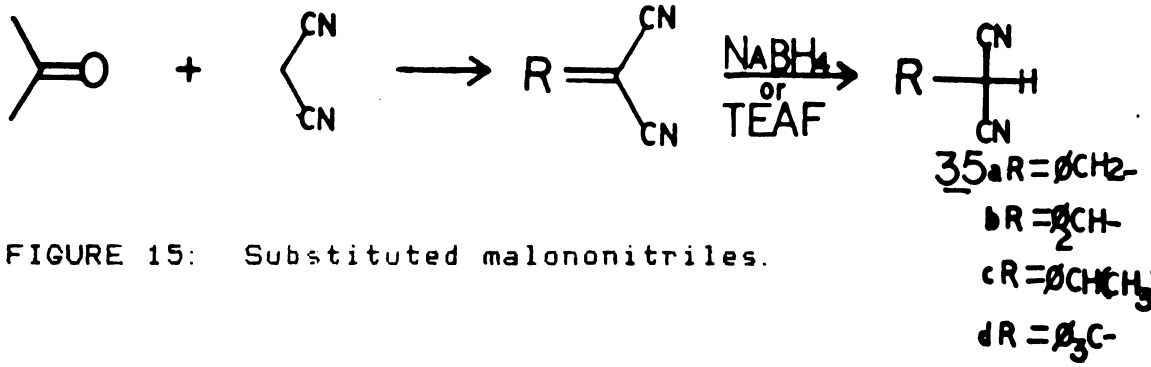


FIGURE 15: Substituted malononitriles.

conditions used for t-butyl-malononitrile, even benzylmalononitrile anion was unable to act as a substituting moiety on the pyridazine ring.

Another approach involved substitution of 22 by dicyano ketene diethyl and ethylene ketals, 36a,b (Figure 16), shown below.

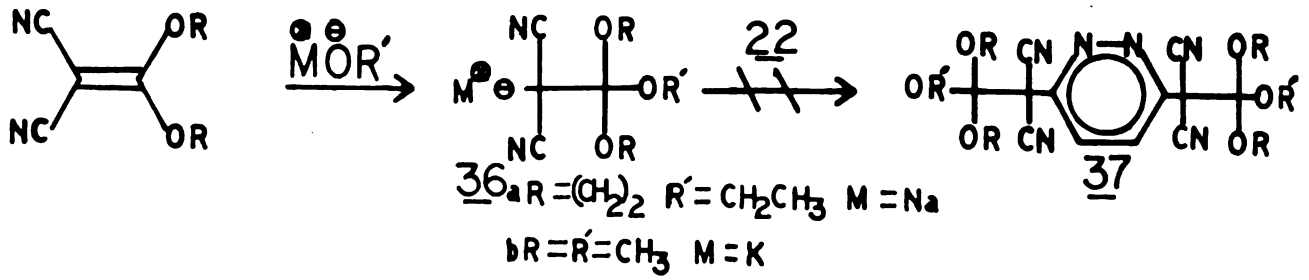


FIGURE 16: Dicyanoketene dialkyl acetals.

Hydrolysis of 37 would give an acid which should spontaneously decarboxylate to yield the 3,6-bismalononitrile pyridazine. Preparation of 36 was straight forward, yielding the salts[32] as powders stable towards air and moisture. However, the high acidity of the proton of the conjugate acids and the hindered nucleophilic site combine to heighten

the stability of this base. Thus it resisted all efforts to effect reaction with 22 under various conditions.

α-Heteroatomic malononitrile molecules were then investigated as possible synthons. The synthesis of N,N-dimethylaminomalononitrile 38, (Figure 17) started with

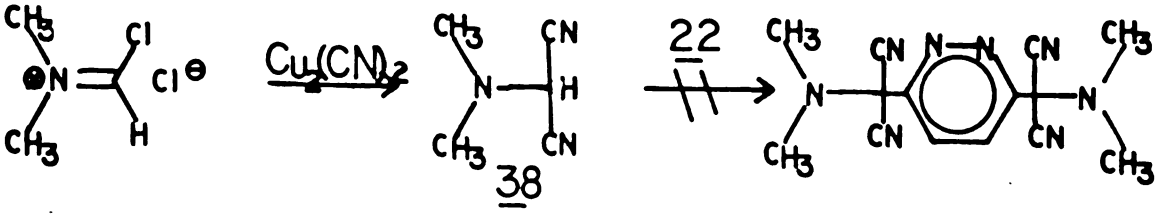


FIGURE 17: Synthesis of N,N-dimethylamino malononitrile.

the preparation of N,N-dimethyl-N-chloromethylammonium chloride from phosgene and dimethylformamide[33]. Addition of excess copper cyanide yielded the product as a fairly stable liquid. Reports on the chemistry of 38 warned of the ambident nucleophilic nature of in this anion[34]. When the anion was reacted with 22, a tarry mixture of products was obtained. Separation and isolation of these products was abandoned in order to pursue more viable routes.

The second class of heteroatomic malononitriles investigated was that incorporating a sulfur in the position. This work was based on the assumption that mild Raney nickel or nickel boride desulfurization of this synthon, following its attachment to an aromatic ring, would lead to the de-

sired product. Initially four compounds of this type were known, 39[35], 40[36], 41[36], and 42[36] (Figure 18). Phenylthiomalononitrile, 39,

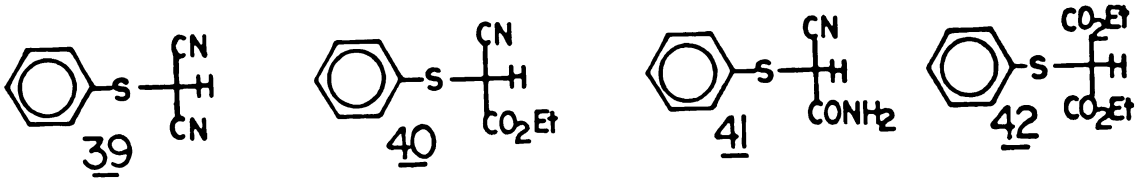


FIGURE 18: α-Sulfenylated active methylene compounds.

was synthesized in a number of ways, the best one being a new, more general method shown in Figure 19, using phenyl toluenethiosulfonate[37], 43, as a

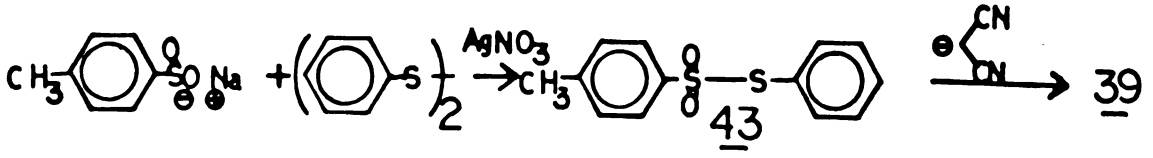


FIGURE 19: New synthesis of phenylthiomalononitrile.

sulfenylating agent. A previously reported synthesis of 39, which was said to proceed in 98% yield, gave in our hands a mixture of monosulfenylated and disulfenylated products[38]. Phenylthiomalononitrile is converted to a stable anion upon treatment with sodium hydride in tetrahydrofuran. However, this anion failed to react with 22 and 13, even on refluxing for long periods.

Assuming steric interference does not account entirely for this failure to react, the stability of the anion must be so great as to preclude this desired substitution. Therefore it was thought that ethyl (phenylthio) cyanoacetate, 40, or (phenylthio) cyanoacetamide, 41, might yield stronger nucleophiles, and they were reacted initially with sodium hydride in tetrahydrofuran or hexamethylphosphoramide, followed by combination with 22. Again, only starting material was recovered from these reactions.

To overcome both the steric and anion stabilizing effects of the phenyl moiety, the next choice of substituent was an alkylthio group. The synthesis of alkylthiomalononitriles has yet to be reported. Attempts toward the synthesis of methylthiomalononitrile, 44, include direct nucle-

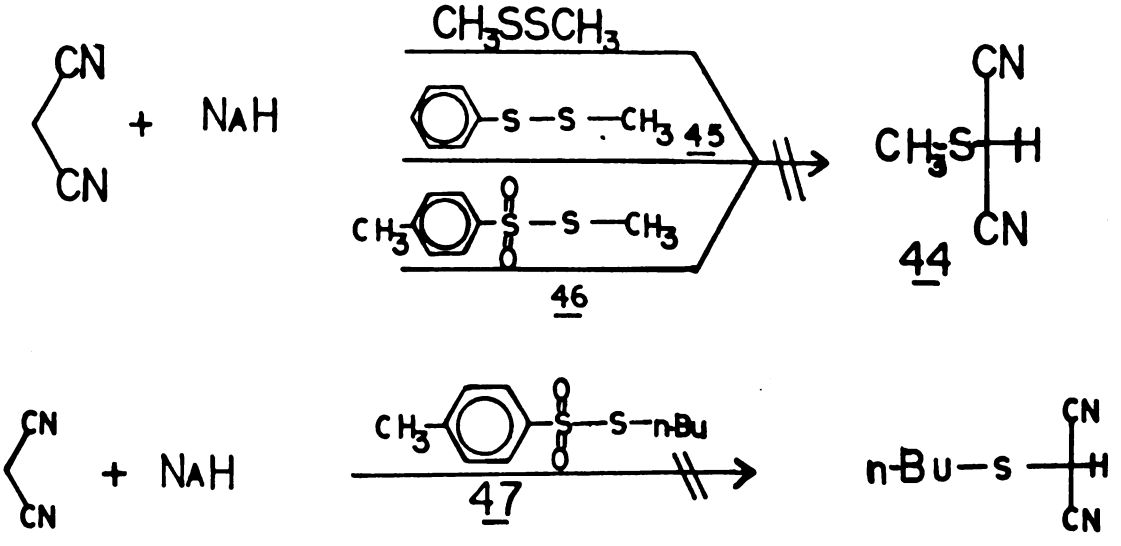


FIGURE 20: Proposed synthesis of methylthiomalononitrile

ophilic attack of the malononitrile anion on dimethyl disulfide (Figure 20) both with and without the presence of silver ion as a catalyst, and using unsymmetrical disulfides as the sulfenylating agent (as in 45). These reactions gave only disulfide residues as products of oxidation. Even when methyl toluenethiosulfonate[37], 46, was prepared, sulfenylation of the active methylene carbon of malononitrile did not occur. This was also the case when n-butyl thiosulfonate, 47, was used. It is possible that disulfenylation may be occuring, since toluenesulfonic acid can usually be retrieved from the products.

Another malononitrile equivalent is the benzylthio derivative, 49. Duplication of the syntheses of sulfenylating agents 43, 46, and 47, using benzyl disulfide gave the corresponding thiolsulfonate, 48, in 90%(Figure 21). Addition of malononitrile anion to

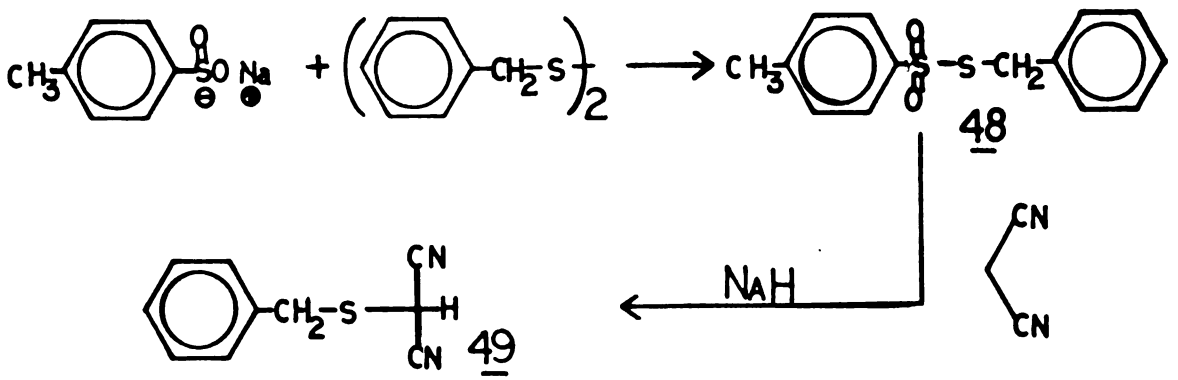


FIGURE 21: Preparation of benzylthiomalononitrile.

48 resulted in formation of benzylthiomalononitrile 49 in 40%. Finally, reaction of this anion with 22 in refluxing tetrahydrofuran for 4 hours led again to recovery of both starting materials. We feel that this evidence confirms the added stability that a sulfur atom lends to an α anion. Thus, substitution reactions of these α-thiomalononitriles with 22 will not occur unless the anion or the ring is further activated.

III. PYRIMIDINE NUCLEUS

An analog of TCNQ involving the pyrimidine ring system, 5, is shown in Figure 22. It differs from the other diazines discussed here in that its two functionalized positions, the two and the five positions, are not equivalent. The position α to the nitrogens, the two position, is quite reactive both in terms of nucleophilic substitutions and oxidation[39]. The carbon positioned "para" to this, the five position, is relatively unreactive toward the conditions necessary for addition of malononitrile. Synthesis of 5 by substitutions of a pyrimidine ring was considered, but due to the lack of derivatives having replacable groups at the two and five positions, this approach was not pursued. Alternatively, we investigated new methods of preparing 2,5-difunctionalized pyrimidines which could lead to the tetracyano product, 5.

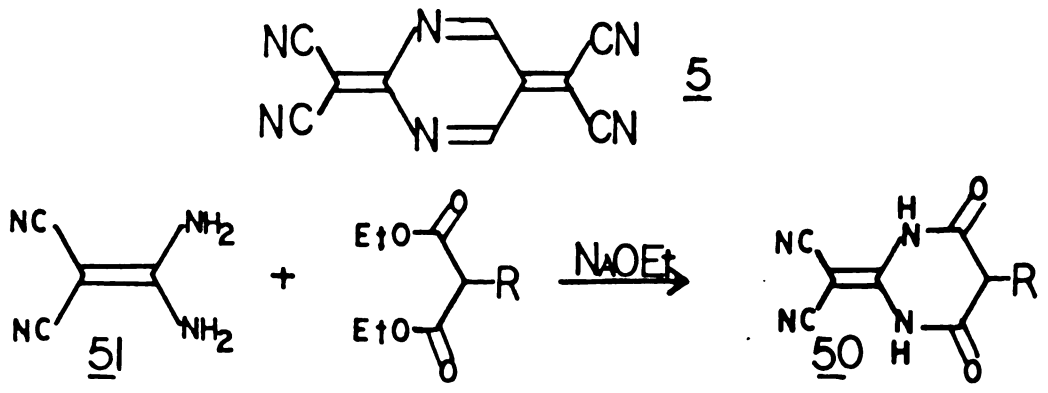


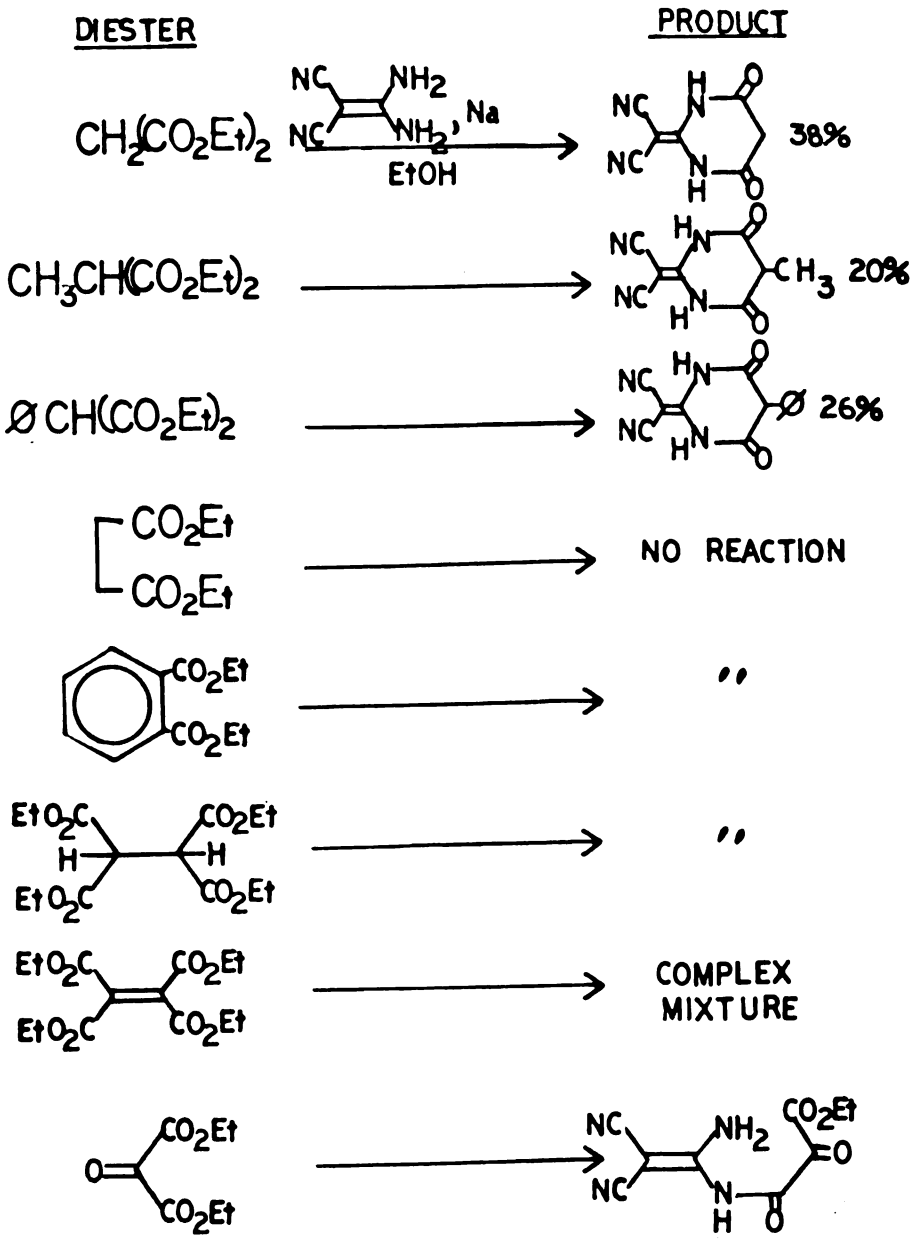
FIGURE 22: Target molecule 5; Previous synthesis of 50.

We have chosen to construct the pyrimidine nucleus from two symmetrical parts. One method is analogous to that discovered by Webster[40] for the synthesis of 50(R=H), a barbituric acid derivative (Figure 22). This molecule was formed by the reaction of diethyl malonate with 1,1-diamino-2,2-dicyanoethylene, 51, in the presence of base. By utilizing a functionalized malonate derivative which could be further transformed to a dicyanomethyl group, the general structure of 5 would be completed. O-alkylation of this modified adduct, e.g. 50, R= $C(C\equiv N)_2$, or treatment with phosphorus oxychloride could then lead to the dimethoxy or dichloro derivatives of 5, respectively.

1,1-Diamino-2,2-dicyanoethylene cyclized with substituted malonate esters. However, varying the length of the carbon chain between the ester groups or allowing the presence of additional functionality led to retrieval of starting materials (Table 4). The fact that the reaction of 50a with phosphorus oxychloride gave rise to ill-defined products caused us to abandon this particular route.

A principal method of constructing reduced pyrimidine rings is by the combination of 1,3-diamino propanes and 1,1-dielectrophiles, e.g. carbonic acid derivatives. The use of guanidines or S-alkyl thioureas for the latter reactants have also yielded tetrahydropyrimidines (Figure

TABLE IV


DIESTER
PRODUCT
CH2(CO2Et)2
NC NH2 NC NH2, Na
EtOH
38%
CH3CH(CO2Et)2
CH3
20%
ØCH(CO2Et)2
Ø
26%
CO2Et CO2Et
NO REACTION
"
"
COMPLEX MIXTURE

23) [41]. By using this methodology with 1,1-bismethylthio 2,2-dicyanoethylene, 52, as the dielectrophile, we hoped that derivatives of 53 would be produced.

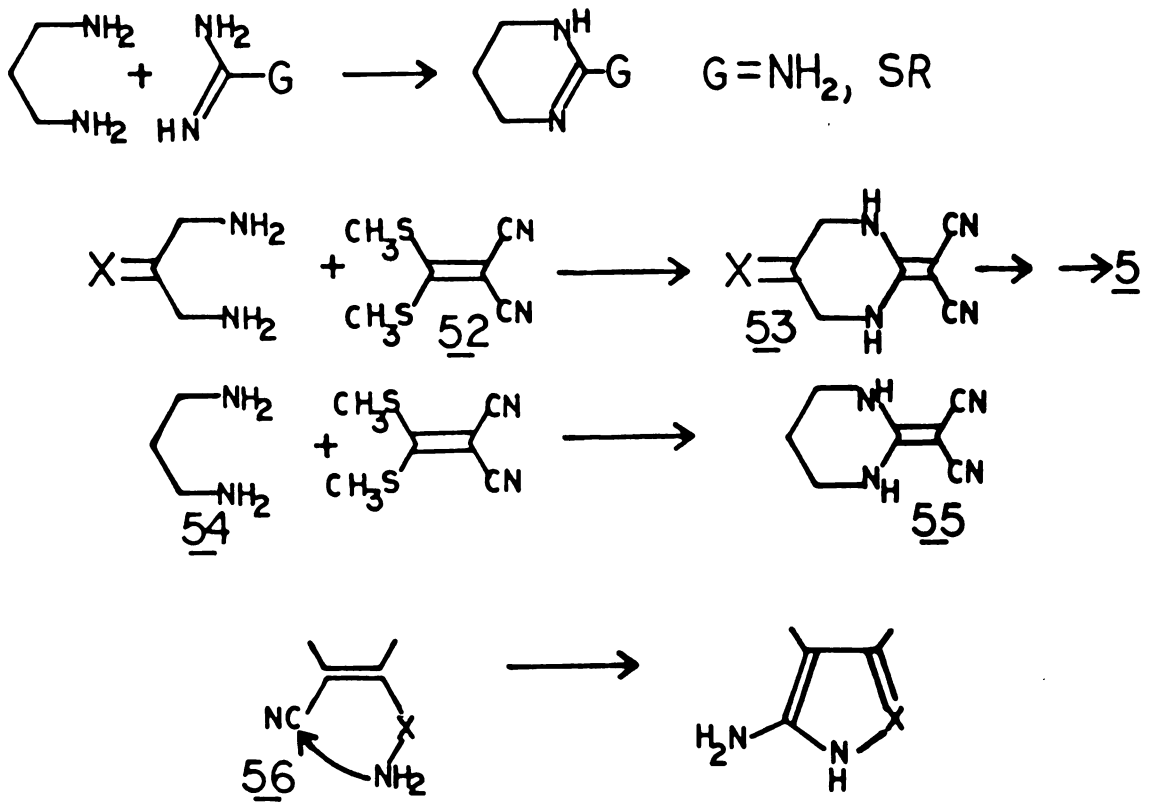


FIGURE 23: Methods for synthesis of tetrahydropyrimidines.

Depending upon the nature of X(Figure 23), further manipulation or oxidation should yield the target molecule, 5. Cyclizations of 52 with 1,2 aliphatic and 1,2 aromatic amines are known[42]. As expected condensation of 52 with 1,3-diamino propane in ethanol resulted in an exothermic reaction from which the adduct, 55, precipitated as a white powder in 80% yield.

In order to obtain 53, where X= $C(C\equiv N)_2$, the diamine moiety would include a γ-amino-αcyanoethylene function. These compounds are known to be unstable[43]. Transformation via an intramolecular cyclization leads, in most cases, to various heterocyclic products as shown for 56. Therefore, a synthetic equivalent of dicyanomethylene is necessary in these diamines. This goal could be attained from the ketone, 57(Figure 24), through a condensation with malononitrile. 1,3-Diamino acetone was reportedly isolated as its dihydrochloride salt in 1895[44].

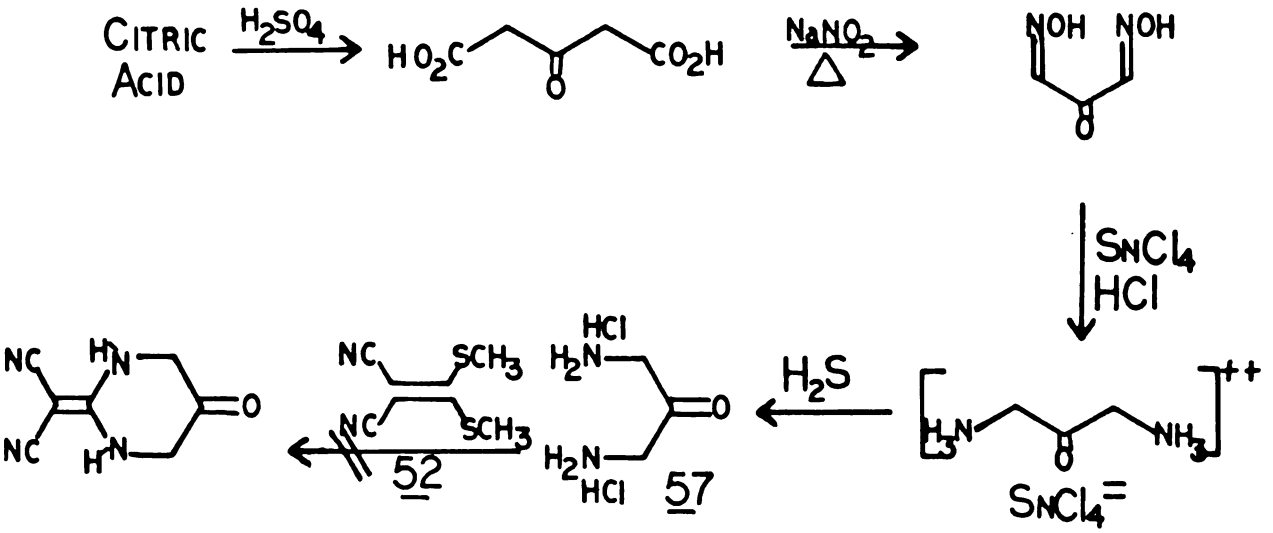


FIGURE 24: First preparation of 1,3-diaminoacetone.

The preparation of 57 shown in Figure 24 is troublesome, and the intermediates are difficult to characterize. Only one report of the use of this compound in heteroatomic synthesis has arisen, namely a cyclization with carbon disulfide in the presence of base[45]. The alleged product, however, was not characterized. A similar cyclization of 57 prepared in

this manner with 58 under various conditions was attempted, but failed.

Since diaminoacetone dihydrochloride was useless as a 1,5-dinucleophile, a commercially available precursor, 1,3-diamino-2-propanol, 58, was chosen as a starting material. The planned synthetic route is shown in Figure 25.

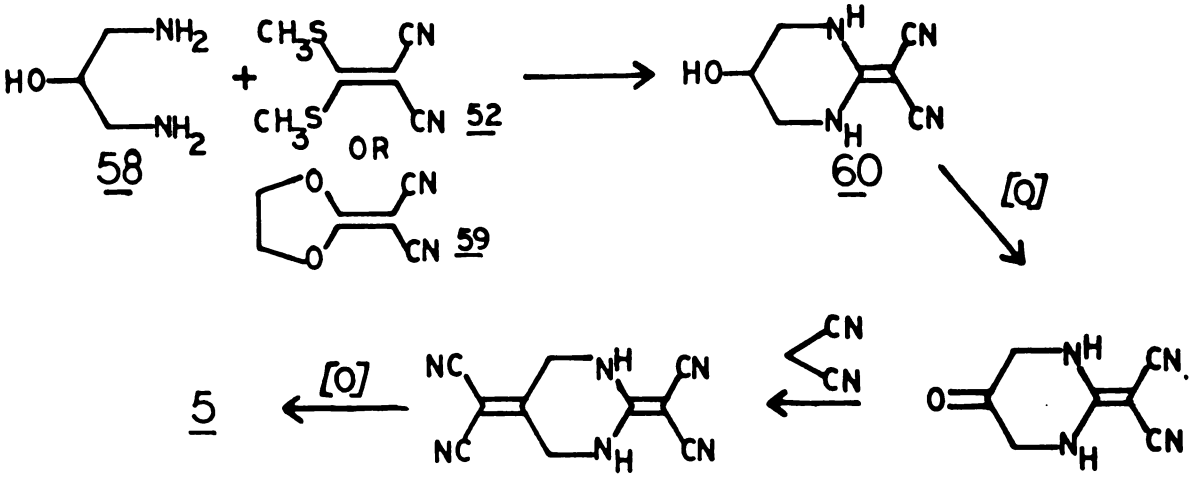


FIGURE 25: Attempted synthesis of 5 from diaminopropanol.

Cyclization of 58 with 52, or the ethylene glycol derivative, 59, offered the alcohol, 60, in 72% and 84% yield, respectively. This compound showed its expected molecular ion from mass spectral analysis at m/e164. Its infrared spectrum exhibited bands at 3300cm-1, 3240cm-1,(O-H, N-H), 2210cm-1, 2170cm-1(C≡N), and its PMR had resonances at δ3.15(br s, CH_2), δ3.92(br tr, HCO), δ5.18(br s, OH), δ7.44 (br s, NH) in dimethyl sulfoxide. This alcohol was soluble in solvents such as dimethyl sulfoxide or dimethyl formamide

and showed remarkable stability toward oxidative conditions. After numerous attempts to convert 60 to the ketone with the reagents listed in Table 5, efforts toward this oxidation were halted.

TABLE V

ENTRY	OXIDIZING AGENT	T(°C)	TIME	SOLVENT
1	$CrO_3 \cdot H_2SO_4$	RT 100	20min	CH_3CCH_3 (O)
2	"	RT	17hrs	DMF
3	"	100	7hrs	"
4	 $\cdot CrO_3Cl^{\ominus}$	"	40min	CH_2Cl_2
5	2 " $\cdot Cr_2O_7^{-2}$	RT	24hrs	DMF
6	$DMSO \cdot DCC \cdot H_3PO_4$	"	"	C_6H_6
7	$DMSO \cdot DCC \cdot TFA$	"	"	"
8	$DMSO \cdot ClC(=O)C(=O)Cl \cdot TEA$	-40	2hrs	CH_2Cl_2
9	$ClC(=O)Cl \cdot TEA$	0 RT	5hrs	THF
10	$SOCl_2$	0 100	2hrs	PYRIDINE
11	$NCS \cdot PYRIDINE$	100	5min	C_6H_6
12	$tBuOCl$	RT	1.5hrs	tBuOH
13	$EtO_2CN{=}NCO_2Et$	"	3 days	DMF
14	MnO_2	"	"	"
15	$AgNO_3, h\nu(350nm)$	"	4hrs	$DMSO/H_2O$

Derivatization of the alcohol, 60, proceeded with mesyl chloride and pyridine to the mesylate, 61, while the tosylate, 62, and the trimethyl silyl ether, 63, were prepared, though in much lower yield(Figure 26). Attempted oxidation of the

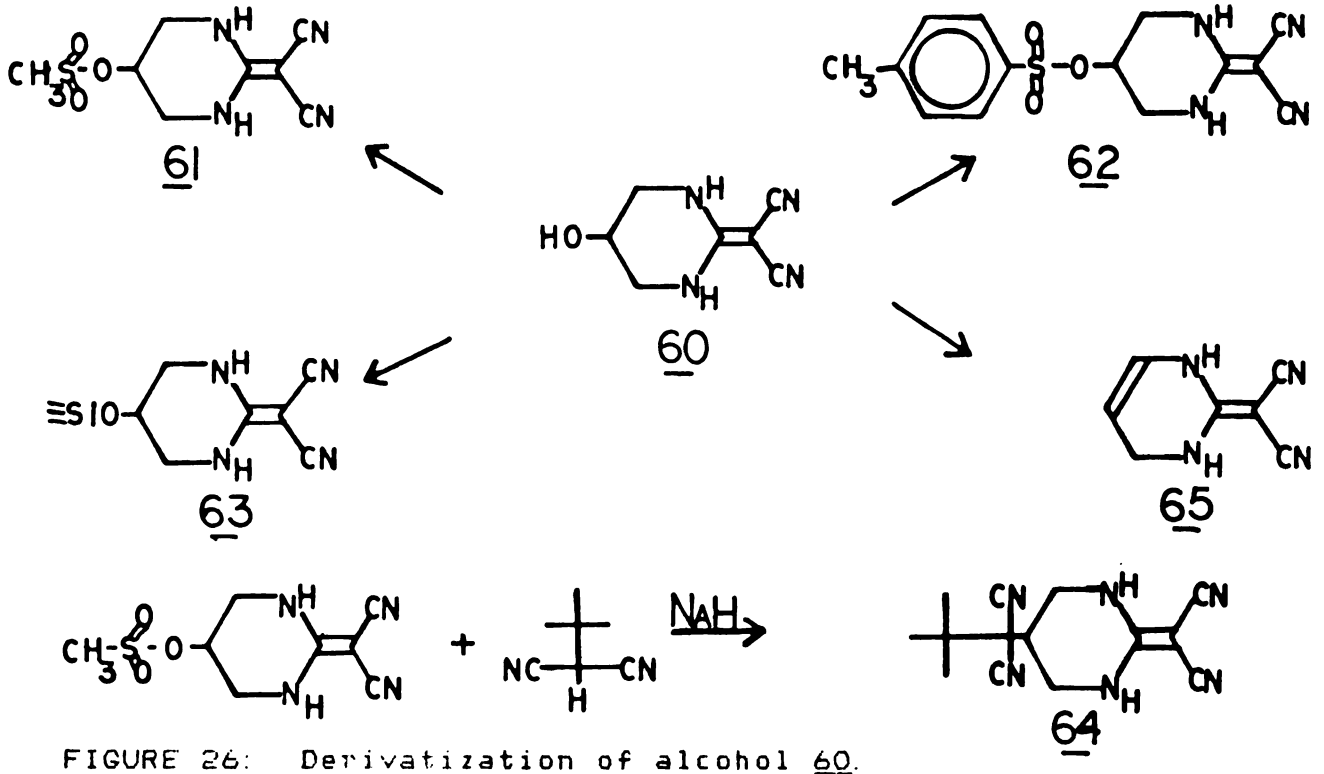


FIGURE 26: Derivatization of alcohol 60.

mesyl and tosyl compounds in dimethyl sulfoxide failed as did the reaction of the silyl ether, 63, with trityl fluoroborate[46]. When the preparation of the triflate was attempted, the only product isolated from the basic reaction mixture was the alkene, 65, in 41%. Nucleophilic displacement of the mesylate with malononitrile anion yielded only the mesylate and the original alcohol on workup. However, a similar reaction with t-butyl-malononitrile resulted in 63%

of the substitution product, 64. Compound 64 proved to be useless as an intermediate product toward the synthesis of 5 and thus, was abandoned.

A thioketal is another synthetically useful carbonyl synthon. Approach to the synthesis of 69a began with the preparation of 2,2-biscarboethoxy-1,3-dithiolane, 67, from ethylene dithiotosylate, 66[47], and malonic ester in quantitative yield. A Japanese group[48] failed to prepare this compound when sodium ethoxide was used as base. Due to the lability of the alkyl dithiotosylate, a less nucleophilic base such as acetate was necessary. We hoped to synthesize the bisamide, 68a, (Figure 27) and reduce this compound to the 1,3 diamine, a useful diamino acetone synthon. Without further purification, the low melting diester,

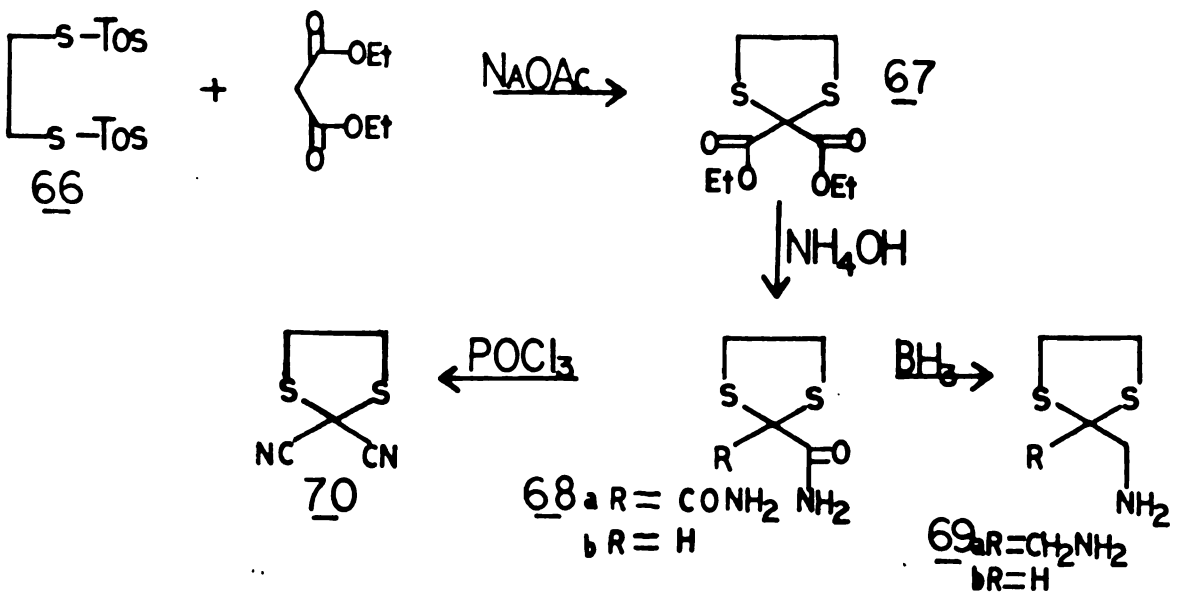


FIGURE 27: Synthesis of diamino thioketal 69a.

67, was warmed with ammonium hydroxide and precipitated a white solid which was characterized not as 68a, but instead, as the monoamide, 68b. This monoamide was also produced when malonamide was refluxed with the sulfenylating agent. This thermal decarbamylation has been noted to occur with a variety of sulfenylated malonamides[48]. However, by combining the diester with ammonium hydroxide at 0° C for 7 hours, the bisamide, 68a, was isolated in 80%.

Lithium aluminum hydride reduction of the bisamide 68a, yielded an oil which showed signs of dithiolane ring opening by PMR analysis. Similar results arose from the use of sodium acyloxyborohydride[49]. When diborane in tetrahydrofuran was used at reflux for 8 hours with a 5:1 molar ratio of reducing agent to diamide, an oil was isolated which contained 2-aminomethyl dithiolane, 69b, and the desired bisaminomethyl dithiolane, 69a. By running this reaction at 0°C for 30 hours, the quantity of side product, 69b, was minimized. The bisamide, 69a, was dehydrated with phosphorus oxychloride to yield the novel dithiolane, 70, albeit in 7.7% yield. Reduction with various reducing agents caused decomposition of 70 without isolation of any diamine, 69a.

Rather than purify this diamine, it was combined with the cyclizing agent 52, (Figure 28) in ethanol, thereby precipitating the thioketal 71, in 53%.

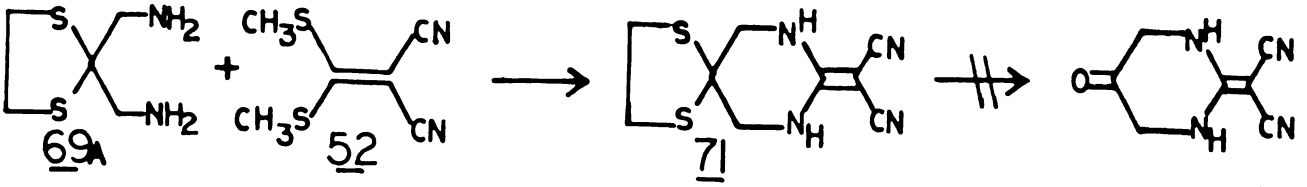


FIGURE 28: Synthesis of thioketal 71.

The PMR spectrum showed three signals at δ3.8(s, S-CH_2), δ3.46(br s, NCH_2), and δ8.00(br s, NH). The infrared spectrum has a cyano pattern very similar to that of the alcohol, 60.

Hydrolysis of thioketal 71 to the desired ketone was attempted with various reagents; however, most yielded only starting material. The use of mercuric chloride and mercuric oxide in methanol or mercuric chloride and cadmium carbonate in dimethyl sulfoxide at both room temperature and 50°C, returned the ketal, 71. Chloramine T, ceric ammonium nitrate, N-bromo succinimide in acetonitrile, sodium periodate, thallium nitrate and magic methyl also gave 71, while N-chloro succinimide and silver nitrate photolysis afforded no isolable products. The variety of deprotecting methods reflects the difficulties involved in the customary removal of thioketal functions.

The use of a more easily hydrolyzed function such as a ketal, may allow formation of the desired ketone. The diaminoacetone synthon, 74, (Figure 29) is unknown, and several

routes toward its synthesis were studied. Initially, substitutions of the

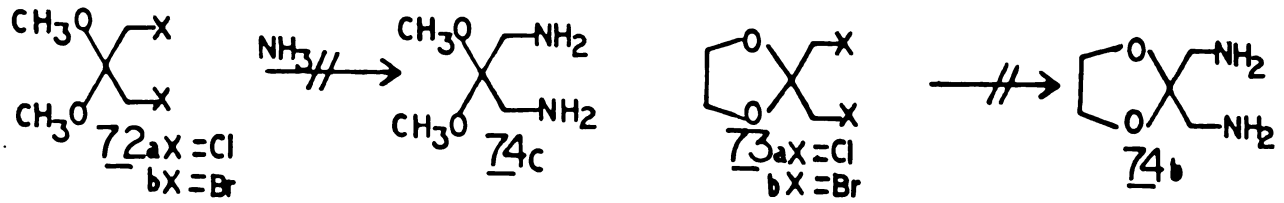


FIGURE 29: Attempts toward the synthesis of 74.

accessible ketal chloride, 72a, and bromide, 72b, by various nitrogen nucleophiles such as ammonia at high temperature and pressure, ammonium hydroxide and azide ion all yielded only starting materials. It was anticipated that displacement of these neopentyl type groups would be slow. In order to reduce the steric hindrance in this substitution, the ethylene ketals of 1,3-dichloroacetone, 73a, and 1,3-dibromoacetone, 73b, were prepared in 43% and 39% yield, respectively. These, too, were completely unreactive toward ammonia, ammonium hydroxide and azide ion. A new amine synthesis utilizing the anion of bisbenzenesulfenimide[50] as a strong nucleophile also failed.

The second route to 74 relied upon the successful work in the synthesis of thioketal 69a. A preparation[51] of the ethylene ketal of diethyl oxomalonate was attained by azeotropic removal of water, but was very dependent upon the particular acidic catalyst used. Due to these difficulties

and the cost of the starting material, a more convenient, though lower yield method of procuring the diethyl ketal was used. Diethyl malonate was brominated directly to the dibromide, 75 in 70%[52]. The ensuing substitution with sodium ethoxide afforded the required ketal, 76, in 16%(Figure 30)[53].

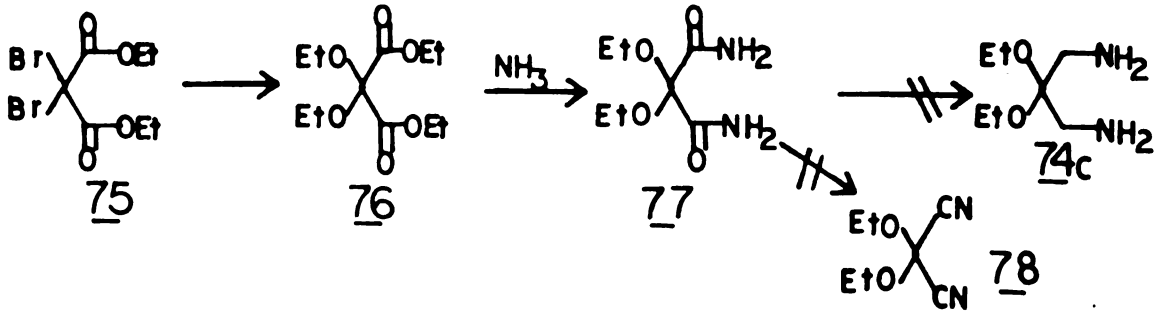


FIGURE 30: Second attempt toward synthesis of 74.

The use of ammonium hydroxide at 0°C with 76 led to only partial ammonolysis, whereas ammonia in a sealed bomb afforded the bisamide 77 in 49% yield. Unfortunately, reduction of this ketal amide as before with lithium aluminum hydride, bismethoxyethoxysodio aluminohydride, sodium acyloxyborohydride, diborane - tetrahydrofuran, and diborane - dimethyl sulfide failed. Expecting that the dinitrile, 78, would lead to a more facile reduction, dehydration of 77 was attempted with both acetic anhydride and its trifluoro derivative, but resulted in extensive decomposition of the starting material.

The third route toward 74 was designed around a recent convenient synthesis of diaminoacetone dihydrochloride, 57[54]. The synthesis is shown below in Figure 31, and succeeds through four steps from glycine ethyl

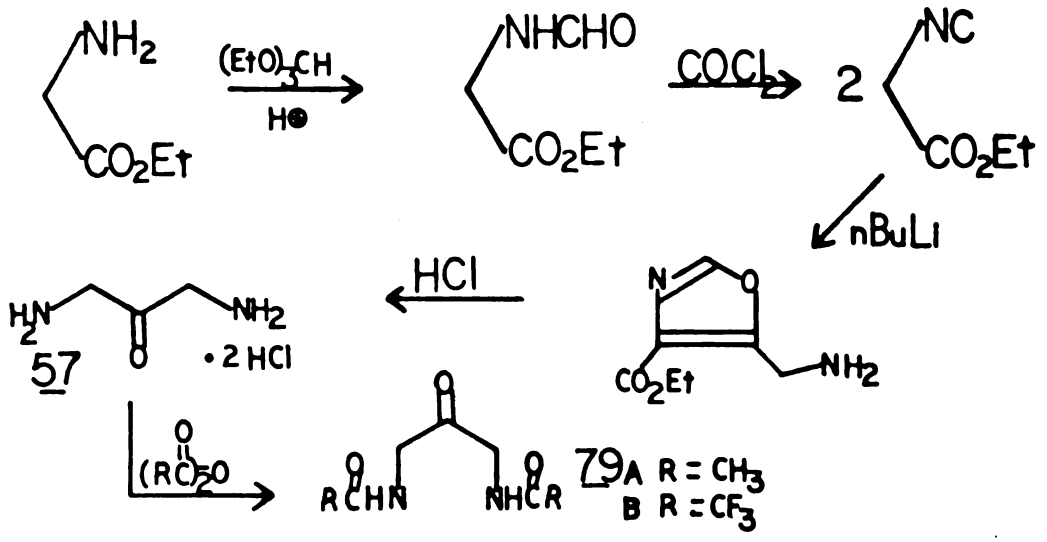


FIGURE 31: Recent synthesis of 57.

ester in 36%. Since quantities of 57 were available, direct neutralization of the hydrochloride and attempts at cyclization were studied under various conditions. None led to the desired ketone. The synthesis of the bisacetamido ketone, 79a, was noted[55], and this procedure was modified to create the bistrifluoroacetamido ketone, 79b. It was presumed that either of these compounds could be ketalized, and hydrolyzed to the corresponding diamine.

Ketalization of the highly insoluble 79b was unsuccess-

ful in various solvents. However, bisacetamide 79a afforded the ketal 80 in 85% by simple azeotropic water removal in benzene with a catalytic amount of hydrochloric acid(Figure 32). This bisacetamido ketal was hydrolyzed to the

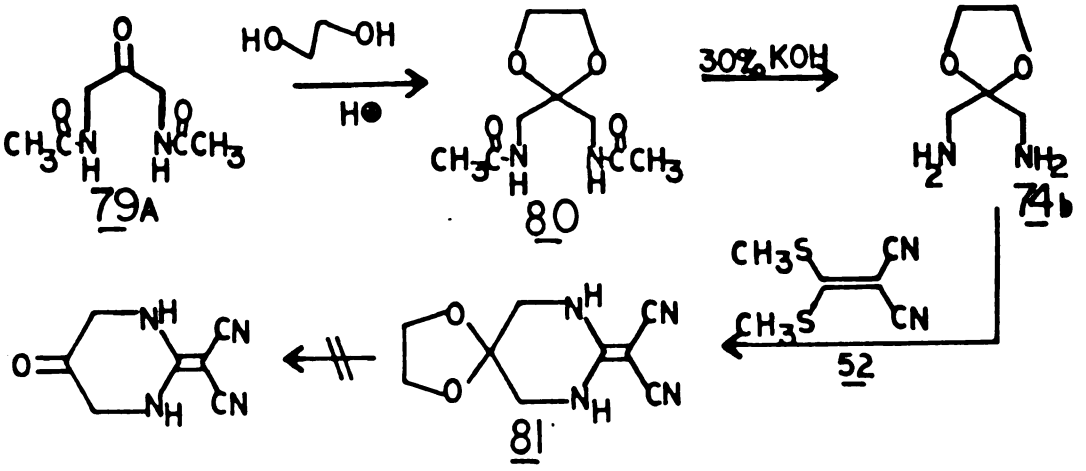


FIGURE 32: Preparation of diaminoacetone synthon 74b.

diamine, 74b, by refluxing in 30% potassium hydroxide for 1 hour. The crude diamine showed a very clean PMR spectrum with three singlets at $\delta 3.95(OCH_2)$, $\delta 2.72(NCH_2)$, and $\delta 1.2(NH_2)$. Without further purification, this compound was combined with the cyclizing agent, 52, and yielded a pure white powder, 81, and which showed the expected molecular ion in its mass spectra. Its PMR and infrared spectra were also similar to the cyclized alcohol, 60, and thioketal, 71. Again, hydrolysis of this ketal, 81, condensation of the ketone with malononitrile followed by oxidation, should yield the target molecule, 5.

All hydrolytic methods applied to ketal 81 failed to produce the desired ketone. With various acids, solvents, and temperatures, the starting material was the lone product isolated from the mixtures. When 81 was heated in dimethyl sulfoxide-10% hydrochloric acid for 10 hours at 90°, complete decomposition into water soluble products occured.

It was suspected that the amide-like N-H group in 81 was the cause of failure of these reactions, probably by more favorable coordination with the hydrolytic reagent. Substitution of these hydrogens by alkyl groups would restrict this coordination and also disallow any tautomeric equilibria. Several methods of acylation were performed on 81, but to no avail, as the starting material was always recovered. Another synthetic pathway to these alkylated derivatives of 81 could be envisioned as starting from the bis-N,N'-dialkyl-1,3-diamines, as shown in Figure 33. If the blocking group is labile, e.g. benzyl, perhaps deketalization to ketone 95 and condensation to tetracyano compound 96 could be carried out. Subsequent removal of the blocking group and ring oxidation could then provide the quinone 5.

The first point to consider in this scheme is whether the cyclization of the more hindered bis-secondary amines, 93, with reagent 52, would be possible. In order to answer

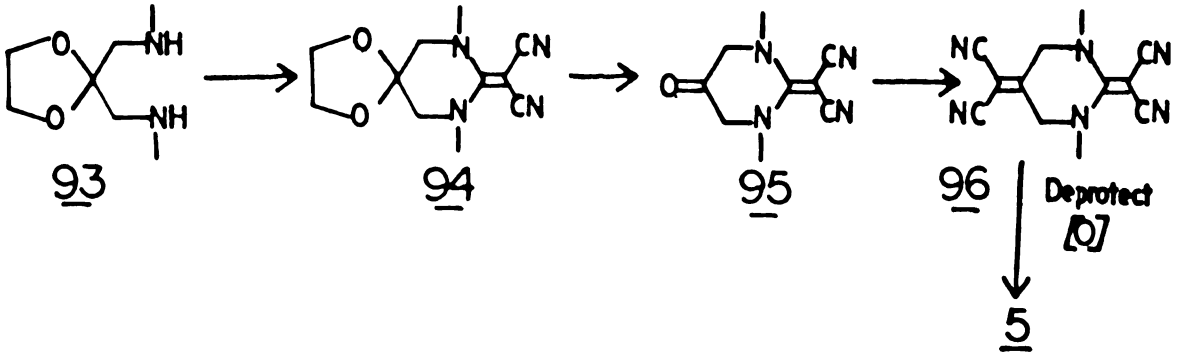


FIGURE 33: Proposed synthesis of 5 via dialkyl diamines.

this question, diamine 82 (Figure 34) was prepared by reduc-

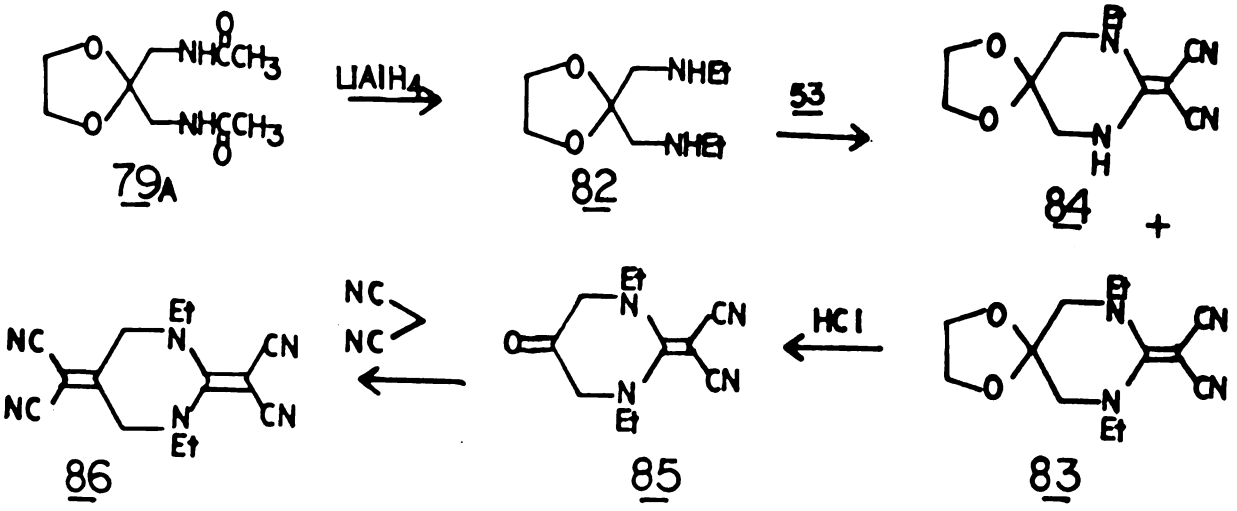


FIGURE 34: Synthesis of N,N'-disubstituted piperimidines.

tion of bis-amide 79a. The cyclization of 82 yielded two products, 83 and 84, which were separated by chromatography. The unsymmetrical diamine 84, was isolated in very low yield and arises from reductive cleavage of the acyl group in 79a. When hydrolysis of ketal 83 was attempted by heating with 10% hydrochloric acid and the ketone 85 was isolated as

white needles in 20%-30% yield. Under these conditions destruction of 83 to water soluble products causes the substantial losses. Nevertheless, upon warming the ketone 85 with malononitrile and water in the presence of alanine, the tetracyano compound, 86, was isolated from a mixture of products, albeit, in low yield.

Since construction of the desired carbon skeleton is now possible, use of diamines with potentially removable groups was studied. The source of such diamines would be dependent upon the long synthetic scheme to diamino acetone(See Figure 31). A more convenient and general method was discovered arising from the commercially available 1,3-diamino-2-propanol, 58(Figure 35). Acylation of 58 by benzoyl or acetic anhydrides led to production of 88 and 92 in 80% and 73% yields, respectively. Oxidation of 88 with pyridinium dichromate, ketalization, and reduction of the bisamide afforded diamine 91, in 50% yield for these three steps. However, attempted cyclization of 91 with reagent 52 under various conditions, led to the recovery of both starting materials. Since the basicity of 91 is assumed to be competitive with the other diamines, the lack of reactiv-

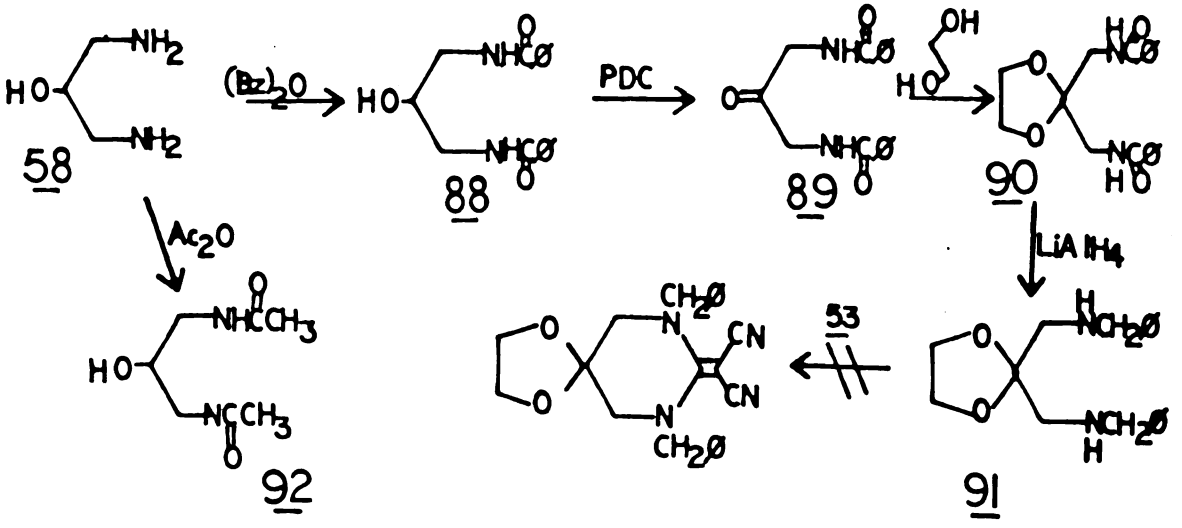


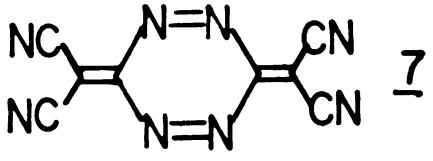
FIGURE 35: Synthesis of 1,3-N,N'-dialkylamino-ketones.

ity must be attributed to the greater bulk of the benzyl groups.

In summary, we report the preparation of the 1,3 diamino acetone ethylene ketal, 74b, and ethylene dithioketal, 69a, along with a general synthetic route to 1,3 bis(alkylamino)acetone ethylene ketal compounds, 93. Several of these 1,5 dinucleophiles have been cyclized with 1,1-diamino-2,2-dicyanoethylene, 52, providing an access to 2,5 disubstituted tetrahydropyrimidines. The use of cyclizing agents such as carbon disulfide, phosgene, or other carbonic acid derivatives with these diamines has not been attempted, but should be done in order to test the generality of this method. Further modification of the ketone function on the cyclized products should also be done.

IV. TETRAZINE NUCLEUS

The 1,2,4,5-tetrazine ring system has been known since 1898, although the majority of work on this system has dealt with the 3,6-diaryl derivatives[56]. The parent ring, s-tetrazine, is unstable in the presence of light or moisture and most of its derivatives are unstable to moderately acidic and basic conditions. Presumedly, a synthesis of 7 could not proceed through the stepwise method of Wheland and Martin (Figure 36) due to the strongly basic conditions known to decompose the ring system[56].



7

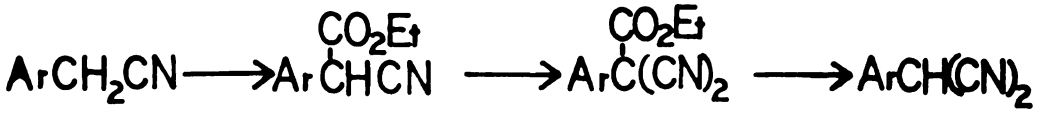


FIGURE 36: 1,2,4,5-Tetrazine analog to TCNQ.

Classically, 3,6-disubstituted tetrazines have been prepared by reacting hydrazine with nitriles, imidates, amidines, or thioamides as shown in Figure 37[56]. These methods would also be inappropriate for formation of 7, as the desired nitrile groups in the sidechain of R would not tolerate these conditions. Therefore the dicyanomethyl moiety would best be introduced onto the tetrazine ring in one

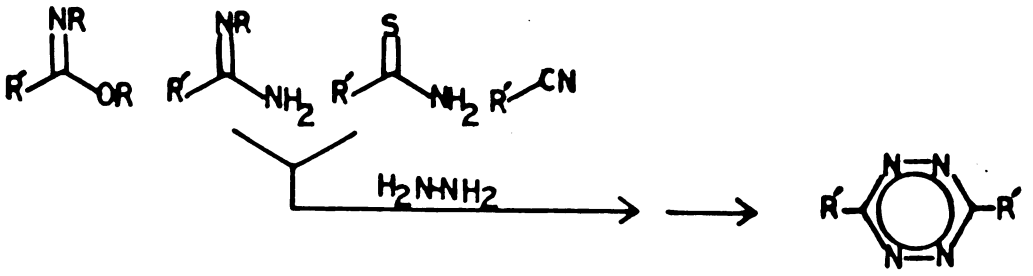


FIGURE 37: Syntheses of 3,6-disubstituted tetrazines.

step, or possibly, the tetrazine ring should be cyclized with previously incorporated dicyanomethyl groups. Only the former route will be described here.

In 1977, Mangia[57] synthesized 1,2,4,5-tetrazines having the potential for systematic nucleophilic substitution at both the 3 position and 6 position. Previously, 1,2,4,5-tetrazines having replacable functionalities at both positions were unknown. His work described the preparation of 3,6 bis-methylthio-1,2,4,5-tetrazine. This tetrazine derivative, 100, can undergo substitution of one methylthio group by hydrazine. Subsequent oxidation in the presence of halide ion affords the halide 101 which can, in turn, be substituted by an appropriate nucleophile. Manzia proposed that the second methylthio group can be dealt with in an analogous manner, thus resulting in 3,6 disubstituted derivatives. The preparation of 100 shown in Figure 38 was also accomplished for the present work.

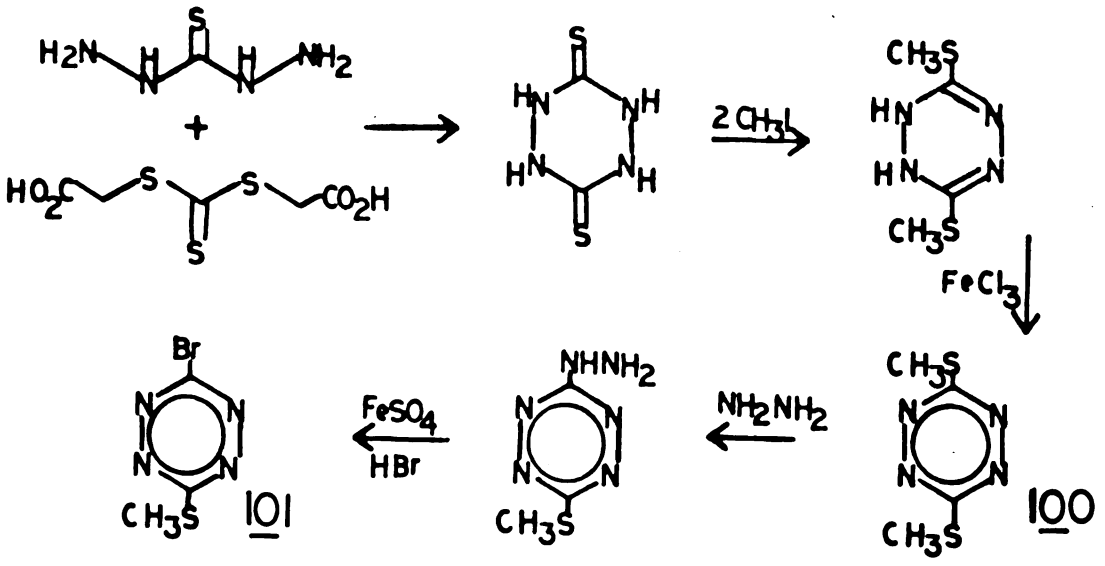


FIGURE 38: Synthesis of 3,6-bismethylthiotetrazine 100.

The proposed synthesis of 7 used malononitrile anion as the nucleophilic species in this method(Figure 39). It was

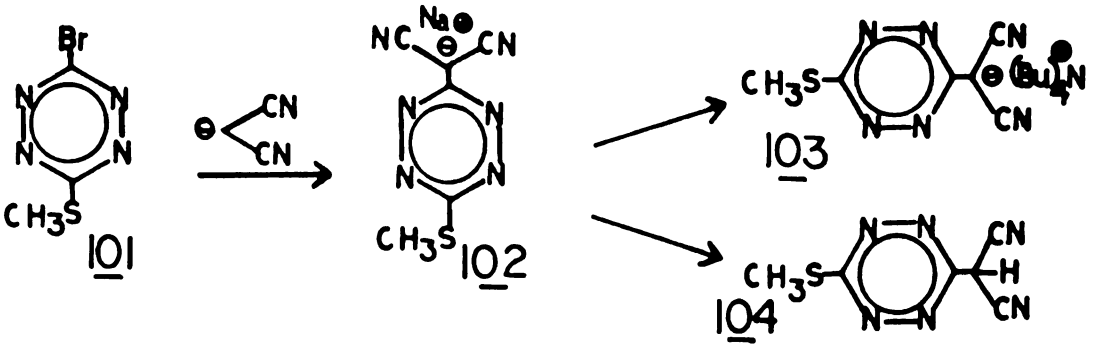


FIGURE 39: Reaction of 101 with malononitrile.

not certain whether the first malononitrile group introduced would be stable toward conditions necessary to replace the second methylthio group. When 3-bromo-6-methylthio-1,2,4,5 tetrazine was reacted with sodiomalononitrile in benzene, a purple powder precipitated from the reaction mixture. This

solid showed infrared bands at 3400cm-1(water), 2200cm-1, 2160cm-1(C≡N), and PMR signals in dimethyl sulfoxide at δ2.52(S-CH_3) and δ3.3(water). Even when the solvent and solid were extensively dried, a signal due to water appeared. The actual precipitation of this salt would not occur until the system was exposed to water or simply atmospheric moisture overnight.

Treatment of this violet solid with tetrabutylammonium iodide in warm water precipitated the metathesized organic salt, 103. After recrystallization from ethanol-water, this compound was collected as shiny violet plates. The sodium salt was acidified with 10% hydrochloric acid to yield 104 as a violet oil. This oil, however, was unstable, and any trace of base immediately returned the salt, 103.

The substitution of the second methylthio group has proven to be difficult, due, primarily, to the enhanced acidity of 104. Reaction of 102 or 104 with hydrazine failed to give the substitution product, yielding instead, starting material in the first case, and a residue containing the methylthio group in the latter. The use of a protected malononitrile such as t-butyl-malononitrile, failed to yield any substitution product, but did cause decomposition of the ring system.

A corresponding substitution with sodio diethylmalonate yielded 105(Figure 40) as a red oil which was isolated by acidification of the reaction mixture and extraction into

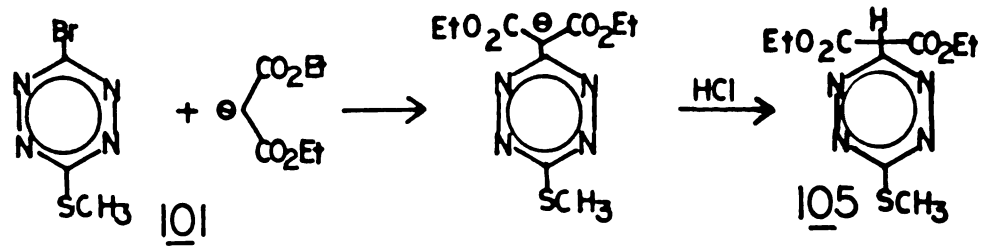


FIGURE 40: Synthesis of diester 105.

ether. The acidic proton in 105 appeared at δ5.15 in the PMR spectrum. Further modification of this diester failed to produce isolable compounds.

Another possible route to tetrazines might be through use of 1,1-diamino-2,2-dicyanoethylene, 106[40]. Coupling of the nitrogens would yield the tetracyano compound, 107 (Figure 41) which presumedly could be oxidized to the product 7.

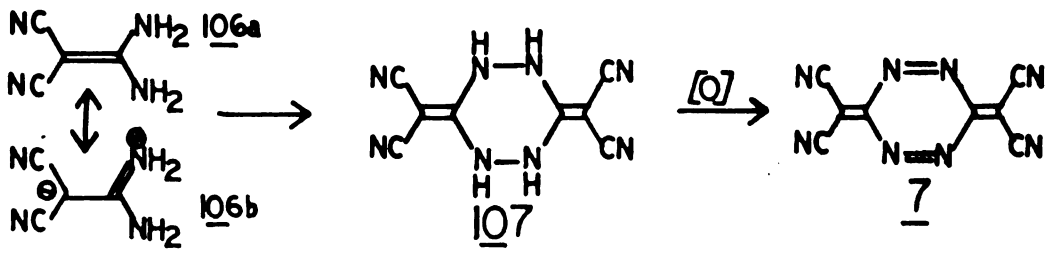


FIGURE 41: Alternate route toward synthesis of 7.

It was thought, at first, that monochlorination of each of the geminal nitrogens in the presence of a tertiary amine base could remove two moles of hydrogen chloride, yielding the condensation product. It was found through various manipulations that the amino groups in 106 are quite non-nucleophilic, due most probably to the predominating resonance form, 106b. This compound showed no reaction when combined with thionyl chloride or ethyl chloroformate, although n-butyl lithium caused the precipitation of an amorphous polymer.

Nevertheless, chlorination with chlorine gas introduced into a suspension of 106 in acetonitrile at -20°C, caused dissolution of the solid after several minutes. Workup yielded a yellow oil which crystallized to whitish needles.

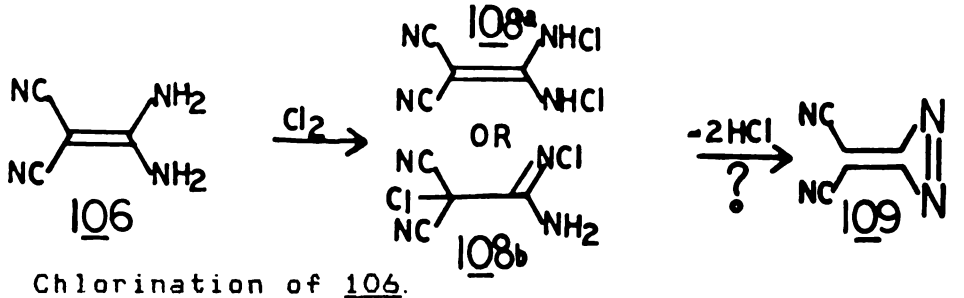


FIGURE 42: Chlorination of 106.

The mass spectrum exhibited a molecular ion containing two chlorines at m/e 176 which may correspond to either 108a or 108b(Figure 42). The infrared spectrum has bands at 3430cm-1, 3340cm-1, 3220cm-1, 3150cm-1, along with a saturated nitrile band at 2252cm-1 and a broad band at 1650cm-1

suggesting structure 108b. Difficulties in reproducing the initial conditions have arisen, and yields of 108 have been inconsistant. Addition of sodium hydroxide, sodium bicarbonate, or even basic alumina to 108 causes the white solid to dissolve into a bright yellow solution. However, isolation of products from these solutions have failed thus far. Besides intermolecular condensation, intramolecular reaction may be occurring to form 109. This molecule may be stable enough to exist since its main resonance form leads to an aromatic system.

V. THIENO[3,2-b]THIOPHENE NUCLEUS

Thieno[3,2-b]thiophenes are aromatic systems similar in many physical and chemical properties to napthalene. Their syntheses have been reviewed recently[58] and mainly stem from the thiophene nucleus. However, work on the elaboration of sidechains has been quite limited. A recent article[59] dealing with the synthesis and properties of 2,5-dihydroxy thieno[3,2-b]thiophenes, 110, showed that oxidation of the corresponding dianion led to solutions of stable radical anions (Figure 43). With this in mind, we attempted to synthesize quinone 8, an analog of tetracyanonapthaquinodimethane, TNAP.

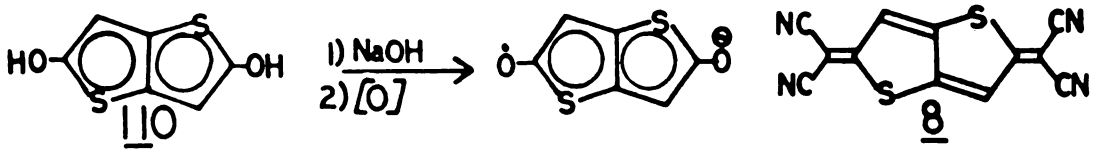


FIGURE 43: Known radical anion of thienothiophene system.

In previous work the dicyanomethyl group has been incorporated onto a thiophene ring by a peculiar condensation of 2,5-dibromothiophene with tetracyano ethylene oxide as in Figure 44[60]. This reaction yielded only starting material when repeated with 2,5-dibromothieno[3,2-b]thiophene. All attempts at the direct substitution of bromine in 118 with sodio malononitrile also failed.

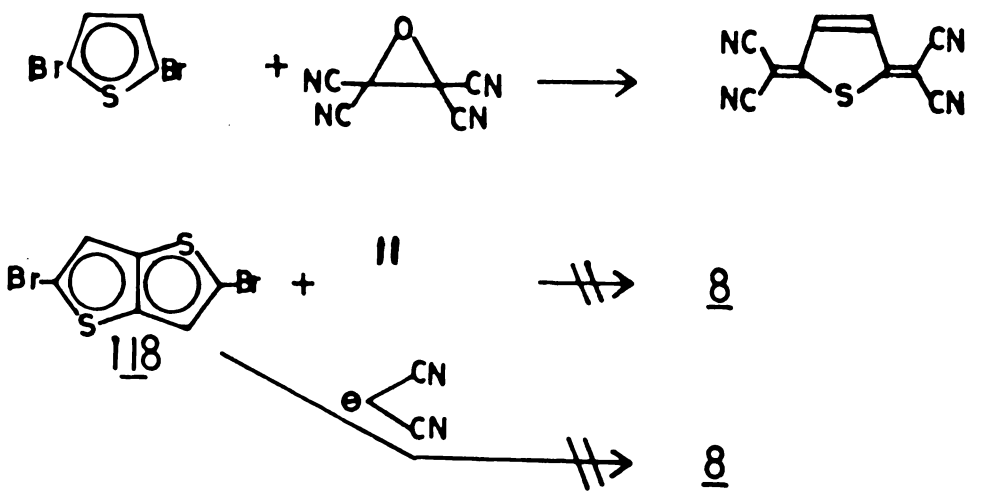


FIGURE 44: Preparation of thiophene analog to TCNQ.

which reflects the high electron density of these rings.

The synthetic approach to 8 made use of a classical route that had been utilized in the synthesis of TNAP. Reduction of the 2,5 dialdehyde, 120(Figure 45),[61] should yield the diol, 121, which through halogenation and substi-

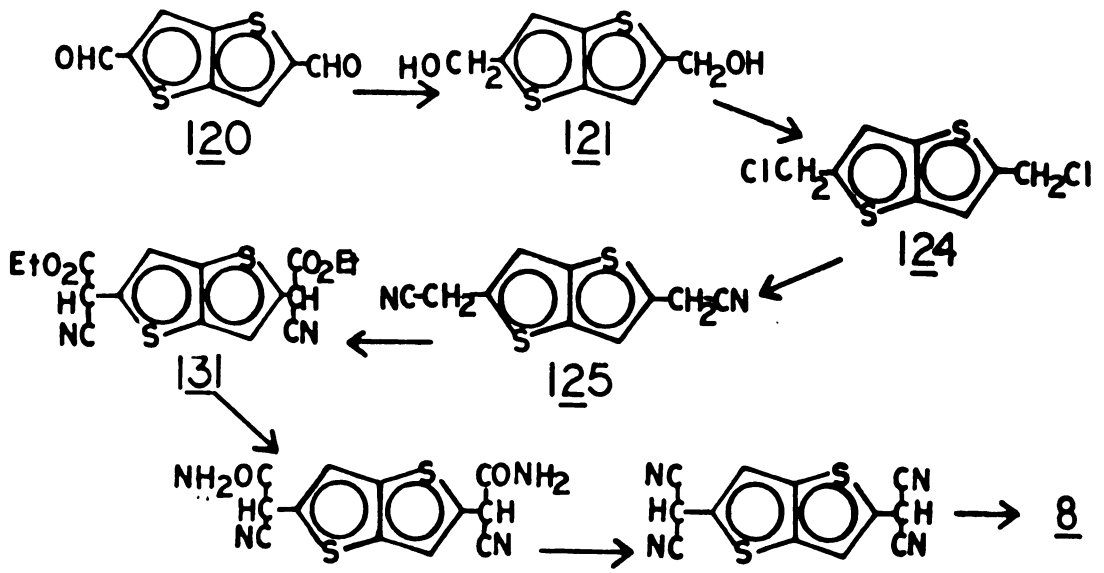


FIGURE 45: Classical route to tetracyanoquinones.

tution by cyanide ion would yield the bis-acetonitrile, 125. Carboalkoxylation of 125, ammonolysis to the amide, and dehydration of this amide, possibly would provide the tetracyano compound 8.

The standard preparation of the parent ring system, thieno[3,2-b]thiophene, 117, an important intermediate for further functionalization, is shown in Figure 46[62].

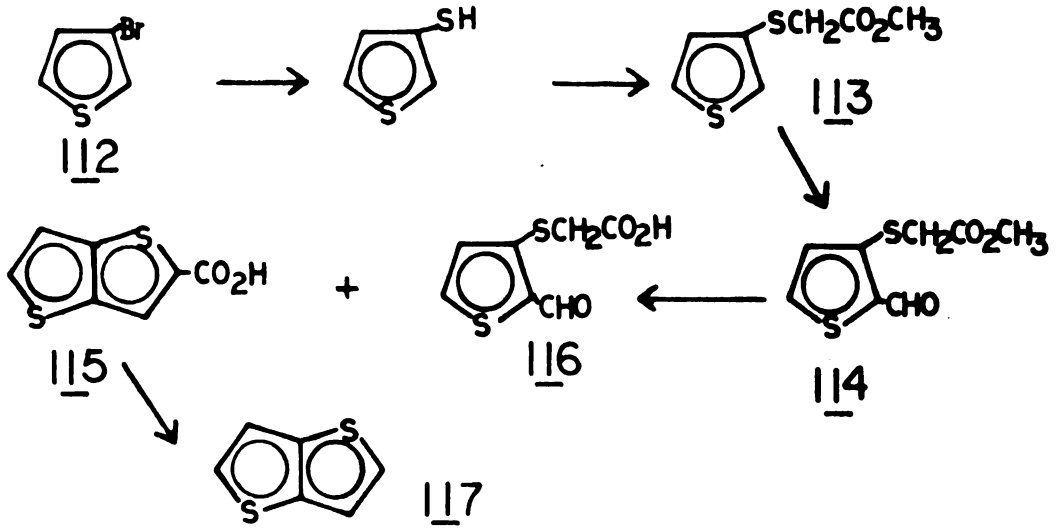


FIGURE 46: Preparation of thieno[3,2-b]thiophene.

Several problems arose when this procedure was repeated in large quantities. First, the separation of ester 113 and aldehyde 114 through fractional distillation is rarely complete. Analysis of the reaction mixtures were performed by thin layer chromatography on silica gel. The subsequent cyclization reaction leading to acid 115, allowed retrieval of this product in a pure state, without traces of either

112, 113, or 114. Therefore, for large scale preparations, the intermediate products were used directly to prepare acid 115 without further purification.

Secondly, the cyclization to the acid 115 was accompanied by hydrolysis of the ester 113 to yield the open chain acid 116. These acids are separated by initial acidification to pH 5, precipitating the cyclized acid, 115. Further addition of hydrochloric acid affords the side product, 116. This thiophene acid, however, can be recycled to the ester by using methyl iodide and sodium bicarbonate stirred in dimethyl acetamide. In this way, the ester 113, is produced in 94%.

The decarboxylation of 115 and bromination[63] are done without purifying the parent compound, 117, and in 88% yield(Figure 47). The dialdehyde, 120, has recently been synthesized in two steps from the dibromide, 118. Combination of 118 with two moles of n-butyl lithium provides 2,5-dilithio thieno[3,2-b]thiophene, 119, which gives the dialdehyde when reacted with dimethyl formamide. This highly insoluble dialdehyde was reduced with lithium aluminum hydride to yield the diol, 121, as light tan flakes in 77%. Compound 121 was also prepared in lower yield directly from the dianion 119, by quenching with paraformaldehyde. Although this latter method involved fewer steps, it was not

as efficient or reproducible as the former route.

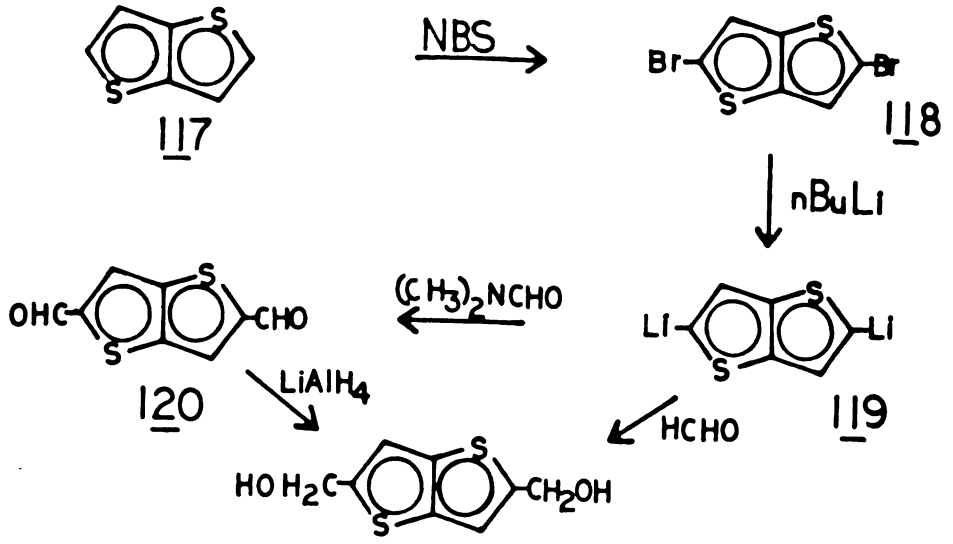


FIGURE 47: Preparation of diol 121.

The tedious synthesis of the diol, 121, could be shortened if direct functionalization of the acid 115, could be attained. Treatment of this acid with two moles of base to form its dianion, 122 (Figure 48), could be followed by addition of carbon dioxide, esterification of this diacid and reduction, affording the diol 121. It was found that upon addition of two moles of lithium diisopropylamide to acid

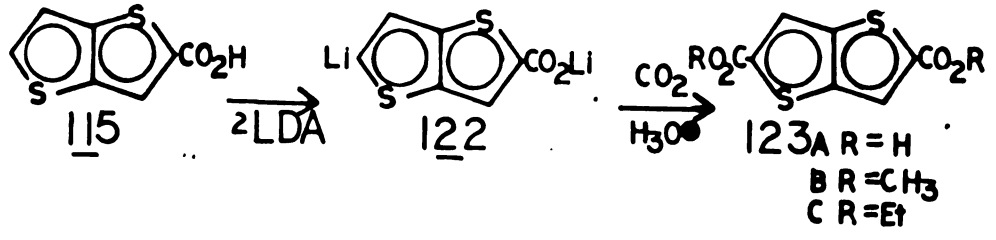


FIGURE 48: Preparation of diacid 123a.

115 at -78°C, followed by warming to -10° C and quenching with carbon dioxide, the diacid, 123a, was prepared in 73% yield. Quantitative esterification to the diester, 123b, with diazomethane succeeded as did lithium aluminum hydride reduction to afford the diol, 121, in 80%. This demonstrates a new and convenient method of functionalizing the thienothiophene ring system.

The 2,5-bis(chloromethyl) thieno[3,2-b]thiophene, 124a, was prepared from diol 121 with thionyl chloride and pyridine in 96%(Figure 49). When sodium cyanide in aqueous acetone was used to make the dicyanide, 125, only a 7% yield

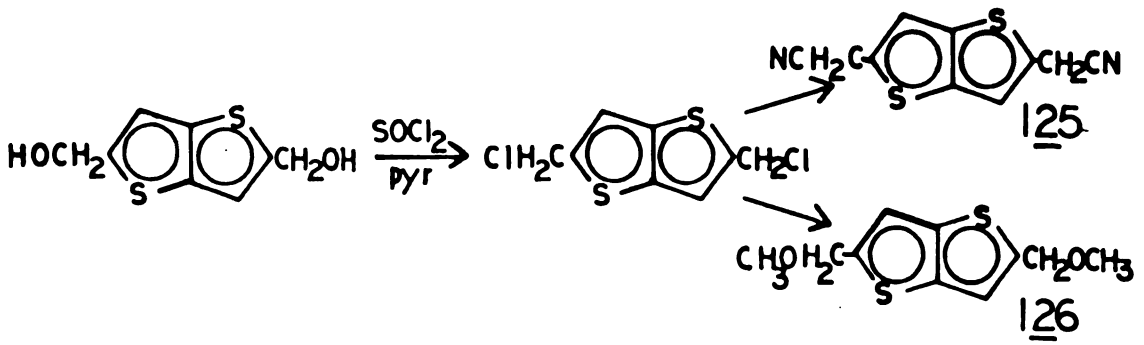


FIGURE 49: Preparation of bis-acetonitrile 125.

was produced. Using dimethyl sulfoxide led to a higher yield of 16%. When potassium cyanide in methanol was used, a 53% yield of 2,5-dimethoxymethyl thieno[3,2-b]thiophene, 126, resulted with no trace of 125. Upon checking the literature for analogous disubstituted systems, this bis-benzylic displacement was found to be of only fair or

poor yield. In the case of TNAP, the published result in dimethyl sulfoxide is 8%[64]. Changing the solvent to methanol in that case gave 25% of the product. It is possible that the cyanide ion may be acting as a base to deprotonate the product or may just be less reactive under such polar conditions.

The preparation of tetraethylammonium cyanide, TEACN, by the metathesis of potassium cyanide and tetraethyl fluoroborate was employed as previously described[65]. TEACN is soluble in methylene chloride, as is the dichloride 124a. Addition of 124a to a solution of TEACN led to rapid darkening of the mixture and production of product 125 in at most 26% yield after chromatography.

By changing the leaving group to bromide as in 124b through the use of phosphorus tribromide on the diol 121, approximately the same yield of 125 was acquired. Since the bis-bromide was less stable than the corresponding chloro derivative, no advantage was to be gained through this method. An attempt to prepare the iodide via trimethyl silyl iodide led to the isolation of a product which darkened on exposure to moisture and decomposed while eluting on silica gel. Reaction of a solution of this bis-iodide led to 125, but in very low yield. Tosylation and mesylation of the diol was attempted by utilizing the respective sulphonyl

chlorides and pyridine, but isolation of these reactive materials was not successful.

Other indirect methods of preparing bis-acetonitrile groups were investigated. A classical method toward this end is the Erlenmeyer azalactone synthesis(Figure 50). In this

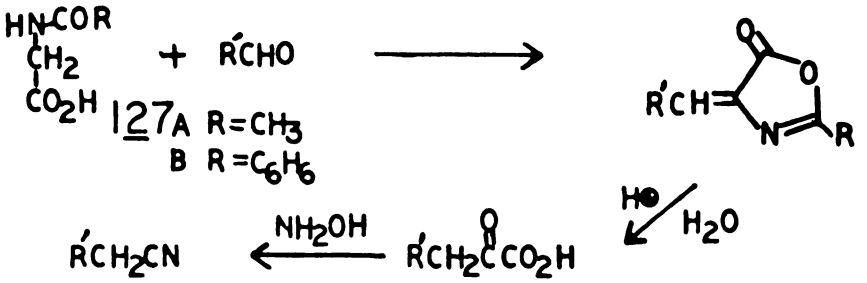


FIGURE 50: Erlenmeyer azalactone synthesis.

process, an aldehyde is condensed with aceturic acid, 127a(Figure 50, R= CH_3), or hippuric acid, 127b(R= phenyl) to afford the azalactone. Initial hydrolysis with base followed by treatment with acid produces the β-keto acid. These derivatives are known to yield acetonitriles when warmed in the presence of aqueous hydroxylamine[66]. Other variations include the use of rhodanine which can be treated as aceturic acid had been to yield the product[67]. Only one report of these methods dealt with an aryl dialdehyde, terephthaldehyde, though its hydrolysis or any further reactions were not reported. When the dialdehyde 120 was heated with acetic anhydride and aceturic acid,(Figure 51) an ex-

tremely insoluble red product was isolated which exhibited molecular ion peaks in its mass spectrum for the monoazalactone and

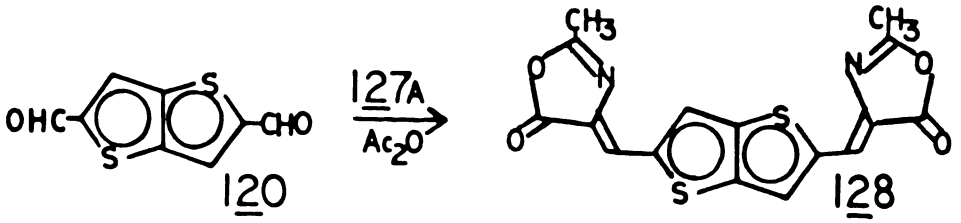


FIGURE 51: Preparation of bis-azalactone 128.

bis-azalactone, 128. Similar results accompanied the experiments employing rhodanine as the homologating agent. Presumedly, the mono-cyclized product was so insoluble that further reaction was unlikely. Both these methods worked well for thiophene producing a fair yield of thienyl acetonitrile in two steps from 2-thiophene carboxaldehyde.

A new method of preparing homologated nitriles from ketones and some aldehydes was reported recently[68]. It dealt with the use of toluenesulfonylmethyl isocyanide, TOSMIC, as the condensing agent with carbonyls to yield the tosylalkenylformamides. Upon treatment with sodium in methanol, these compounds undergo a rearrangement to the acetonitriles, as shown in Figure 52[69]. Again, no examples of difunctional molecules were reported. Thiophene gave 75% of 129 when treated with TOSMIC and potassium t-butoxide in tetrahydrofuran. Terephthaldehyde was also used as a model

system and yielded 68% of the bis-amide. Treatment of 120 under the same conditions, led mainly to the recovery of starting material.

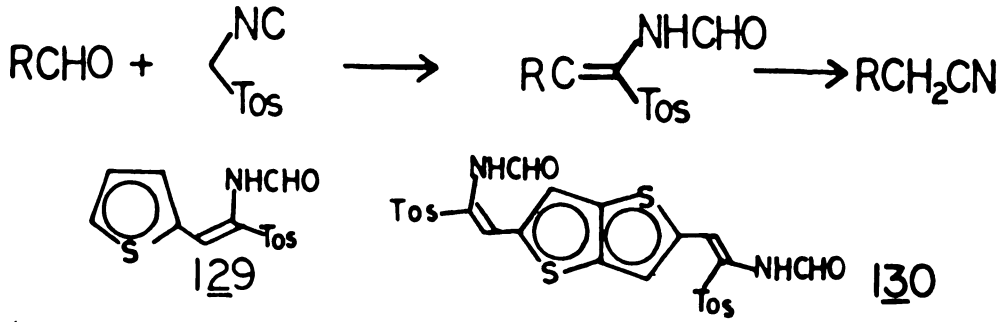


FIGURE 52: Recent synthesis of arylacetonitriles.

When a mixture of dimethyl sulfoxide and tetrahydrofuran was used as the solvents, terephthaldehyde gave 84% of the bis-amide, and the dialdehyde, 120, yielded only one product, its corresponding bis-amide, 130, in 77% yield. Rearrangement of 130 under basic conditions, followed by purification, led to 14.5% yield of the desired dicyanide, 125. This quantity could not be increased by varying conditions of either step. Since this was, in total, less efficient than the previous reduction, halogenation, cyanation sequence, further application of this potentially useful reaction was rejected.

The addition of a carboxy group to of 125 results in

the bis-cyanoester, 131 (Figure 53), being produced in 72%

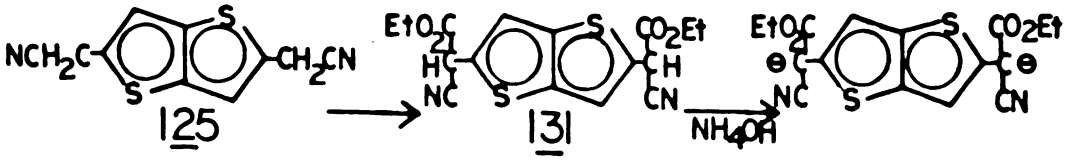


FIGURE 53: Attempted ammonolysis of ester 131.

yield. The ammonolysis of 131 with ammonium hydroxide at room temperature or liquid ammonia at 0°C, on workup mainly returns starting material. It is thought that the cyanoester 131, may be more acidic than its benzene or napthalene analogs. The greater pKa would stabilize the resultant anion and thus, slow attack of ammonia upon the ester carbonyl. This could also explain lower yields due to side products in the use of cyanide ion as a nucleophile.

Nevertheless, in order to proceed on the synthetic route toward 8, an alternate method designed by Wheland and Martin at du Pont was used[10]. Rather than transform the carboethoxy group into a cyano group, the method obtains the conjugate base of the cyanoester(See Figure 36), and cyanates with cyanogen chloride. Thus, in a stepwise manner, a protected malononitrile group has been prepared. The process continues with the aqueous base hydrolysis of the ester and acidification, to release carbon dioxide and obtain the aryl malononitrile. Oxidation in situ is normally used to directly provide the quinone, 8. Cyanation of ester 131 has

led to the dicyano acetate 132 in low yield. Purification of this compound has been complicated by its reactivity with various chromatographic supports. The crude 132 was combined without further purification with aqueous base yielding a highly fluorescent solution after dissolution of the solid 132 with heat. Acidification of this mixture in order to isolate 133 (Figure 54), or direct oxidation of the acidified solution to yield 8 has failed. Only highly

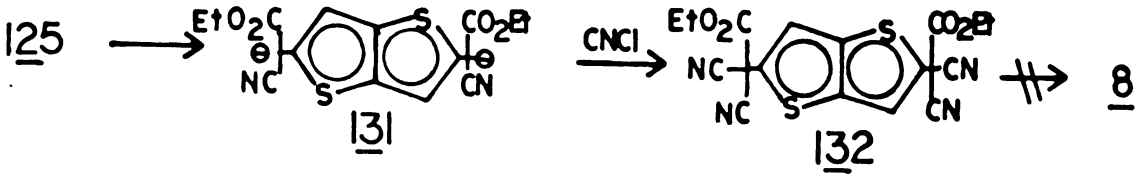


FIGURE 54: Synthesis of diester 132.

insoluble products have been obtained from the fluorescent solutions. This fluorescence fades upon standing overnight at room temperature, and the solids which precipitate have not yet been successfully characterized.

Access to the dialdehyde 120 encouraged efforts toward the synthesis of derivatives of TTF with extended π frameworks, e.g. 134(Figure 55). The availability of 3,4-dimercaptotoluene 135, promoted its use in our work.

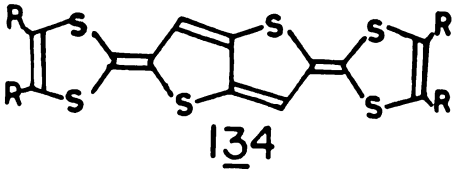


FIGURE 55: Synthetic target system of thienothiophene.

Upon refluxing 120 in benzene with two moles of 135, and a catalytic amount of toluenesulfonic acid, there precipitates a tan solid whose mass spectrum exhibits a molecular ion peak at m/e 472, corresponding to the bis-dithiole 136(Figure 56). However, when 1,2 dimercaptobenzene, 137, was used in

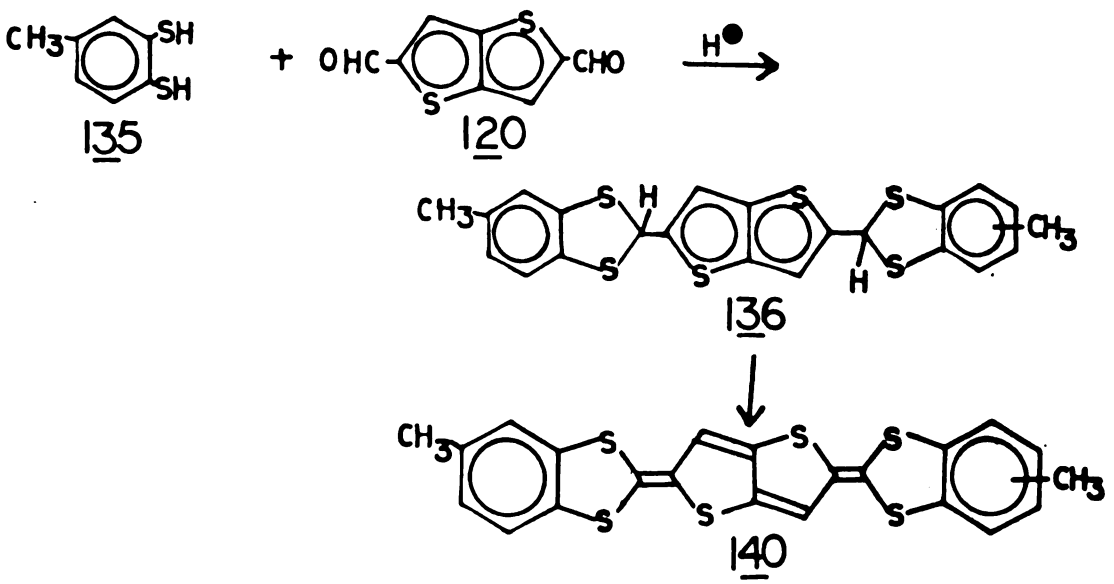


FIGURE 56: Synthesis of bis(methylbenzo)dithiole 140.

this same way only the mono benzdithiole, 138, was isolated in low yield (Figure 57). Either the insolubility of 138 or the lower stability of the dithiol may have caused this loss in yield. Changing the reaction conditions by stirring the dithiol 135 in ethanol, saturated with hydrogen chloride at room temperature, led to a 73% yield of 136 being produced. No trace of the oxidized product 140 or of any disulfides was present from PMR and mass spectral

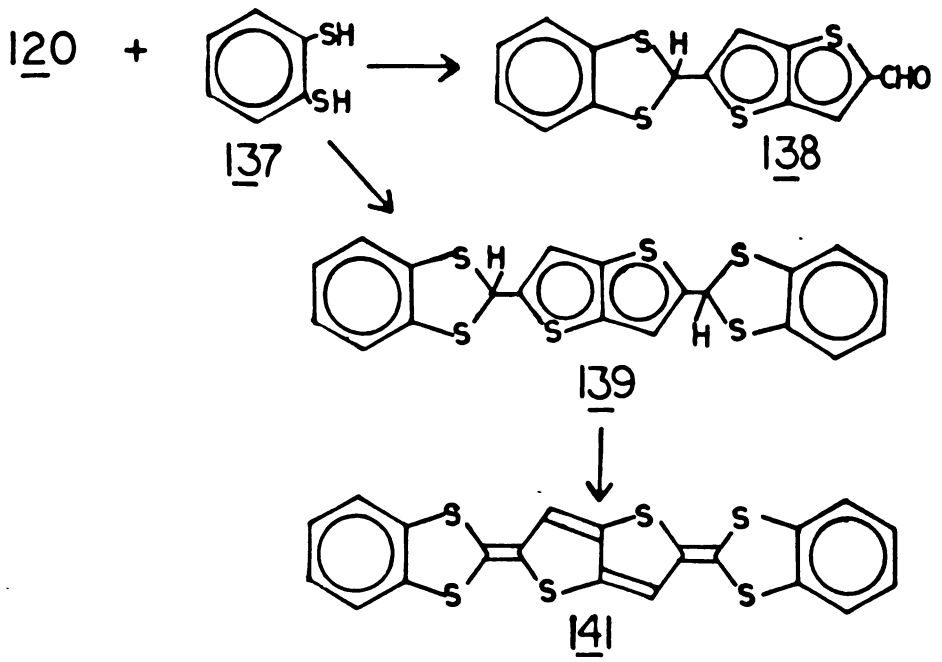


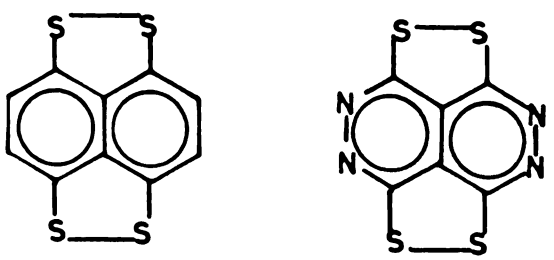
FIGURE 57: Synthesis of bis-benzodithiole 141.

analysis. Application of these same conditions to the unstable dithiol, 137, led to a 62% yield of 139.

When 136 and 139 was treated with a solution of dichloro dicyano quinone in tetrahydrofuran, dark solids precipitated and show molecular ions at m/e 470 and m/e 442 agreeing with that expected of the oxidized products, 140 and 141. Unfortunately, most of the product consists of very insoluble and non-volatile compounds which may be the charge transfer complexes of 140 and 141 with DDQ.

VI. PYRIDAZINO[4,5-d]PYRIDAZINE NUCLEUS

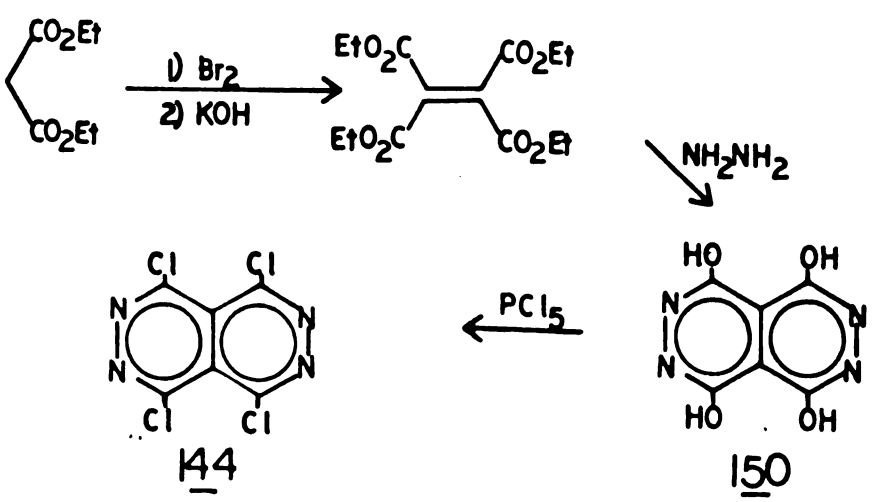
As shown in Table I, the napthalene bis disulfide, 145 (Figure 58) forms a highly conducting complex with TCNQ. The substitution of heteroatoms in this ring system as in 10 may result in equally interesting electronic properties. We



145 10

FIGURE 58: TTN, 145, and proposed analog, 10.

attempted to synthesize 10 since it should be quite accessible from the known tetrachloro compound, 144, prepared as shown below (Figure 59)[71].



144 150

FIGURE 59: Tetrachloro-tetra-azanapthalene, 144.

Since positions α to an aromatic nitrogen as in 144 are easily functionalized, the synthesis of 10 should be less arduous than that of the carbocyclic system. Numerous methods of introducing sulfur to these positions are present in the literature. Furthermore, thiol sulfurs that are positioned peri to each other have been shown to be easily oxidized to the cyclic disulfide. From initial experiments, 144 was found to be quite reactive toward nucleophiles. Displacement of one chlorine by a hydroxy group had been found to occur while it was stirred with aqueous sodium carbonate at room temperature.

Fusion of 144 with sulfur using conditions similar to preparations of 145 failed to give any 10. In fact, treating 144 with sulfur in various nucleophilic forms, KSH or dipotassium sulfide, 146, and even potassium ethylxanthate, 147, or potassium thiolacetic acid yielded insoluble red-brown powders (Figure 60). The mass spectra of these

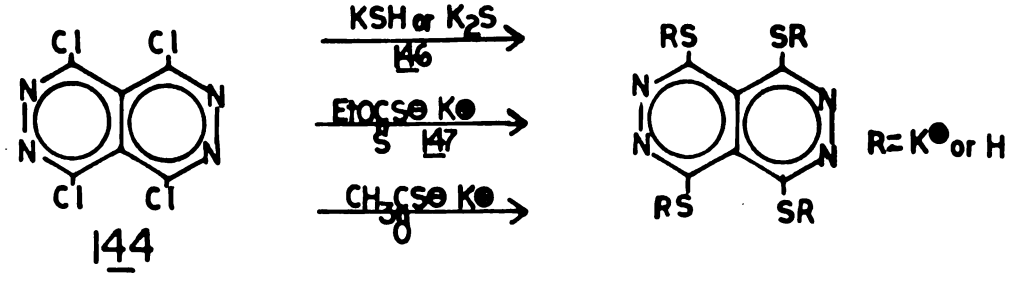


FIGURE 60: Attempts at sulfur incorporation of 144.

samples often exhibited a molecular ion at m/e 256.

Although this is the correct weight for 10, it is also that for elemental sulfur. All samples were washed with excessive amounts of carbon disulfide to extract out any sulfurous residues, however, this did not change the spectral results. Identification through the study of the fragmentation ions is complicated by the coincidental weight of m/e 128 for the desulfurated ring nucleus of 10 and S_4, an important fragment of sulfur itself.

A recent method involving the in situ production of a dilithio disulfide species in the absence of larger sulfur fragments was also used with 144 (Figure 61). A stoichimetric amount of sulfur

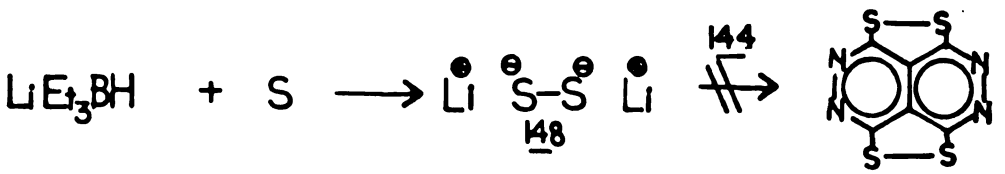


FIGURE 61: Attempted synthesis of 10.

and of lithium triethylborohydride in tetrahydrofuran were mixed together yielding a clear solution of 148. However, when this solution was added to 144, a resinous product resulted which, after chromatography, showed a large fragment ion for ethyl in its mass spectrum.

Treatment of the known tetramethoxy 149, or tetrahydroxy compounds 150 (Figure 62), with phosphorus pentasul-

fide under various conditions gave products displaying sulfur-containing mass spectra after washing with water,

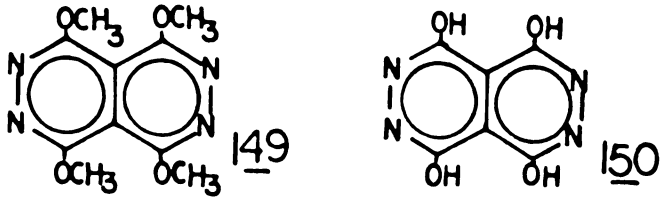


FIGURE 62: Oxygen derivatives of 144.

hot carbon disulfide and ether. When 144 was reacted with thiourea similar intractable products were obtained. These reactions took place immediately, and the solution darkened long before all reagent was added. In most cases, no starting material could be recovered.

If the problem was one of the initially formed mercaptide ion, 151 (Figure 63), undergoing an intermolecular substitution, then utilizing a protected sulfur nucleophile

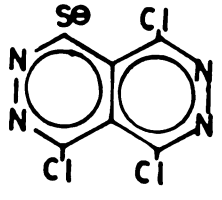


FIGURE 63: Possible intermediate from sulfurization of 144.

would obstruct this side reaction. Although potassium thiocyanate in ethanol was used with 144 under various condi-

tions, it failed to produce the tetrasubstituted compound. It has been shown in the 3,6-dichloropyridazine system[72] that that only one thiocyanate group will substitute on the ring.

The protection of protein thiol groups has gained importance recently, and studies in this field have utilized a number of compounds that 1) can act as a protected sulfur nucleophile, and 2) after substitution, allow facile removal of this group[73]. One of the more well known protected thiols is t-butyl mercaptan. When this thiol is mixed with potassium hydroxide in ethanol and reacted with 144, there resulted a bright yellow compound, 152, in 48%(Figure 64). Mass spectral analysis

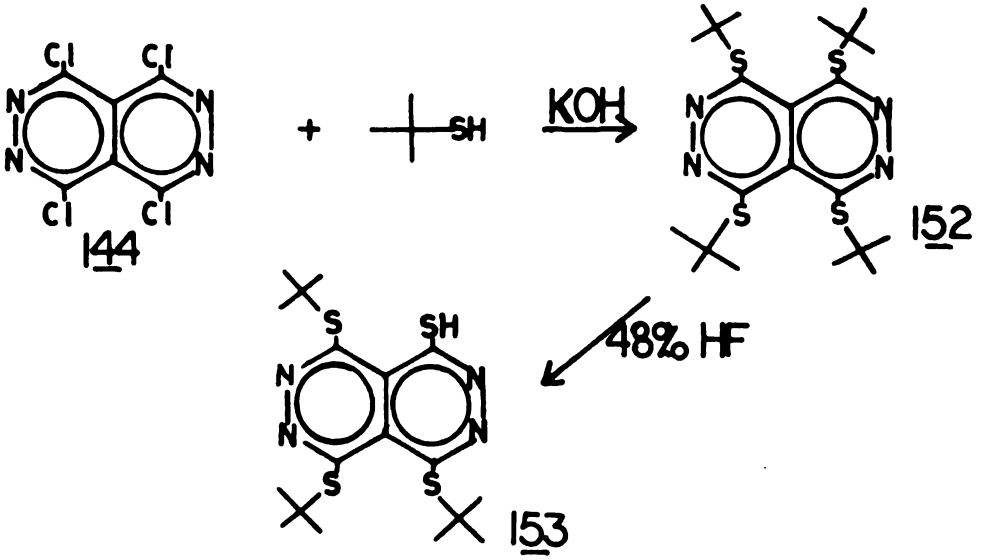


FIGURE 64: Tetra-t-butylthio-tetra-azanapthalene, 152.

showed large fragment signals corresponding to loss of all

the t-butyl groups, and other spectral evidence agreed with expected values. Cleavage of the t-butyl moiety was attempted by heating 152 in trifluoroacetic acid. The dark insoluble product again showed a peak at m/e 256 along with other minor peaks at higher molecular weights. The physical properties of this solid were similar to those of the previous products. Stirring 152 in 48% hydrofluoric acid at room temperature led to a mixture of at least five products, the slowest eluting compound being the tri-t-butyl monomercapto product, 153. Efforts to force this reaction to completion led to decomposition of the starting material and products. A more recent method of cleavage utilizing mercuric bis-trifluoroacetate[74] gave products which showed the presence of mercury in their mass spectra.

Another classical sulfur protecting species is the benzyl group. Synthesis of the tetrabenzylthio derivative, 154, from benzyl mercaptan proceeded as previously described for the t-butyl derivative (Figure 65). A common procedure

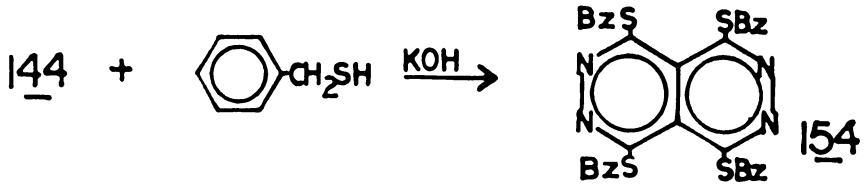


FIGURE 65: Tetrabenzylthio-tetra-azanapthalene, 154.

for deprotection of benzylthio ethers relies on reduction by

sodium in ammonia. When 154 was added to the ammonia solution, a reaction was evident as dissolution of the solid took place. Quenching with ice, followed by neutralization, led to a dark precipitate that also exhibited a molecular ion in its mass spectra at m/e 256. In order to determine whether these insoluble products were, in fact, 10, or whether they were polymeric in nature, elemental analyses were taken. The results differed from calculated values by as much as 2-3% for carbon and nitrogen. This shows that though the isolated products are carbon containing materials, further purification would be necessary in order to properly characterize these solids.

VII. DIAZEPINO[4,5,6,7-d,e,f]FLUORENE NUCLEUS

Although azulene is isomeric to napthalene and exhibits considerable aromatic behavior, the differences in the electronic system in this structure is well known. The azulene derivative 156 (Figure 66), corresponding to TNAP (Table II, entry 4) would be of great interest and as yet, has not been reported. However, a similar structure, 157,

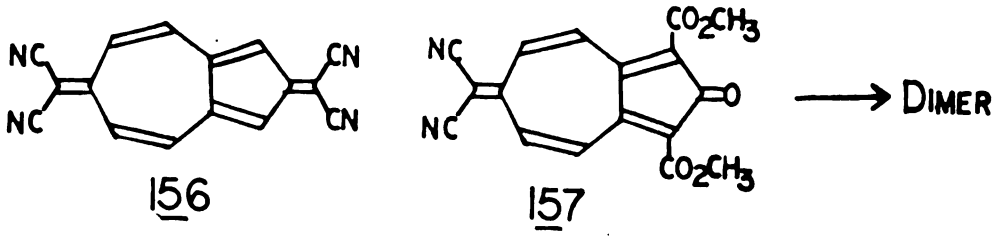


FIGURE 66: Azulene quinone target and derivative.

has been prepared[75], and when isolation was attempted, facile dimerization took place. This result reflects the inherent instability of azulene quinones, and establishes the need for stabilizing groups in order to isolate such a system. Extending the π system of azulene via its fusion to benzene rings is one way to increase the stability of this compound and perhaps allow isolation.

The diaza analog, 11, was chosen as the synthetic target since its synthesis could lead advantageously from the accessible fluorenone, 158[76]. The proposed synthetic

scheme is shown in Figure 67. It was thought that a Knoevenagel condensation of the carbonyl group in 158 with malononitrile would yield the dicyanofluorenylidene, 159.

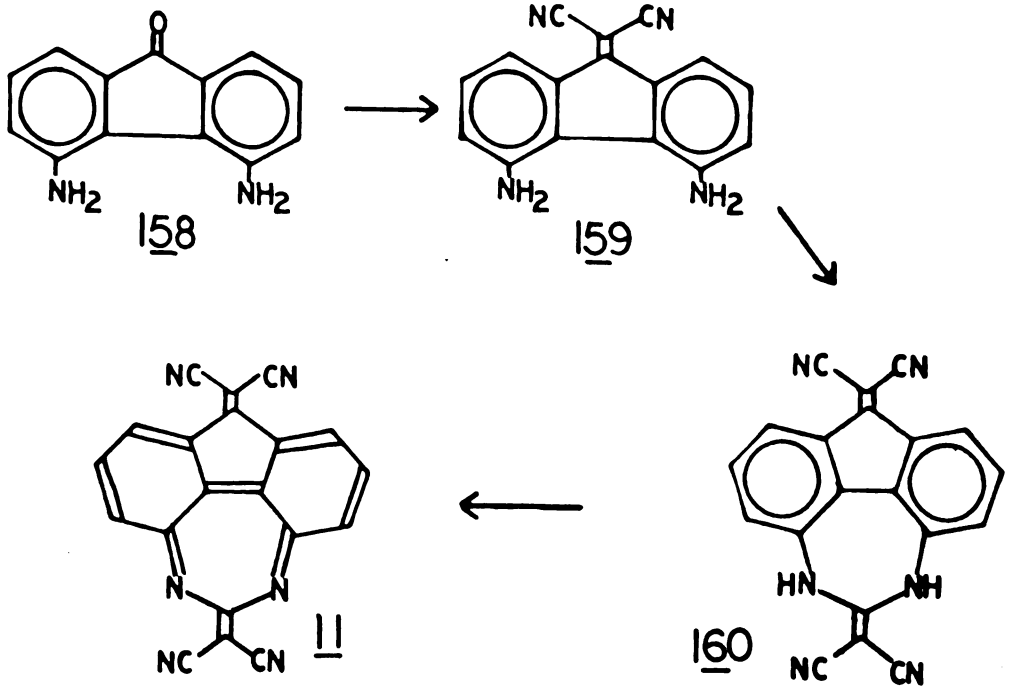


FIGURE 67: Proposed route to tetracyano derivative 11.

Although reagent 52 has never been applied to the synthesis of 1,3-diazepines from 1,4-diamines, it was hoped that this reaction could be used as a new and convenient method toward this end. If subsequent cyclization of 159 with reagent 52 should lead to 160, then an oxidation of 160 would be expected to provide 11.

The starting material, 4,5-diaminofluorenone, 158, was previously prepared from phenanthraquinone in the multi-step sequence described in Figure 68[77]. All attempts at acid

catalyzed condensation of 158 with malononitrile

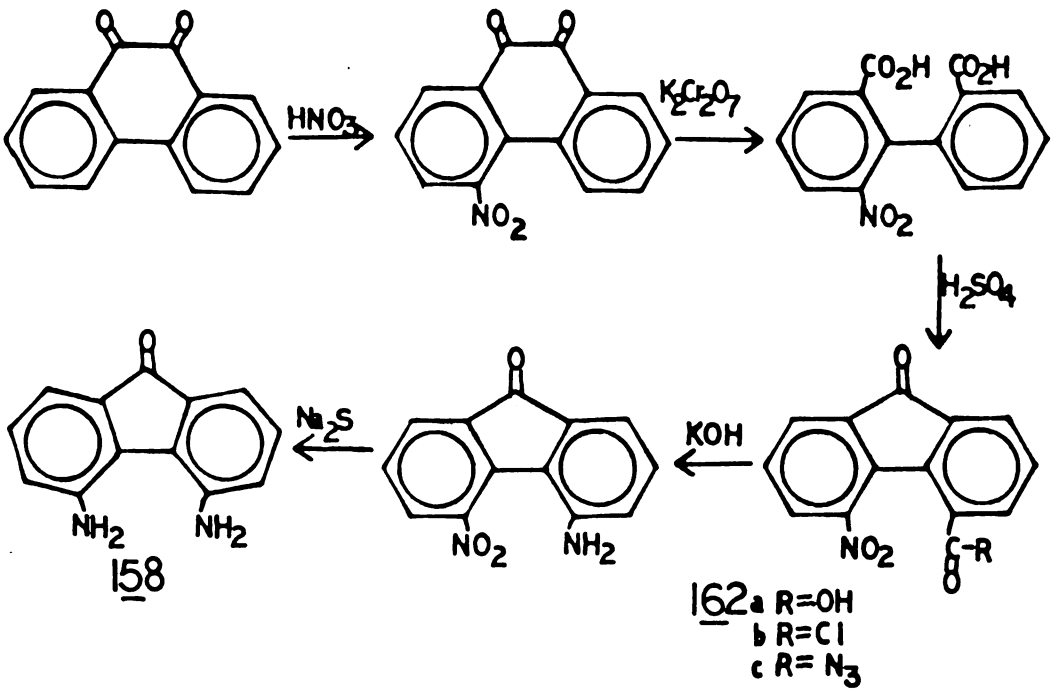


FIGURE 68: Synthesis of 4,5-diaminofluorenone.

failed even when excess acid was used. However, using piperidine as the catalyst resulted in the isolation of a very dark green solid which showed the expected spectral values for product 159. Condensation of 159 with cyclizing agent 52 in the presence of a tertiary amine gave no 160, but instead, led to uncharacterized products of higher molecular weight. The amino groups in 159 were expected to be weaker nucleophiles than those in the corresponding ketone, 158, and the reduced reactivity possibly caused this reaction to fail.

This problem can be solved by exchanging the synthetic

steps, i.e. by initially preparing the 2-dicyanomethylene 1,3-diazepine ring, and following this reaction by the Knoevenagel condensation with 161(Figure 69). In this way, the preparation of the highly insoluble 161 succeeded in 46%

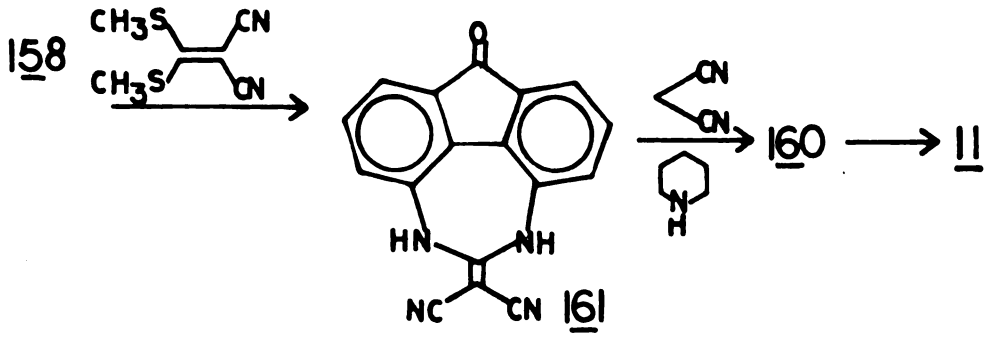


FIGURE 69: Modified synthetic route to 11.

yield. When ketone 161 was heated with malononitrile in dimethyl formamide in the presence of piperidine, the tetracyano compound, 160, was isolated in 95% yield. All attempts to oxidize 160 to 11 thus far, have returned only starting material. Destruction of the aromaticity in the biphenyl system in 160 would occur upon oxidation to 11. It is possible that the desired quinone, 11, is not stable relative to the diprotonated form 160.

EXPERIMENTAL

GENERAL PROCEDURES

The melting points were determined on a Thomas Hoover Uni-melt melting point apparatus and are uncorrected. The infrared spectra were recorded on a Perkin-Elmer Model 237B or 137 spectrometer. The PMR spectra were obtained on a Varian T-60 spectrometer with chemical shifts reported in δ-units from tetramethylsilane as the internal standard. A Hitachi Perkin-Elmer RMU-6 model and a Finnagan 4000 model mass spectrometer were used to obtain the mass spectra. Elemental analyses were performed by Guelph Chemical Laboratories Ltd. Tetrahydrofuran, THF, was used after distillation from potassium metal. Ether was used directly from sealed metal containers having less than 0.01% water. Sodium hydride was used as a 50% dispersion in mineral oil.

4-Chloropyridine 1-dicyanomethylide (16)

To a solution of 4-chloropyridine hydrochloride (8.43g, 56.6 mmoles) in the minimum amount of water, is added sodium carbonate (3g, 0.0283 moles). The basic aqueous layer is extracted three times with ether (50ml), and the combined organic layers are dried over sodium carbonate. Filtration and evaporation of the ether yields an oil that is combined with benzene (100ml) and water (1ml), and cooled in an ice bath. A pipet is used to bubble nitrogen into the stirred

solution throughout the reaction. Tetracyanoethylene oxide, TCNEO, (7.09g, 0.0492 moles) is added to this solution with a solid addition funnel. The mixture is stirred in the cold for 8 hours and then filtered. The solid is air dried, and by concentrating the mother liquor more solid is able to be obtained. The solids are combined and dissolved in methylene chloride/ethyl acetate, 4:1. Chromatography on alumina absorption using this solvent combination at first, and changing to ethyl acetate yields 5g (57%) of 16: mp 126°; IR (Nujol): 3100, 2200, 2150, 1210, 835; PMR (DMSO): 7.8 (d, 2H), 8.4 (d, 2H); MS: m/e = 177 (parent).

Potassium 4-dicyanomethylpyridine 1-dicyanomethylide (17)

Potassium hydride (3.7g, 25% in mineral oil, 0.023 moles) is suspended under nitrogen in dry THF (50ml) at 0 . To this suspension is added malononitrile (0.75g, 0.0113 moles) dissolved in THF (10ml). Following hydrogen evolution, 16 (2g, 0.0113 moles) in THF (100ml) is added dropwise to the anion. The mixture is refluxed for 1 day, cooled, and the brown solid is collected by filtration, triturated with ether and dried to give 2.9g (56%) of 17. mp >300°; IR (Nujol): 2200, 2160, 2125, 1620, 875; PMR (DMSO): 6.75 (d, 2H), 7.8 (d, 2H).

Anal. Calcd for 17: C, 53.86; H, 1.64; N, 28.55; Found: C, 54.05; H, 1.67; N, 29.04.

4-Ethoxypyridine 1-dicyanomethylide (18)

Sodium (0.15g, 6.52 mmoles) is added to absolute ethanol (10ml), and once dissolved, 16 (0.57g, 3.22 mmoles) is added all at once. The solution is stirred for 2 hours at room temperature. The reaction mixture is then filtered and the mother liquor is evaporated to a yellow brown solid. Recrystallization of this solid with ethanol yields 0.26g (43%) of 18: mp 145°; IR (Nujol): 2190, 2150, 1030, 800; PMR (Chloroform): 1.44 (tr, 3H), 4.17 (q, 2H), 7.0 (d, 2H), 8.23 (d, 2H); MS: m/e = 187 (parent).

4-t-Butyldicyanomethylpyridine 1-dicyanomethylide (19)

To sodium hydride (0.2g, 50% in mineral oil, 4.16 mmoles) is added dry ether (10ml) under nitrogen. To this stirred suspension is added t-butylmalononitrile (0.2g, 1.64mmoles) in dry ether (5ml). It is allowed to stir at room temperature for 1 hour. All at once, 16 (0.228g, 1.29 mmoles) is added, and the mixture is stirred overnight. Excess sodium hydride is decomposed by cautious addition of water, and the solution is filtered. The bright yellow solid is rinsed with cold ether and vacuum dried to give 0.27g (81%) of 19: mp 218°; IR (Nujol) : 2200, 2160, 860; PMR (DMSO): 1.15 (s, 9H), 7.65 (d, 2H), 8.38 (d, 2H); MS: m/e = 263 (parent).

4-Bis(ethoxycarbonyl)methylpyridine 1-dicyanomethylide (20)

Sodium (0.016g, 0.7 mmoles) is dissolved in absolute ethanol (3ml). Diethyl malonate (0.05g, 0.34mmoles) is dissolved in ethanol (1ml), and this solution is added all at once to the basic solution. The mixture is stirred at room temperature for 5 minutes and then 16 (0.060g, 0.34 mmoles) in THF (5ml) is added. After 1 hour, the ethanol is evaporated, and ether and 5% sodium hydroxide are added to dissolve all solids. The ethereal layer is extracted twice with 5% sodium hydroxide (5ml), and the aqueous layers are separated, combined and acidified with 5% hydrochloric acid at which point a light yellow solid precipitates. This solid is collected by filtration, and the acidic aqueous layer is extracted twice with ether. Evaporation of the solvent leaves a solid which, combined with the previous solid, can be recrystallized from ethanol yielding 42.6mg (41%) of 20: mp 173-174°; IR (Nujol): 2200, 2160, 1740, 1160, 1045; PMR (chloroform): 1.15 (tr, 6H), 4.08 (q, 4H), 4.62 (s, 1H), 7.6 (d, 2H), 8.38 (d, 2H); MS: m/e = 301 (parent).

4-Aminopyridine 1-dicyanomethylide

To concentrated ammonium hydroxide solution (1.62ml of 58%) is added 20 (0.0426g, 0.14 mmoles) and this mixture is warmed on a steam bath for 1.5 hours. Water is added to the cooled solution, and the precipitated solid is filtered.

More solid can be attained by ether extraction of the aqueous layer: IR (Nujol): 3250, 2260, 2180, 1625; PMR (chloroform): 2.52 (s, 2H), 7.3 (d, 2H), 8.32 (d, 2H); MS: m/e = 158 (parent).

3-Dicyanomethyl-6-chloropyridazine (23a)

To a suspension of sodium hydride (3.8g, 50% in mineral oil, 0.079 moles) in dry THF (150ml), malononitrile (5.2g, 0.079 moles) in THF (50ml) is added dropwise with stirring under nitrogen at room temperature. To this white suspension is quickly added 3,6-dichloropyridazine (5g, 0.0335 moles) in THF (75ml). The mixture is refluxed overnight, cooled, and the solvent is evaporated. The solid is triturated with ether and collected by filtration. Dissolution of this solid in water (200ml) with stirring gives a solution that is filtered, acidified with concentrated hydrochloric acid, and refiltered. This filtered solid is washed several times with water and is vacuum dried yielding 4.22g (71%): mp 258°; IR (Nujol): 3050, 2225, 2180, 1610, 1560, 1255, 1020, 820; PMR (DMSO): 7.45 (s, 2H), 13.3 (br s, 1H); MS: m/e = 178 (parent).

2-N-Methyl-3-dicyanomethylene-6-chloropyridazine (26)

To a stirred suspension of sodium hydride (0.135g, 50% in mineral oil, 2.8 mmoles) in THF (10ml), is added 23a

(0.5g, 2.8 mmoles) as a solid at room temperature under nitrogen. The mixture is refluxed 0.5 hours and cooled in ice while triethyloxonium fluoroborate (0.41g, 2.8 mmoles) dissolved in THF (70ml) is added dropwise. The ice bath is removed, and the reaction is stirred overnight. The solvent is evaporated, water added, and the remaining solid is filtered, triturated with ether and refiltered leaving 0.22g (41%) of 26: mp 142-142.5°; IR (Nujol): 3100, 2201, 1625; PMR (chloroform): 4.15 (s, 3H), 6.9 (d, 1H), 7.46 (d, 1H); MS: m/e = 192 (parent).

3,6-Bis-(t-butyldicyanomethyl)pyridazine (29)

To a suspension of potassium hydride (4.2g, 25% in mineral oil, 0.027 moles) in THF (25ml), is added dropwise a solution of t-butyl malononitrile (3.3g, 0.027 moles) in THF (25ml). After the initial reaction is over, the mixture is stirred until the evolution of hydrogen has quelled. At this point, 3,6-dichloropyridazine (2g, 0.0134 moles) in THF (20ml) is added quickly, and the mixture is refluxed for 60 hours. Afterwards, the solvent is evaporated, and water is cautiously added. The aqueous mixture is extracted with chloroform until it extracts no more color. Evaporation of the solvent gives a dark brown solid. Column chromatography of this solid on neutral alumina with chloroform yields a solid which can be recrystallized from ethanol. 1.35g (31%): mp 221-222°; IR (Nujol): 2245, 1415, 1175, 940;

PMR (chloroform): 1.27 (s, 9H), 7.84 (s, 1H) ; MS: m/e = 264 (parent - isobutylene).

3,6-Bis-(methylsulfonyl)pyridazine (30)

Chlorine gas was slowly entered into a solution of 3,6-bis-(methylthio)pyridazine (7.4g, 8.14 mmoles) in methanol (140ml) and water (0.6ml) cooled to -5°. A white precipitate gradually forms. After 25 minutes, the mixture is cooled to -20°, and the solid is collected by filtration giving 1.6g (83%) of 30: mp 250°; IR (Nujol): 3100, 3030, 3005, 1550, 1310, 852; PMR (DMSO): 3.53 (s, 3H), 8.5 (s, 1H); MS: m/e = 236 (parent).

3-Dicyanomethyl-6-t-butyldicyanomethylpyridazine (31)

To a solution of refluxing phenyl ether (20ml) is added all at once, 29 (0.2g, 0.625 moles). After 5 minutes, the solution is cooled to room temperature. The reaction mixture is treated with 5% sodium bicarbonate, and these aqueous solutions are extracted several times with ether to remove the residual phenyl ether. Acidification of this aqueous layer with 5% hydrochloric acid precipitates a solid which is collected by filtration and washed thoroughly with water. After drying in a vacuum for several hours, there remains 0.1g (61%) 31: mp 235-240°; IR (Nujol): 3150, 2201, 2175, 1640, 1585, 805; PMR (chloroform): 1.27 (s,

9H), 7.12 (s, 2H), 7.45 (s, 1H); MS: m/e = 264 (parent).

Phenylthiomalononitrile (39)

Sodium hydride (0.364g, 50% in mineral oil, 7.6 mmoles) is suspended in THF (10ml) and to this ice cooled solution is added malononitrile (0.5g, 7.6 mmoles) dissolved in THF (5ml). After evolution of hydrogen is complete, the mixture is warmed to room temperature and pipetted with an eye dropper into a stirred solution of phenyl toluenethiosulfonate (2g, 7.6 mmoles) in THF (100ml). As the anion adds, a dense white precipitate forms. The thick suspension is stirred overnight, and the solvent is evaporated. Water is added and the mixture is extracted three times with ether. The organic solution is dried over sodium sulfate and evaporated to an oil which crystallizes on standing to yield 30% of 39. All spectral data concur with literature values[38]..

n-Butyl toluenethiolsulfonate (47)

Silver nitrate (2.16g, 12.7 mmoles) is dissolved in water (10ml). n-Butyl disulfide (1.88g, 10.5 mmoles) is dissolved in acetone (30ml), and this solution is combined with the aqueous solution. The mixture is stirred at room temperature in an open flask. Sodium toluenesulfinate (2.07g, 11.7 mmoles) is added as a solid to the stirred mix-

ture and immediately creates a thick precipitate. The mixture is stirred for 2 hours, filtered, and the inorganic solids are washed with acetone. The mother liquor and acetone are concentrated, and the remaining slush is extracted three times with ether. This organic solution is dried over sodium sulfate and the solvent is evaporated. The crude oil is flash chromatographed on silica gel with methylene chloride yielding 1.54g (51%) of 47: IR (Neat): 2950, 1600, 1350, 1140, 812; PMR (chloroform): 0.83 (tr, 3H), 1.42 (m, 4H), 2.4 (s, 2H), 2.9 (tr, 2H), 7.13 (d, 2H), 7.62 (d, 2H); MS: m/e = 260 (parent).

Benzyl toluenethiolsulfonate (48)

The same procedure was used as that shown above for 47. Using silver nitrate (10.4g, 0.061 moles), benzyl disulfide (12.3g, 0.05 moles) in acetone (200ml) and water (75ml) together with sodium thiolsulfinate (10g, 0.056 moles) yielded 12.4g (89%) of 48. The crude material can be purified by flash chromatography on silica gel using pet ether:ethyl acetate, 3:1, as the eluent: mp 56-57°; IR (Nujol): 1590, 1325, 1135, 700; PMR (chloroform): 2.36 (s, 3H), 4.15 (s, 2H), 7.05 (s, 5H), 7.1 (d, 2H), 7.55 (d, 2H); MS: m/e = 278 (parent).

Benzylthiomalononitrile (49)

Malononitrile (2.37g, 0.036 moles) dissolved in THF (10ml) is added to a suspension of sodium hydride (1.75g, 50% in mineral oil, 0.036 moles) in THF (20ml) cooled by an ice bath. After evolution of the hydrogen had ceased, an eyedropper was used to add the anion dropwise into a solution of 48 in THF (200ml). As it adds, a dense white precipitate forms, and after stirring at room temperature for 1 hour, the solid is filtered and washed with ether. The organic solvents are evaporated to a moist solid that is collected by filtration with pentane. The crude solid is flash chromatographed over silica gel with methylene chloride yielding 2.7g (40%) of 49: mp 66-69°; IR (Nujol): 2275, 1180, 1020; PMR (chloroform): 4.06 (s, 2H), 4.12 (s, 1H), 7.12 (s, 5H); MS: m/e = 188 (parent).

2-Dicyanomethyl-3,5-dihydroxy-4-methylpyrimidine (50b)

A solution of sodium ethoxide is prepared by dissolving sodium (0.167g, 7.26 mmoles) in ethanol (25ml). To this solution is added diethyl methylmalonate (1.21g, 6.95 mmoles) and 1,1-diamino-2,2-dicyanoethylene[40] (0.75g, 6.95 mmoles). The mixture is refluxed for 2.5 hours and precipitates a white solid. This solid is collected by filtration and dried by washing with ether. The solid is dissolved in water and acidified, precipitating a white solid that was collected by filtraytion and washed with water. After drying in vacuum there was given 0.21g (16%) of 50b: mp 300°;

IR (Nujol): 3530, 3460, 2235, 2220, 1750; PMR (DMSO): 1.7 (s), other signals are very broad due to solvent; MS: m/e = 190 (parent).

2-Dicyanomethyl-3,5-dihydroxy-4-phenylpyrimidine (50c)

The same procedure was used as for 50b. In this way 1,1-diamino-2,2-dicyano ethylene (0.5g, 4.6 mmoles), diethyl phenylmalonate (1.1g, 4.6 mmoles) were added to sodium (0.11g, 4.6 mmoles) in ethanol resulting in 0.3g (26%) of 50c: mp 260°; IR (Nujol): 3375, 3060, 2225, 2200, 1560; PMR (DMSO): 7.2 (s, 5H), 11.17 (s, 3H), other signals are very broad due to solvent; MS: m/e = 252 (parent).

2-Dicyanomethylene piperimidine (55)

To a warm solution of 1,1-bismethylmercapto 2,2-dicyanoethylene, 52, (1g, 5.88 mmoles) in ethanol (50ml), is added 1,3-diaminopropane (0.435g, 5.88mmoles) in ethanol (10ml) dropwise with stirring. The mixture is stirred for 0.5 hour and cooled before filtering the precipitated solid. This solid is washed with ether to dryness to yield 0.7g (81%) of 55: mp 300°; IR (Nujol): 3290, 2190, 2160, 1585, 1200; PMR (DMSO): 1.79 (p, 2H), 3.2 (tr, 4H), 7.5 (br s, 2H); MS: m/e = 148 (parent).

5-Hydroxy-2-dicyanomethylene piperimidine (60)

A solution of 1,3-diamino-2-propanol (0.5g, 5.55 mmoles) in ethanol (25ml) is stirred at room temperature. To this solution is added an equimolar amount of 52 or dicyanoketene ethylene acetal, 59[40], either in solution or as solids. The respective mixtures are refluxed for 2 hours and allowed to cool slightly before the precipitated solids are collected by filtration. This solid is washed to dryness with ether giving 0.74g (81%) of 60: mp 267°; IR (Nujol): 3300, 3050, 2205, 2170, 1601, 1580, 1200; PMR (DMSO): 3.15 (br s, 4H), 3.9 (p, 1H), 5.15 (br s, 1H), 7.4 (br s, 2H); MS: m/e = 164 (parent).

2-Dicyanomethylene piperimidine-5-mesylate (61)

A solution of 60 (1g, 6.1 mmoles) in pyridine (15ml) is stirred at 0° while methanesulfonyl chloride (0.695g, 6.1 mmoles) is added dropwise. The mixture is stirred for two hours before quenching with water. The precipitated solid is washed with water and vacuum dried to yield 1.4g (95%) of 61: mp 240°; IR (Nujol): 3230, 3045, 2200, 2170, 1630, 1590, 1350, 930; PMR (DMSO): 3.28 (s, 3H), 3.42 (br s, 4H), 5.1 (br s, 1H), 7.7 (br s, 2H); MS: m/e = 242 (parent).

2-Dicyanomethylene piperimidine-5-tosylate (62)

A solution of 60 (0.5g, 3.05 mmoles) in pyridine (10ml)

is cooled to 0°and stirred while toluenesulfonyl chloride (0.58g, 3.05 mmoles) is added as a solid over several minutes. After stirring for 1 hour, the yellow mixture is evaporated and combined with water and ether. Some suspended solid is filtered from these layers, and the organic layer is then separated. The aqueous layer is extracted twice with ether. The organic layers are combined and evaporated to an oil which is crystallized by addition of a small amount of water. The white crystalline solid is dried in a vacuum overnight: mp 230°; IR (Nujol): 3275, 2220, 2200, 1630, 1600, 1155; MS: m/e = 318 (parent).

5-Trimethylsiloxy-2-dicyanomethylene piperimidine (63)

A solution of 60 (0.5g, 3.05 mmoles) in pyridine (5ml) is stirred at room temperature while trimethylsilyl chloride (0.33g, 3.05 mmoles) is added dropwise. After 1 hour, the mixture was evaporated, and the residue was warmed with chloroform. Undissolved solids are filtered, and the mother liquor is combined with pet ether and cooled in order to precipitate the product: mp 265-267°; IR (Nujol): 3300, 2200, 2165, 1620, 1600, 1200, 875; PMR (DMSO): 0.17 (s, 9H), 3.2 (m, 4H), 4.2 (br s, 1H), 7.45 (br s, 2H); MS: m/e = 236 (parent).

2-Dicyanomethyl-(3H,4H)-dihydropyrimidine (65)

Into a flask chilled to 0°and protected by a drying tube, is charged 60 (0.41g, 2.5 mmoles) and pyridine (3.5ml). To this stirred solution is added trifluoromethanesulfonyl anhydride (0.71g, 2.5 mmoles) dropwise. The yellow suspension is stirred for 3 hours at room temperature before quenching with water (40ml). The precipitated solid is collected by filtration and washed with water and rinsed dry with ether yielding 0.15g (41%) of 65: mp 285-289°; IR (Nujol): 3290, 3075, 2220, 2190, 1700, 1680, 1225; PMR (DMSO): 3.78 (m, 2H), 4.9 (m, 1H), 5.97 (m, 1H), 7.7 (br s, 1H), 9.0 (br s, 1H); MS: m/e = 146 (parent).

2,2-Dicarboethoxy 1,3-dithiolane (67)

Ethylene dithiolsulfonate (3g, 7.46 mmoles), diethyl malonate (1.25g, 7.81 mmoles), and potassium acetate (2g, 20.2 mmoles) are combined and refluxed in ethanol (50ml) for 6 hours. The ethanol is evaporated and the oily solid is extracted into ether. The organic layer is washed once with 10% sodium carbonate, and once with saturated sodium chloride solution. After drying with sodium sulfate, evaporation of the solvent leaves an oil that is of adequate purity for further reactions, 1.86g (95%): IR (Neat): 2980, 1740, 1230, 1030; PMR (chloroform): 1.33 (tr, 3H), 3.45 (s, 2H), 4.27 (q, 2H); MS: m/e = 250 (parent).

2,2-Biscarbamoyl 1,3-dithiolane (68a)

A solution of 67 (3.1g, 12.4 mmoles) in the minimum amount of ether is poured into concentrated ammonium hydroxide (50ml) at 0°. The mixture is vigorously stirred at this temperature for 1 hour, then allowed to warm to room temperature for 4 hours. The white solid is filtered and rinsed dry with ether. The mother liquor is evaporated to leave a residue which contains a 50:50 mixture of the product diamide and the side product, 2-carbamoyl 1,3-dithiolane. Total yield of product 68a is 1.9g (80%): mp 247°; IR (Nujol): 3400, 3200, 1650, 1350; PMR (DMSO): 3.25 (s, 4H), 7.26 (br s, 4H); MS: m/e = 192 (parent).

2,2-Bis(aminomethyl)-1,3-dithiolane dihydrochloride (69a)

Diborane:tetrahydrofuran complex (43.5ml of 0.94M solution, 41 mmoles) is stirred under nitrogen at 0°while 68a (1.57g, 8.12 mmoles) is added as a solid. The mixture is stirred at room temperature for 24 hours. The recooled solution is quenched with 10% hydrochloric acid (6.6ml), and the solvents are evaporated to a slush. With cooling, water (5ml) is first added followed by several pellets of potassium hydroxide, making the mixture alkaline. The basic aqueous layer is then extracted three times with chloroform, and this organic solution is dried over sodium sulfate. The oily diamine can be used for further reactions by evaporation of the solvent. Isolation of the dihydrochloride salt

can be accomplished by entering dry hydrogen chloride into the cooled chloroform solution. Filtration of the solid and regassing of the clear mother liquor is repeated until no further solid precipitates. This method yields 0.95g (50%) of 69a:2HCl : mp>300°; IR (Nujol): 3000, 2100, 1585, 1050, 970; PMR (chloroform): 2.18 (s, 4H), 2.88 (s, 4H), 3.21 (s, 4H).

2,2-Dicyano-1,3-dithiolane (70)

Acetamide (1.04g, 17.6 mmoles) and 69a (0.8g, 4.2 mmoles) are combined with phosphorus oxychloride (2ml) and refluxed for 2 hours. The dark tarry mixture is cooled, and some ice is cautiously added until all solids dissolve. This mixture is extracted three times with ether, and the organic layer is, in turn, washed with water and dried over sodium sulfate. Evaporation of the solvent leaves an orange oil which crystallizes on standing. The solid residue is recrystallized from carbon tetrachloride with darco to yield 0.05g (7.7%) of 70: mp 76-77°; IR (Nujol): 2225, 1455, 1280; PMR (chloroform): 3.68 (s); MS: m/e = 156 (parent).

2-Dicyanomethylene-5-piperimidone ethylene dithioketal (71)

A solution of the oily 69a (1.62g, 9.87 mmoles) in ethanol (25ml) is combined with 52 (1.68g, 9.87 mmoles) and re-

fluxed for 2 hours. The mixture is allowed to cool slightly, and the precipitated solid is collected by filtration. This solid is washed with ether to dryness yielding 0.65g (53%) of 71: mp >260°; IR (Nujol): 3280, 2250, 2160, 1620, 1580; PMR (DMSO): 3.35 (s, 4H), 3.42 (br s, 4H), 8.0 (br s, 2H); MS: m/e = 238 (parent).

2,2-Bisaminomethyl-1,3-dioxolane (74b)

A mixture of 80 (3.1g, 14.4 mmoles) is refluxed in 30% potassium hydroxide solution (25ml) for 1 hour. The clear mixture is cooled and saturated with several pellets of potassium hydroxide. The basic aqueous solution is extracted three times with chloroform. This organic solution is dried over anhydrous sodium carbonate, and the solvent is evaporated to a clear oil weighing 2.25g (84%). This diamine is used without further purification for subsequent reactions: IR (Neat): 3360, 1600, 1025; PMR (chloroform): 1.2 (s, 4H), 2.72 (s, 4H), 3.96 (s, 4H).

Diethoxymalonamide (74c)

Ammonia (25ml) is condensed into a stainless steel bomb cooled to -78°in a dry ice/ acetone bath. Diethyl diethoxymalonate[53] (10g, 52.1 mmoles) is dissolved in a minimum of ethanol and slowly combined with the ammonia. The bomb is sealed and allowed to warm to room temperature for 48 hours.

The bomb is then recooled, opened, and its contents are emptied by washing several times with boiling ethanol. One recrystallization of the crude solid from ethanol yields 4.3g (56%) of 74c contaminated with a trace of the corresponding acetamide: mp 206-207°; IR (Nujol): 3470, 3400, 3380, 1670, 1125, 1080; PMR (DMSO): 1.2 (tr, 6H), 3.4 (q, 4H), 7.13 (br d, 3H); MS: m/e = 190 (parent).

1,3-Bistrifluoroacetamidoacetone (79b)

1,3-Diaminoacetone dihydrochloride (2g, 11.2 mmoles) and sodium acetate (1.84g, 22.4 mmoles) are stirred in ether (30ml) in a flask cooled in an ice bath and protected by a drying tube. To this suspension is added trifluoroacetic anhydride (14.9g, 70.9 mmoles) dropwise. The mixture is allowed to warm to room temperature for 8 hours. The solid is collected by filtration, triturated in 1% hydrochloric acid solution (25ml), refiltered, and rinsed to dryness with ether. After vacuum drying for several hours, there is produced 2g (64%) of 79b: mp 223-226°; IR (Nujol): 3300, 3100, 1730, 1700, 1560, 1175, 1030; PMR (DMSO): 4.18 (d, 4H), 9.54 (br tr, 2H); MS: m/e = 281 (parent).

1,3-Diacetamidoacetone ethylene ketal (80)

Ethylene glycol (6.8ml), three drops of concentrated hydrochloric acid, and 1,3-diacetamidoacetone[55] (3.4g,

19.8 mmoles) are refluxed in benzene (150ml) with a water separator. After 5 hours, the mixture is cooled, and the solvent is evaporated. The residue is triturated with 4:1 ether:acetone, yielding, after drying, 3.7g (87%) of 80: mp 162-163°; IR (Nujol): 3290, 3060, 1700, 1570, 1220; PMR (DMSO): 1.99 (s, 6H), 3.3 (d, 4H), 3.93 (s, 4H), 6.3 (br s, 2H); MS: m/e = 216 (parent).

2-Dicyanomethylene-5-piperimidone ethylene ketal (81)

The diamine, 74b (2.05, 15.5 mmoles), is dissolved in ethanol (20ml), and to this solution is added 52 (2.65g, 15.5 mmoles) all at once. This mixture is refluxed for 0.5 hours and allowed to cool slightly before collecting the precipitated solid by filtration. This solid is washed with ether to dryness yielding 1.68g (53%) of 81: mp >300°; IR (Nujol): 3250, 3040, 2205, 2170, 1625, 1585, 860; PMR (DMSO): 3.1 (d, 4H), 3.9 (s, 4H), 7.68 (br s, 2H); MS: m/e = 206 (parent).

N,N'-Diethyl-1,3-diaminoacetone ethylene ketal (82)

The ketal 80 (1.14g, 5 mmoles), is added as a solid to a suspension of lithium aluminum hydride (0.5g, 13.15 mmoles) in tetrahydrofuran (25ml) stirred at room temperature. After the addition, the mixture is refluxed for 8 hours. The suspension is then cooled, and water (0.5ml),

15% potassium hydroxide solution (0.5ml), and water (1.5ml) are cautiously added in order. After stirring for 1 hour, the inorganic solids are collected by filtration and washed with THF. The solvent is evaporated, and the residue is combined with enough water (1ml) to dissolve several pellets of potassium hydroxide. The basic aqueous layer is extracted three times with ether. The ether solution is dried over anhydrous sodium carbonate and upon evaporation of the solvent, there results an oil, 0.92g (93%) of 82. This diamine is used in subsequent reactions without further purification: PMR (chloroform): 1.08 (tr, 6H), 1.48 (br s, 2H), 2.6 (q, 4H), 2.72 (s, 4H), 3.9 (s, 4H); MS: m/e = 188 (parent).

1,3-N,N'-Diethyl-2-dicyanomethylene-5-piperimidone ethylene ketal (83) and 1-N-ethyl-2-dicyanomethylene-5-piperimidone ethylene ketal (84)

The ketal 82 (0.79g, 4.2 mmoles) is combined with 52 (0.714g, 4.2 mmoles) in ethanol (20ml) and refluxed for 1 hour. The precipitated solid is filtered from the reddish reaction mixture and yields 0.31g (51%) of 83: mp 150-152°; IR (Nujol): 2190, 2170, 1560, 1520, 900, 813; PMR (chloroform): 1.3 (tr, 6H), 3.1 (s, 4H), 3.35 (q, 4H), 3.92 (s, 4H); MS: m/e = 262 (parent).

Evaporation of the mother liquor gives a mixture of 83 along with another product which can be separated by column

chromatography. Elution of the crude solid with ethyl acetate on alumina absorption isolates 84: mp 140-141°; IR (Nujol): 3250, 2190, 2170, 1575; PMR (chloroform): 1.3 (tr, 3H), 3.1 (br s, 4H), 3.6 (q, 2H), 3.99 (s, 4H), 6.0 (br s, 1H); MS: m/e = 234 (parent).

1,3-N,N'-Diethyl-2-dicyanomethylene-5-piperimidone (85)

The ketal 83 (0.3g, 1.15 mmoles) is combined with 10% hydrochloric acid (10ml) and heated on a steam bath for 5 hours. The mixture is filtered hot from any suspended solid and cooled in ice to precipitate clear needles. The product is collected by filtration and vacuum dried to give 85: mp 198-200°; IR (Nujol): 2190, 2170, 1750, 1530, 1500; PMR (DMSO): 1.2 (tr, 6H), 3.48 (q, 4H), 3.85 (s, 4H); MS: m/e = 218 (parent).

N,N'-Bisbenzoyl-1,3-diamino-2-propanol (88)

1,3-Diamino-2-propanol (1g, 11.1 mmoles) is dissolved in methanol (15ml) with stirring. To this solution is added benzoic anhydride (5.1g, 22.5 mmoles) within 5 minutes warming the solution considerably. After 0.5 hours, the solvents are evaporated and saturated sodium bicarbonate is added to the residue. The white solid is collected by filtration and washed, first with water, followed by ether. After vacuum drying there remains 2.6g (80%) of 88: mp

134-135.5°; IR (Nujol): 3480, 3300, 1640, 1580, 1115, 800; PMR (DMSO): 3.3 (br tr, 4H), 3.78 (m, 1H), 5.13 (br s, 1H), 7.3 (m, 6H), 7.78 (m, 4H), 8.32 (br s, 2H); MS: m/e = 280 (parent - water).

1,3-Bisbenzamidoacetone (89)

The alcohol 88 (0.3g, 1 mmole) is dissolved in dimethylformamide (2ml) and added at once into a similar solution of pyridinium dichromate[79] (0.57g, 1.5 mmoles). The dark red mixture is capped and stirred at room temperature for 48 hours. Water is added to precipitate a solid that is washed with water and vacuum dried yielding 0.17g (57%) of 89: mp 191-192.5°; IR (Nujol): 3300, 1740, 1640, 1300; PMR (DMSO): 4.12 (d, 4H), 7.3 (m, 6H), 7.78 (m, 4H), 8.65 (br tr, 2H); MS: m/e = 191 (parent - benzoyl).

1,3-Bisbenzamidoacetone ethylene ketal (90)

Ethylene glycol (0.142g, 2.3 mmoles) and ketone 89 (0.11g, 0.37 mmoles) are combined in benzene (15ml) along with one drop of concentrated hydrochloric acid. A water separator and drying tube are used as this mixture is refluxed for 12 hours. As the mixture cools a solid precipitates and is collected by filtration. Saturated sodium chloride solution is added to the mother liquor, and the organic layer is separated, dried over anhydrous sodium carbo-

nate and evaporated to yield a white solid. The two solids are combined to yield 0.105g (84%) of 90: mp 173-176°; IR (Nujol): 3300, 1640, 1550, 1310, 690; PMR (DMSO): 3.6 (d, 4H), 4.0 (s, 4H), 7.22 (br m, 8H), 7.78 (m, 4H); MS: m/e = 340 (parent).

1,3-Bis(benzylamino)acetone ethylene ketal (91)

The ketal 90 (0.1g, 0.29 mmoles) is dissolved in THF (5ml) and added dropwise to a stirred suspension of lithium aluminum hydride (0.028g, 0.74 mmoles) in THF (10ml) under nitrogen. After refluxing for 4 hours, the mixture is then cooled and to it is added, water (0.05ml), 15% sodium hydroxide (0.05ml), and water (0.15ml) in order. The solids are filtered and washed with THF. Evaporation of the combined solvents leaves an oily residue. Water (1ml) and several pellets of potassium hydroxide are added to this residue before it is extracted twice with ether. The organic solution is dried with sodium sulfate and evaporated to a light yellow oil. The crude yield is 0.09g (100%) of 91: PMR (chloroform): 2.1 (s, 2H), 2.78 (s, 4H), 3.72 (s, 4H), 3.85 (s, 4H), 7.15 (s, 10). This diamine was used in subsequent reactions without further purification.

1,3-Bisacetamido-2-propanol (92)

1,3-Diamino-2-propanol (1g, 11.1 mmoles) is dissolved

in methanol with stirring. To this solution is added acetic anhydride (2.5g, 24.5 mmoles) within 5 minutes warming the solution considerably. After 1 hour, the solvents are evaporated, leaving an oil which is crystallized by adding methylene chloride. The yield of white crystalline 92 is 1.41g (73%). The product can be recrystallized by adding methylene chloride/pet ether: mp 98-100°; IR (Nujol): 3380, 3320, 3100, 1660, 1580, 1125; PMR (DMSO): 1.8 (s, 6H), 3.0 (br tr, 5H), 4.9 (d, 1H), 7.7 (br s, 2H); MS: m/e = 174 (parent).

3-Dicyanomethyl-6-methylthio-1,2,4,5-tetrazine sodium salt (102)

Sodium hydride (1.3g, 50% in mineral oil, (27.1 mmoles) was suspended in benzene (25ml) and malononitrile (0.16g, 2.43 mmoles) in benzene (10ml) was added dropwise with stirring under nitrogen at room temperature. To this anion is added 3-bromo-6-methylthio-1,2,4,5-tetrazine, 101 (0.5g, 2.43m moles) in benzene (10ml) in a dropwise manner. Following this addition, the vessel is opened to the air and stirred vigorously for 2 hours. From the red solution a dark solid precipitates which is collected by filtration and rinsed dry with ether yielding 0.95g of a hydrated violet powder: mp >300°; IR (Nujol): 3400, 2200, 2180, 2160, 1620; PMR (DMSO): 2.52 (s), 3.3 (water).

3-Dicyanomethyl-6-methylthio 1,2,4,5-tetrazine tetrabutyl ammonium salt (103)

The sodium salt 102 is dissolved in water and to this solution is added a warm clear solution of a slight excess of tetrabutylammonium iodide in water. Upon combination, a violet solid precipitates. This metathesized solid is collected by filtration and is recrystallized from 95% ethanol: mp 114-115°; IR (Nujol): 2180, 2155, 1200, 1050.

3-Dicyanomethyl-6-methylthio-1,2,4,5-tetrazine (104)

The sodium salt 102 (1.25g) is dissolved in water (50ml) and is then treated with 10% hydrochloric acid to pH 2. Extraction with ether several times gives a dark tarry oil which reverts into the anionic form upon standing overnight in glassware: PMR (chloroform): 2.53 (s), 5.77 (br s).

3-Bis(carboethoxy)-6-methylthio-1,2,4,5-tetrazine (105)

Sodium hydride (0.13g, 50% in mineral oil, 2.7 mmoles) is suspended in benzene (10ml) and diethyl malonate (0.4g, 2.5 mmoles) is dissolved in benzene (10ml) and added dropwise causing evolution of gas. To the suspension of the anion is added a solution of 101 (0.5g, 2.43 mmoles) in benzene (20ml). Addition causes darker solution to occur. After stirring 1 hour at room temperature, solids are col-

lected by filtration. These solids are dissolved in 5% sodium hydroxide solution and extracted with ether. The basic aqueous layer is acidified with 10% hydrochloric acid and extracted three times with ether. The ether solution is dried over sodium sulfate and evaporated to give a red oil as the product, 105: IR (Nujol): 1725, 1370, 1160, 1025; PMR (carbon tetrachloride): 1.32 (tr, 6H), 2.75 (s, 3H), 4.3 (q, 4H), 5.15 (s, 1H); MS: m/e = 286 (parent).

Chlorination product of 1,1-diamino-2,2-dicyanoethylene (106)

1,1-Diamino-2,2-dicyanoethylene (0.2g, 1.85 mmoles) is suspended in dry acetonitrile (20ml) cooled to -20° with a dry ice/carbon tetrachloride bath. Chlorine gas is entered into the mixture with stirring at a steady rate and after several minutes a light yellow precipitate is seen. Soon all of the solids dissolve as chlorine is bubbled in for a total of 0.5 hours. The mixture is allowed to warm to room temperature, and the solvents are evaporated. Water is added along with ether and the organic layer is separated, dried over magnesium sulfate and evaporated to leave a pale yellow oil. This oil crystallizes upon standing and is collected by filtration with hexane. Column chromatography with silica gel and ether as the eluent proceeds to afford the purified product: IR (Nujol): 3430, 3340, 3220, 3150, 2252, 1650; MS: m/e = 176.

3-(Thienyl-2-carboxaldehyde)-mercaptoacetic acid (114)

The preparation of thieno[3,2-b]thiophene 2-carboxylic acid was followed as in reference 62. To the basic aqueous layer, 10% hydrochloric acid is added until a pH of 5 is reached. The precipitate is collected by filtration, and the mother liquor is acidified further to pH of 1-3. The latter solid that precipitates is mainly that of 116: PMR (DMSO): 3.88 (s, 2H), 7.15 (d, 1H), 7.97 (d, 1H), 9.72 (s, 1H).

Thieno[3,2-b]thiophene-2,5-dicarboxylic acid (123a)

Thieno[3,2-b]thiophene-2-carboxylic acid[62] (1g, 4.39 mmoles) is added as a solid to a solution of lithium diisopropyl amide (7.47ml 1.6M n-BuLi, 1.21g diisopropylamine) in THF (50ml) at -78° under nitrogen. The stirred suspension is allowed to warm to -10° for 0.5 hours at which time an excess of dry carbon dioxide is bubbled into the mixture. After 0.5 hours, the solvents are evaporated, and the remaining solids are vacuum dried overnight. The product is dissolved in a minimum of water and extracted two times with ether. The basic aqueous layer is cooled in an ice bath and acidified by dropwise addition of 10% hydrochloric acid. The mixture is stirred for 10 minutes, and the precipitated solid is collected by filtration and vacuum dried yielding 0.9g (73%) of 123a: mp >300°; IR (Nujol): 3100, 1660, 1300, 1150, 750; PMR (DMSO): 8.0 (s); MS: m/e = 228

(parent).

Diethyl thieno[3,2-b]thiophene-2,5-dicarboxylate (123b)

The diacid 123a (0.2g, 0.88 mmoles) is suspended in methylene chloride (25ml) and to this mixture is added diisopropylethylamine (0.226g, 1.75 mmoles) and triethyloxonium fluoroborate (0.37g, 1.94 mmoles). The mixture is capped and stirred for 24 hours. Extraction three times with 1N hydrochloric acid, three times with 1N sodium bicarbonate, and once with saturated sodium chloride gave an organic solution that was dried over sodium sulfate and evaporated to yield 0.12g (48%) of 123b;: IR (Nujol): 3090, 1702, 1235; PMR (DMSO): 1.4 (tr, 6H), 4.32 (q, 4H), 7.8 (s, 2H); MS: m/e = 256 (parent - ethyl).

Dimethyl thieno[3,2-b]thiophene-2,5-dicarboxylate (123c)

The diacid 123a is added as a solid to a cold solution of distilled diazomethane (from N,N'-dimethyl-N,N' dinitrosoterephthalimide[78] 2.5g). The mixture is stirred overnight at room temperature. Acetic acid is added dropwise to destroy excess diazomethane. Evaporation of the solvent and trituration of the solid with water followed by drying in vacuum gave 0.18g (80%) of 123c: mp 233°; IR (Nujol): 1720, 1230; PMR (chloroform): 3.82 (s, 6H), 7.97 (s, 2H); MS: m/e = 256 (parent).

2,5-Bis(hydroxymethyl)thieno[3,2-b]thiophene (121)

Thieno[3,2-b]thiophene-2,5-dicarboxaldehyde 120 (22.15g, 0.113 moles) is added as a solid to a suspension of lithium aluminum hydride (17.06g, 0.449 moles) in THF (400ml) at 0°. The mixture is stirred at room temperature overnight. To the recooled mixture is then added water (34ml), 15% sodium hydroxide (34ml), and water (34ml) in order. The inorganic solids are collected by filtration and washed several times with hot THF. The organic solution is evaporated to yield 17.45g (77%) of the crude 121 which can be used without further purification for subsequent steps. This diol can be purified from THF and darco, by filtration and precipitation with hexane: mp 145°; IR (Nujol): 3200, 1635, 1145, 1040, 1000, 820 ; PMR (DMSO): 4.6 (d, 4H), 5.4 (tr, 2H), 7.11 (s, 2H); MS: m/e = 200 (parent). O.

2,5-Bis(chloromethyl)thieno[3,2-b]thiophene (124a)

The diol 121 (17.45g, 87.25 mmoles) is combined in chloroform (250ml) with pyridine (13.1ml). To this stirred suspension is added thionyl chloride (18.9ml) in chloroform (50ml) under nitrogen. The hot mixture is refluxed for 0.5 hours, cooled, and quenched by pouring cautiously onto ice and is stirred for 0.5 hours. The organic layer is separated and washed with 10% hydrochloric acid (50ml), with 10% sodium carbonate (50ml), and with water (50ml). The organic solution is then warmed with calcium chloride and darco, and

filtered. The organic solution is evaporated to yield 17.9g (87%) of crude 124a. Further purification is possible by column chromatography with silica gel using ether as the eluent: mp 136-137°; IR (Nujol): 1465, 1250, 1150, 1120, 835; PMR (DMSO): 5.12 (s, 4H), 7.5 (s, 2H); MS: m/e = 236 (parent).

2,5-Bis(bromomethyl)thieno[3,2-b]thiophene (124b)

The diol 121 (1g, 5 mmoles) is dissolved in THF (25ml), and to this solution is added dropwise at 0° a solution of phosphorus tribromide (1ml) in THF (10ml). The mixture is stirred for 2 hours at 0°, 1 hour at room temperature, and then quenched by pouring on ice. The precipitated solid is filtered and vacuum dried. The organic solvent is evaporated and more solid is collected, yielding 0.6g (70%) of 124b: PMR (chloroform): 5.2 (s, 4H), 7.4 (s, 2H); MS: m/e = 345 (parent).

2,5-Bis(cyanomethyl)thieno[3,2-b]thiophene (125)

The bis-chloromethyl compound 124a (16.75g, 0.071 moles) is dissolved in dry methylene chloride (700ml) in a flask equipped with a drying tube. To this stirred solution at room temperature is added tetraethylammonium cyanide (22.35g, 0.143 moles) in dry methylene chloride (350ml), and this mixture is refluxed for 2 hours. The solvent is evapo-

rated, and the residue is chromatographed on silica gel with methylene chloride/ether 50:1, yielding 4g (26%) of 125: mp 155-158°; IR (Nujol): 2250, 1215, 825; PMR (DMSO): 4.35 (s, 4H), 7.3 (s, 2H); MS: m/e = 218 (parent).

Reaction of potassium cyanide in methanol with 124a

The bis-chloromethyl compound 124a (0.59g, 2.5 mmoles) is dissolved in methanol (25ml) and to this solution is added, all at once with stirring, a solution of potassium cyanide (0.335g, 5.1 mmoles) in methanol (50ml). The mixture is refluxed overnight, cooled, and the solvent is evaporated. The residue is triturated with water, and the aqueous mixture is extracted three times with ether. The organic solution is dried over sodium carbonate, heated with darco, filtered and evaporated to yield 0.3g (53%) of 2,5-bis(methoxymethyl) thieno[3,2-b]thiophene, 126: mp 60-70°; PMR (chloroform): 3.32 (s, 4H), 4.57 (s, 4H), 7.0 (s, 2H); MS: m/e = 228 (parent).

2,5-Bis(carboethoxycyanomethyl)-thieno[3,2-b]thiophene (131)

The bis-cyanomethyl compound 125 (0.5g, 2.3 mmoles) is dissolved in THF (15ml) along with dimethyl carbonate (0.413g, 4.6 mmoles), and this solution is added dropwise under nitrogen to a room temperature suspension of sodium hydride (0.22g, 50% in mineral oil, 4.58 mmoles) in THF

(10ml). After 10 hours the solvent is evaporated, and the residue is acidified with acetic acid and is extracted 4 times with chloroform. The organic solution is washed with water and warmed over sodium sulfate and darco. Once filtered and evaporated, this solution yields 0.55g (72%): IR (Nujol): 2250, 2210, 1750, 1280, 1025, 840; PMR (DMSO): 3.7 (s, 6H), 6.0 (br s, 2H), 7.4 (s, 2H); MS: m/e = 334 (parent).

2,5-Bis-(5-methylbenz-1,3-dithiolyl) thieno[3,2-b]thiophene (136)

Dial 120 (0.628g, 3.2 mmoles) and 4-methyl-1,2-benzenedithiol 135 (1g, 6.41 mmoles) are both added at once to ethanol (25ml) which had been saturated with hydrogen chloride. The vessel is capped, and the heterogenous mixture is stirred for 20 hours at room temperature. The solids are collected by filtration and washed with ethanol followed by ether. There results 1.1g (73%) of 136: mp 156-159°; IR (Nujol): 1125, 800; PMR (chloroform): 2.23 (s, 6H), 6.15 (s, 2H), 6.9 (m, 8H); MS: m/e = 472 (parent).

2,5-Bis-(benz-1,3-dithiolyl) thieno[3,2-b]thiophene (139)

The same procedure was followed as described above for 136. Dial (0.345g, 1.76 mmoles) and 1,2-benzenedithiol 137

(0.5g, 3.52 mmoles) were combined in ethanol-hydrogen chloride (25ml) yielding 0.7g (62%) of 139: mp 225-230°; PMR (DMSO): 6.62 (s, 2H), 7.2 (m, 10H); MS: m/e = 444 (parent).

Tetra-t-butylthiopyridazino[4,5-d]pyridazine (152)

To a solution of potassium hydroxide (0.25g, 4.39 mmoles) in ethanol (10ml) is pipetted t-butylmercaptan (0.39g, 4.33 mmoles). The mixture is stirred under nitrogen and transferred into a dropping funnel. This basic solution is then added dropwise to a stirred suspension of tetrachloro pyridazino[4,5-d]pyridazine, 144 (0.29g, 1.08 mmoles) in ethanol (20ml). After the addition, the dark mixture is refluxed for 2 hours, cooled, and the solvent is evaporated. The residue is combined with water and chloroform, and the aqueous layer is extracted twice more with chloroform. Combining the organic layers, drying with sodium sulfate, and evaporation of the solvent yields the crude products. Column chromatography on neutral alumina absorption with chloroform yields 1.1g (30%) of 152: mp 199-201°; IR (Nujol): 1420, 1368, 1275, 1162, 648; PMR (chloroform): 1.6 (s); MS: m/e = 484 (parent).

Washing the column with ethyl acetate-methanol yields a sideproduct, the mono hydroxy tri-t-butylthio derivative, 16%: MS: 412 (parent).

Tetrabenzylthiopyridazino[4,5-d]pyridazine (154)

To a solution of potassium hydroxide (0.5g, 8.77 mmoles) in ethanol (25ml) is pipetted benzylmercaptan (0.925g, 7.46 mmoles). The solution is stirred for 15 minutes under nitrogen (at RT) and 144 (0.5g, 1.86 mmoles) is added all at once. The mixture is refluxed for 3 hours, then cooled, and the solvent is evaporated. The residue is washed and filtered from water, and after column chromatography on neutral alumina absorption with chloroform as eluent, 0.54g (47%) of 154 was yielded: mp 222-226°; IR (Nujol): 1600, 1490, 1280; PMR (chloroform): 3.5 (s, 2H), 7.03 (s, 5H); MS: m/e = 529 (parent - benzyl).

9-Dicyanomethylene-4,5-diaminofluorene (159)

Fluorenone 158 (0.5g, 2.38 mmoles) is combined with malononitrile (0.19g, 2.88 mmoles) and piperidine (1ml) in benzene (50ml). This mixture is refluxed for 3 hours, then cooled, and the solids are collected by filtration. After washing with ether there results 0.3g (49%) of 159: mp>300°; IR (Nujol): 3410, 2255, 1620, 1540, 730; PMR (DMSO): 5.8 (br s, 4H), 6.94 (m, 4H), 7.55 (m, 2H); UV (chloroform): λ (max) 590, 420, 300, 248; MS: m/e = 258 (parent).

2-Dicyanomethylene-1,3-diazepino [4,5,6,7-d,e,f] 9-dicyano-

methylfluorene (160)

Compound 161 (0.05g, 0.176 mmoles) is combined with malononitrile (0.1g, 1.52 mmoles) in dimethylformamide (5ml). After adding 3 drops of piperidine, the mixture is heated on a steam bath for one hour. After cooling, water is added precipitating a brown solid which is collected by filtration. After washing with water and ether, this solid is vacuum dried to give 0.06g (95%) of 160: mp >300°; IR (Nujol): 3420, 2210, 2180, 1660, 1600, 720; MS: m/e = 332 (parent).

2-Dicyanomethylene-1,3-diazepino[4,5,6,7-d,e,f] fluorenone (161)

4,5-Diaminofluorenone (0.4g, 1.9 mmoles) is refluxed in eythanol (150ml) with triethylamine (0.12ml) and 1,1-bis methylmercapto-2,2-dicyanoethylene (0.32g, 1.88 mmoles). After 4 hours of reflux, the mixture is cooled slightly, and the precipitated solid is collected by filtration. This solid is washed with warm ethanol (50ml), ether (50ml), and vacuum dried to yield 0.25g (46%) of 161: mp >300°; IR (Nujol): 3240, 3100, 2190, 1725, 1660, 1625; MS: m/e = 284 (parent).

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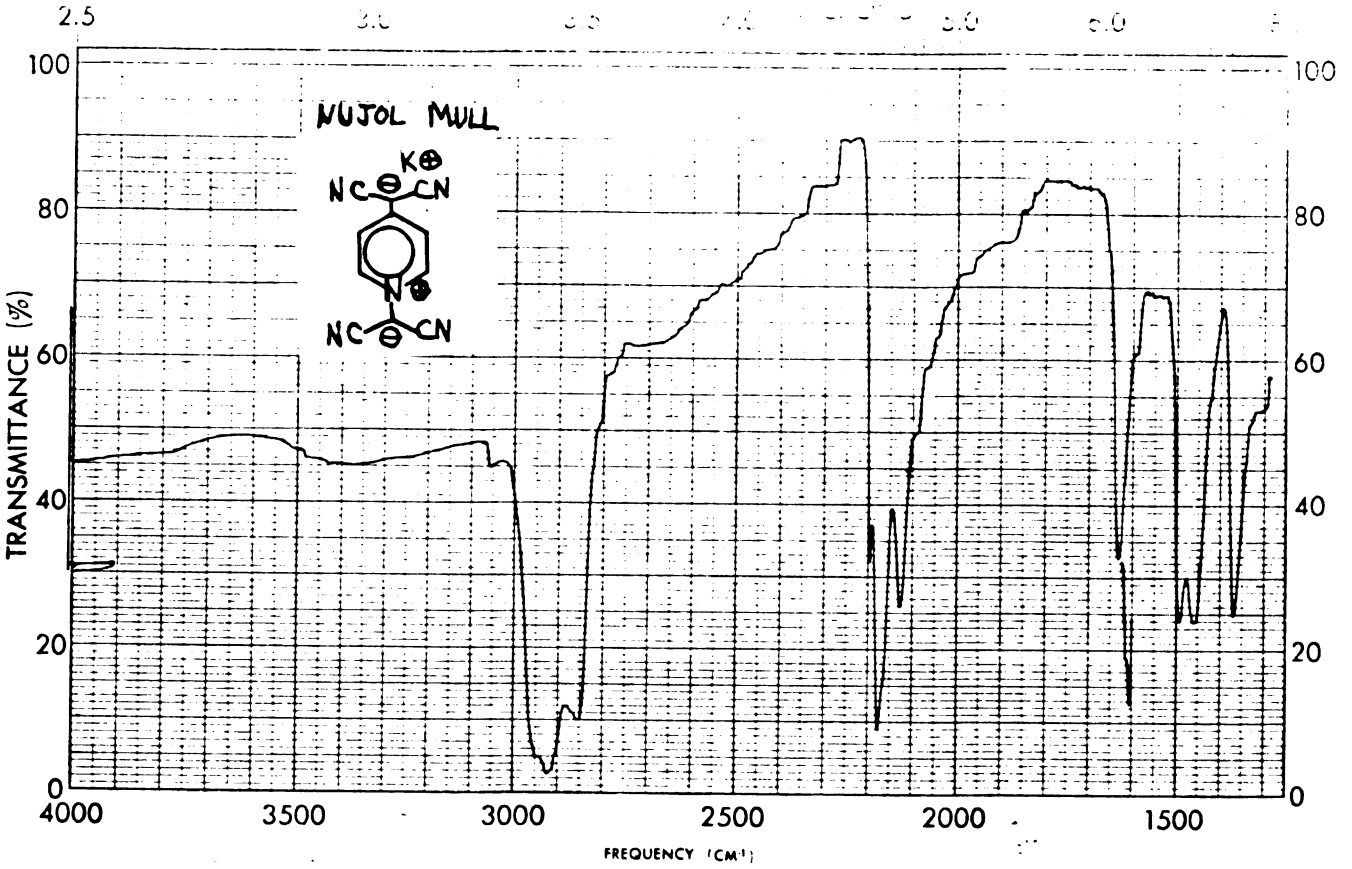
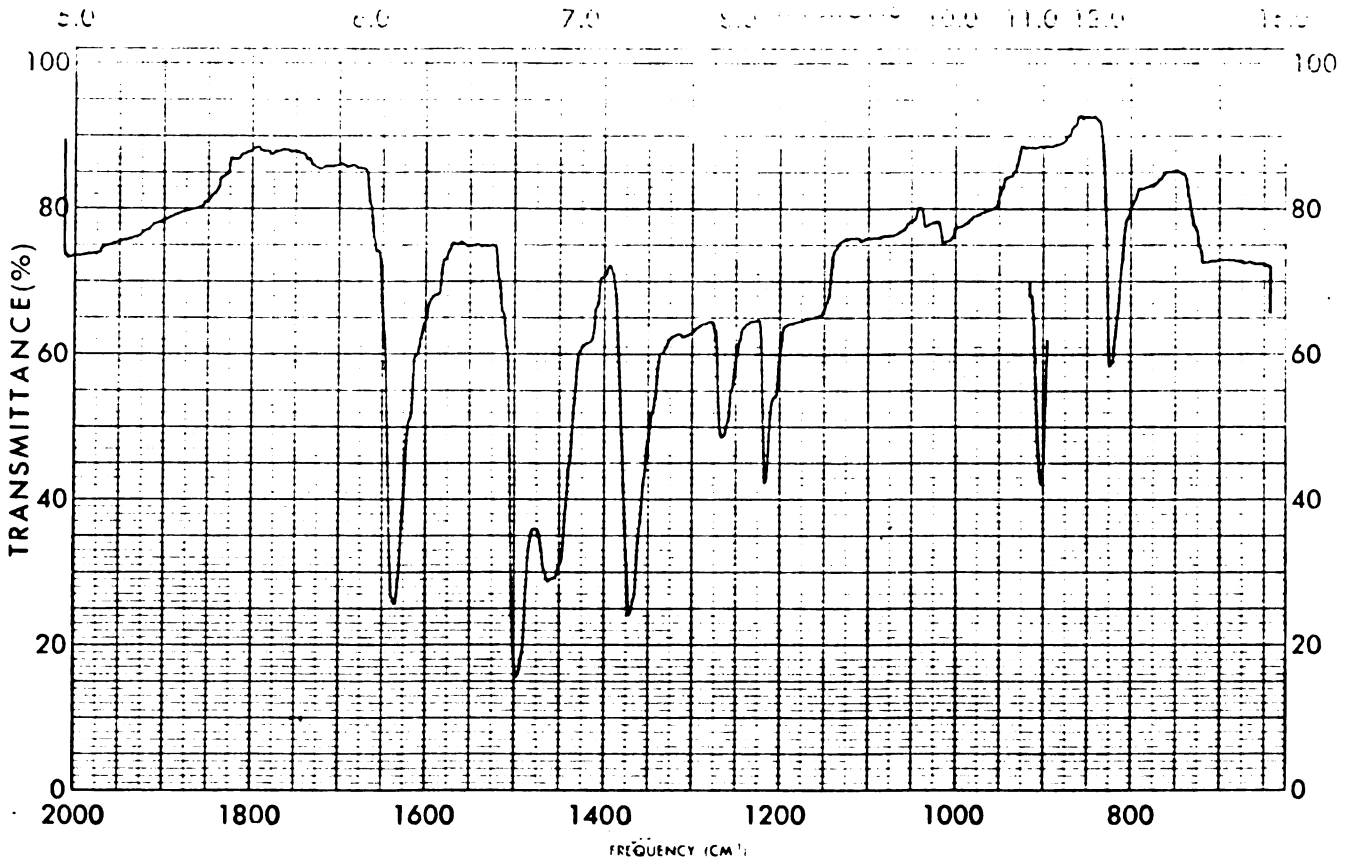
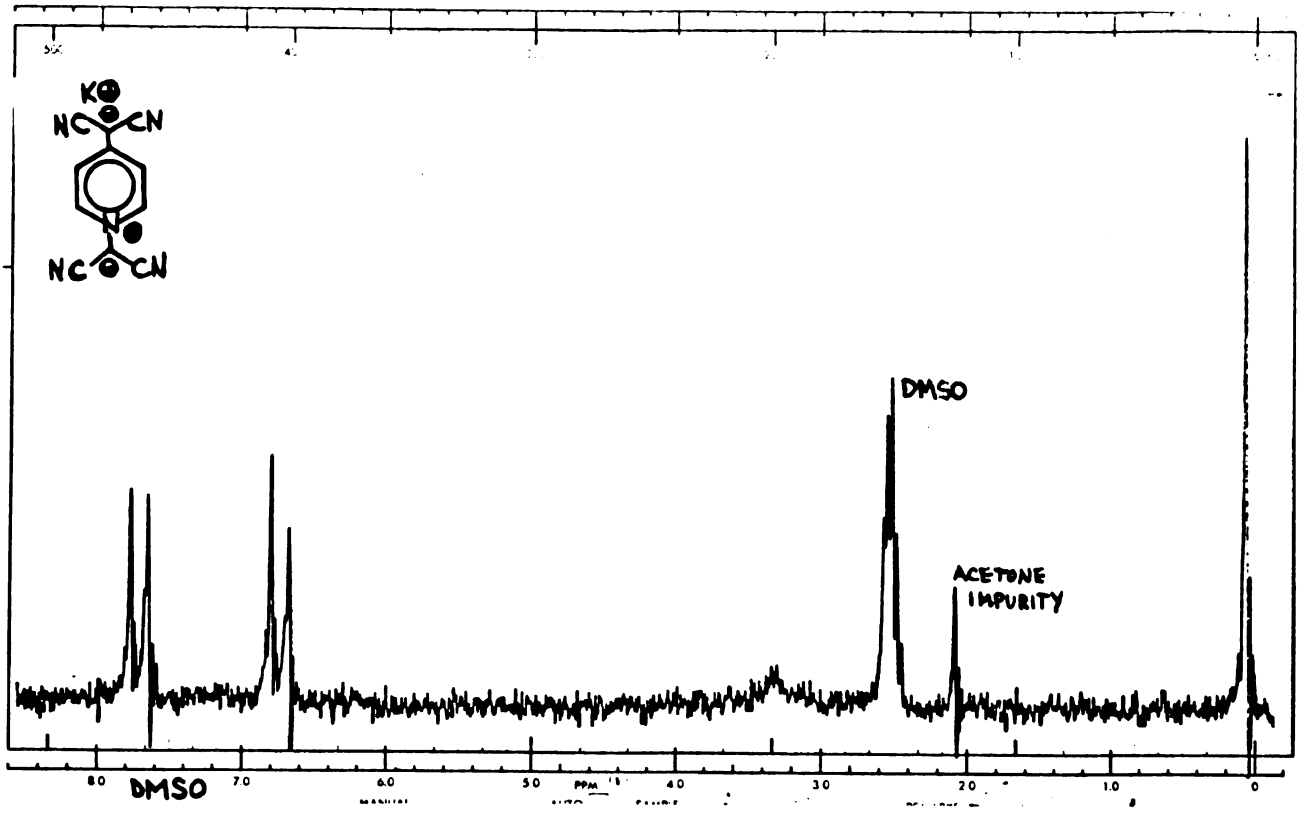
APPENDIX

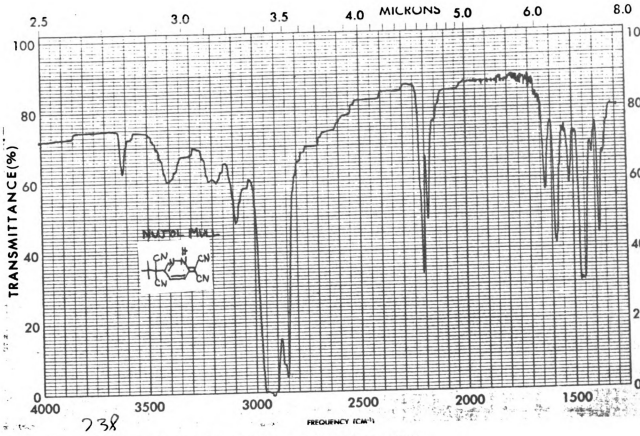


1. Infrared spectra of potassium salt (17)





2. PMR spectra of potassium salt (17)



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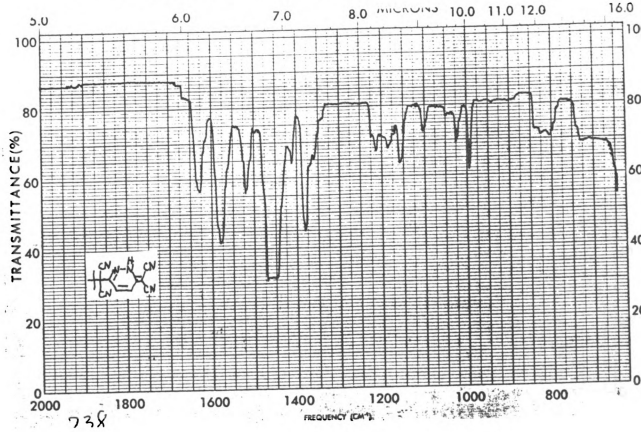
3. **Infrared spectra of pyridazine (31)**



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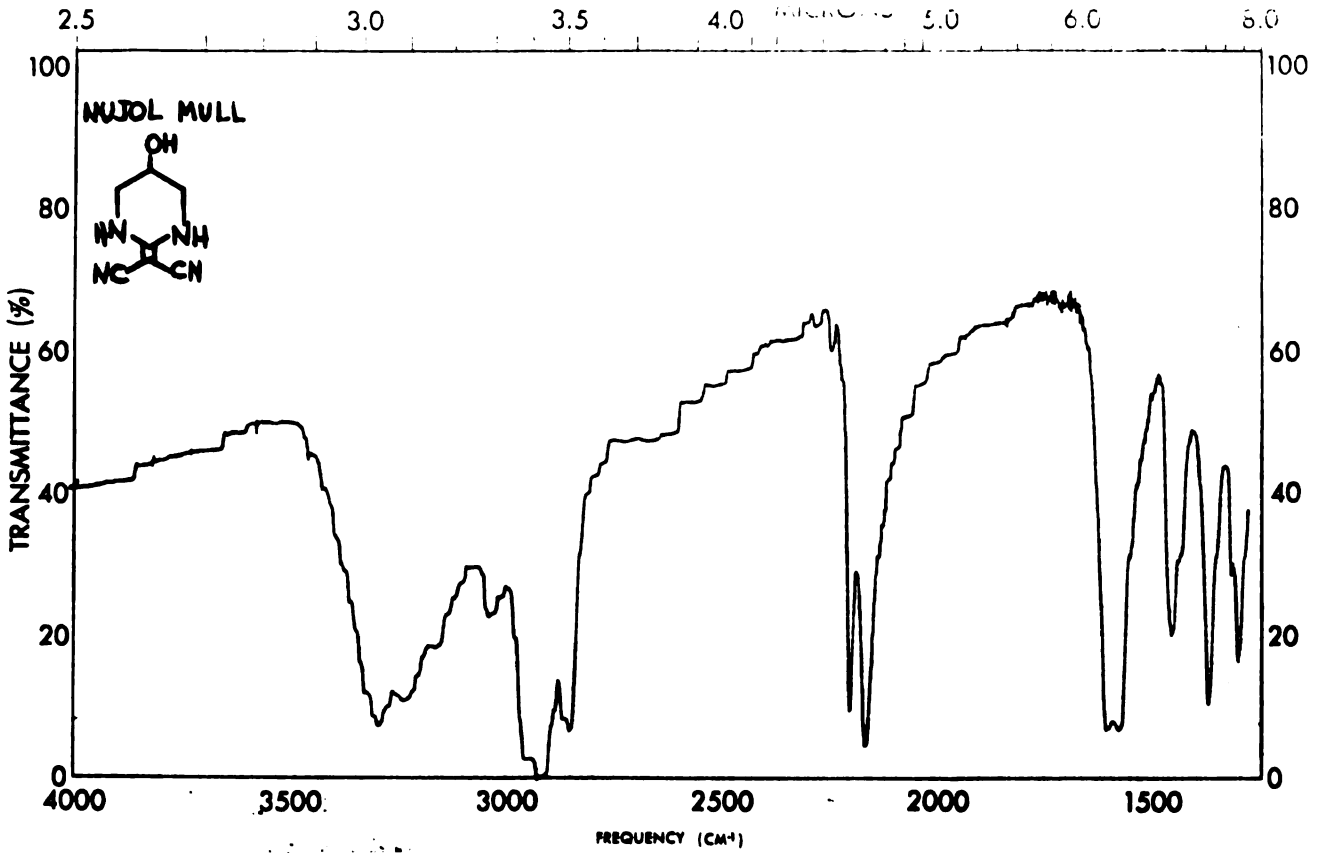
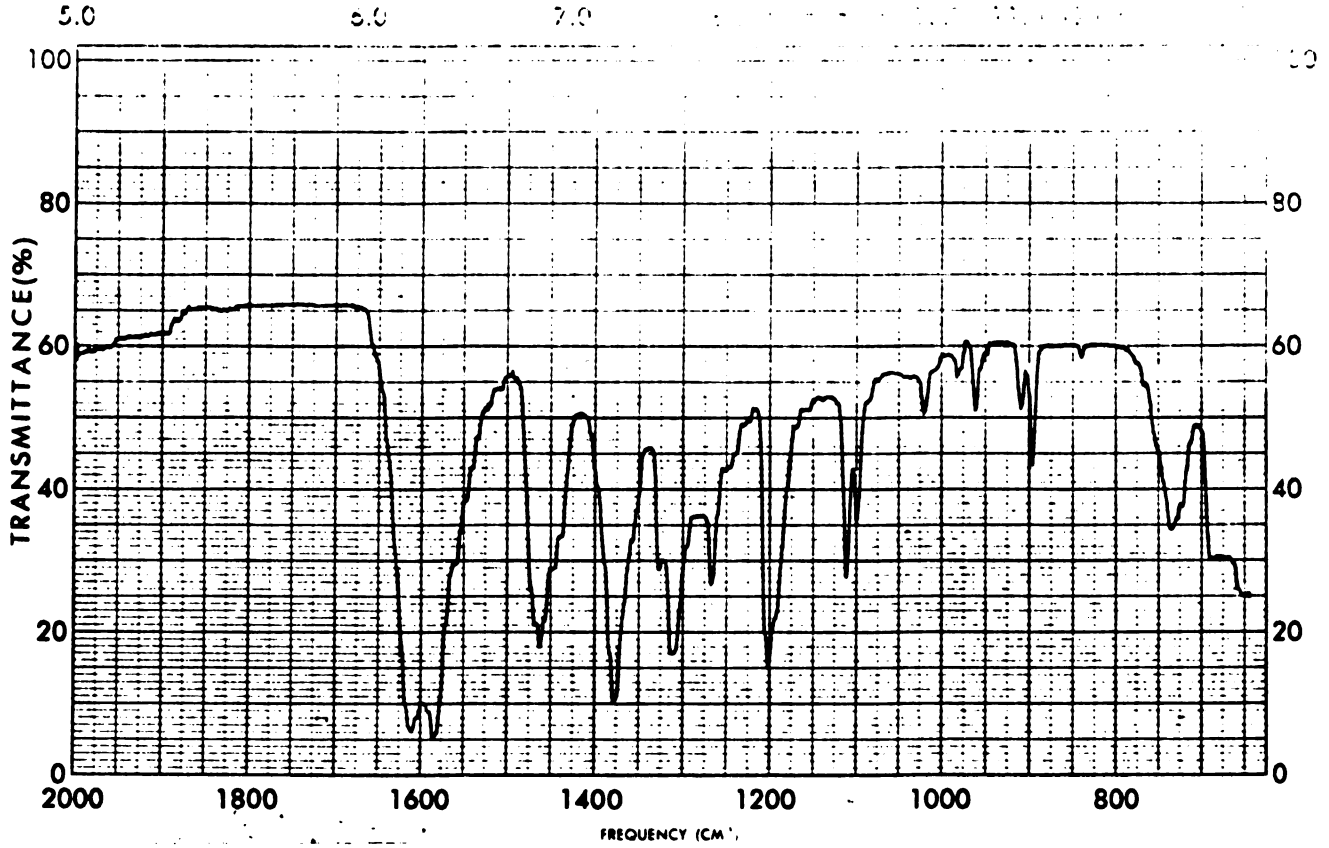
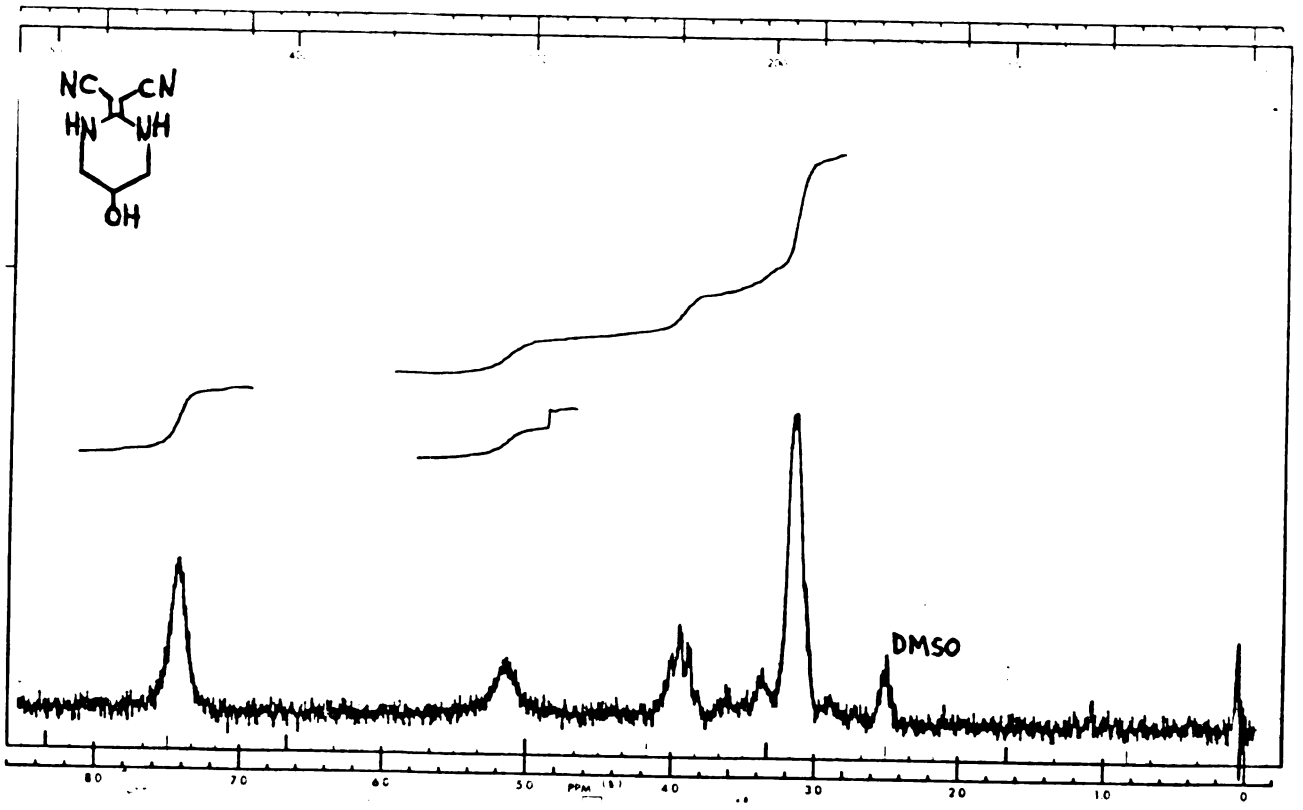
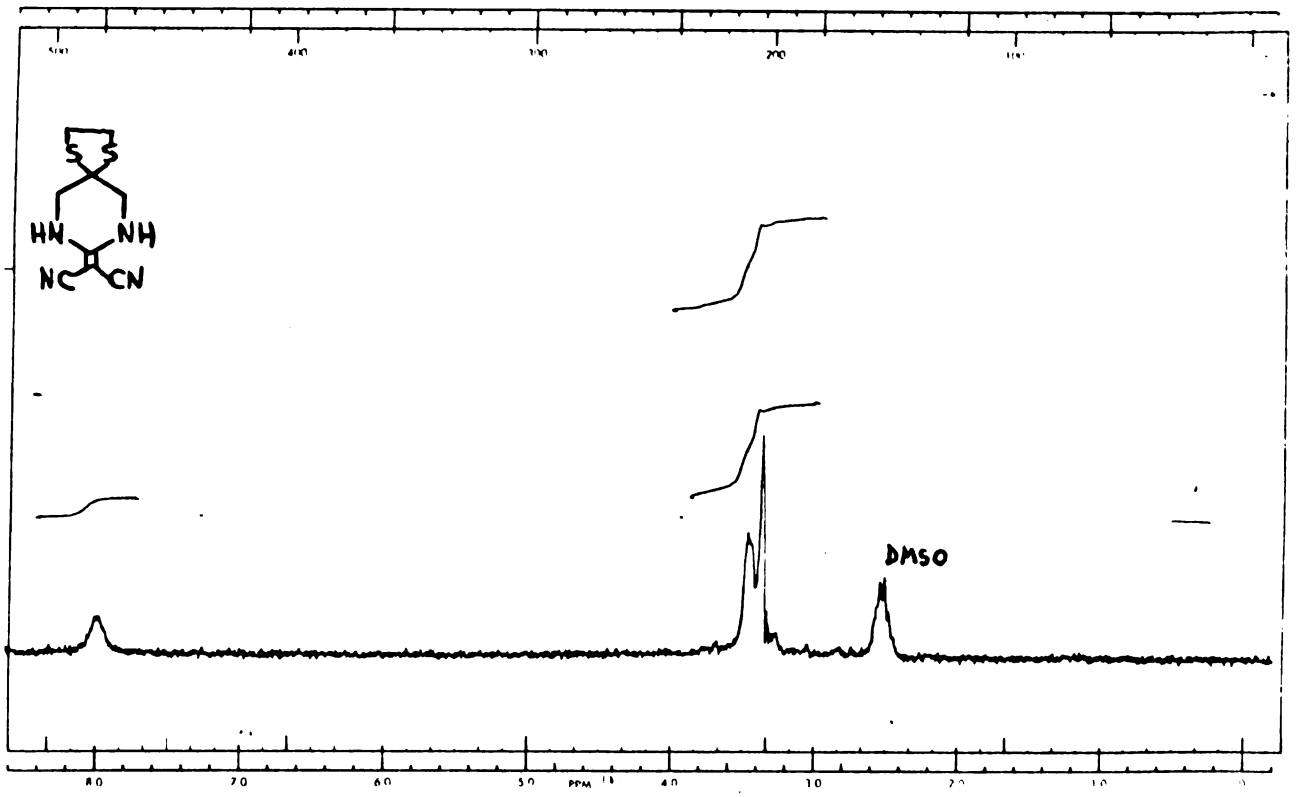


4. Infrared spectra of hydroxy-piperimidine (60)

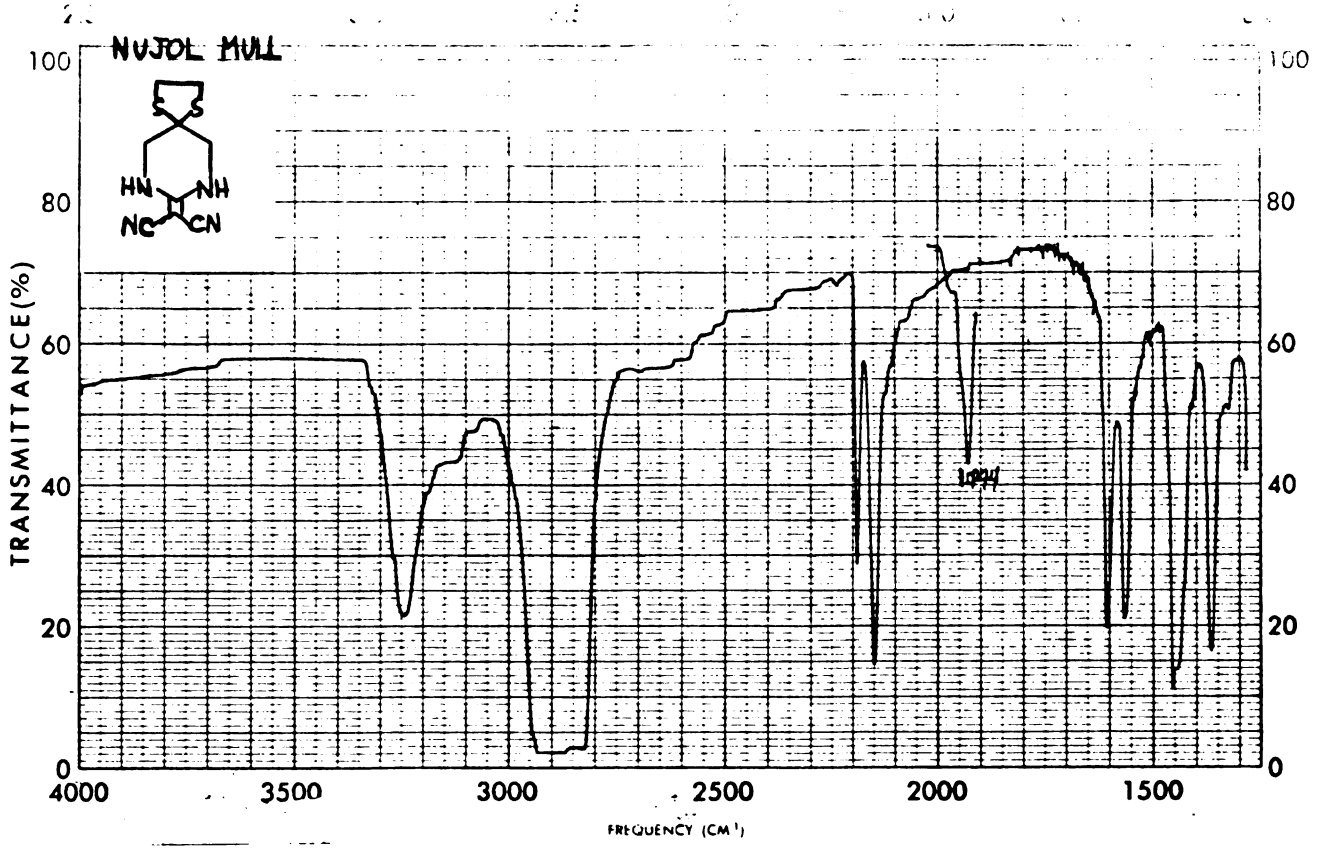




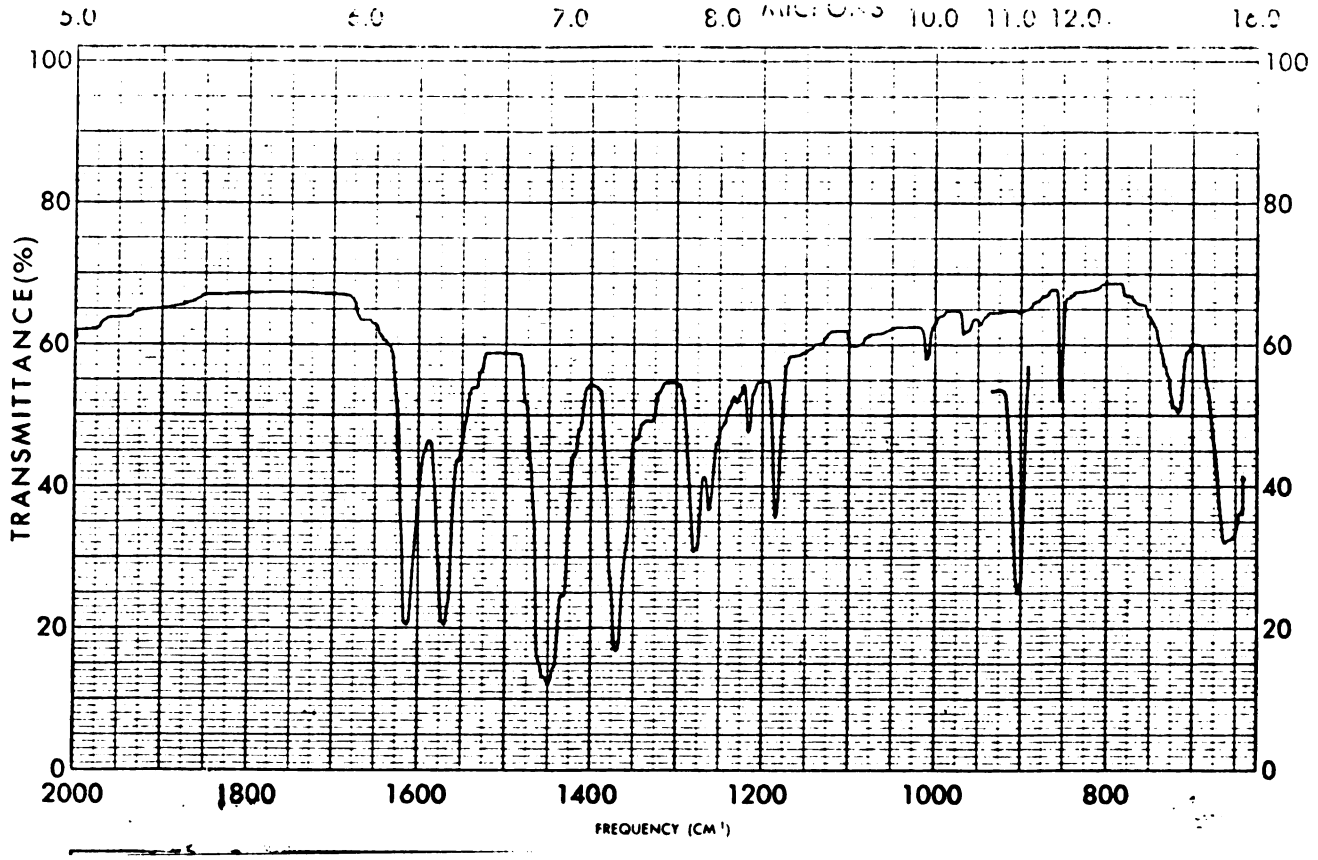
5. PMR spectra of hydroxy-piperimidine (60)

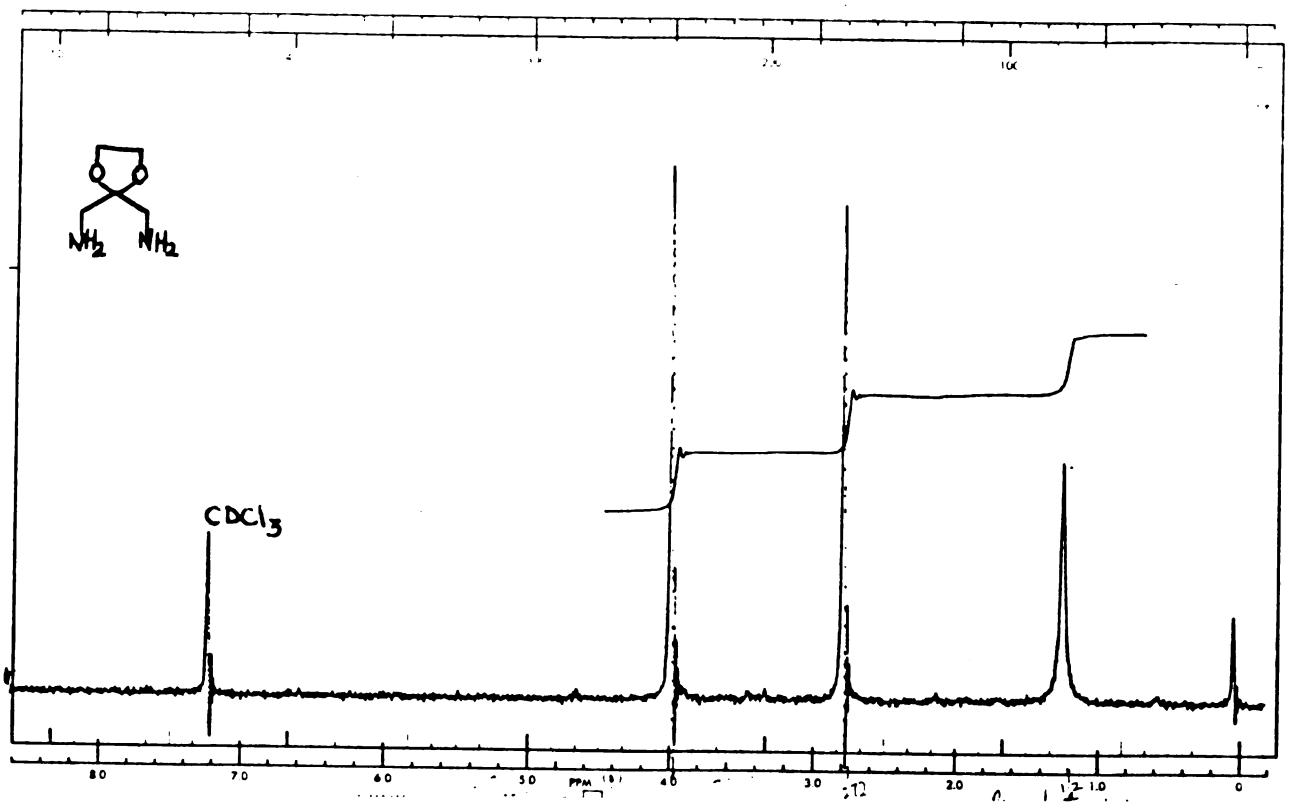


6. PMR spectra of dithiolane (67)

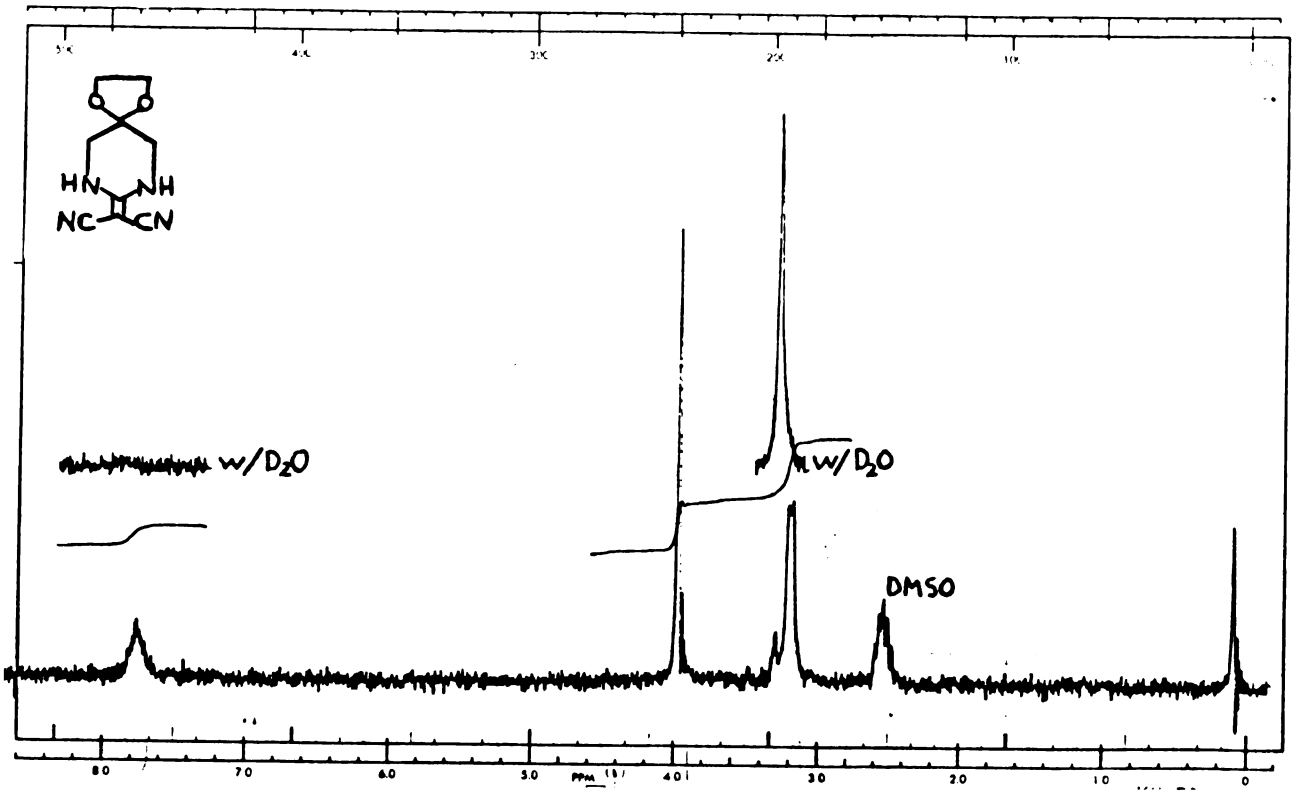


7. **Infrared spectra of dithiolane (67)**

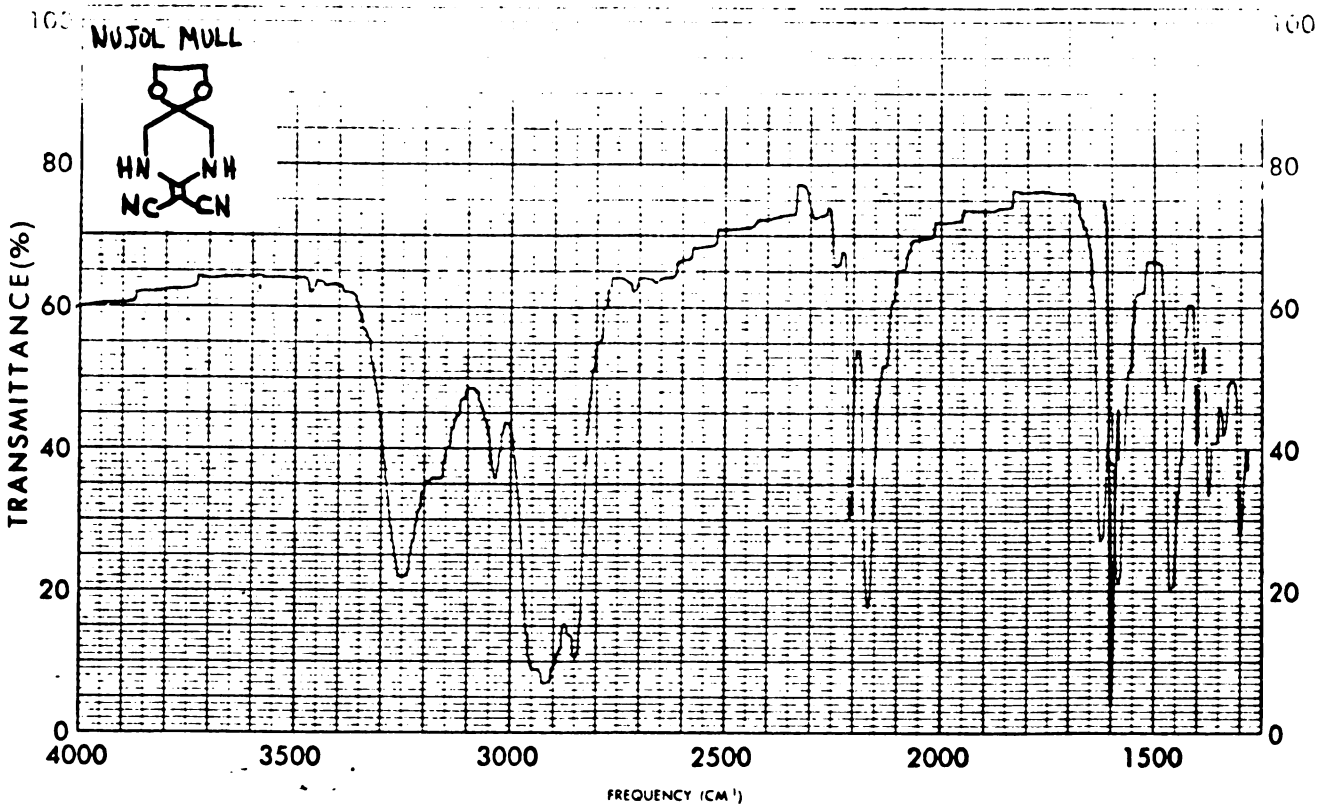




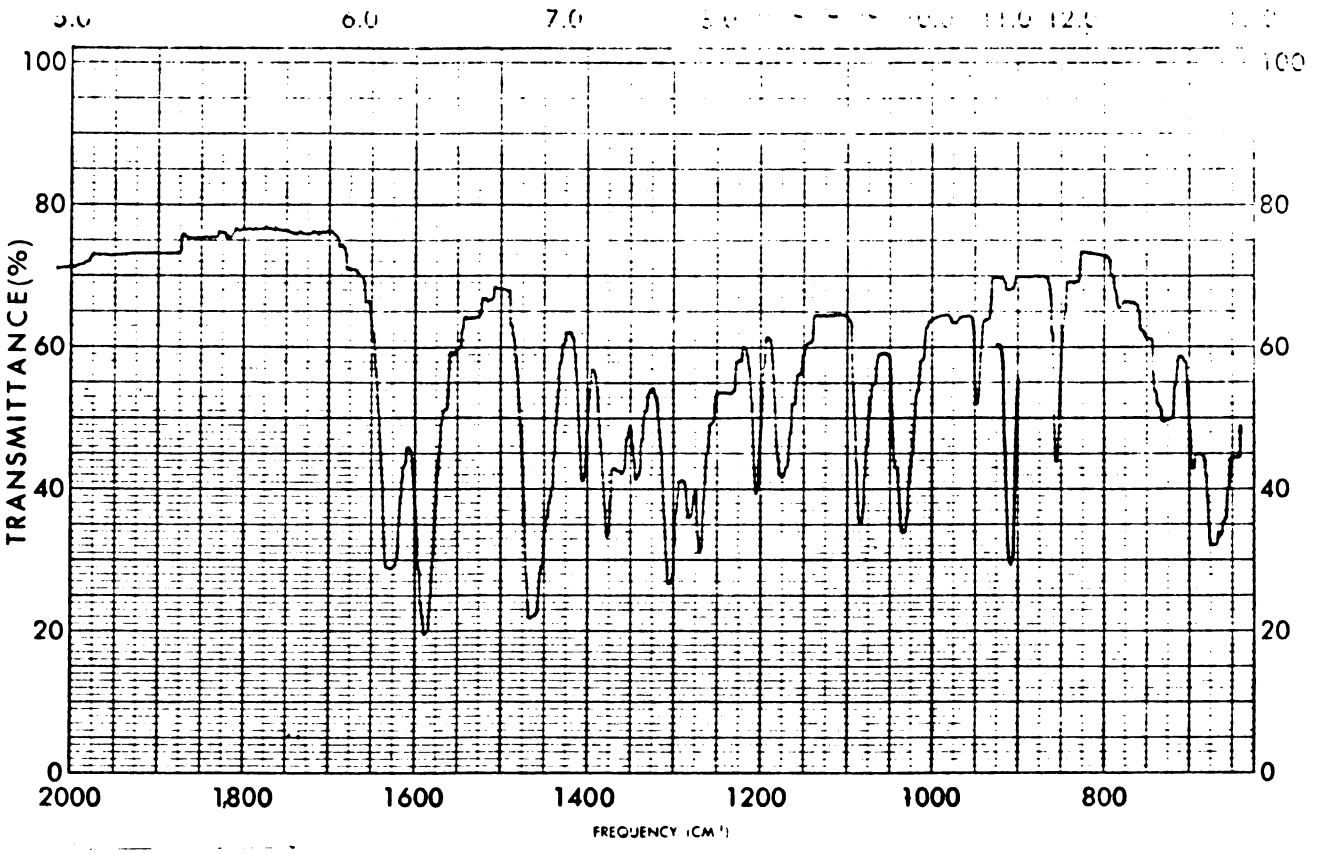
8. PMR spectra of diamine (74b)

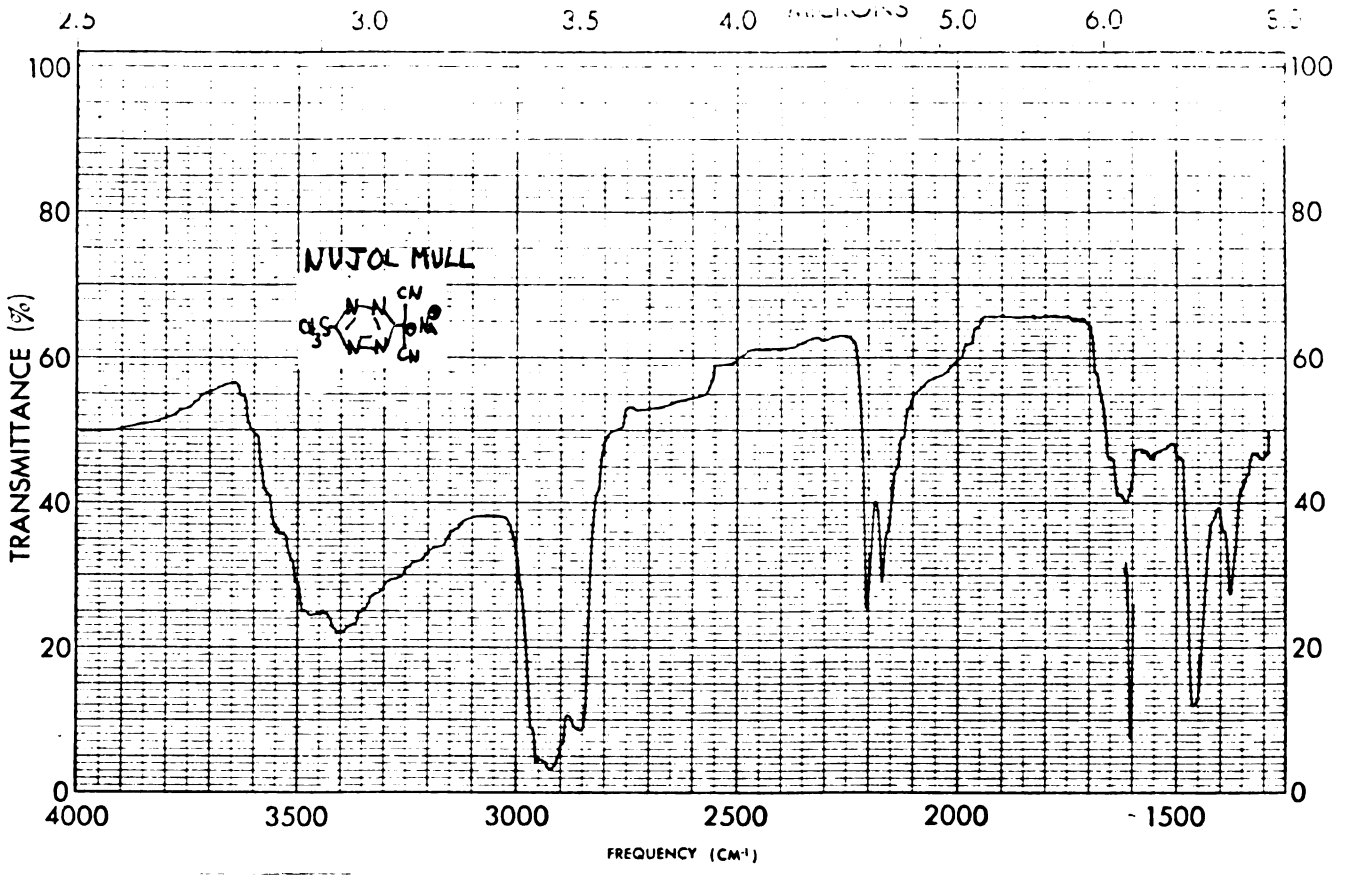


9. PMR spectra of dioxolane (81)

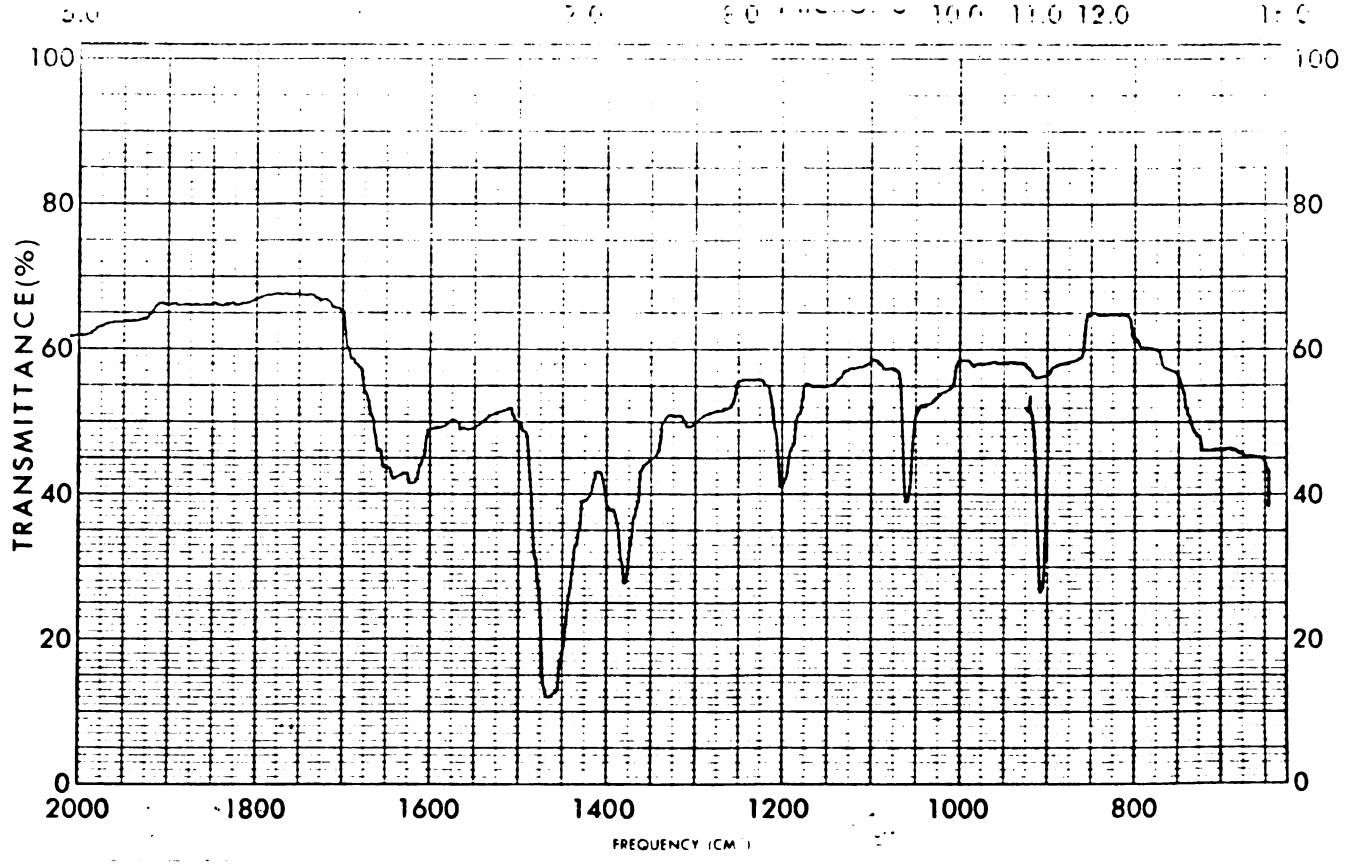


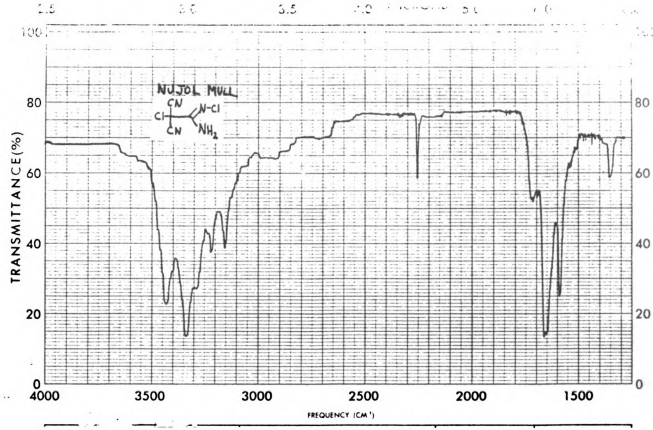
10. **Infrared spectra of dioxolane (81)**



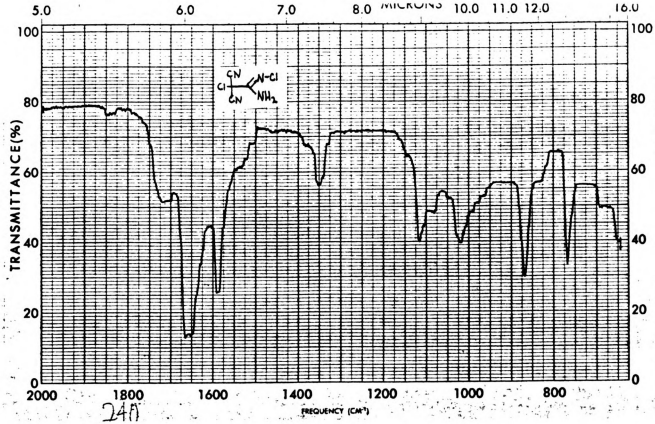


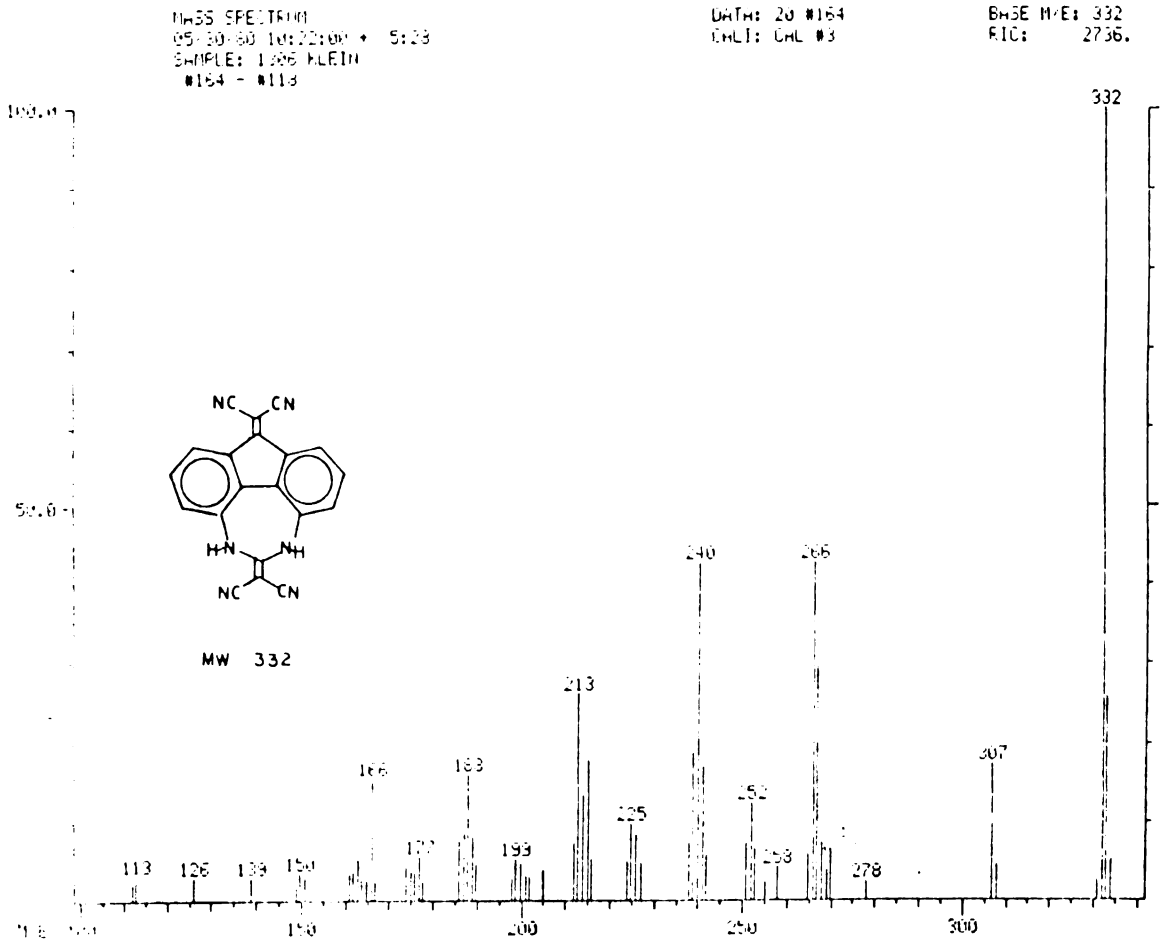
11. Infrared spectra of tetrazine sodium salt (102)





12. Infrared spectra of chlorination product of 106





13. Mass spectra of tetracyano compound (160)