CONDENSATION OF PHTHALONITRILE
WITH ACTIVE METHYLENE COMPOUNDS
DIRECTED TOWARDS MACROCYCLES
AND POLYMERS

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The work described in this thesis is concerned with condensation reactions between phthalonitrile and biscyanomethylene substituted compounds with a view to synthesising methine linked macrocycles analogous to the series of well known aza-linked macrocycles which have been well characterized and extensively investigated. Another objective was to prepare condensation products which might serve as monomers for possible polymeric materials.

Model condensation reactions were carried out, using phthalonitrile and benzyl cyanide as reactants, in order to establish the necessary conditions for condensation to take place. Two and 'three-unit' condensation products were obtained and their structure was investigated.

Using the established reaction conditions, phthalonitrile was reacted with p-dicyanoxylylene, m-dicyanoxylylene, 2,6-biscyanomethylpyridine and 4,4-di(cyanomethyl)phenyl ether. In each case only the 'two-unit' and 'three-unit' condensation products were obtained. No evidence of macrocycle formation was found even when very stringent reaction conditions were employed.

Attempts to synthesise macrocycles by 'ring-closure' of the 'three-unit' bis-isoindoline compounds, by reacting them with the appropriate dicyanomethylene compound or aromatic diamines were also unsuccessful. However, m-di[cyano-(3-imino-1-isoindoleninyl) methyl] benzene reacted with 1,3-
diiminoisoindoline to give the di-methine linked macrocycle.

Among the model compounds prepared were the 'two-unit' and 'three-unit' condensation products from the reaction of phthalonitrile with 3-cyanomethyl-5-phenyl-1-2,4-triazole and 2-cyanomethylthiophene. These products had the expected characteristics.

Attempted synthesis of 3,5-biscyanomethyl-1-2,4-triazole gave an anomalous product which spectroscopic analysis proved to be 2-cyanomethyl-4,6-diaminopyrimidine. This compound failed to condense with phthalonitrile.

The reaction of 2,5-biscyanomethyl-thiophene with phthalonitrile in 2-ethoxyethanol containing sodium as catalyst gave a mixture of polycondensation products.
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CHAPTER 1
Historical Introduction

The discovery of phthalocyanine in 1928 and the elucidation of its structure by Linseström and his colleagues \(^1-9\) in the early 1930's stimulated interest in macrocyclic compounds because of their valuable tinctorial properties and their high thermal stability.

The phthalocyanine class of compounds consists of metal derivatives of phthalocyanine (I). The two hydrogen atoms in the centre of the molecule have been replaced by metals from every group in the Periodic Table. In addition, from 1 to 16 of the peripheral hydrogen atoms in the 4 benzene rings in the phthalocyanine molecule have been replaced by halogen atoms and by numerous organic groups. It has been found that the stability of these substituted phthalocyanines were generally lower than that of phthalocyanine itself. \(^10,11\)

The most common methods used in the synthesis of the metal phthalocyanines were (i) the reaction of phthalonitrile with a metal or metal salt \(^9,12\); (ii) the reaction of phthalic anhydride, phthalic acid or phthalamide, with urea, metal salts and a catalyst \(^13,14\); (iii) the reaction of o-cyanobenzamide with a metal. \(^9,12,15,16,17\)

The metal-free phthalocyanine was prepared, originally, by the removal of the metal from a labile metal phthalocyanine.\(^2\) However, with the isolation of 1,3-di-iminoisoindoline (II), \(^18,19\) a convenient route to the metal-free phthalocyanine was achieved. When this compound is heated in hydrogen donating
solvents it undergoes self-condensation giving phthalocyanine in high yield.\textsuperscript{20,21}

The discovery of 1,3-di-iminoisoindoline and the realization that it is a precursor of phthalocyanine formation led to the investigation of its potential as the starting material for other types of macrocycles.

The oxo-derivative of (II), 1-imino-3-oxoisooindoline (III) had been reported as early as 1907 by Braun and Tcherniac,\textsuperscript{22} who prepared it by the thermal isomerization of o-cyanobenzamide at 200°. Further investigation of this compound proved that the exocyclic imino-group was reactive and that condensation with primary amines took place readily.\textsuperscript{23} Similarly, 1,3-diiminoisoindoline reacted easily at both imino groups with primary amines such as 2-aminopyridine to give 1:3-di-2'-pyridyliminoisoindoline (IV) which was capable of forming complexes with metals.\textsuperscript{19}

The investigation of these condensation reactions was extended to aromatic diamines. In 1952, Elvidge and Linstead\textsuperscript{24} reported the first of a new series of novel macrocycles formed by the condensation of 1,3-di-iminoisoindoline and 2,6-diaminopyridine (V).

The new macrocycle was similar to phthalocyanine in many respects. Both compounds were thermally stable and capable of forming complexes with metals. Both compounds had a central 16-numbered ring of the same size and shape, but in the new compound (V) the pyridine nitrogen atoms performed
a co-ordinating function similar to those of the second pair of isoindoline nitrogen atoms in phthalocyanine.

The macrocycle (V) differed from phthalocyanine in one major respect. It was cross-conjugated, containing only the partial chromophores of related linear compounds, unlike phthalocyanine which is fully conjugated. However, when the macrocycle (V) was complexed with a metal, a marked bathochromic shift was observed in the light-absorption spectrum. This shift, which is not observed in the phthalocyanine complexes, is probably due to the fact that the metal derivatives of (V) have a fully conjugated cyclic system as in (VI), whereas the parent macrocycle has the cross-conjugated system as in (V). X-ray analysis of metal complexes of (V) tended to confirm this view.  

Further investigation of the reaction of 1,3-diiminoisoidoline with primary aromatic diamines led to the synthesis of a series of macrocycles of the general type (VII) where R was m-phenylenediamine, 3,5-diaminopyridine, 2,7-diaminonaphthalene, 2,8-diaminoacridine and 2,4-diaminotoluene. More recently, macrocycles of this type, have been synthesized by condensing 1,3-diiminoisoidoline with 2,7-diamino-diphenylenesulphone, 2,7-diaminofluorene and with guanazole. 

In the preparation of these macrocycles, it was found, by altering the reaction conditions and the relative concentration of the reactants that a number of intermediates and adducts could be isolated. The isolation of these intermediates indicated that macrocycle formation
took place in a step-wise manner. Thus the intermediate compound (VIII) was found to condense readily with m-phenylene diamine to give the expected macrocycle. The isolation of these intermediate compounds also provided a route to the synthesis of new 'mixed' macrocycles. When compound (VIII) was treated with the appropriate quantity of 1,3-diminoisoindoline condensation took place to give the new 'benzene-tri-isoiindole' macrocycle (IX). $^{27}$ This new macrocycle, although it has three-quarters of the phthalocyanine chromophore, is not fully conjugated. Like the pyridine macrocycle (V) its metal complexes produce a bathochromic shift indicating a completion of the conjugated system. $^{32}$

Other 'mixed' macrocycles have been prepared by this step-wise synthesis including a fully conjugated macrocycle, obtained from the reaction of succinimidine and 1,3-diminoisoindoline, in which the benzene ring of (IX) is replaced by a pyrrole ring. $^{33}$

Despite the high thermal stability recorded for phthalocyanine and related macrocyclic pigments, the published literature has concentrated on the use of these compounds as pigments rather than as stable polymer materials. The phthalocyanine polymers that have been reported can be divided into three groups: (i) phthalocyanines in which the phenylene rings are connected in the manner of a diphenyl bond; $^{35}$ (ii) phthalocyanines in which the monomers are joined together by substituents attached to the phenylene rings; $^{36,37,38}$ and (iii) phthalocyanines which share
phenylene rings in common. 37,38,39

Some of these polymers have enhanced semi-conducting properties compared to the monomeric materials. They have been used as a high temperature dielectric film coating on copper surfaces, 35 as a metal lubricant for use over a wide temperature range 40 and as an efficient curing agent for polyepoxide resins. 41

More recently a novel class of thermally stable macrocyclic polymers have been reported 42,43 which can be considered as a special case of the ladder polymers previously described by Marvel. 44 When 1,2,4,5-tetracyanobenzene was reacted with aromatic diamines, polymeric macrocyclic compounds (X) and related open-chain polymers (XI) were obtained. In the case of m-phenylenediamine a dark red polymeric powder was produced. Thermal gravimetric analysis in air (4°/min.) showed a 10% loss in weight of the polymer at 540°. In argon the polymer was stable to 600°. It was capable of being moulded under pressure at temperatures in the range 350° - 400° to give specimens with tensile strengths up to 13,000 psi.

Other aromatic diamines that have been successfully used in the synthesis of this type of polymer include p-phenylene-diamine, 4,4'-diaminodiphenyl ether, 4,4'-diaminodiphenyl-methane and hexamethylenediamine.

Hitherto, the efforts to synthesize macrocycles have concentrated on the condensation of 1,3-diiminoisoindoline
or phthalonitrile with aromatic diamines. A methine linked macrocycle of the type (XII) would be of interest since it would resemble both the aza-linked macrocycle (V) and porphin (XIII). In addition, it could serve as a monomer for related polymeric compounds which might feasibly be formed by substituting phthalonitrile with 1,2,4,5-tetra-cyanobenzene.

The literature does contain some reports of the condensation of 1-imino-3-oxo-isoiindoline and 1,3-diiminoisoiindoline with active methylene compounds. Fitt has condensed the former compound with 2-picoline to give 1-(2'-pyridyl-methylene)-3-oxoisoiindoline (XIV) but the condensation only took place under extremely vigorous reaction conditions. However, with compounds containing a rather more active methylene group condensation occurred readily. Thus with acetoacetic acid and malonic esters, condensation products (XV) were obtained \( R = \text{CH}_3\text{CO} \) and \( \text{CO}_2\text{C}_2\text{H}_5 \). Ethyl cyanoacetate has been reacted with 1,3-diiminoisoiindoline to give the condensation product (XVI), and with succinimidine to give product (XVII). Succinonitrile has also been shown to react with ethyl cyanoacetate to give the same condensation product (XVII). Similar condensation reactions have been carried out using phthalonitrile instead of succinonitrile.

The ease with which 1,3-diiminoisoiindoline or phthalonitrile condensed with compounds containing an active methylene group suggested that this would be a suitable route to the synthesis of a methine-linked macrocycle or to condensed
linear products.

The basis of the work carried out in this thesis was the study of the condensation reactions of phthalonitrile with active methylene compounds with a view to preparing and investigating these condensation products which could have particular interest in the polymer field.
CHAPTER 2
Model reactions of phthalonitrile with benzyl cyanide to give 'two-unit' and 'three-unit' condensation products.

The condensation of benzyl cyanide with phthalonitrile to give 1-phenylcyanomethylene-3-iminoisoindoline (XVIII) has been reported. The ease with which this condensation takes place indicates that this type of reaction might be utilized in macrocycle formation and in polymer synthesis. Before embarking on the attempted condensation of phthalonitrile with di-cyanomethyl substituted compounds it was decided to study this condensation reaction in detail and to examine the fine structure of the reaction products.

In a preliminary experiment equivalent quantities of phthalonitrile (purified by distillation into methanol) and benzyl cyanide were dissolved in a small quantity of ethanol containing an equivalent amount of sodium and stirred at room temperature. On the addition of the reactants, the reaction mixture immediately turned dark red. After fifteen minutes stirring a reddish yellow solid began to separate from the solution. Filtration yielded a yellow-orange powder which was found to decompose above 350°. Upon recrystallisation from nitrobenzene yellow crystals were obtained which melted at 285°. The reaction only takes place in the presence of a base catalyst. Therefore the following mechanism has been ascribed to it (See Fig. 1).

The product could have any one of the three structures shown in Fig. 2. The preferred structure was established by the following spectral data.
FIG. 1
FIG. 2
a) **Infrared Absorption:** Strong bands occur at 2200 cm$^{-1}$, 1670 cm$^{-1}$, 1660 cm$^{-1}$ and 1520 cm$^{-1}$. These bands can be ascribed to $\alpha,\beta$-unsaturated $\text{-C=N}$ absorption, a $\text{-C=N}$ absorption, a $\text{-C=C}$ absorption and an amidine (possibly amidine $\text{-NH}$ deformation) respectively. The adsorption at 1520 cm$^{-1}$ seems genuinely to be associated with the amidine system since it disappears when the compound is hydrolysed and other amidines show absorption in this region of the spectrum.

b) **Ultra-violet and Visible Light Absorption:** The maximum absorption of the reaction product occurs at 388 nm. This is at substantially longer wavelength than 1-cyanomethylene-3-iminoisoindoline which absorbs up to 320 nm. Therefore an extended conjugated system must have been produced; hence a double bond lies between the two aromatic rings as in structures (XVIII) and (XVIIIa) in Fig. 2. The actual fine structure of the compound is considered at greater length at the end of this chapter.

c) **Proton Magnetic Resonance:** It is important if macrocycle formation is to take place by the condensation of phthalonitrile and aromatic diacetonitrile compounds that the aromatic rings should be trans to each other, i.e. the reaction product should have structure (XVIII) rather than (XVIIIa). The proton magnetic resonance spectrum does in fact indicate that the compound exists in form (XVIII).

The P.M.R. spectrum of compound (XVIII) (Fig. 4) shows an ill-defined singlet centred at 1.3 $\gamma$ of two proton intensity
DESHIELDING EFFECT OF NITRILE GROUP

FIG. 3
FIG. 4

Compound (XVIII) Deuterated

Compound (XVIII) in DMSO Solution
which is attributed to the \(-\text{NH}\) protons. On the addition of deuterium oxide to the sample, proton exchange takes place and this signal disappears. Multiplets occur centred at 1.55\(\gamma\), 1.9\(\gamma\) and 2.5\(\gamma\) corresponding to one, three and five protons. The high field signal was attributed to the protons of the phenyl ring. The low field signal can be assigned to proton \(H_A\) (fig. 3) which is deshielded by the nitrile group if the compound has configuration (XVIII). In this case \(H_A\) is sterically orientated alongside the centre of the triple bond of the nitrile group (depending upon its position in relation to the triple band, the proton will be shielded or deshielded because of the anisotrophy of the triple bond). The spectrum indicates deshielding of approximately 0.6 ppm. The remaining signal at 1.9\(\gamma\) has been assigned to the remaining three protons of the isoindoline nucleus. There was no evidence of a methine proton signal so that structure (XVIIIb) can be ruled out.

d) **Mass Spectrometry:** A mass spectrum of the product gave a molecular ion with \(m/e\) 245.

On the addition of hydrochloric acid to a cold methanolic solution of 1-phenylcyanomethylene-3-iminoisoindoline the hydrochloride (XIX) was obtained. A noticeable difference in the infrared spectra of compounds (XVIII) and XIX) is the shift in the \(-\text{C=N}\) stretching frequency from 1670 cm\(^{-1}\) to 1695 cm\(^{-1}\) on protonation.

Treatment of compound (XVIII) with hot hydrochloric acid
The proton magnetic resonance spectrum of compound (XX) has a singlet at -1.17 which has been attributed to the -NH proton. This signal appears further downfield than the -NH proton signal in the spectrum of compound (XVIII), perhaps because of intermolecular hydrogen bonding between the -NH and the -C=O functional groups. On the addition of deuterium oxide to the sample, proton exchange takes place and this signal disappears. Multiplets occur centred at 1.5\(\gamma\), 2.1\(\gamma\), 2.45\(\gamma\) of one, three and five proton intensities respectively. The low field signal has been assigned as before to the proton of the isoindoline ring closest to the nitrile group. The other signals are attributed to the remaining protons of the isoindoline ring and to the phenyl group.

Compound (XVIII) was found to undergo a self condensation reaction with the elimination of ammonia, when heated above
A dark red coloured product (XXI) was obtained which on extraction (Soxhlet) from benzene yielded fine, dark red needles. Quantitative hydrolysis of this compound yielded two equivalents of 1-phenylcyanomethylene-3-oxoisooindoline. This evidence suggested structure (XXI) which is formed by the elimination of one molecule of ammonia from two molecules of 1-phenylcyanomethylene-3-iminoisoindoline. The visible light spectrum of the condensation product revealed that a lengthening of the conjugated system had taken place. The assigned structure (XXI) was also supported by the mass spectrometric molecular weight of 473. In the fragmentation pattern major peaks occurred at m/e 243 and 229 which were due to the rupture of the molecule into two parts at the single bond of the linking nitrogen atom. The p.m.r. spectrum is similar to that of the spectrum of compound (XVIII) except that the signal from the aromatic protons is increased in intensity.

Another model compound which could theoretically be formed is the "three-unit" compound 1,3-di(phenylcyanomethylene)-isoindoline (XXII). Similar conditions were used to those for the synthesis of 1-phenylcyanomethylene-3-iminoisoindoline, but the reactant ratio was altered to 2 : 1 in favour of benzyl cyanide and refluxing was continued for 6 hours. By this time a reddish brown powder had separated from solution. Mass spectroscopic analysis of this product indicated that mono-condensation only had taken place. The experiment
was repeated and the reaction mixture was refluxed for a total of 30 hours. Again there was no evidence for the desired "three-unit" material being formed. If this condensation reaction were to take place ammonia must be eliminated. Nitrogen was passed through the reaction vessel to maintain an inert atmosphere and sweep out ammonia, but in neither of the experiments was any ammonia detected in the effluent nitrogen.

The reaction was repeated in a sodium butoxide solution and a reflux time of 48 hours. On this occasion ammonia was liberated from the reaction vessel and when this had ceased (after 40 hours), the refluxing was continued for a further 8 hours. By this time a reddish brown powder had precipitated from solution. The visible spectrum of the crude reaction product showed a maximum absorption at 414 nm. This indicated that the "three-unit" material had, in fact, been formed since the maximum absorption of 1-phenylcyano-methylene-3-iminoisoindoline occurs at 388 nm. However, the mass spectrum of the reaction product showed a parent peak at m/e 284 which is correct for the "two-unit" compound. This apparent contradiction was solved when the mass spectrum was run at a lower temperature (90° instead of 150°). Then the mass spectrum gave a molecular ion at 345. The other major peaks can also be explained in terms of the assigned structure. The infra-red shows the usual absorption bands for -NH (3300 cm⁻¹), -C≡N (2200 cm⁻¹) and -C=C (1620 cm⁻¹). However, the amidine absorption band characteristic of the "two-unit" compound is not present.
The P.m.r. spectrum had a multiplet of two proton intensity at 1.4 \( \tau \) corresponding to the two isoindoline protons adjacent to the nitrile groups. A ten proton multiplet centred at 2.55 \( \tau \) was attributed to the protons of the phenyl groups. The remaining protons of the isoindoline ring gave rise to a signal of two proton intensity at 2.1 \( \tau \).

(ii) Condensation of phthalonitrile with p-dicyano-xylylene to give 'two-unit' and 'three-unit' condensation products. The model condensation reactions described in section (i) show the ease with which phthalonitrile condenses with active methylene compounds. This system offers a synthetic route to the methine linked macrocyclic compounds or to polymeric materials by the condensation of aromatic diacetonitriles and phthalonitrile in the presence of a base catalyst. Geometrical requirements indicate that a \( m \)-di-substituted compound would be the most suitable for cyclisation.

Most of the literature concerned with the condensation of 1,3-diiiminoisoindoline with aromatic diamines to give aza-linked macrocycles utilized the \( m \)-substituted compounds.

However the condensation of \( p \)-phenylenediamine with 1,3-diiiminoisoindoline to yield a macrocycle has been reported.\(^ {42} \) There is also reference in the literature to the preparation of a mixed macrocycle in which a \( p \)-substituted aromatic diamine participated.\(^ {48} \) Since the possibility of forming polymers was also a consideration in carrying out this work, it was decided to study the condensation of phthalonitrile and \( p \)-dicyanoxylylene.
In a preliminary experiment 1 : 1 stoichiometric proportions of p-dicyanoxylylene and phthalonitrile were dissolved in a small quantity of ethanol containing sodium ethoxide as catalyst. The reaction mixture was stirred at room temperature under a stream of nitrogen for 4 hours. A reddish brown precipitate was formed which spectral data and microanalytical figures indicated was 1-(4-cyanomethylphenylcyanomethylene)-3-iminoisoindoline (XXIII).

The spectral characteristics of compound (XXIII) were similar to those of 1-phenylcyanomethylene-3-iminoisoindoline, as required by the similarity in structure. The infrared spectrum had the same strong absorption bands at 2200 cm\(^{-1}\), 1670 cm\(^{-1}\), 1600 cm\(^{-1}\) and 1520 cm\(^{-1}\) corresponding to \(-\text{C=N}, -\text{C=N}, -\text{C=C}\) and amidine absorptions. The visible absorption spectrum shows a maximum absorption at 388 nm, identical in position to the maximum absorption band of compound (XVIII). The p.m.r. spectrum had signals at 1.6\(\tau\) of one proton intensity corresponding to the aromatic proton shifted downfield by the anisotropic effect of the nitrile group, and at 1.9\(\tau\) and 2.5\(\tau\) of three and four proton intensity corresponding to the aromatic protons of the isoindoline ring and the phenyl ring. There was also a signal of two proton intensity at 6\(\tau\) corresponding to the protons of the cyano-methylene group and at 1.4\(\tau\) of two proton intensity corresponding to the amidine protons. Finally, mass spectroscopic analysis showed a parent ion at m/e 284, and a fragmentation pattern consistent with the assigned structure.

p-Dicyanoxylylene has two active methylene groups. There-
fore there are two reaction sites at which condensation could take place. Surprisingly, no trace of polymeric or macrocyclic or even "three-unit" material could be found in the reaction product.

Gentle refluxing of compound (XXIII) in a hydrochloric acid-ethanol mixture yielded a bright yellow crystalline powder. Spectroscopic data proved it to be the oxo-derivative, 1-(4-cyanomethylphenylcyanomethylene)-3-oxoisoindoline (XXIV). Under the reaction conditions used, there was no tendency for the cyanomethylene group to undergo hydrolysis.

The infra-red spectrum shows the usual strong bands at 2200 cm\(^{-1}\) and 1600 cm\(^{-1}\) corresponding to \(-\text{C} = \text{N}\) and \(-\text{C} = \text{C}\).

As found on the hydrolysis of compound (XVIII) to (XX) the amidine band in (XXIII) has disappeared and the \(-\text{C} = \text{N}\) band at 1670 cm\(^{-1}\) has been replaced by a \(-\text{C} = \text{O}\) stretching frequency at 1720 cm\(^{-1}\), consistent with structure (XXIV). The replacement of an imino group by an oxo group again resulted in a hypsochromic shift in the position of the visible absorption maximum from 388 to 342 nm. The p.m.r. spectrum of (XXIV) was similar to that of compound (XX) apart from the intensity of the aromatic proton signals and the signal of two proton intensity at 6.7 from the 4-methylene group.

The reaction of p-dicyanoxylylene and phthalonitrile under 1:2 stoichiometric conditions was undertaken in a similar fashion to the previous condensation reaction, using ethanol as solvent and sodium ethoxide as catalyst. The solution was stirred at room temperature for 20 hours under an atmos-
phere of nitrogen, after which time a red-brown solid had
separated from solution. Repeated re-crystallisations
from N-methyl-2-pyrrolidene yielded brilliant yellow crystals,
with a melting point of 312°. The expected structure (XXV)
was confirmed by micro-analysis and by the following spectral
data.

a) **Visible Light Absorption Spectrum**: The maximum absorption
band in the visible spectrum occurs at 464 nm. This cor-
responds to a bathchromic shift of 76 nm over the "two-unit"
compound 1-(4-cyanomethylphenylcyanomethylene)-3-iminoisoin-
doline (XXIII). This large bathochromic shift can be ex-
plained by the fact that the second isoindoline residue is
fully conjugated with the "two-unit" residue.

b) **Infrared Spectrum**: The infrared spectrum shows the ex-
pected bands at 3500 cm⁻¹ and 3350 cm⁻¹ (−N–H stretching),
2200 cm⁻¹ (−C≡N), 1660 cm⁻¹ (−C=N), 1600 cm⁻¹ (−C=C) and
1530 cm⁻¹ corresponding to the amidine stretching frequency.

c) **P.M.R. Spectrum**: The p.m.r. spectrum of the reaction
product shows a singlet of four proton intensity centred
at 1.3 τ which can be attributed to the NH proton. Addition
of deuterium oxide to the p.m.r. sample causes the signal
to disappear. A multiplet of two proton intensity centred
at 1.5 τ can be attributed to the aromatic isoindoline protons
shifted downfield because of the anisotropic effect of the
sterically adjacent nitrile groups. A singlet of four pro-
ton intensity can be attributed to the four equivalent protons
of the phenyl ring. The remaining multiplets at 2\( \gamma \) and 2.4\( \gamma \) are attributed to the remaining protons of the isoindoline ring.

d) **Mass Spectrum:** A mass spectrum of the reaction product gave a parent molecular ion at m/e 412. The fragmentation pattern of the sample was consistent with the assigned structure.

Unlike 1-phenylcyanomethylene-3-iminoisoindoline (XVIII), 1,4-bis[cyano(3-imino-isoindolinylidene)methyl]benzene (XXV) was found to be insoluble in hot hydrochloric acid and attempts to hydrolyse it to the di-oxo compound (XXVI) using this reagent were unsuccessful. It did dissolve in warm concentrated sulphuric acid. However, attempts to hydrolyse it with sulphuric acid resulted in the formation of phthalimide only.

Compound (XXV) can also be obtained by a stepwise synthesis i.e. by the reaction of equimolar quantities of phthalonitrile and p-dicyanoxylylene to give 1-(4-cyanomethylphenylcyanomethylene)-3-iminoisoindoline (XXIII) and the subsequent condensation of this compound with phthalonitrile in the presence of a base catalyst (page 41). It is theoretically feasible that compound (XXIII) could condense with phthalonitrile through its terminal imino group to give compound (XXVIII). However the product isolated from the condensation reaction was composed only of compound (XXV).

Since benzyl cyanide and phthalonitrile were found to condense in 2:1 stoichiometric proportions to give the "three-
unit" material (XXII) an attempt was made to carry out the synthesis of 1,3-di(cyanomethylphenylcyanomethylene)isoindoline. Using dry n-butanol as solvent and sodium butoxide as catalyst, the reagents in the appropriate molar ratios, were refluxed under an atmosphere of nitrogen for 48 hours. Ammonia was evolved from the reaction. Filtration of the reaction mixture yielded a black insoluble material. Thermal analysis showed it decomposed at 410°. This may be the polymeric material (XXIX).

Work up of the filtrate provided a dark brown powder for which spectroscopic analysis indicated the structure (XXVII). Repeated attempts to crystallise it were unsuccessful.

(iii) Attempted Hydrolysis of the Nitrile group of 1-phenylcyanomethyl-3-iminoisoindole.

When 1-phenycyanomethylene-3-iminoisoindoline (XVIII) was hydrolysed to its oxo-derivative (XX) there was no evidence of the nitrile group having undergone hydrolysis. Now since one of the objectives of this work was to produce a methine-linked macrocycle analogous to the aza-linked macrocycles, hydrolysis of the nitrile group of compound (XVIII) was attempted with the intention of subsequently de-carboxylating the reaction product to give compound (XXX). p-Dicyanoxylylene is readily hydrolysed by a mixture of sulphuric acid and glacial acetic acid to give p-phenylenedic acid. However using a variety of reaction conditions, the attempted hydrolysis of compound (XVIII) resulted only in the formation of the oxo-derivative (XX) or of phthalimide. The most
likely explanation for the resistance of the nitrile group to undergo hydrolysis is its steric orientation. The p.m.r. spectrum of (XVIII) has shown that the nitrile group deshields the adjacent aromatic proton and this in turn means that the phenyl group is very close and so probably prevents hydrolytic attack on the nitrile. This explanation is supported by the fact that the 4-cyanomethyl group of 1-(4-cyanomethylphenylcyanomethylene)-3-iminoisoindoline (XXIII) undergoes hydrolysis quite readily whereas the second nitrile group resists hydrolysis.

(iv) Fine Structure of Condensation Products

The fine structure of the aza-linked analogues of the compounds described in this chapter have been studied in detail. Comparison of the visible-light absorption spectra with those of the aza-linked compounds reveals some significant differences. Fig 8 lists the maximum absorption bands of both the aza-linked and the cyanomethine-linked compounds. All of these compounds can theoretically exist in either the iminoisoindoline form (A) or in the aminoisoinndoline form (B).
A consideration of the light absorption data of the aza-linked compounds has shown that where there is an endo-cyclic double bond the maximum u.v. absorption is 20-40 nm further into the visible region than where it is exocyclic. From this it was deduced that the two unit compound 1-phenylimino-3-iminoisoindoline existed as a mixture of the two tautomers because it showed absorption bands both in the 300-320 nm region and in the 360 nm region. This is supported by the absorption of the three-unit compound 2-methyl-1,3-diphenyl-iminoisoindoline where both double bonds are of necessity exo-cyclic. This compound absorbs only 5 nm further into the visible than the two-unit compound. One expects that removal of any contribution from an endo-cyclic form will reduce the longest wavelength absorption and this is slightly more than compensated by the addition of a phenyl group to the conjugated system.

Turning to the cyanomethine-linked compounds it can be seen from fig. 5 that, invariably, a cyanomethine linked compound absorbs at a longer wavelength than its aza-linked analogue. As might be expected the difference is greater in the three-unit compounds than in the two-unit compounds. This difference may very well be due to a difference in the excited states of the molecules. It is not due simply to the two types existing in different tautomeric forms because a) the aza-linked compounds are tautomers of both forms and b) because the difference persists in fixed bond structures as in 3-morpholino-1-phenyliminoisoindoline (XXXV) and 3-morpholino-1-phenylcyanomethylene-isoindoline. Nor can this difference be attributed to the nitrile group since 1-(2'-
max. = 388 nm
max. = 344 nm
max. = 360 nm
max. = 338 nm
max. = 412 nm
max. = 412 nm
max. = 412 nm
max. = 365 nm
max. = 375 nm
FIG. 5
pyridylmethylene)\textsuperscript{-3-oxoisoidolone (XIV) absorbs at a longer wavelength (373 nm) than the aza-linked analogue (338 nm).\textsuperscript{44}

Fig. 5 gives the light absorption data for the cyano-methine linked compounds. 1-Phenylcyanomethylene-3-iminoisoidolone has a maximum absorption band at 388 nm. Unlike its aza-analogue it has no other absorption bands in this region of the spectrum. Therefore it seems that the compound exists in either the endo or the exo-cyclic form rather than as a tautomer. Also the fixed bond compound, 1-phenylcyano-methylene-3-morpholinoiisoindolone has a maximum absorption at 415 nm. This represents a shift of 27nm. Therefore the parent compound must exist in the iminoisoidolone form. This is further confirmed by the fact that the three unit compound 1,3-di(phenylcyanomethylene)-isoindolone has a maximum absorption at 412 nm which represents a bathochromic shift of 24 nm over the two unit compound. This is due to the extension of the conjugated system as a result of the addition of the phenyl group. Now in the aza-linked analogue no such bathochromic shift is observed; the three-unit compound, 1,3-diphenyliminoisoidolone, absorbs at approximately the same wave length as the two-unit compound, 1-phenylimino-3-iminoisoidolone, the chromophoric effect of the additional phenyl group being approximately the same as the contribution of the endocyclic form.
CHAPTER 3
(i) Attempted Synthesis of a Methine-linked Macrocycle by the Condensation of Phthalonitrile with p-Dicyanoxylylene in a Single stage Reaction.

p-Dicyanoxylylene is a potential starting material for the synthesis of either a methine-linked macrocycle (XXXVI) or polymer. Indeed there are references in the literature to such condensation reactions of this compound to form polymers.49,50

For macrocycle formation it is theoretically feasible to use either a one stage synthesis or a stepwise synthesis. The aza-linked macrocycles formed by the condensation of 1,3-diiminoisoindoline with aromatic diamines have been prepared by both of these routes.27,48 Under the conditions used to form the model compounds described in Chapter II no trace of polymeric or macrocyclic material was found. It was evident, therefore, if such materials were to be formed, that much more vigorous reaction conditions would be required, because otherwise condensation would not proceed beyond the first or second stage. Accordingly reaction conditions, analogous to those used in the synthesis of the aza-linked macrocycles, were employed.

1 : 1 Stoichiometric proportions of p-dicyanoxylylene and phthalonitrile were dissolved in a small quantity of n-butanol containing sodium butoxide as catalyst and the reaction mixture was refluxed for 48 hours. The resulting reddish brown precipitate proved on examination to be the two-unit material 1-(4-Cyanomethylphenylcyanomethylene)-3-
iminoisoindoline (XXIII).

No trace of higher molecular weight material was formed. The experiment was repeated using sodium hydride as catalyst and dry dimethylformamide as solvent. This solvent had some advantages in that compound (XXIII) was soluble in it and it had a reasonably high boiling point with little decomposition when refluxing under an atmosphere of nitrogen. The reaction mixture was refluxed for 24 hours. Examination of the brown reaction product showed it to be compound (XXIII). In a further experiment the reactant ratios were altered to 2 : 1 in favour of phthalonitrile, but otherwise the reaction was carried out as before. Work up gave a dark brown powder. Spectroscopic analysis proved this to be 1,4-bis \( \text{cyano-}(3\text{-imino-1-isoindoleninylidene})\text{methyl} \) benzene (XXV).

Even more drastic reaction conditions were employed in an effort to obtain the desired polmeric materials. To molten \( p \)-dicyanoxylylene were added equimolar quantities of phthalonitrile and sodium hydride. The reaction mixture was maintained at 200° for 30 minutes under a nitrogen atmosphere. Extraction of the black molten mass with dimethylformamide showed that it contained sodium phthalocyanine and the three-unit compound 1,3-di-(4-cyanomethylphenylcyanomethylene)isoindoline (XXVII).

In these condensation reactions there was no evidence of the required macrocycle or polymer having been formed. It would seem that the two-unit compound was formed very readily, but that there was no great tendency for the reaction to proceed further either at the imino group or the free
cyanomethylene group. In the last reaction attempt conditions were such that some sodium phthalocyanine was formed leaving an excess of p-dicyanoxylylene, which then combined with phthalonitrile to give the three-unit compound (XXVII).

(ii) Attempted Synthesis of a Methine-linked Macrocyle using 'three-unit' condensation Products as precursors.

Since a one-step synthesis of a methine-linked macrocycle was unsuccessful, attention was turned to the possibility of forming a macrocycle by a stepwise synthesis. The obvious precursors for this type of synthesis were compounds (XXV) and (XXVII). The bis-isoindolenyl compound formed by the condensation of m-phenylenediamine and 1,3-diiminoisoindoline has been used as a precursor in the synthesis of some mixed aza-linked macrocycles. 27

The attempted synthesis of the methine linked macrocycle (XXXVI) by the condensation of 1,4-di[cyano-(3-imino-1-isoindoleninyl)methyl] benzene (XXV) and p-dicyanoxylylene was undertaken. Equimolar quantities of compound (XXV) and p-dicyanoxylylene were refluxed in n-butanol, with sodium butoxide as catalyst, for 24 hours. Work up of the reaction product yielded a dark brown solid which spectroscopic analysis showed to be the starting materials. Even using more severe reaction conditions namely, dimethyl formamide as solvent and sodium hydride as catalyst, the desired macrocycle was not obtained. Another theoretically possible route to cyanomethine linked macrocycles is from 1,3-di(cyanophenylcyanomethylene)isoin-
doline (XXVII) and phthalonitrile as starting materials.

Details of the preparation of compound (XXVII) were given in Chapter 2. Equimolar amounts of the crude material and phthalonitrile were added to n-butanol containing two equivalents of sodium. The reaction mixture was refluxed for 48 hours under a stream of nitrogen. The solvent was reduced to small volume and taken up in ethanol. The black precipitate formed proved on mass spectrometric analysis to be a mixture of the three unit starting material (XXVII) and phthalocyanine. More severe reaction conditions using dimethylformamide as solvent and sodium hydride as catalyst yielded similar reaction products. Evidently the ease with which phthalocyanine is formed from phthalonitrile is very much greater than the ease of its condensation with compound (XXVII).

(iii) Attempted Formation of Diaza-dimethine-linked Macrocycles.

Since the attempts to prepare the fully methine-linked macrocycle by either a one step synthesis or by a stepwise synthesis were unsuccessful, the possibility was considered of preparing a partly methine-linked macrocycle of the type:
Macrocycles of this type could theoretically be formed:
(a) by condensing 1,4-bis[cyanocarbonyl-(3-imino-1-isoindoleninyl) methyl]benzene (XXV) with an aromatic diamine.
(b) by the initial condensation of 1-(4-cyanomethylphenyl-cyanomethylene)-3-iminoisoindoline (XXVII) with an aromatic diamine and the subsequent condensation of the product with phthalonitrile in the presence of a basic catalyst.

Both methods were used in the attempted synthesis of these macrocycles.

Aza-linked bis-isoindoleninyl compounds condense quite readily with suitable aromatic diamines to give fully aza-linked macrocycles. It was expected that compound (XXV) would also condense with diamines in the same manner and with the same facility. With this in mind, 1:1-stoichiometric proportions of compound (XXV) and p-phenylenediamine were added to n-butanol and refluxed under an atmosphere of nitrogen for a period of 48 hours. No appreciable concentrations of ammonia were evolved during the course of the reaction. Examination of the reaction product showed the presence of uncondensed starting materials only. The reaction was repeated using dry dimethylformamide as solvent. Here again, condensation failed to take place. Equally unsuccessful were attempts to condense compound (XXV) with other aromatic diamines such as m-phenylenediamine, 2,7-diaminoanthraquinone, 2,6-diaminopyridine, 2,8-diaminoacridine (fig. 6).
XXXV

\[ \text{NC} \quad \text{H} \quad \text{NH} \quad \text{NC} \quad \text{H} \quad \text{NH} \]

\[ \text{H}_2\text{N} \quad \text{R} \quad \text{NH}_2 \]

XXXVIII

FIG.6
The second theoretically possible route to a di-methine, di-aza linked macrocycle involves 1-(4-cyanomethylphenyl-cyanomethylene)-3-iminoisoindoline as starting material. This compound was found to condense quite readily with amino-compounds through its imino group. If the compound condensed with diamines then the products should, if condensed further with phthalonitrile, give the desired type of macrocycle or alternatively polymeric material (fig. 7). Accordingly a number of intermediate compounds were synthesised by condensing compound (XXIII) with p-phenylenediamine, m-phenylene-diamine, 2,6-diaminopyridine, 2,7-diaminoanthraquinone and 2,8-diaminoacridine. Boiling n-butanol was found to be a satisfactory medium in which the reaction could take place. During the course of the reaction ammonia was evolved and the condensations were judged to be complete when the evolution of ammonia had ceased. The reaction products were invariably dark brown powders. These products were characterized by light absorption and infrared spectroscopy and mass spectrometry.

The attempted syntheses of the partly methine-linked macrocycles were carried out by refluxing equivalent quantities of the intermediates and phthalonitrile in n-butanol with sodium butoxide as catalyst. The reaction mixtures were refluxed for periods up to 48 hours. In each case the reaction product proved to be mixtures of the starting materials and sodium phthalocyanine. Evidently under these reaction conditions phthalocyanine formation takes place much more easily than the condensation of phthalonitrile with the intermediate three-unit compounds. These attempted condensations
\[
\text{XXIII} \quad \xrightarrow{\text{base}} \quad \text{XXVII}
\]

\[
\begin{align*}
\text{H}_2\text{N} \quad &\quad \text{R} \quad \text{NH}_2 \\
\text{NC} \quad &\quad \text{CH}_2\text{CN} \\
\text{NH} \quad &\quad \text{N} \quad \text{R} \quad \text{NH}_2 \\
\text{NH} \quad &\quad \text{N} \quad \text{R} \quad \text{NH}_2 \\
\end{align*}
\]

\[
\text{CN} \quad \text{CN}
\]

FIG. 7
were repeated using ethanol as solvent and sodium ethoxide as catalyst. Again, although phthalocyanine was not formed, there was no evidence of the formation of condensation products.

(iv) **Suggested Reasons for the Failure to Obtain the desired Macro-cyclic Products and Polymers.**

The failure of the bis-isoindolinyl compound (XXV) to condense further with \( \sigma \)-dicyanoxylylene can perhaps be partly explained in terms of the stereochemistry of the structures involved. It appeared from atomic models of compound (XXV) and of the methine-linked macrocycle, that conversion into the latter by the addition of \( \sigma \)-dicyanoxylylene would be most unlikely. The structure of such a methine linked macrocycle would be highly strained. In a scale drawing of compound (XXV) in which the bond angles and bond lengths used are based on those of phthalocyanine and relevant compounds in the Chemical Society Tables, the spacing between the two imino groups of compound (XXV) was found to be 7.4\( \AA \), whereas the spacing between the reacting centres of \( \sigma \)-dicyanoxylylene is 5.6\( \AA \).

It is interesting to note here that attempts to form the methine linked macrocycle by condensing phthalonitrile and \( m \)-dicyanoxylylene (Chap. 4) were equally unsuccessful. In this case there were no obvious steric reasons why macrocycle formation should not take place.

The lack of reactivity of the bis-isoindoleninyl compound towards \( \sigma \)-dicyanoxylylene was not altogether surprising in
the light of the results of the model reactions carried out with benzyl cyanide and phthalonitrile. Phthalonitrile was found to condense with benzyl cyanide in the presence of a base catalyst, at room temperature to give the two-unit compound (XVIII). When the reactant ratios were altered to 2:1 in favour of benzyl cyanide the three-unit compound (XXII) was obtained quite readily. However, the stepwise synthesis of this compound was unsuccessful. This suggested that the actual mechanism of formation of compound (XXII) did not involve compound (XVIII) as an intermediate (fig. 8). Perhaps there is addition of benzyl cyanide anion to each of the phthalonitrile cyano groups before there is cyclisation and elimination of ammonia.

The failure to synthesise the fully methine linked macrocycle by the condensation reaction of compound (XXVII) and phthalonitrile might again be attributed to steric reasons. A consideration of atomic models of compound (XXVII) and the macrocycle indicated that conversion to the latter would be unlikely because of the strain involved. In a scale drawing of compound (XXVII) the band angles and band lengths used again being based on those of phthalocyanine and related compounds, it is found that the spacing between the two methylene groups is 6.9\AA, whereas the spacing between the nitrile groups of phthalonitrile is 4.7\AA.

These steric considerations do not explain why no open-chain or polymeric materials were formed by the condensation of compound (XXVII) with phthalonitrile. A possible explana-
\[
\text{base} \quad \begin{array}{c}
\text{NC} \\
\text{NC}
\end{array} + 2 \quad \begin{array}{c}
\text{NC} \\
\text{CH}_2\text{CN}
\end{array}
\]

\[
\text{base} \quad \begin{array}{c}
\text{NC} \\
\text{NC}
\end{array} \quad \begin{array}{c}
\text{NC} \\
\text{NC}
\end{array}
\]

\[
\text{base} \quad \begin{array}{c}
\text{NC} \\
\text{NC}
\end{array} \quad \begin{array}{c}
\text{NC} \\
\text{NC}
\end{array} + \quad \begin{array}{c}
\text{NC} \\
\text{CH}_2\text{CN}
\end{array}
\]

FIG. 8
tion is that, under the reaction conditions used, phthalocyanine is the most easily formed product and so the phthalonitrile is rapidly consumed in that way and does not have the opportunity of interacting in the required manner.

The steric factors which militate against the formation of the methine linked macrocycle would also apply to the attempted formation of the partly methine linked macrocycle from the 'three-unit' compounds. The spacing between the reacting centres of the various diamines used in the attempted condensations with compound (XXV) are as follows:

- \( p \)-Phenylenediamine \( 5.74 \, \text{Å} \)
- \( m \)-Phenylenediamine \( 4.8 \, \text{Å} \)
- 2,6-diaminopyridine \( 4.8 \, \text{Å} \)
- 2,7-diaminoanthraquinone \( 9.676 \, \text{Å} \)
- 2,8-diaminoacridine \( 9.962 \, \text{Å} \)
- 2,7-diaminonaphthalene \( 7.395 \, \text{Å} \)

The spacing between the imino groups of compound (XXV) was \( 7.4 \, \text{Å} \). Save for 2,7-diaminonaphthalene all these compounds seemed either too small or too large for condensation to take place. However, even with 2,7-diaminonaphthalene no condensation product was obtained. Thus it seemed there were other considerations preventing macrocycle formation from these compounds.
CHAPTER 4
(i) Reaction of Phthalonitrile with m-Dicyanoxylylene to give 'Two-unit' and 'Three-Unit' Condensation Products.

The condensation of p-dicyanoxylylene with phthalonitrile, depending on the molar ratio of the reactants gave three different compounds (XXIII) (XXV) and (XXVII). However, attempted formation of macrocycles from these compounds either by a direct synthesis or by a stepwise synthesis was unsuccessful, perhaps because the macrocycles so formed would be highly strained. If m-dicyanoxylylene were used in the condensation reactions rather than p-dicyanoxylylene there should be no steric hindrance to the formation of macrocyclic compounds. Therefore the Thorpe condensation of m-dicyanoxylylene with phthalonitrile was examined in detail.

Using the same reaction conditions as in Chapter 2 equimolar quantities of phthalonitrile and m-dicyanoxylylene were found to condense to give 1-(3-cyanomethylphenylcyanomethylene) -3-iminoisoindoline (XXXIX). The structure of this compound was established by elemental analysis and by its spectral properties. Its infra-red spectrum was similar to that of compound (XXIII), with characteristic NH stretching vibrations at 3450 cm⁻¹ and 3350 cm⁻¹, and strong absorption bands at 2200 cm⁻¹, 1670 cm⁻¹, 1600 cm⁻¹ and 1520 cm⁻¹ corresponding to -C=N, -C=N, -C=C and amidine absorptions. The visible absorption spectrum shows a maximum absorption at 388 nm which is identical in position to the maximum absorption band of compound (XXIII).

Therefore it can be assumed that compound (XXXIX) exists
in the same tautomeric form as compounds (XVIII) and (XXIII), with a double band conjugating the two benzenoid rings of that structure. The p.m.r. spectrum of (XXXIX) is also similar to that of compound (XXIII). Signals occur at 1.3\(\gamma\) and 1.5\(\gamma\) of two and one proton intensity corresponding to the amidine-NH protons and to the aromatic proton shifted downfield by the anisotropic effect of the adjacent nitrile group. Signals also occur at 1.9\(\gamma\), 2.5\(\gamma\) and 6\(\gamma\) of three, four and two proton intensity corresponding to the aromatic protons of the isoindoline and phenyl rings and to the protons of the cyanomethylene group. The mass spectrum of compound (XXXIX) has a parent ion at m/e 284 and a fragmentation pattern consistent with the assigned structure.

Compound (XXXIX) was hydrolysed to give 1-(3-cyano-methyl-phenylcyanomethylene)-3-oxoisoindoline (XL) by refluxing in ethanol in hydrochloric acid. Characterisation of compound (XL) was achieved by elemental analysis and by spectroscopic data. The infra-red spectrum has strong absorption bands corresponding to \(-\text{C}=\text{N}\) at 2200 cm\(^{-1}\), \(-\text{C}=\text{C}\) at 1600 cm\(^{-1}\) and \(-\text{C}=\text{O}\) at 1720 cm\(^{-1}\). The amidine band of compound (XXXIX) has been replaced by the \(-\text{C}=\text{O}\) stretching frequency. The visible spectrum has a maximum absorption at 346 nm. Compared with the maximum shown by compound (XXXIX) this represents a hypsochromic shift of 42 nm. The p.m.r. spectrum of (XL) has a singlet centred at \(-1.1\gamma\) which is attributed to the \(-\text{NH}\) proton. On addition of deuterium oxide to the sample, proton exchanges take place
and this signal disappears. This signal appears further down-field than the amidine -NH proton signal of the parent compound (XXXIX). Intermolecular hydrogen bonding between the -NH and -C=O functional groups may be the explanation for this down-field shift. Multiplets occur at 1.5γ, 2γ and 2.5γ of one, three and four proton intensity corresponding to the proton of the isoindoline ring closest to the nitrile group, the remaining three aromatic protons of the isoindoline ring and the protons of the phenyl ring. An additional signal occurs at 6γ of two proton intensity which can be ascribed to the cyanomethylene protons.

Finally a mass spectrum of this compound gave a molecular ion with m/e 285, and a fragmentation pattern consistent with the structure assigned to compound (XL).

The meta analogue of compound (XXV) was prepared by refluxing m-dicyanoxylylene and phthalonitrile in 1:2 stoichiometric proportions using ethanol as solvent and sodium as catalyst. After refluxing for 20 hours a yellow-brown solid separated from solution. Repeated recrystallisations from N-methyl-2-pyrrolidone yielded bright yellow crystals which melted at 305°. The expected structure (XLI) was confirmed by the following spectroscopic data and by microanalysis.

Visible Absorption Spectrum: The maximum absorption band in the visible spectrum occurs at 412 nm. This is considerably shorter than the maximum absorption band of compound (XXIII) which occurs at 464 nm. This is to be expected
since in the latter compound the molecule is fully con­jugated through the bridging phenyl ring whereas compound (XLI) is only cross-conjugated.

**Infra-red Spectrum:** The infra-red spectrum shows the ex­pected N-H stretching frequencies at 3500 cm\(^{-1}\) and 3350 cm\(^{-1}\). Absorption bands also occur at 2200 cm\(^{-1}\) (C≡N), 1660 cm\(^{-1}\) (C=N), 1600 cm\(^{-1}\) (C=C) and 1530 cm\(^{-1}\), the last corresponding to the amidine stretching frequency.

**The P.m.r. Spectrum:** The p.m.r. spectrum of compound (XLI) has a singlet of four proton intensity centred at 1.4\(\gamma\) which is attributed to the NH protons. Multiplets occur at 1.5\(\gamma\) and 1.7\(\gamma\) of two and four proton intensity respectively. These are attributed to the anisotropically shielded protons of the isoindoline rings and the protons of the substituted benzene ring. Other multiplets occur at 2.0\(\gamma\) and 2.3\(\gamma\) of two and four proton intensity which can be ascribed to the remaining protons of the isoindoline rings.

**Mass Spectrum:** A mass spectrum of compound (XLI) gave a parent molecular ion at m/e 412 and the fragmentation pattern of the sample was consistent with the assigned structure.

Refluxing of compound (XLI) in ethanol in hydrochloric acid yielded the di-oxo derivative 1,3-di[cyano(3-oxo-1­isoindolinylidene)methyl] benzene (XLII). The infrared spectrum of this compound shows no amidine absorption band (1530 cm\(^{-1}\)) but there is strong carbonyl absorption at 1710 cm\(^{-1}\).
In common with the products of other hydrolysis reactions already described, the visible absorption maximum of compound (XLII) was shifted 70 nm hypsochromically from that of the precursor (XLI).

The meta analogue of compound (XXVII) was also prepared from phthalonitrile and m-dicyanoxylylene using 1:2 stoichiometric proportions and refluxing in 2-ethoxyethanol containing a catalytic amount of sodium for a period of 24 hours. A dark brown precipitate separated. The spectral characteristics of this compound were similar to compound (XXVII) indicating that the 'three-unit' material (XLV) was, indeed, formed. However, the mass spectrum of the reaction product indicated that trace amounts of higher molecular weight material corresponding to the uncondensed '4-unit material' (XLVI) was present.

(ii) Attempted preparation of a methine-linked macrocycle by the condensation of phthalonitrile with m-dicyanoxylylene in a single stage synthesis.

Phthalonitrile and m-dicyanoxylylene condensed very readily to give two and three unit compounds. Indeed in one case the mass spectrum of the reaction product indicated that traces of higher molecular weight material was present. Accordingly an attempt was made to prepare the carbon-linked 4-unit macrocycle (XLIII) by the direct condensation of phthalonitrile and m-dicyanoxylylene by using more drastic reaction conditions than for the preparation of the two and three unit compounds.
Phthalonitrile and m-dicyanoxylylene in 1:1 stoichiometric proportions were added to dry dimethylformamide containing a catalytic amount of sodium hydride. The reaction mixture was refluxed for 24 hours. Work up of the reaction product showed the presence of the two unit material (XXXIX) only.

The attempted condensation was repeated by adding equimolar quantities of phthalonitrile and sodium hydride to an excess of molten m-dicyanoxylylene. The reaction mixture was maintained at 200° for 30 minutes under a nitrogen atmosphere. The dark molten mass was extracted with dimethyl formamide. Spectroscopic examination of the reaction product showed that it was composed of sodium phthalocyanine and the three unit material (XLV).

(iii) **Attempted Preparation of a Methine-linked Macrocycle using Intermediate Condensation Products as Precursors.**

The stepwise synthesis of the macrocycle using as starting materials compounds (XXXIX) and (XLI) was also attempted. To dry dimethyl formamide containing a catalytic amount of sodium hydride, equimolar quantities of m-dicyanoxylylene and compound (XLI) were added. The reaction mixture was refluxed for a 12 hour period during which no ammonia was evolved. Spectroscopic examination of the reaction product indicated that it was composed of the starting materials only.

Using the same reactions conditions as above the attempted
condensation of phthalonitrile and compound (XLV) gave a reaction product which on examination was revealed to be a mixture of the starting 'three unit' compound and sodium phthalocyanine.

(iv) **Attempted Synthesis of the Diaza-Dimethine-linked Macrocycle using the Intermediate Compounds as precursors.**

Since attempts to synthesise the fully methine-linked macrocycle were unsuccessful attention was turned to the possibility of forming the diaza-dimethine linked macrocycles (XLVIII). There are references in the literature to the formation of mixed aza-linked macrocycles. These have been formed by the condensation of an aza-linked bis-isoindoleninyl compound with aromatic diamines or 1,3-di-iminoisoindoline to give fully aza-linked macrocycles. Since the methine-linked bis-isoindoleninyl compound (XLI) can be formed with such facility, it is the obvious precursor for the dimethine-diaza linked macrocycles.

Accordingly m-phenylene diamine and compound (XLI) in 1:1 stoichiometric proportions were added to dry dimethyl formamide and the reaction mixture refluxed for 18 hours. No significant amounts of ammonia were evolved during the period of refluxing. The reaction mixture was allowed to cool and decanted into water. The dark brown precipitate formed was extractively crystallised from o-dichlorobenzene. Spectroscopic examination of the product showed it to be the starting material (XLI) although the mass spectrum indicated the presence of the macrocycle (XLVIII).
and the uncyclised compound (XLVII, \( R = \text{C}_6\text{H}_5\text{NH}_2 \)).

In an attempt to prepare a significant amount of these higher molecular weight products more drastic reaction conditions were employed. To molten \( m \)-phenylenediamine was added a small quantity of compound (XLI). The reaction mixture was maintained at 200° under a nitrogen atmosphere for a period of 30 minutes. The molten mass was extracted with dimethyl formamide. Spectroscopic examination of the extracted product showed no significant amounts of the desired higher molecular weight compounds.

Equally unsuccessful were attempts to condense compound (XLI) and 2,6-diaminopyridine using the same reaction conditions.

The other theoretically feasible route to the formation of the diaza-dimethine linked macrocycles, namely via the two unit compound (XXXIX) was also explored. Like its para analogue, 1-(3-cyanomethylphenylcyanomethylene)-3-iminoisoindoline condenses readily with aromatic diamines. Thus the three unit compound (XLIXA) was prepared by refluxing equimolar proportions of compound(XXXIX) and \( m \)-phenylenediamine in \( n \)-butanol for 8 hours after which time the evolution of ammonia had ceased.

The structure assigned to compound (XLIXA) was confirmed by spectroscopic data. In the same manner, 1-(3-cyanomethylphenylcyanomethylene)-3-iminoisoindoline (XXXIX) was condensed with 2,6-diaminopyridine to give the three unit com-
Subsequent attempts to condense these three unit compounds with phthalonitrile were not successful. Under the reaction conditions used (the same as those used for the analogous para substituted compounds in chapter III) only starting materials and phthalocyanine were obtained.

(v) Condensation of 1,3-Bis [cyano(3-imino-1-isoindolinyl-dene)methyl] benzene with 1,3 di-iminoisoindoline.

However the bis-isoindoleninyl compound was found to condense with 1,3-diiminoisoindoline to give the triisoindoline macrocycle (L). Equimolar proportions of 1,3-diiminoiso-indoline and compound (XLIV) were added to dry n-butanol and the reaction mixture was refluxed under a stream of nitrogen for 20 hours. Ammonia was evolved. Upon cooling a dark red precipitate separated out of solution. Repeated extractive crystallisations from o-dichlorobenzene gave the macrocycle (L). Confirmation of the structure came from consideration of the following spectroscopic data.

Visible Spectrum: The visible light absorption spectrum shows a maximum at 460 nm. This represents a considerable lengthening in the conjugated system compared to the bis-isoindoleninyl compound which had a maximum absorption band at 412 nm, but the absorption is not so far to the red as in the aza-linked triisoindoline benzene macrocycle (IX) which absorbs at 507 nm. This was claimed to be characteristic of the triisoindoline chromophore which con-
stitutes three quarters of the phthalocyanine chromophore.

**Infrared Spectrum:** The infrared spectrum shows only one-NH stretching vibration at $3280 \text{ cm}^{-1}$ in contrast to the two and three unit compounds which had two NH stretching vibrations. Other absorption bands occur at $2200 \text{ cm}^{-1}$, $1670 \text{ cm}^{-1}$ and $1600 \text{ cm}^{-1}$ corresponding to $-\text{C=N}$, $-\text{C=N}$ and $-\text{C=C}$. The characteristic amidine absorption band at $1520 \text{ cm}^{-1}$ of the two and three unit compounds has disappeared.

**Mass Spectrum:** A mass spectrum of compound (L) gave a parent molecular ion at $m/e$ 523 and the fragmentation pattern of the sample was consistent with the assigned structure.
(vi) Condensation of Phthalonitrile with 2,6-Biscyanomethyl-pyridine

Although the synthesis of a cyanomethine-linked macrocycle from the condensation of m-dicyanoxylylene and phthalonitrile was not achieved, it was decided to investigate the possibility of preparing a methine-linked macrocycle (LII) analogous to the aza-linked pyridine macrocycle reported by Elvidge and Linstead. With this in view 2,6-biscyanomethyl-pyridine was prepared according to the method outlined by Barker.

The reaction scheme is as follows:-
2,6-Lutidine was converted to dipicolinic acid by permanganate oxidation using the method of Soine and Buchdahl and esterified to give dimethylpyridine-2,6-dicarboxylate. Subsequent reduction using sodium borohydride in dry diglyme in the presence of magnesium chloride gave 2,6-dihydroxymethylpyridine in high yield. The 2,6-dimethanol was easily converted by thionyl chloride to the corresponding bis-chloromethylpyridine. Treatment with sodium cyanide in dry dimethylsulphoxide gave 2,6-biscyanomethylpyridine.

Like its benzene analogue 2,6-biscyanomethylpyridine was found to condense quite readily with phthalonitrile in 2:1 stoichiometric proportions to give the bis-isoindolinyldene compound (L1). The infrared spectrum of this compound has strong absorption bands at 2200 cm\(^{-1}\), 1650 cm\(^{-1}\) and 1530 cm\(^{-1}\) corresponding to \(-C=N\), \(-C=N\) and amidine stretching frequencies respectively. The maximum absorption band in the visible spectrum occurs at 420 nm. The mass spectrum has a parent molecular ion at m/e 413 and a doubly charged ion at m/e 206.5.

The further condensation of 2,6-bis[cyano(3-imino-1-isoindolinyldene)methyl] pyridine with 2,6-biscyanomethylpyridine was examined. Accordingly, equimolar proportions of these two compounds were added to dry dimethylformamide containing a catalytic amount of sodium hydride and refluxed for a period of 8 hours. No evolution of ammonia was detected during the refluxing period. Spectroscopic examination of the reaction product showed that no further condensation had taken place.
Using the same reaction conditions attempts were made to condense the 'three-unit' compound (LI) with 2,6-diamino-pyridine and 1,3-diiminoisoindoline. In both cases the main products were the uncondensed starting materials, although mass spectra of the reaction products indicated that traces of higher molecular weight compounds corresponding to the uncyclised 'four-unit' and to the macrocyclic materials were present. In this respect the methine linked bis-isoidoline compounds (LI) and (XLI) resemble their aza-linked counterparts. A macrocycle containing three-quarters of the phthalocyanine molecule (LIX, R = m-phenylene) has been synthesised by interacting the bis-isoidoline compound (LIII, R = m-phenylene) with 1,3-diiminoisoindoline. However, compound (LIX, R = 2,6-pyridyl) has not been achieved by a similar condensation of compound (LIII, R = 2,6-pyridyl) with 1,3-diiminoisoindoline, although metal derivatives of the macrocycle have been prepared by a template synthesis. This technique may well offer a route to either the fully methine linked macrocycle (LII) or to the partly methine linked tri-isoidoline macrocycle (LV).
(i) Introduction

The condensation of phthalonitrile or 1,3-diiminoisoindoline with oxydianiline and the related compounds aminodianiline and methanedianiline have been reported. The structures of these aza-linked macrocycles have not been examined in detail. In fact some unusual macrocycles have been claimed to be formed by the self-condensation of the bis-isoindoline intermediates (fig 9).

Before embarking on the attempted synthesis of the analogous methine-linked macrocycle (LIX) it was decided to examine the synthesis of these aza-linked macrocycles in greater detail. 1:1-Stoichiometric proportions of 1,3-diiminoisindoline and oxydianiline were refluxed in dry ethanol for 20 minutes, during which time ammonia was evolved. On cooling, an orange precipitate separated. Spectroscopic analysis of the product showed it to be the aza-linked macrocycle (LVIII).

The same product was obtained by refluxing equimolar proportions of phthalonitrile and oxydianiline in ethanol using sodium alkoxide as catalyst (fig.10). The synthesis of the bis-isoindolinyl derivative formed by the condensation of phthalonitrile and oxydiaminile in 2:1 stoichiometric proportions has also been reported by Packham and Davies and by Wolf.

Wolf prepared this compound as well as the aminodianiline and methane dianiline bis-isoindoline compounds by dissolving
FIG. 9

\[ \text{Compounds LVI and LVII are shown.} \]
the appropriate diamine and phthalonitrile in methanol containing two equivalents of sodium metal, and maintaining the mixture at 50° until the reactants had dissolved. Upon cooling an orange-brown product (LVI) separated out of solution.

When these bis-isoindoline compounds were heated in nitrobenzene to 200 - 250° for twenty minutes ammonia was evolved. It was claimed that ring-closure had taken place to give the 'three-unit' macrocycle (LVII).

(ii) Preparation of 4,4'-Di(cyanomethylphenyl)Ether

The obvious starting materials for the methine-linked macrocycle are phthalonitrile and 4,4'-di(cyanomethylphenyl)ether. Accordingly the preparation of the latter material was undertaken. This compound can be prepared by the direct chloromethylation of biphenyl and the subsequent replacement of the chloro groups by nitrile groups, or by the halogenation of 4,4'-dimethylphenyl ether and the conversion of the dihalide derivative to the di-nitrile compound. Since 4,4'-dimethylphenyl ether was readily available the second synthetic route was adopted.

However, a survey of the literature has shown that the dihalide derivative can be prepared in high yields using N-bromosuccinimide as reagent and benzoyl peroxide as catalyst. Over a period of twenty minutes N-bromosuccinimide was added to a refluxing solution of 4,4'-dimethylphenyl ether and benzoyl peroxide in benzene. The cooled solution was filtered from succinimide and washed.
with aqueous sodium hydroxide. Concentration of the solution yielded the di-bromo derivative in 76% yield. Extractive recrystallisation from light petroleum gave colourless crystals with a melting point of 98°.

Conversion to the dinitrile derivative was achieved using the method of Pleininger. 2:1 Stoichiometric proportions of sodium cyanide and 4,4′-di(bromomethylphenyl)ether were refluxed in acetone containing a catalytic amount of sodium iodide for a period of 36 hours. The solvent was evaporated and the residue was diluted with water and extracted with diethyl ether. The ether solution was dried and evaporated leaving behind an oil. On cooling the residual oil, solid 4,4′-di(cyanomethylphenyl)ether separated. Repeated recrystallisation from ethanol gave a white crystalline product with a melting point of 68°.
FIG. 10

LVIII
(iii) Condensation of Phthalonitrile with 4,4'-Di(cyano-methylphenyl) Ether.

Equimolar quantities of 4,4'-di(cyano-methylphenyl) ether and phthalonitrile were added to dry ethanol containing a catalytic amount of sodium. The mixture was refluxed for two hours, then decanted into cold water with vigorous stirring, and neutralized with 2N-hydrochloric acid. The yellow precipitate was filtered and dried. Spectroscopic analysis showed the product to be 1-(4-cyanomethyl-4'-cyano-methylene-diphenyl ether)-3-iminoisoindoline (LX).

The visible light absorption spectrum shows a maximum at 385 nm. The model compound (XVIII) had a maximum at 392 nm. Because there is no extension of conjugation through the ether linkage in compound (LX) it is not surprising that the maximum absorption of this compound should be in the same region as that of compound (XVIII). The infrared spectrum shows the usual absorption bands at 3450 cm⁻¹ and 3350 cm⁻¹ characteristic of the -NH stretching vibrations and strong absorption bands at 2200 cm⁻¹, 1670 cm⁻¹, 1610 cm⁻¹ and 1520 cm⁻¹ corresponding to -C≡N, -C=N, -C=C and amidine -NH absorptions. Unlike compound (XVIII) however it does possess a strong absorption band at 1240 cm⁻¹ corresponding to the C-O stretching frequency of the ether linkage. The mass spectrum of compound (LX) has a parent ion at m/e 376 and a fragmentation pattern which is consistent with the assigned structure.
Compound (LX) underwent hydrolysis upon refluxing in a mixture of ethanol and hydrochloric acid to give the oxo-derivative (LXI). Like similar hydrolysis products already described, its light absorption spectrum showed a hypsochromic shift of 30 nm. The infrared spectrum was characterized by the replacement of the amidine -NH stretching frequency at 1520 cm$^{-1}$ by strong carbonyl absorption at 1720 cm$^{-1}$.

The synthesis of the bis-isoindoline compounds by the reaction of phthalonitrile with both meta and para-dicyanoxylylene proceeded quite smoothly at room temperature. The condensation of oxydianiline and phthalonitrile in 1:2 -stoichiometric proportions to give the aza-linked bis-isoindoline compound also took place at room temperature. However using the same reaction conditions, phthalonitrile and 4,4'-di(cyanomethylphenyl) ether in the appropriate proportions failed to condense to give the bis-isoindoline compound (LXII). More severe reaction conditions were also tried with 2:1 stoichiometric proportions of phthalonitrile and 4,4'-di(cyanomethylphenyl) ether in boiling n-butanol for 6 hours with sodium present as catalyst. No evidence for the formation of the 'three-unit' material was found. The attempted condensation was equally unsuccessful when dimethylformamide was used as solvent and sodium hydride as catalyst. In this respect, 4,4'-di(cyanomethylphenyl) ether resembles di(aminophenyl) sulphone, in that condensation of the latter with phthalonitrile or with 1,3-diiminoisoindoline gave only the two unit compound. There
was no tendency for the condensation with the ether to proceed further to give the bis-isoindoline compound or the macrocycle.

However, under extreme conditions the methine-linked bis-isoindoline compound (LXII) was formed. To molten 4,4-di(cyanomethylphenyl) ether was added phthalonitrile and a trace amount of sodium hydride. The reaction mixture was then maintained at approximately 150° for 30 minutes under a nitrogen atmosphere. Extraction of the black molten mass with dimethylformamide gave a dark brown product. Spectroscopic data indicated that this crude product was indeed the desired bis-isoindoline compound (LXII) although repeated efforts to purify it by Soxhlet extraction and recrystallisation were unfortunately not successful.

No evidence could be obtained for formation of the methine-linked 'four-unit' macrocycle (LIX) or of a 'three-unit' partly methine-linked macrocycle analogous to the aza-linked macrocycle (LXIII). Nevertheless further attempts were made to synthesise these macrocycles and also to obtain the di-aza di-methine linked macrocycle using the crude bis-isoindoline compound as starting material.

1:1-Stoichioimetric proportions of compound (LXII) and 4,4'-di(cyanomethylphenyl) ether were added to dry dimethylformamide and refluxed for 48 hours under a stream of nitrogen. No detectable amounts of ammonia were emitted during the course of the reaction. Work-up of the reaction product showed the presence of starting materials only. Even when
extreme reaction conditions were used, namely the addition of compound (LXII) to molten 4,4'-di(cyanomethylphenyl) ether no evidence of macrocycle formation was found.

The same reaction conditions were used in the attempted condensation of compound (LXII) with oxydianiline. Here again, examination of the reaction products showed the presence of starting materials only.

In an attempt to prepare the partly methine linked 'three-unit' macrocycle (LXIII), the same reaction conditions were employed as were used in the synthesis of the aza-linked analogue (LVII) from its bis-isoindoline precursor. Accordingly compound (LXII) was added to nitrobenzene and maintained at 200° for twenty minutes. No ammonia was evolved and the uncondensed starting material was recovered.
(i) **Introduction**

Recently the condensation of 1,3-diiminoisoindoline with five-membered heterocyclic diamines has been studied in detail. Some interesting macrocycles have been prepared which were capable of chelating metals. The extension of this work to cyanomethylene-linked compounds was considered. If methine-linked macrocycles could be formed they would be of particular interest in that the unsaturated system would be fully conjugated rather than cross-conjugated. In this respect they would resemble haem or phthalocyanine and might be expected to support an induced ring current.

Since guanazole was found to condense very readily with 1,3-diiminoisoindoline to give the aza-linked triazole macrocycle (LXVIII) the synthesis of the analogous methine-linked compounds was examined.

A literature search showed that the required starting material for macrocycle formation, namely, 3,5-dicyanomethyl-1,2,4-triazole (LXXII) had not been reported. However, reference was found to the preparation of the mono-cyanomethyl derivative. Klosa reported that the compound could be prepared by condensing cyanoacethydrazide with formamide.

\[
\begin{align*}
\text{HC} & \quad \text{H}_2\text{N} - \text{NH} \\
\text{NH}_2 & \quad \text{C} - \text{CH}_2\text{CN} \\
\rightarrow & \\
\text{N} & \quad \text{N} \\
\text{CH}_2\text{CN} & \quad + 2\text{H}_2\text{O}
\end{align*}
\]
The synthesis was carried out by heating the reactants on a steam bath for three hours. The reaction mixture was cooled and diluted with ethanol, whereupon a bright red solid separated out of solution. Recrystallisation from glacial acetic acid gave crystals which melted with decomposition at $300^\circ$. Spectroscopic analysis did not confirm the assigned structure. The infrared spectrum lacked the characteristic nitrile absorption band and the most abundant peak in the mass spectrum occurred at m/e 218, whereas the expected molecular ion of 3-cyanomethyl-1,2,4-triazole would have m/e 108. Brown and Polya have claimed that this bright red product is related to the red polymers obtained when cyanomethyl-triazoles or the acylamidrazone intermediates are overheated.

(ii) Synthesis of 3-Cyanomethyl-5-phenyl-1,2,4-Triazole

Postovskii and Vershchagine $^{66}$ and Brown and Polya $^{65}$ have prepared di-substituted 1,2,4-triazoles by the condensation of acylhydrazines (LXV) with imidic esters (LXIV):

\[ \text{LXIV} \quad \text{LXV} \]

\[ \text{LXVI} \quad \text{LXVII} \]
The intermediate acylamidrazones (LXVI) were found to cyclise spontaneously or under moderate conditions (mild heating or treatment with dilute alkali). 3-Cyanomethyl-5-phenyl-1,2,4-triazole (LXVII R=CH\textsubscript{2}CN, R' = C\textsubscript{6}H\textsubscript{5}) and 3-cyanomethyl-5-methyl-1,2,4-triazole (LXVII R=CH\textsubscript{2}CN, R' = CH\textsubscript{3}) were reported. It was decided to prepare these mono-cyanomethyl-substituted triazoles and to study their possible condensation with phthalonitrile. Accordingly, cyanoacetyldrazide was prepared following the method of Rotherburg\textsuperscript{67} and the methyl and methyl benzimidate hydrochloride according to the method outlined by Sah.\textsuperscript{68}

The imidic ester was added to dry methanol containing sodium hydroxide and the precipitated salt filtered. An equimolar quantity of the cyanoacetyldrazide was added to the filtrate and the mixture was refluxed for 40 minutes. The solution was concentrated and treated with ether, whereupon a cream powder was precipitated. Repeated recrystallisation from ether-light petroleum gave 3-cyanomethyl-5-phenyl-1,2,4-triazole in one case, and the substituted acylamidrazone in the other. When heated, the acylamidrazone cyclised to give 3-cyanomethyl-5-methyl-1,2,4-triazole.

(iii) Condensation of Phthalonitrile with 3-Cyanomethyl-5-phenyl-1,2,4-triazole

The condensation of one of these triazoles, namely, 3-cyanomethyl-5-phenyl-1,2,4-triazole with phthalonitrile was examined in detail. Stoichiometric proportions of
the reactants were added to ethanol containing an equivalent amount of sodium. The mixture was refluxed for 30 minutes during which time it turned a deep red colour. On cooling some of the starting materials separated out of solution. Filtration and neutralization of the filtrate with dilute hydrochloric acid yielded a yellow precipitate. Spectroscopic data indicated that this was the desired 'two-unit' compound 1-(3-cyanomethylene-5-phenyl-1,2,4-triazole)-3-iminoisoindoline (LXIX).

When the experiment was repeated with a refluxing time of 6 hours no starting materials were recovered. Instead a yellow flocculent precipitate was formed upon neutralizing the reaction mixture. Filtration and drying yielded a bright yellow powder with a melting point of 240°. The compound showed a molecular ion (the most abundant peak in the mass spectrum) of m/e 312. Two major fragment ions occur at m/e 184, corresponding to the substituted triazole and at m/e 129 corresponding to the isoindole system. Thus the major fragments arise from cleavage of the molecule into its two components. The infrared spectrum showed two sharp bands at 3300 cm⁻¹ and 3500 cm⁻¹ (NH), as well as prominent bands at 2200 cm⁻¹ (C≡N), 1640 cm⁻¹ (C=N) and 1520 cm⁻¹ (amidine). The maximum absorption in the visible spectrum occurs at 420 nm. This is at a substantially longer wavelength than the model compound 1-(phenylcyanomethylene)-3-iminoisoindoline which absorbs up to 388 nm. The phenyl in the triazole ring extends the conjugated system.
(iv) Attempted Synthesis of Bis-cyanomethyl-1,2,4-triazole

Since the condensation of phthalonitrile and 3-cyanomethyl-5-phenyl-1,2,4-triazole took place so readily, an attempt was made to synthesize the bis-cyanomethyl-triazole. Vershchagina's method for the synthesis of 1,2,4-triazoles seemed to offer the most convenient route to the di-cyanomethyl derivative. The proposed synthetic route was as follows:

\[
\begin{align*}
\text{NCH}_2\text{C} & \quad \text{C} \\
\text{C} & \quad \text{N} \\
\text{NH} & \quad \text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{EtO} & \quad \text{C} \\
\text{CH}_2\text{CN} & \quad \text{NH}
\end{align*}
\]

\[
\begin{align*}
\text{NCH}_2\text{C} & \quad \text{C} \\
\text{C} & \quad \text{NCH}_2\text{CH}_2\text{CN}
\end{align*}
\]

\[
\begin{align*}
\text{NCH}_2\text{C} & \quad \text{C} \\
\text{C} & \quad \text{N} \\
\text{CH}_2\text{CN}
\end{align*}
\]

Ethyl cyanoacetimidate hydrochloride was prepared according to the method of McElvain and Schroeder and the free base isolated. Equimolar quantities of cyanoacethydrazide and the imidic ester were refluxed in ethanol. After 15 minutes a white flocculent precipitate was formed. Filtration and drying gave a white powder with a melting point of 160°. Repeated recrystallisation from water gave a
white crystalline compound with a melting point of 164°, and microanalytical figures corresponding to C₆H₇N₅O, which is correct for the intermediate amidrazone (LXXI). A mass spectrum confirmed the elemental analysis giving a molecular ion of m/e 165. The infrared spectrum showed no strong hydroxyl absorption band at 3400 cm⁻¹ as well as prominent bands at 3200 cm⁻¹ (NH) and 2250 cm⁻¹ (C=N). There was no evidence of a carbonyl absorption band. Presumably the compound does not exist as structure (LXXI), but as a combination of the many possible tautomers.

Unexpectedly the cyclodehydration of this amidrazone was not achieved. Unlike the amidrazone precursor of 3-cyano-methyl-5-methyl-1,2,4-triazole, heating or treating with sodium hydroxide in ethanol did not result in the expected cyclisation.

(v) Condensation of Phthalonitrile with the Di(cyanomethyl)- Amidrazone (LXXI).

Despite the failure to cyclise compound (LXXI), it was decided to examine the condensation of this compound with phthalonitrile. Since the condensation is carried out in an alkaline medium the possibility that cyclisation might occur during condensation was considered.

1:1 Stoichiometric quantities of phthalonitrile and the di-(cyanomethyl)-amidrazone were added to 2-ethoxyethanol containing a catalytic amount of sodium and refluxed for
20 minutes. The reaction mixture changed from bright yellow to dark brown. On cooling a red brown product separated out of solution. Filtration and drying yielded a light brown powder which melted with decomposition at 350°.

Mass spectral analysis gave a molecular ion at m/e 717. An open-chain compound consisting of three amidrazone and two isoindole moieties has a molecular weight of 717. The fragmentation pattern of the spectrum was consistent with such a structure.

Alternative methods for the synthesis of 3,5-bis(cyanomethyl)-1,2,4-triazole were considered. Imidic esters can be easily converted to their corresponding amidines by ammonolysis. Cyanoacetamididine would be expected to condense with cyanoacethydradzide to give the desired triazole on the elimination of ammonia and water.
Cyanoacetamidine was prepared by adding ethyl cyanoacetimidate hydrochloride to a cooled saturated solution of ammonia in anhydrous ethanol. The mixture was stirred for 10 minutes and the precipitated ammonium chloride filtered. Cyanoacethydrazide was added to the filtrate, and the mixture refluxed until the evolution of ammonia ceased. On cooling a white solid separated. Repeated recrystallisation from water gave white crystals with a melting point of 240° and microanalytical figures corresponding to C₆H₇N₅. The mass spectrum showed a molecular ion at m/e 149 which confirmed the elemental analysis. The bis-cyanomethyl-triazole has a molecular weight of 147 and a formula of C₆H₅N₅.

A survey of the literature showed that the attempted condensation of cyanoacetamidine with malonic ester was studied by McElvain and Tate. These workers found that cyanoacetamidine failed to condense with malonic ester, but underwent self-condensation to give a product with the same chemical formula as that obtained above. They proposed the following mechanism for the self-condensation:

\[
\begin{align*}
\text{NCHC} &= \text{C} \left( \begin{array}{c} \text{NH}_2 \\ \text{NH}_2 \end{array} \right) \quad + \quad \text{CN} \quad \frac{\text{H}_2\text{N} - \text{C} \left( \begin{array}{c} \text{NH}_2 \\ \text{NH}_2 \end{array} \right)}{\text{NH}_3} \\
\text{NCHG} &= \text{C} \left( \begin{array}{c} \text{N} \\ \text{H} \\ \text{C} \left( \begin{array}{c} \text{NH} \\ \text{NH}_2 \end{array} \right) \right) \quad \xrightarrow{\text{LXXIII}} \quad \text{NCH}_2\text{C} \left( \begin{array}{c} \text{N} \\ \text{NH}_2 \end{array} \right) \\
\text{NCHG} &= \text{C} \left( \begin{array}{c} \text{N} \\ \text{H} \\ \text{C} \left( \begin{array}{c} \text{NH} \\ \text{NH}_2 \end{array} \right) \right) \quad \text{LXXIII} \quad \xrightarrow{\text{NCH}_2\text{C} \left( \begin{array}{c} \text{N} \\ \text{NH}_2 \end{array} \right)}
\end{align*}
\]
This anomalous behaviour of cyanoacetamidine may be the result of the low basicity of the amidine resulting from electronegativity of the nitrile group. It is interesting to note that McElvain and Tate found that carbethoxyacetamidine also behaved in this anomalous manner. These workers have also pointed out that the relatively low basicities of these amidines is evident in their preparation by the ammonolysis of the respective imidic esters in alcohol solution. In these reactions ammonium chloride precipitated from the alcohol solution. In the preparation of other amidines it was the amidine hydrochloride which precipitated from solution.

Investigations into the Condensation of Phthalonitrile with 2-Cyanomethyl-4,6-diaminopyrimidine:

The product formed by the self-condensation of cyanoacetamide is itself of interest in that it possesses three functional group theoretically capable of condensing with phthalonitrile or 1,3-diiminoisoindoline. It is potentially a starting material for a partly-methine linked macrocycle (LXXV). Original work of Elvidge and Clark \(^47\) reported that 2,4-diaminopyrimidine condensed with 3-imino-1-oxoisoindoline in 2-ethoxyethanol to give the two unit compound (LXIV). However, more recent work on the condensation of 2,6-diaminopyrimidine with 1,3-diiminoisoindoline has shown that the functional group in the 2-position is subject to electron-withdrawing effects of both of the ring nitrogen atoms and is thus less reactive than the 4-sub-
Indeed, attempts to form an aza-linked pyrimidine macrocycle by the condensation of 1,3-diiminoisoindoline with 2,6-diamino-pyrimidine failed. Since compound (LXXIII) has the cyanomethyl group in the 2-position and since the Thorpe condensation involved the formation of a carbanion, it was expected that this electron deficient character of the pyrimidine ring would increase the stability of the carbanion and thus assist condensation in the desired sense.

Attempts to condense 2-cyanomethyl-4,6-pyrimidine with phthalonitrile to give compound (LXXV) by refluxing equimolar proportions of the reactants in 2-ethoxyethanol with sodium present as catalyst proved abortive. Equally unsuccessful were attempts to condense the pyrimidine with 1,3-diiminoisoindoline using the same reaction conditions.

A closer examination of the spectroscopic data of 2-cyanomethyl-4,6-diaminopyrimidine might provide an explanation for its failure to condense with these compounds. The pyrimidine ring proton in the 5-position would be expected to produce a signal at 2.63 γ. The position of the cyanomethyl protons can be predicted using the Modified Shoolery Rules:

\[ \gamma_{-\text{alkyl}} = 9.767 - \sum_{i} \delta_{i\text{eff}} \]

where \(\gamma_{-\text{alkyl}}\) is the proton frequency in the system.
$x' - \text{CH}_2 x^2$ and $\sigma_{\text{eff.}}$ is the effective shielding constant of $x^i$. The term 9.676 is the $\gamma$-value of methane. On this basis the cyanomethyl protons should provide a signal at:

$$\gamma = 9.797 - 1.7 + 2.2)$$

$$= 5.8 \gamma.$$

The p.m.r. spectrum of compound (LXXIII) shows no signals at either of these two frequencies. Instead a singlet of two-proton intensity occurs at 4.9 $\gamma$ and a multiplet of four proton intensity occurs at 4.2 $\gamma$. On deuteration the multiplet disappears.

Thus no assignment of signals can be made which would correspond to the substituted pyrimidine (LXXIIIb). A tentative assignment can be made for the tautomer (LXXIIIA). The singlet at 4.9 $\gamma$ can be ascribed to the two olefinic protons and the other lines near 4.2 $\gamma$ to the N-H protons.

If the compound exists in the tautomeric form (LXXIIIA) as suggested by the p.m.r. spectrum, then its ability to
undergo the Thorpe condensation with phthalonitrile perhaps might be reduced.
CHAPTER 7
(i) **Condensation of Phthalonitrile with 2-Cyanomethyl-thiophene:**

Another cyanomethyl-substituted five-membered heterocyclic compound which might be capable of condensing with phthalonitrile to form a macrocycle or polymeric compounds could be derived from thiophene. Indeed polymeric materials reported to be related to phthalocyanine and to aza-linked benzene macrocycles have been formed from 2,5-diamino-3,4-dicyanothiophene. 74,75

Before embarking on the synthesis of 2,5-dicyanomethylthiophene the condensation reaction of phthalonitrile and the monosubstituted compound was studied in detail.

Equimolar quantities of phthalonitrile and 2-cyanomethyl-thiophene were added to dry ethanol containing an equivalent amount of sodium. The mixture was stirred at room temperature until all the phthalonitrile had dissolved and then refluxed for 4 hours. After cooling the reaction mixture and neutralizing it with dilute hydrochloric acid, a yellow-orange solid precipitated. Purification of the product on a column of alumina, using benzene/ethyl acetate as eluent gave a yellow powder with a melting point of 184°. Elemental microanalysis gave an empirical formula of $C_{14}H_{9}N_3S$ which is consistent with the structure (LXXVI) assigned to the product.

The mass spectrum of the product showed a molecular ion at m/e 251. A major fragment ion occurs at m/e 123, corresponding to the cyanomethylthiophene portion of the molecule.
plus 2H and another at m/e 129 corresponds to isoindole system less 1H. Thus the major fragments arise from the cleavage of the protonated molecule into its two components.

The infrared spectrum showed the presence of sharp bands at 3450 cm\(^{-1}\) and 3380 cm\(^{-1}\) attributable to N-H stretching modes. Sharp bands also occur at 2220 cm\(^{-1}\), 1660 cm\(^{-1}\) and 1540 cm\(^{-1}\) attributable to C=\(\equiv\)N, C=N and NH deformation respectively.

The compound (LXXVI), in which the thiophene ring is conjugated with the isoindole nucleus, has a maximum wavelength absorption band at 416 nm. There is here a bathochromic shift much larger than expected, the maximum wavelength absorption band of 1-phenylcyanomethylene-3-iminoisoindoline (XVIII) occurring at 388 nm. The morpholino-derivative of (XVIII), with its fixed bond isoindole structure absorbed at the longer wavelength of 412 nm. It seems that compound (LXXVI), in solution, exists in the aminoisouindole form B rather than the iminoisoindoline form A.
This was surprising since the aza-linked 'two-unit' compound (LXXVII) has a maximum absorption of 355 nm which closely parallels that of 1-imino-3-phenyliminoisoindoline in both position (360 nm) and intensity.

The p.m.r. spectrum of compound (LXXVI) showed a singlet at 1.2 $\gamma$ of two-proton intensity attributable to the NH protons. Another low field signal also occurred at 1.6 $\gamma$ attributed to the $H_A$ proton of the isoindole ring, deshielded by the sterically adjacent nitrile group. Ill-resolved multiplets occurred at 2.0 $\gamma$ and 2.3 $\gamma$ of one and two proton intensity respectively. These were attributed to the remaining protons of the isoindole ring. Two other multiplets occurred, centred at 2.5 $\gamma$ and 2.9 $\gamma$ of two and one proton intensity respectively. These were attributed to the $\beta$ and $\alpha$ protons of the thiophene ring.
2-Cyanomethylthiophene and phthalonitrile in 2:1 stoichiometric proportions condensed to give the three-unit compound 1,3-di(2-cyanomethylenethiophene)-isoindoline (LXXVII). Initial attempts to prepare this compound by refluxing the reactant in n-propanol with sodium present as catalyst resulted in the formation of the two-unit compound (LXXVI) only. However, when n-butanol was used as solvent and the reactants refluxed for 48 hours the desired three-unit compound was obtained.

Because of its insolubility, attempts to purify this compound were unsuccessful. However, the structure was established by spectroscopic data. The mass spectrum showed a molecular ion at m/e 357. Two major fragments occurred at m/e 246 and m/e 123, corresponding to a cleavage of the type encountered before. The light absorption spectrum of compound (LXXVII) showed a maximum wavelength band at 424 nm. This represented a bathochromic shift of only 8 nm over the 'two-unit' compound (LXXVI) and may indicate that compound (LXXVII) exists in the aminoisooindole form, since the removal of any contribution from an endo-cyclic form will reduce the longest wavelength absorption and this is slightly more than compensated by the addition of a thiophene ring to the conjugated system.
(ii) **Preparation of 2,5-bis-cyanomethylthiophene:**

Since no difficulties were encountered in condensing phthalonitrile and 2-cyanomethylthiophene, it was decided to extend this study to the condensation of phthalonitrile and 2,5-bis-cyanomethylthiophene with the objective of synthesising the methine linked thiophene macrocycle (LXXIX).

The synthesis of 2,5-bis-cyanomethylthiophene has been reported in the literature \(^{76,77}\) and involves the following reaction scheme:
When added to a cooled solution of formalin and hydrochloric acid, thiophene underwent chloromethylation in the 2 and 5-positions quite readily. After the reaction mixture was stirred for 20 minutes the oily layer was siphoned off and washed with cold water. On refrigeration, it solidified to give pale brown crystals with a melting point of 42°. This crude bis-chloromethylthiophene was added portionwise to a stirred mixture of sodium cyanide in anhydrous dimethylformamide. There was an immediate increase in temperature and the solution rapidly darkened. Cooling was applied to maintain a temperature below 90°. After the reaction mixture had been stirred at room temperature for 2 hours, it was extracted with chloroform. Evaporation of the solvent gave a brown oil which on refrigeration gave the yellow-brown solid 2,5-bis-cyanomethylthiophene.

ii) Condensation of Phthalonitrile with 2,5-bis-cyanomethylthiophene:

Condensation of the crude 2,5-bis-cyanomethylthiophene with phthalonitrile was achieved by refluxing equimolar quantities of the reactants in 2-ethoxyethanol containing sodium as catalyst. After a reaction time of 4 hours a brown-black solid precipitated. Filtration and drying yielded a highly insoluble powder with a melting point greater than 350°. One of the most abundant peaks in the mass spectrum of this product occurred at m/e 563 which is correct for the uncyclised 'four-unit' compound (LXXX). Intense peaks also occurred for higher m/e values, indicating the product contained polycondensation products.
In a recent study of the interaction of 1,3-diiminoisoindoline with 2,5-diamino-3,4-dicyanothiophene it was concluded that, contrary to a previous report in the literature the aza-linked thiophene macrocycle (LXXXI) could not be formed. The factors which prevent the formation of the aza-linked macrocycle would also prevent the formation of the methine-linked macrocycle. The geometry of the thiophene ring is such that the cyanomethyl groups in the 2 and 5 positions are close to a linear orientation with respect to each other.

Thus the sterochemical arguments used to explain the failure of p-dicyanoxylylene to form macrocycles (Chap. III) also apply in the present case.
CHAPTER 8
1. All condensation reactions carried out between phthalonitrile and cyanomethylene compounds were stirred magnetically and protected from water vapour by soda-lime drying tubes.

2. All solvents were dried and distilled before use.

3. Elemental microanalyses were carried out by:
   
   Dr Alfred Bernhardt,
   Mikroanalytisches Laboratorium
   5251 Elbach uber Engelskirchen
   Fritz-Pregl-Strasze 14-16
   West Germany.

   or

   Microanalytical Services,
   Dept. of Chemistry,
   University of Surrey,
   Guildford,
   Surrey.

4. All melting points are uncorrected.

5. Infra-red spectra were recorded on a Unicam SP 200 Spectrophotometer. Samples were prepared as mulls in Nujol, hexachlorobutadiene and fluorolube. The instrument was calibrated using the 1601 cm$^{-1}$ or 1029 cm$^{-1}$ bands of polystyrene. Absorption band intensities are indicated by the following letters in parenthese after each frequency value:
   
   s = strong; m = medium; w = weak.
The calculation of shifts in the wavelength of absorption of deuterated species was carried out using the following equations and approximations.

The relationship between the wavenumber of the absorption band arising from the band x-y in the diatomic molecule xy and the masses of the relevant atoms is given by the equation:

\[ v_{x-y} = \frac{1}{2\pi c} \sqrt{\frac{K}{M_x M_y}} \frac{1}{M_x + M_y} \]  

(1)

Where:

- \( \nu \) = Fundamental stretching frequency in cm\(^{-1}\)
- \( c \) = Velocity of light.
- \( K \) = Force constant of the X-Y band.
- \( M_x \) = Mass of X.
- \( M_y \) = Mass of Y.

For a molecule containing an X-Y band, where the mass of X is much greater than that of H and the X-H vibration does not mix with other vibrations, then the following approximation can be made:

If \( M_x \gg M_y \)

Then \( \frac{M_x M_H}{M_x + M_H} \approx \frac{M_x M_H}{M_x} = M_H \)  

(2)

Hence \( v_{X-H} = \frac{1}{2\pi c} \sqrt{\frac{K}{M_H}} \)
Similarly \( \sqrt{X-D} = \frac{1}{2 \sqrt{K}} \sqrt{\frac{K}{M_D}} \)

Thus providing \( K_{X-H} \approx K_{X-D} \)

Then \( \frac{\sqrt{X-H}}{\sqrt{X-D}} = \sqrt{\frac{M_D}{M_H}} = \sqrt{2} = 1.414 \ldots \ldots \ldots (3) \)

Thus providing the molecule is heavy enough, exchanging an 
X-H bond by an X-D bond should move the absorption frequency 
to a lower value by an amount approximately equal 0.707 times 
the original frequency.

6. Ultra-violet and visible light spectra were recorded as 
solutions on a Unicam SP800 spectrophotometer. Points of 
inflection are indicated by an asterisk (*) following the 
wavelengths at which they appear. Molar extinction co-
efficient values are calculated from the equation:

\[ e = \frac{A}{c \cdot l} \]

Where 
- \( e \) = Molar Extinction coefficient 
- \( A \) = Absorbance 
- \( c \) = Molar concentration 
- \( l \) = Pathlength (1cm)

7. Mass spectra were recorded on an AEI MS12 Mass Spectro-
meter. Samples were introduced into the instrument using 
a direct insertion probe.

8. Proton Magnetic Resonance Spectra were recorded on a Perkin 
Elmer R10 instrument operating at 60 MHz. and at a temperature
of $34^\circ$. Spectra were recorded in deuterochloroform, dimethyl-
sulphoxide and N-methyl-2-pyrrolidone. Tetramethyilsilane
was used as internal reference. Signal multiplicities are
indicated by the following letters in parenthesis after
each value:

- $s$ = singlet;
- $d$ = doublet;
- $t$ = triplet;
- $q$ = quadruplet;
- $m$ = multiplet.
(ii) 1-\(\alpha\)-Cyanobenzylidene-3-iminoisoindoline

To a solution of sodium ethoxide from sodium (0.92g, 0.04 mol) in dry ethanol (50 ml) phthalonitrile (5.12g, 0.04 mol) and benzyl cyanide (4.68g, 0.04 mol) were added. The solution was swirled to dissolve the phthalonitrile. The reaction mixture immediately turned dark red. After 15 minutes stirring, a reddish yellow solid began to separate from solution. The reaction mixture was allowed to stand for 20 minutes and then poured into water (50 ml) 2N-hydrochloric acid (20 ml) was added producing a dark yellow solid (8.1g, 82%) which decomposed above 350°. Repeated recrystallisation from nitrobenzene gave yellow crystals which melted at 285°. Molecular ion m/e 245.

P.m.r. (Acetone) 1.3\(\tau\) (b,s) 2 protons, 1.55\(\tau\) (m) 1 proton, 1.9 \(\tau\) (m) 3 protons, 2.5 \(\tau\) (m) 5 protons.

\(\nu_{\text{max}}\) (Nujol): 3460 (w) (NH); 2200 (s) (C\(=\)N); 1660 (s) (C\(=\)N); 1605 (w), 1590 (w) (C=C); 1525 (s) (amidine); 1300 (w), 1215 (s), 1165 (w), 1145 (w) and 1090 (s), 770 (s), 745 (s) and 700 (s) cm\(^{-1}\) (aryl C-H).

\(\lambda_{\text{max}}\) (96% EtOH): 212, 239, 388 nm. (\(\varepsilon\): 33320, 34545, 27440 respectively).

Found: C, 78.17; H, 4.68; N, 17.28.

C\(_{16}\)H\(_{11}\)N\(_3\) requires C, 78.35; H, 4.52; N, 17.13%.

Hydrochloride

1-\(\alpha\)-Cyanobenzylidene-3-iminoisoindoline (2.45g, 0.01 mol) was dissolved in ethanol (30 ml) and 3N-hydrochloric acid
(10 ml) was added. On standing a yellow solid precipitated
(2.29g, 81%). The compound was recrystallised from methanol
to give the hydrochloride, m.p. 220°(decomposition).

$\nu_{\text{max.}}$ (Nujol): 3460 (w) (NH); 2200 (s) (C≡N); 1690
(s) (C=N); 1625 (m), 1610 (w) and 1595 (w) (C=C); 1290
(w), 1260 (s), 1160 (w), 1120 (w), 1090 (s), 760 (s), 730
(s) and 700 (w) cm$^{-1}$ (aryl C-H).

$\lambda_{\text{max.}}$ (96% EtOH): 209, 236, 270, 358 nm ($\varepsilon$: 27540,
33720, 16860, 29790 respectively).

Found: C, 68.04; H, 4.46; Cl, 12.62; N, 14.76 Calc. for
C$_{16}$H$_{12}$ClN$_{3}$: C, 68.21; H, 4.29; Cl, 12.58; N, 14.92%.

$\alpha$-Cyanobenzylidene-3-oxoisooindoline

$\alpha$-Cyanobenzylidene-3-iminoisooindoline (4.9g, 0.02 mol)
was dissolved in ethanol (100 ml) and 3N-hydrochloric acid
(20 ml) was added. The solution was refluxed for 4 hours.
The hot solution was neutralized with 3N-sodium hydroxide.
On cooling, $\alpha$-cyanobenzylidene-3-oxoisooindoline separated
as pale yellow crystals (3.5g, 70%). Recrystallisation
from ethanol/benzene (3:1) gave a bright yellow crystallline
compound which melted at 228°. Molecular Ion m/e 246.

P.m.r. (DMSO) $-1.1 \gamma$ (s) 1 proton; $1.5 \gamma$ (m) 1 proton;
2.1 $\gamma$ (m) 3 protons; 2.45 $\gamma$ (m) 5 protons;

$\nu_{\text{max.}}$ (Nujol): 3300 (s) (NH); 2200 (s) (C≡N) 1730 (s)
(C=O); 1610 (s) and 1590 (w) (C=C); 1300 (s) 1250 (w),
1200 (w), 1160 (w), 1140 (m), 1090 (m), 1020 (m), 790
(w), 770 (s), 695 (s) and 690 (s) cm$^{-1}$ Aryl (C-H).

$\lambda_{\text{max.}}$ (96% EtOH): 227, 293, 344 nm ($\varepsilon$: 20 172, 9840,
18200 respectively).
The Self-Condensation of 1-α-Cyanobenzylidene-3-iminoisoindoline.

1-α-Cyanobenzylidene-3-iminoisoindoline (XVIII) (2.45 g, 0.01 mol) was heated in a nitrogen atmosphere to 230° approximately and maintained at that temperature for 90 minutes. The colour of the compound changed from orange to dark red and ammonia was evolved. After extractive crystallisation (Soxhlet) from benzene, dark red needles of the condensation product (XXI) were obtained which melted at 310°.

m/e (M+) 473, (M++) 236.5 P.m.r. (CDCl₃) 1.5 τ (m) 2 protons, 2.2 τ - 3.0 τ (m) 16 protons.

V max. (Nujol): 2200 (s) (C=N); 1600 (bs) (C=C and C=N); 1260 (m), 1180 (m), 1150 (w), 1120 (w), 1100 (w), 760 (s), 720 (w) and 680 (s) cm⁻¹ (Aryl C-H).

λ max. (96% EtOH): 490, 400, 345 nm (ε: 14 200, 11500 and 39000 respectively).

Found: C, 81.43; H, 4.22; N 14.74.
Calculated for: C₃₂H₁₉N₅: C, 81.17; H, 4.02; N, 14.80%

Hydrolysis of Compound (XXI):

Compound (XXI) (0.095g, 0.0002 mol) was suspended in a mixture of ethanol (75 ml) and conc. hydrochloric acid (75 ml). The suspension was refluxed for 18 hours. The solution was neutralized with aqueous sodium hydroxide, whereupon a yellow solid separated. Recrystallization from ethanol/
benzene (3:1) gave 1-α-cyanobenzylidene-3-oxoisooindoline (0.089g., 91%), m.p. 227 - 230°, mixed m.p. 228°.

1,3-Bis-α-cyanobenzylidene-isoindoline:

(1) To a solution of sodium ethoxide from sodium (2.2g, 0.10 mol) and dry ethanol (50 ml), phthalonitrile (6.4g, 0.05 mol) and benzyl cyanide (11.70g, 0.10 mol) were added. The solution was swirled to dissolve the phthalonitrile and the reaction mixture refluxed for 6 hours. Filtration yielded a reddish brown powder (9.8g).
Spectroscopic data indicated that the compound was 1-α-cyanobenzylidene-3-iminoisoindoline.

(2) The above experiment was repeated with a reaction time of 30 hours, but the same product resulted.

(3) To a solution of sodium butoxide from sodium (2.2g, 0.10 mol) in dry n-butanol (50 ml), phthalonitrile (6.4g, 0.05 mol) and benzyl cyanide (11.70g, 0.10 mol) were added. The mixture was swirled to dissolve the reactants. It immediately turned dark red. The mixture was refluxed under a stream of nitrogen for 48 hours. By this time a dark brown precipitate had been formed. The n-butanol was reduced in volume and the residue was taken up in ethanol (100ml). The ethanolic solution was decanted into an excess of water (300ml), and the brown precipitate was allowed to coagulate. Filtration and drying yielded a solid (10.8, 63%). Extractive crystallisation (Soxhlet)
from methanol gave bright yellow crystals, m.p. 192°.

m/e (M+) 345. P.m.r. (CDCl₃) 1.4 γ (m) 2 protons; 2.1 γ (m) 2 protons; 2.55 γ (m) 10 protons,

ν max. (Nujol): 3500 (b) (N-H); 2200 (s) (C=≡N); 1620 (bs) (C≡N); 1260 (w), 1215 (m), 1150 (w), 1110 (w), 780 (s), 730 (w) and 700 (s) cm⁻¹ (Aryl C-H);

λ max. (96% EtOH): 230, 260⁺, 310, 412 nm (ξ: 26740, 20700, 15720, 16220 respectively).

Found: C, 83.45; H 4.39; N, 12.41.

Calc. for C₂₄H₁₅N₃: C, 83.46; H, 4.38; N, 12.17%.

1-(α-Cyano-4-cyanomethylbenzylidene)-3-iminoisoindoline:

To a solution of sodium ethoxide from sodium (0.69g, 0.03 mol), in dry ethanol (25ml) p-dicyanoxylylene (4.68g, 0.03 mol) and phthalonitrile (3.84g, 0.03 mol) were added. The reaction mixture was stirred at room temperature under a stream of nitrogen for 4 hours. A yellow colour developed rapidly, gradually turning dark brown. The mixture was poured into water (200 ml) with vigorous stirring. A slight excess of 2N-hydrochloric acid was added, causing the finely divided precipitate to coagulate (yield, 6.7g, 78.6%). Extractive crystallisation (Soxhlet) from methanol gave bright yellow crystals, m.p. 283°. m/e (M⁺) 284.

P.m.r. (DMSO) 1.4 γ (m) 2 protons; 1.6 γ (m) 1 proton
1.9 γ (m) 3 protons; 2.5 γ (m) 4 protons.

ν max. (Nujol): 3450 (w) (N-H); 2200 (s) (C≡N); 1665 (s) (C≡N); 1605 (w) (C≡N); 1530 (s) (amidine); 1320 (m), 1250 (m), 1210 (s), 1160 (w), 1110 (w), 770 (s), 740 (m) and 700 (s) cm⁻¹ (Aryl C-H).
Amax. (EtOH): 242, 294, 388 nm (ε: 21560, 8520, 17948).

Found: C, 76.19; H 4.43; N, 19.52. Calc. for C_{18}H_{12}N_{4}:
C, 76.04; H, 4.2; N, 19.71%.

1-(α-Cyano-4-cyanomethylbenzylidene-3-oxoisoindoline:

1-(α-Cyano-4-cyanomethylbenzylidene-3-iminoisoindoline
(5.68g, 0.02 mol) was dissolved in ethanol (100 ml) and
2N-hydrochloric acid added (20ml). The solution was
refluxed for 4 hours. The hot reaction mixture was neutralized with 2N-sodium hydroxide solution. On cooling a
yellow brown precipitate separated from solution. Filtra­
tion and drying gave 4.2g (74% yield) of 1-(α-cyano-4-cyano-
methylbenzylidene-3-oxoisoindoline. Extractive crystallisa­
tion (Soxhlet) from methanol gave light brown needles, m.p.
258°. m/e (M⁺) 285. P.m.r. (DMSO) 1.55 γ (m), 1 proton;
2.2 γ (m), 3 protons; 2.5 γ (m), 4 protons;

ν max. (Nujol): 3400 (w) (N-H); 2200 (s) (C=N); 1720
(s) (C=O); 1620 (s) (C=C); 1300 (m), 1290 (w), 1215
(m), 1160 (w), 1110 (m), 880 (w), 850 (m), 770 (s), 740
(w) and 700 (m) cm⁻¹ (Aryl C-H).

Amax. (96% EtOH): 227; 240; 290; 342 nm. (ε:19 380,
10540, 10690, 19520 respectively.)

Found: C, 75.67; H 4.07; N, 14.73; Calc. for C_{18}H_{11}N_{3}O:
C 75.78; H 3.89; N, 14.73%

1,4-Bis [cyano(3-imino-1-isoindolinylidene)methyl] -benzene:

To a solution of sodium ethoxide from sodium (0.46g, 0.02
mol) in dry ethanol (60ml) p-dicyanoxylylene (1.56g, 0.01
mol) was added and dissolved by swirling. Phthalonitrile (2.56g, 0.02 mol) was added to the solution, and the mixture was stirred at room temperature for 20 hours. The reaction was carried out in a nitrogen atmosphere. The mixture was decanted into an excess of water (500 ml) and neutralized with 3N-hydrochloric acid (10 ml). On neutralization, the fine precipitate coagulated. Filtration and drying gave 3.67g. (89% yield) of a dark red powder. Recrystallisation from N-methyl-2-pyrrolidone gave bright yellow crystals of 1,4-bis-[cyano(3-imino-l-isoindolinylidene) methyl] benzene (XXV), m.p. 312° m/e (M⁺) 412. P.m.r. (DMSO): 1.3 γ (s), 4 protons; 1.55 γ (m), 2 protons; 1.7 γ (s), 4 protons; 2.0 γ (m), 2 protons; 2.4 γ (m), 4 protons;

γ max. (Nujol): 3500 (s) (NH); 2200 (s) (C=N); 1660 (s) (C=N); 1600 (w) (C=C) 1530 (s) (amidine); 1260 (m), 1200 (s), 1160 (s), 1150 (m), 1110 (m), 870 (w), 840 (w), 760 (s), 740 (w) and 710 (w) cm⁻¹ (aryl C-H).

λ max. (DMF): 464, 395, 372 nm (ε; 32000, 16150, 13500 respectively).

Found: C, 75.58; H, 3.80; N, 20.53.
Calc. for C₂₆H₁₆N₆: C, 75.71; H, 3.91; N, 20.38%

Hydrolysis of 1,4-Bis [cyano(3-imino-l-isoindolinylidene) methyl] benzene:

1. 1-4-Bis [cyano(3-imino-l-isoindolinylidene)methyl] benzene (0.412g, 0.001 mol) was suspended in concentrated hydrochloric acid (20ml) and refluxed gently for 30 minutes. The product
did not dissolve and was recovered unchanged on cooling the solution.

2. Compound (XXV) (0.412g, 0.001 mol) was stirred with warm concentrated sulphuric acid for 30 minutes, after which the deep orange colour of the solution had faded and crystals began to separate. The mixture was cooled in ice, and phthalimide was then collected (0.216g), m.p. and mixed m.p. 228-230°.

Synthesis of 1,4-Bis cyano-3-imino-1-isoindolenylidene)methyl benzene (XXV):

To a solution of sodium ethoxide from sodium (0.23g, 0.01 mol) and dry ethanol (100 ml) phthalonitrile (1.28g, 0.01 mol) and 1-(4-cyanomethylphenyl cyanomethylene)-3-imino-isoindoline (2.84g, 0.01 mol) were added. The mixture was stirred at room temperature until the reactants had dissolved, and then refluxed for 30 minutes under a stream of nitrogen. On decanting the cooled solution into an excess of water (250ml) and neutralization with 2N-hydrochloric acid, an orange-coloured precipitate formed (yield, 3.46g, 84%). Recrystallisation from N-methyl-2-pyrrolidone gave bright yellow crystals of 1,4-Bis [cyano-3-imino-1-isoindolenylidene)methyl benzene (XXV), m.p. and mixed m.p. 310 - 312°.

1,3-Bis(N-cyano-4-cyanomethylbenzylidene)-isoindoline:

To a solution of sodium butoxide, from sodium (2.2g, 0.10
mol) in dry n-butanol (150 ml) phthalonitrile (6.4g, 0.05 mol) and p-dicyanoxylylene (15.6g, 0.10 mol) were added. The mixture was stirred at room temperature until the reactants dissolved and was then refluxed under a stream of nitrogen for 48 hours. Ammonia was evolved. By this time a black deposit had separated from solution. Filtra­tion yielded 6.3g. The filtrate was reduced in volume and the residue was taken up in ethanol (100ml). The ethanolic solution was decanted into an excess of water (300 ml) and the brown precipitate formed was allowed to coagulate. Filtration and drying yielded a solid (11.84g, 58%), m.p. 294°. m/e (M⁺) 423.

νmax. (Nujol): 3400 (b,w) (N-H); 2200 (s) (C≡N); 1620 (s) (C≡N) and (C=C); 1270 (w), 1215 (m), 1110 (w) (aryl C-H), 780 (s), 720 (w) and 700 (w) cm⁻¹ (aryl C-H).

λmax. (96% EtOH): 237, 260 310 412 nm (ε:18170, 13800, 14040, 15830).

3-Morpholino-l-κ-cyanobenzylidene-isoindoline:

l-κ-Cyanobenzylidene-3-iminoisoindoline (7.35g, 0.03 mol), morpholine (2.55g, 0.03 mol, redistilled) and ethanol (80ml) were heated under reflux for 24 hours. Ammonia was evolved during the refluxing period. The hot solution was treated with charcoal, evaporated to small bulk, and cooled. The 3-morpholino-l-κ-cyanobenzylidene-isoindoline crystallised from benzene to give bright yellow needles (6.39g, 68%), m.p. 176°. m/e (M⁺) 313.
P.m.r. (DMSO) 1.5 χ (m), 1 proton, 1.9 χ (m), 3 protons, 2.5 χ (m), 5 protons.

ν max. (Nujol): 2200 (s) (C≡N); 1760 (s) (C=N); 1600 (w) (C=C); 1320 (m), 1250 (w), 1210 (s), 1160 (w), 1150 (w), 1090 (m), 770 (s), 750 (m) and 700 (s) cm⁻¹ (Aryl C-H).

λ max. (96% EtOH): 246, 258, 320 and 415 nm (ε: 18900, 17140, 8060, 18650).
Condensation of Phthalonitrile with p-Dicyanoxylylene

(a) To a solution of sodium butoxide from sodium (0.92g, 0.04 mol) in dry n-butanol (40 ml), phthalonitrile (5.12g, 0.04 mol) and p-dicyanoxylylene (6.24g, 0.04 mol) were added. The reaction mixture was refluxed under a stream of nitrogen for 48 hours, the colour changing from an initial bright yellow to a dark brown. The solvent was reduced in volume and the residue was taken up in ethanol (100 ml). The ethanolic solution was poured into an excess of water with vigorous stirring. Neutralization with 2N-hydrochloric acid (20 ml) produced a light brown precipitate. Filtration and drying gave 9.2g (81%) of 1-(α-cyano-4-cyano-methylbenzylidene)-3-iminoisoindoline (XXIII), m/e 284 (M^+).

(b) To a suspension of sodium hydride (0.72g, 0.03 mol) in dry dimethylformamide (40 ml) were added phthalonitrile (3.84g, 0.03 mol) and p-dicyanoxylylene (4.68g, 0.03 mol). The reaction mixture was refluxed under an atmosphere of nitrogen for 24 hours. Dilution with water (200 ml) gave a brown flocculent precipitate. Filtration and drying yielded 6.3g (74.2%) of compound (XXIII), m/e 284 (M^+).

(c) To a suspension of sodium hydride (0.48g, 0.02 mol) in dry dimethylformamide (50 ml) were added phthalonitrile (2.56g, 0.02 mol) and p-dicyanoxylylene (1.56g, 0.01 mol). The reaction mixture was refluxed under an atmosphere of nitrogen for 24 hours. Dilution with water gave a reddish brown precipitate. Filtration and drying yielded 3.48g (84.5% yield) of 1,4-bis[α-cyano-(3-imino-1-isoindolinylylidene)methyl]benzene (XXV), m/e 412 (M^+).
(d) To molten p-dicyanoxylylene (7.80g, 0.05 mol) maintained at 200° under a nitrogen atmosphere, phthalonitrile (1.92g, 0.015 mol) and sodium hydride (0.72g, 0.03 mol) were added. The reaction mixture was maintained at 200° for 30 minutes. After being cooled, the black molten mass was extracted (Soxhlet) with dry dimethylformamide (100 ml). Dilution with water gave a dark brown flocculent precipitate. Filtration and drying yielded 1.14g (18%) of 1,3-di-(4-cyanomethylphenylcyanomethylene)-isoindoline (XXVII), m/e 423. The insoluble residue was identified as phthalocyanine.

Attempted Condensation of 1,4-Bis \[
\text{cyano-(3-imino-1-isoin-dolinylidene)methyl}\] benzene (XXV) with p-Dicyanoxylylene

(a) Compound (XXV) (4.12g, 0.01 mol) and p-dicyanoxylylene (1.56g, 0.01 mol) were added to a solution of sodium butoxide from sodium (0.46g, 0.02 mol) in dry n-butanol (100 ml). The reaction mixture was refluxed for 24 hours. The solvent was reduced in volume and the residue taken up in ethanol (100 ml). A brown solid precipitated out of solution. Filtration and drying gave 3.34g (81% yield) of unreacted compound (XXV), m/e 412 (M⁺).

(b) To a suspension of sodium hydride (0.48g, 0.02 mol) in dry dimethylformamide (50 ml), compound (XXV) (4.12g, 0.01 mol) and p-dicyanoxylylene (1.56g, 0.01 mol) were added. The reaction mixture was refluxed for 48 hours. Cooling and diluting with water (100 ml) gave a dark brown precipitate. Filtration and drying yielded 3.67g (91% recovery) of compound (XXV), m/e 412 (M⁺).
Attempted Condensation of 1,3-di(4-cyanomethylphenylcyano-
methylene)-isoindoline (XXVII) with phthalonitrile:

(a) To a solution of sodium butoxide from sodium (0.46g, 0.02 mol) in dry n-butanol (100 ml) compound (XXVII)(4.23g, 0.01 mol) and phthalonitrile (1.20g, 0.01 mol) were added. The reaction mixture was refluxed under a stream of nitrogen for 48 hours. The solvent was reduced to small volume and the residue was taken up in ethanol. A brown-black precipitate separated. Filtration and drying yielded a black solid. Dimethylformamide extraction (Soxhlet) of the solid and subsequent dilution of the extract gave the uncondensed starting material (XXVII) (3.68g, 87% recovery).

(b) Compound (XXVII)(4.23g, 0.01 mol) and phthalonitrile (1.28g, 0.01 mol) were added to dry dimethylformamide (50 ml) containing sodium hydride (0.48g, 0.02 mol). The resulting mixture was refluxed under a stream of nitrogen for 48 hours. On cooling, a blue-black solid separated. Filtration and drying gave phthalocyanine (0.63g). The filtrate was diluted with water whereupon a brown precipitate was formed. Filtration and drying yielded compound (XXVII) (3.16g, 74% recovery).

Attempted Condensation of 1,4-Bis[cyano(3-imino-1-isoin-
dolinyldene) methyl] benzene (XXV) and aromatic diamines.

(i) With p-Phenylenediamine

(a) Compound (XXV) (5.12g, 0.01 mol) and p-phenylenediamine (1.08g, 0.01 mol) were added to dry n-butanol (50 ml). The reaction mixture was refluxed in a nitrogen atmosphere
for 48 hours. No detectable amounts of ammonia were evolved during the course of the reactions. The solvent was reduced to small volume and the residue was taken up in ethanol. A light brown powder separated out of solution. Filtration and drying yielded the uncondensed starting material, compound (XXV) (3.44g, 81.6% recovery), m/e 412 (M⁺).

(b) Compound (XXV) (4.12g, 0.01 mol) and p-phenylenediamine (1.08g, 0.01 mol) were added to dry dimethylformamide (50 ml). The reaction mixture was refluxed for 48 hours in an atmosphere of nitrogen. No ammonia was evolved during the course of the reaction. Upon cooling and diluting with water, a light brown precipitate was formed. Filtration and drying yielded the uncondensed starting material, compound (XXV) (3.6g, 87.4% recovery), m/e 412 (M⁺).

(ii) With m-Phenylenediamine
Reaction conditions as in (i). Starting material recovered unchanged.

(iii) With 2,6-Diaminopyridine
Reaction conditions as in (i). Starting material recovered unchanged.

(iv) With 2,7-diaminoanthraquinone
Reaction conditions as in (i). Starting material recovered unchanged.

(v) With 2,8-Diaminoacridine
Reaction conditions as in (i). Starting material recovered unchanged.
Condensation Reactions of 1-(α-Cyano-4-cyanomethylbenzylidene)-3-iminoisoindoline (XVIII) and aromatic diamines.

(i) With p-Phenylenediamine

Compound (XVIII) (2.84 g, 0.01 mol) and p-phenylenediamine (1.08 g, 0.01 mol) were added to dry n-butanol (50 ml). The mixture was swirled at room temperature until the reactants had dissolved. The solution was then refluxed for 12 hours, by which time the evolution of ammonia had ceased. The solvent was reduced to small volume and the residue was taken up in ethanol (80 ml). The ethanolic solution was decanted into an excess of water (250 ml) with vigorous stirring. A light brown flocculent precipitate was formed. Filtration and drying yielded 3.18 g (84.9%) of 1-(α-cyano-4-cyanomethylbenzylidene)-3-(4-aminophenyl-imino)-isoindoline (XXXVIIA) m.p. 310°, m/e 375 (M+).

υmax. (Nujol)

345 (s) (NH); 2200 (s) (C=O); 1650 (s) (C=O); 1605 (w), 1500 (w) (C=C); 1520 (s) amidine; 1310 (w), 1280 (s), 1220 (w), 1170 (w), 1150 (w), 1120 (w), 770 (s) and 700 (s) cm⁻¹ (aryl C-H).


Found: C, 76.7; H, 4.6; N, 17.7. C24H17N5 required C, 76.7; H, 4.6, N, 18.65%.
(ii) With m-Phenylenediamine

Compound (XVIII) (2.84g, 0.01 mol) and m-phenylenediamine (1.08g, 0.01 mol) were added to dry n-butanol (50 ml). The reaction mixture was swirled at room temperature until the reactants had dissolved and was then refluxed for 12 hours, during which time ammonia was evolved copiously. The solvent was reduced to small volume and the residue taken up in ethanol (80 ml). The ethanolic solution was diluted with water whereupon a brown precipitate separated out of solution. Filtration and drying yielded 2.87g (76.4% yield) of crude 1-(α-cyano-4-cyanomethylbenzylidene)-3(amo-no-phenylimino)-isoindoline (XXXVIIIB). Repeated extraction (Soxhlet) from dimethyl formamide gave a light brown powder, m.p. 303°C (decomp.) m/e 375 (M+).

\[ \text{\( \nu_{\text{max.}} \) (Nujol)} \]

3450 (s) NH; 2200 (s) (C≡N); 1650 (s) (C=N) 1610 (w), 1590 (w) (C=C); 1520 (s) amidine; 1320 (w), 1280 (s), 1220 (w), 1180 (w), 1150 (w), 1110 (w), 750 (s) and 710 (s) cm\(^{-1}\) (aryl C-H).

\[ \text{\( \lambda_{\text{max.}} \) (DMF):} \quad 330, 434 \text{ nm (\( \varepsilon: \)} 18680, 32480). \]

Found: C, 76.6; H, 4.7; N, 18.5. C\(_{24}\)H\(_{17}\)N\(_{5}\) required C, 76.8; H, 4.6; N, 18.65%.
(iii) With 2,6-diaminopyridine

Compound (XVIII) (2.83g, 0.01 mol) and 2,6-diaminopyridine (1.09g, 0.01 mol) were added to dry n-butanol (50 ml). The mixture was swirled at room temperature until the reactants had dissolved. The solution was then refluxed until the evolution of ammonia had ceased (14 hours). The solvent was reduced to small volume and the residue taken up in ethanol (80 ml), and the ethanolic solution was decanted into an excess of water (250 ml) with vigorous stirring. A brown flocculent precipitate settled out of solution. Filtration and drying yielded 3.15g (83.7%) of 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-6-pyridyliminoo)-isoindoline (XXXVIIIC) m.p.313° (decomp.), m/e 376 (M+).

$\nu_{\text{max.}}$ (Nujol)

3450 (s) NH; 2200 (s) (C≡N); 1660 (s) (C=N); 1605 (w), 1590 (w), (C=C); 1520 (s) amidine; 1410 (w), 1380 (s), 1280 (w), 1210 (s), 1160 (w), 1110 (w), (aryl C-H); 770 (s), 700 (s), cm⁻¹ (aryl C-H).

$\lambda_{\text{max.}}$ (DMF): 335, 425 nm (ε: 24350, 37030).

(iv) With 2,7-diaminoanthraquinone

Compound (XVIII) (2.84g, 0.01 mol) and 2,7-diaminoanthraquinone (2.38g, 0.01 mol) were added to dry n-butanol (60 ml).
The reaction mixture was refluxed for 14 hours. During the course of the reaction ammonia was evolved. The solvent was reduced to small volume and the residue was taken up in ethanol (80 ml). Dilution of the ethanolic solution with an excess of water (250 ml) gave a dark brown flocculent precipitate. Filtration and drying yielded 3.65g (72.3%) of the anthraquinone adduct (XXXVIIIC) m.p. 332° (decomp.), m/e 505 (M+).

\[ \text{\( \nu \text{, max. (Nujol)} \)} 
3400 \text{ (s), (NH)}; \ 2200 \text{ (s), (C=N)}; \ 1620 \text{ (s) (C=O): 1600 (w), 1580 (w) (C=C); 1520 (s) amidine; 1380 (s), 1280 (s), 1220 (w), 1170 (w), 1140 (w), 1100 (w), 770 (s), 700 (s), cm}^{-1} \text{ (aryl C-H).} 
\[ \text{\( \lambda \text{, max. (DMF): 336, 445 nm (\varepsilon: 16640, 28950) \)}} 

(v) With 2,8-diaminoacridine

Compound (XVIII) (2.8g, 0.01 mol) and 2,8-diaminoacridine (2.09g, 0.01 mol) were added to dry n-butanol (60 ml). The reaction mixture was refluxed until the evolution of ammonia had ceased (12 hours). The solvent was reduced in volume and the residue was taken up in ethanol (80 ml). Upon decanting the ethanolic solution into a large excess of water (250 ml) a dark brown precipitate separated.
Filtration and drying yielded 3.68g (74.6% yield) of 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-8-acridylimino)-isoindoline (XXXVIIIE) m.p. (decomposition) 328°, m/e 476 (M⁺).

\( \nu_{\text{max.}} \) (Nujol)

3500 (s) (NH); 2200 (s) (C≡N); 1650 (s) (C=N); 1610 (w) 1590 (w) (C=C); 1520 (s) amidine; 1340 (s), 1250 (s), 1160 (s), 1160 (w), 1120 (w), (aryl C-H); 760 (s), 710 (s) cm⁻¹ (aryl C-H).

\( A_{\text{max.}} \) (DMF): 334, 440 nm (ε: 20140, 34640).

Attempted Interaction of Phthalonitrile with '3-unit' Compounds.

(i) With 1-(α-cyano-4-cyanomethylbenzylidene)-3-(4-amino-phenylimino)-isoindoline (XXXVIIIA).

Compound (XXXVIIIA) (1.88g, 0.005 mol) and phthalonitrile (0.64g, 0.005 mol) were added to dry dimethylformamide (40 ml) containing sodium hydride (0.24g, 0.01 mol). The resulting mixture was refluxed under a stream of nitrogen for 48 hours. On cooling a blue-black solid separated. Filtration and drying gave phthalocyanine (0.47g). On diluting the filtrate with water compound (XXXVIIIA) was precipitated, m/e 375 (M⁺).

(ii) 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(3-aminophenyl-imino)-isoindoline (XXXVIIB).

Reaction conditions as in (i). Compound (XXXVIIB) recovered.
(iii) 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-6-pyridylimino)-isoindoline (XXXVIIC).

Reaction conditions as in (i). Compound (XXXVIIC) recovered.

(iv) Anthraquinone adduct (XXXVIID)

Reaction conditions as in (i). Compound (XXXVIID) recovered.

(v) 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-8-acridylimino)-isoindoline (XXXVIE).

Reaction conditions as in (i). Compound (XXXVIE) recovered.

(vi) 1-(α-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-7-naphthylimino)-isoindoline (XXXVIF).

Reaction conditions as in (i). Compound (XXXVIF) recovered. unchanged.
1-(α-Cyano-3-cyanomethylbenzylidene)-3-imino-isoindoline
(XXXIX)

To a solution of sodium ethoxide from sodium (0.23g, 0.01 mol) in dry ethanol (30 ml) m-dicyanoxylylene (1.56g, 0.01 mol) and phthalonitrile (1.28g, 0.01 mol) were added. The reaction mixture was stirred at room temperature for 6 hours. The colour of the reaction mixture changed rapidly from yellow to dark brown. The mixture was decanted into an excess of water (100 ml) with vigorous stirring. Neutralisation of the solution with 2N-hydrochloric acid caused the finely divided precipitate to coagulate. Filtration and drying yielded 2.3g (81%) of 1-(α-cyano-3-cyanomethyl-benzylidene)-3-imino-isoindoline (XXXIX). Crystallisation from N-methyl-2-pyrollidone gave bright yellow needles, m.p. 276°, m/e 284 (M⁺). P.m.r. (DMSO): 1.3 γ (m), 2 protons; 1.5 γ, 1 proton; 1.8 γ (m), 3 protons; 2.5 γ (m), 4 protons.

vₗₘₐₓ. (Nujol): 3450 (w), 3350 (w) (NH); 2200 (s) (C≡N); 1670 (s) (C=N); 1600 (w) (C=C); 1520 (s) amidine; 1260 (w), 1210 (s), 1160 (m), 1100 (w), 780 (w), 770 (s), 690 (s) cm⁻¹ (aryl C-H).


Found: C, 75.9; H, 4.4; N, 19.6; Required for C₁₈H₁₂N₄: C, 76.0; H, 4.25; N, 19.7%.

1-(α-Cyano-3-cyanomethylbenzylidene)-3-oxo-isoindoline
(XL).

1-(α-Cyano-3-cyanomethylbenzylidene)-3-iminoisoindoline
(1.42g, 0.05 mol) was dissolved in ethanol (20 ml) and 2N-hydrochloric acid added (5 ml). The solution was refluxed for 4 hours. The hot reaction mixture was neutralised with 2N-sodium hydroxide solution. On cooling a yellow powder separated out of solution. Filtration and drying gave 1.24g (86% yield) of 1-(N-Cyano-3-cyanomethyl-benzylidene)-3-oxoisooindoline (XL). Crystallisation from aqueous methanol gave bright yellow needles, m.p. 253°, m/e 285 (M+). P.m.r. (DMSO)-1.1 (s) 1 proton; 1.5 (m) 1 proton; 2.0 (m) 3 protons; 2.5 (m) 4 protons. 

\[ \text{\textit{v}}_{\text{max.}} \text{ (Nujol):} 3400 \text{ (w) (NH), } 2200 \text{ (s) (C=N)}, 1720 \text{ (s) (C=O); } 1610 \text{ (m) (C=C); } 1270 \text{ (w), } 1210 \text{ (m), } 1145 \text{ (m); 770 (s), } 720 \text{ (w) and } 690 \text{ (s) cm}^{-1} \text{ (aryl C-H).} \]

\[ \text{\textit{A}}_{\text{max.}} \text{ (96\% EtOH):} \text{ 346, 293, 228 nm. (} \varepsilon = 22800, 13100, 22100 \text{ respectively).} \]

Found: C, 75.7; H, 4.0; N, 14.9 Required for C₁₆H₁₁N₃O
C, 75.8; H, 3.9; N, 14.7%.

\[ 1,3-\text{Bis[cyano(3-imino-1-isoindolinylidene) methyl] benzene} \]

(XLI).

To a solution of sodium ethoxide from sodium (0.46g, 0.02 mol) in dry ethanol (50 ml), m-dicyanoxylylene (1.56g, 0.01 mol) was added and dissolved by swirling. Phthalonitrile (2.56g, 0.02 mol) was added to the solution, and the mixture was stirred at room temperature for 24 hours. The mixture was cooled and then decanted into an excess of water (100 ml) with vigorous stirring. Neutralisation with 2N-hydrochloric acid caused the finely divided precipitate to coagulate.
Filtration and drying gave 3.58g, (87%) of a reddish-brown powder. Crystallisation from N-methyl-2-pyrrolidone gave bright yellow crystals of 1,3-bis [cyano(3-imino-l-isoin-dolinylidene)methyl] benzene (XLI), m.p. 305°, m/e 412 (M⁺). P.m.r. (DMSO): 1.4 γ(s), 4 protons, 1.7 γ(m) 2 protons; 2.0 γ(m), 2 protons; 2.3 γ(m) 4 protons.  

υ max. (Nujol): 3500 (w), 3300 (w) (NH), 2200 (s) (C≡N), 1680 (s) (C=N), 1620 (s) (C=C); 1520 (s) amidine; 1300 (m), 1280 (m), 1240 (m), 1220 (m), 1170 (w), 1150 (w), 1020 (w) (aryl C-H): 810 (w), 765 (s), 750 (w), 720 (w) and 690 (s) cm⁻¹ (aryl C-H).

λ max. (DMF): 294, 310, 412 nm. (ε = 17580, 15600, 32960 respectively).

Found: C, 75.6; H, 4.0; N, 20.3: Required for C26H16N6: C, 75.7; H, 3.9; N, 20.4%.

Hydrolysis of 1,3-Bis [cyano(3-imino-l-isoin-dolinylidene) methyl] benzene (XLI).

Compound (XLI) (1.03g, 0.0025 mol) was suspended in ethanol (20 ml), to which was added 2N-hydrochloric acid (10 ml). The solution was refluxed for 6 hours. The hot reaction mixture was neutralised with 2N-sodium hydroxide and allowed to cool. A bright yellow precipitate separated. Crystallisation from dimethyl acetamide gave yellow needles (0.7g, 68%); m.p. 214°, m/e 414 (M⁺).

υ max. (Nujol): 3250 (s) (NH); 2200 (s), (C≡N); 1730 (s) (C=O); 1615 (m) and 1605 (s) (C=C); 1330 (m), 1260 (w), 1205 (w), 1145 (m), 1100 (w), 775 (s), 760 (s), 730 (w) and 700 (s) cm⁻¹ (aryl C-H).
$\lambda_{\text{max}}$ (DMF): 291, 342 nm. ($\varepsilon = 27300, 18200$).

1,3-Bis ($\alpha$-cyano-3-cyanomethylbenzylidene)-isoindoline (XLV):

To 2-ethoxyethanol (30 ml) containing sodium (0.046g, 0.002 mol) were added m-dicyanoxylylene (0.312g, 0.002 mol) and phthalonitrile (0.128g, 0.001 mol). The reaction mixture immediately developed a deep yellow odour which during the course of 24 hours refluxing turned dark brown. On cooling and dilution with water (100 ml) a brown precipitate was formed. Filtration and drying yielded 0.274g (64.8%) of a brown powder with m.p. 334°. Mass spectrometry gave a parent molecular ion of m/e 423 and a low intensity peak at 551.

Condensation of Phthalonitrile with m-Dicyanoxylylene

(a) To a suspension of sodium hydride (0.48g, 0.002 mol) in dry dimethyl formamide (20 ml) were added phthalonitrile (0.128g, 0.001 mol) and m-dicyanoxylylene (0.156g, 0.001 mol). The reaction mixture was refluxed under an atmosphere of nitrogen for 24 hours. Dilution with water (50 ml) gave a dark brown precipitate. Filtration and drying yielded 0.235 g (83%) of 1-($\alpha$-Cyano-3-cyanomethylbenzylidene)-3-iminoisoindoline (XXXIX), m.p. and mixed m.p. 276°.

(b) To molten m-dicyanoxylylene (1.56g, 0.01 mol) maintained at 200° under a nitrogen atmosphere, phthalonitrile (3.84g, 0.03 mol) and sodium hydride (0.48g, 0.02 mol) were added.
The reaction mixture was maintained at 200°C for 30 minutes. After being cooled, the black molten mass was extracted (Soxhlet) with dry dimethylformamide (30 ml). Dilution with water gave a brown flocculent precipitate. Filtration and drying yielded 0.98 g (23 g) of 1,3-bis(α-cyano-3-cyano-methylbenzylidene)-isoindoline (XLV), m/e 423 (M⁺).

The insoluble residue was identified as phthalocyanine.

**Attempted Condensation of 1,3-Bis(α-cyano(3-imino-1-isindolinylidene)methyl) benzene (XLI) and m-Dicyanoxylylene**

Compound (XLI) (0.824 g, 0.002 mol) and m-dicyanoxylylene (0.156 g, 0.002 mol) were added to a suspension of sodium hydride (0.096 g, 0.004 mol) in dry dimethyl formamide (30 ml). The reaction mixture was refluxed for 12 hours in a nitrogen atmosphere. No evolution of ammonia was detected during the course of the reaction. The mixture was cooled and diluted with water (50 ml). The dark brown precipitate formed, was filtered and dried to give 0.66 g (78%) of compound (XLI) m/e 412 (M⁺).

**Attempted Condensation of 1,3-Bis(α-cyano-3-cyanomethyl-benzylidene)-isoindoline (XLV) and Phthalonitrile**

Compound (XLV) (0.846 g, 0.002 mol) and phthalonitrile (0.256 g, 0.002 mol) were added to dry dimethyl formamide (30 ml) containing sodium hydride (0.096 g, 0.002 mol). The resulting mixture was refluxed under a stream of nitrogen for 24 hours. On cooling, a blue-black solid separated. Filtration and drying yielded phthalocyanine (0.19 g). Dilution of the
filtrate with water gave a dark brown precipitate. Filtration and drying yielded compound (XLV) (0.53g, 63% recover), m/e 423 (M+).

Condensation Reactions of 1-(α-Cyano-3-cyanomethylbenzylidene)-3-iminoisoindoline (XXXIX) and Aromatic Diamines:

(i) With m-phenylenediamine

Compound (XXXIX)(0.568g, 0.002 mol) and m-phenylenediamine (0.216g, 0.02 mol) were added to dry n-butanol (30 ml). The mixture was swirled at room temperature until the reactants had dissolved. The solution was refluxed for 8 hours, by which time the evolution of ammonia had ceased. The solvent was reduced to small volume and the residue was taken up in ethanol (50 ml). The ethanolic solution was decanted into water (100 ml) with vigorous stirring. A brown flocculent precipitate was formed. Filtration and drying yielded 0.54g (73%) of 1-(α-Cyano-3-cyanomethylbenzylidene)-3-(3-aminophenylimino)-isoindoline (XLIXA) m.p. decomp. 306°, m/e 375 (M+).

\[ \nu_{\text{max. (Nujol): 3600 (s), (NH); 2200 (s), (C=N); 1650 (s), (C=N), 1600 (w), (C=C); 1520 (s), amidine; 1310 (w), 1290 (s), 1230 (w), 1190 (w), 1150 (w), 1120 (w), (aryl C-H); 750 (s) and 710 (s) cm}^{-1} \text{ (aryl C-H).} \]

(ii) With 2,6-Diaminopyridine

Compound (XXXIX)(0.568g), 0.002 mol) and 2,6-diaminopyridine
(0.218g, 0.002 mol) were added to dry n-butanol (30 ml). The mixture was swirled at room temperature until the reactants had dissolved. The solution was then refluxed for 10 hours by which time the evolution of ammonia had ceased. The solvent was reduced to small volume and the residue taken up in ethanol (40 ml), and the ethanolic solution poured into an excess of water (100 ml) with vigorous stirring. A brown precipitate was formed, which on filtration and drying yielded 0.51g (69%) of 1-(&-Cyano-4-cyanomethylbenzylidene)-3-(2-amino-6-pyridylimino)-isoindoline (XLIXB) decomp. 310°, m/e 376 (M+).

$\nu_{\text{max.}}$ (Nujol)

3450 (s), (NH); 2200 (s) (C≡N); 1660 (s), (c=N) 1600 (w), (C=N); 1570 (s) amidine; 1390 (w), 1370 (s), 1280 (w), 1210 (s), 1150 (w), 1110 (w), 770 (s) and 710 (s) cm$^{-1}$ (aryl C-H).

Attempted Interaction of Phthalonitrile with '3-Unit' Compounds, (XLIXA) and (XLIXB).

(i) With 1-(&-Cyano-3-cyanomethylbenzylidene-3-(3-amino-phenylimino)isoindoline (XLIXA).

Compound (XLIXA) (0.376g, 0.001 mol) and phthalonitrile (0.128g, 0.001 mol) were added to dry dimethylformamide (30 ml) containing sodium hydride (0.02g, 0.002 mol). The resulting mixture was refluxed under a stream of nitrogen for 48 hours. Upon cooling, a blue-black solid separated. Filtration and drying gave phthalocyanine (0.07g). On
dilution of the filtrate with water, compound (XLIXA) was precipitated. Filtration and drying gave 0.19g (57%), m/e 375 (M⁺).

(ii) With 1-(\(\alpha\)-Cyano-3-cyanomethylbenzylidene-3-(2-amino-6-pyridylmino)-isoindoline (XLIXB).

With reactions conditions as in (i), compound (XLIXB) m/e 376 (M⁺) and phthalocyanine were recovered.

Attempted Condensation of 1,3-Bis \(\text{Cyano}(3\text{-imino-1-isoindinylidene})\)methyl benzene (XLI) with Aromatic Diamines:

(i) With m-Phenylenediamine
Compound (XLI) (0.824g, 0.002 mol) and m-phenylenediamine (0.216g, 0.002 mol) were added to dry dimethyl formamide (20 ml). The reaction mixture was refluxed for 48 hours. No detectable amounts of ammonia were evolved during the period of refluxing. Upon cooling and diluting with water, a dark brown precipitate was formed. Filtration and drying yielded compound (XLI). (0.65g, 79%) m/e 412 (M⁺).

(ii) With 2,6-Diaminopyridine
Reaction conditions as in (i). Starting material recovered uncondensed.

Condensation of 1,3-Bis \(\text{Cyano}(3\text{-imino-1-isoindolineylidene})\)methyl benzene (XLI) and 1,3-Diminoisoinindle.
Compound (XLI) (0.824g, 0.002 mol) and 1,3-diminoisiodoine (0.29g, 0.002 mol) were added to dry n-butanol (20ml) and the reaction mixture was refluxed under a stream of nitrogen for 20 hours. Ammonia was evolved during the period of refluxing. Upon cooling a dark red solid separated out of solution. Repeated extractive crystallisation (Soxhlet) from o-dichlorobenzene gave the macrocycle (L) (0.48g, 46%), decomp. at 220°, m/e 523 (M+).

$\nu_{\text{max}}$ (Nujol): 3280 (s), (NH); 2200 (s), (C=N); 1670 (m), (C=N); 1600 (w), (C=C); 1260 (s), 1180 (w), 1150 (w), 1120 (s), 1100 (w) and 1020 (s), 720 (s) and 690 (s) cm$^{-1}$ (aryl C-H).

$\lambda_{\text{max}}$ (o-Dichlorobenzene): 360, 460 nm ($\varepsilon$ = 40500, 11620).

Preparation of 2,6-Dipicolinic Acid

2,6-Lutidine (53.5g, 0.5 mol) and potassium permanganate (321g, 2.03 mol) were added to water (2000 ml) and refluxed for 48 hours. The hot solution was filtered, and the filtered material washed with boiling water. The combined filtrate and washings were concentrated on the steam bath. Concentrated hydrochloric acid was added to the cooled solution (pH 1.5). Hydrated dipicolinic acid separated out of solution. Recrystallisation from water gave 76g (36%) of 2,6-dipicolinic acid hydrate, m.p. 235° (Lit. m.p. 235-7°).

Preparation of Dimethyl Dipicolinate

Dipicolinic acid hydrate (101.5g, 0.5 mol) was refluxed with purified thionyl chloride (300 ml) for 48 hours.
The excess of thionyl chloride was distilled and the residue taken up in carbon tetrachloride. Methanol (55 ml) was added to the solution. During the addition the temperature of the solution was maintained between 50 and 60°. Crude dimethyl dipicolinate precipitated on cooling the solution. The crude ester was purified by vacuum distillation (b.p. 155 - 160° at 0.5 mm Hg) to give 79.9 g (82%) of dimethyl-dipicolinate, m.p. 124° (Lit m.p. 125°), m/e 195 (M+).

Preparation of 2,6-Dihydroxymethylpyridine

Dimethyl dipicolinate (10 g, 0.051 mol) and sodium borohydride (2.4 g, 0.063 mol) were stirred in dry diglyme (15 ml). Then anhydrous magnesium chloride (3.6 g, 0.036 mol) was added and the mixture stirred at room temperature for 30 minutes during which time an orange colour developed. After further stirring for 4 hours at 85° the mixture was acidified with 2N-hydrochloric acid to dissolve the solids. The solution was then made alkaline with a slight excess of sodium carbonate solution and evaporated to dryness. The solid residue was crushed and continuously extracted (Soxhlet) with chloroform. Evaporation of the extract gave 5.6 g of product which was extracted with water and dried to give 2,6-dihydroxymethylpyridine (4.8 g, 67%), m.p. 114° (after sublimation), m/e 139 (M+).

\[ \nu_{\text{max. (Nujol)}}: 3400 \text{ (s) (OH); } 1605 \text{ (s) and } 1580 \text{ (w), pyridine; } 1230 \text{ (OH); } 1165 \text{ and } 1120 \text{ (pyridine (C-H)) } 1080 \text{ (s), (OH); } 1030, 980 \text{ 830 (s) and } 780 \text{ cm}^{-1} \text{ (pyridine C-H).} \]

Found: C, 60.3; H, 6.7; N, 10.2. Calc. for C₇H₉NO₂: C, 60.4; H, 6.5; N, 10.1%.
Preparation of 2,6-Dichloromethylpyridine

Thionyl chloride (40 ml) was slowly added to 2,6-dihydroxy-
methylpyridine (6.95g, 0.05 mol) at 0°. The mixture was
warmed on the water bath for 4 hours, cooled and treated
with benzene (100 ml). The precipitated hydrochloride
(5.2g) was filtered and washed with benzene. The free
base was isolated by dissolving the hydrochloride in water
and neutralising the solution with sodium carbonate.
2,6-dichloromethylpyridine was collected and recrystallised
from light petroleum (b.p. 40-60°) as colourless needles
(3.6g, 41%), m.p. 75° (Lit. m.p. 74-75°) m/e 175 (M+).

Preparation of 2,6-Dicyanomethylpyridine

Dry sodium cyanide (1.96g, 0.04 mol) was placed in a flask
equipped with a reflux condensor (fitted with drying tube)
stirrer and dropping funnel. Dry dimethyl sulphoxide
(7 ml) was added and the suspension stirred and heated to
100°. A solution of 2,6-dichloromethylpyridine (3.5g,
0.02 mol) in dry dimethyl sulphoxide (7 ml) was added drop-
wise over a period of 15 minutes. Stirring and heating
was continued for a further 30 minutes. The dark reaction
mixture was allowed to cool. Chloroform (30 ml) was added
and the mixture poured into saturated sodium carbonate
solution (60 ml). The chloroform layer was run off and
the upper layer further extracted with chloroform (2 x 25 ml).
The combined extracts were washed with saturated sodium
carbonate solution (25 mls), dried (Na₂SO₄) and evaporated
leaving a solution of the dinitrile in dimethyl sulphoxide. The solvent was distilled off at 100°/0.1 mm. The residue was taken up in ethanol and treated with charcoal. Filtration of the charcoal and reduction of the ethanolic solution to small volume caused the 2,6-dicyanomethylpyridine to precipitate as colourless crystals, (0.97g, 33%). After recrystallisation from methanol it had m.p. 96°–97° (Lit. m.p. 97°–98°).

Preparation of 2,6-Bis[cyano-(3-imino-1-isoindolinylidene)methyl]pyridine (LI).

To a solution of sodium ethoxide (from sodium (0.046g, 0.002 mol) in dry ethanol (20 ml), 2,6-dicyanomethylpyridine (0.157g, 0.001 mol) and phthalonitrile (0.25g, 0.002 mol) were added. The solution was stirred at room temperature for 5 hours, after which it was poured into water (100 ml) with vigorous stirring. Filtration yielded a light brown powder which was recrystallised from dimethyl acetamide to give yellow crystals of 1,3-bis[cyanoc(3-imino-1-isoindolinylidene)methylpyridine] (LI) (0.36g, 86%), decomp. at 310°, m/e 413 (M+).

ν<sub>max.</sub> (Nujol): 2200 (s), (C=N); 1650 (s), 1610 (s), (C=N): 1590 (w), 1580 (w), (C=C); 1520 (s), (amidine); 1340 (s), 1260 (m) 1240 (m), 1210 (s), 1180 (m), 1120 (w), 1100 (w), 1040 (w), (aryl and pyridine C-H); 940 (s) 890 (m), 870 (m), 810 (s), (Pyridine C-H) 770 (s), 740 (m), 715 (m), 690 (s) cm<sup>-1</sup> (aryl-pyridine C-H).
Attempted Condensation of 2,6-Bis cyano(3-imino-1-isoindolinylidene)methyl pyridine (LI) with 2,6-Biscyanomethylpyridine:

Compound (LI) (0.103g, 0.00025 mol) and 2,6-biscyanomethylpyridine (0.04g, 0.00025 mol) were added to dry dimethyl formamide (20 ml) in which was suspended sodium hydride (0.012g, 0.0005 mol). The reaction mixture was refluxed for 8 hours. No detectable amount of ammonia was evolved. Dilution of the cooled solution with water (20 ml) produced a brown flocculent precipitate. Filtration and drying yielded the starting material, compound (LI) (0.1g, 93%), m/e 413 (M⁺).

Attempted Condensation of Compound (LI) with 2,6-Diamino-pyridine:

Compound (LI) (0.103g, 0.00025 mol) and 2,6-diaminopyridine (0.027g, 0.00025 mol) were added to dry dimethyl formamide (20 ml). The reaction mixture was refluxed for 8 hours. Evolution of ammonia was not detected. The cooled solution was decanted into water (30 ml) with vigorous stirring. A fine brown solid separated. Filtration and drying yielded the starting material, 2,6-bis cyano(3-imino-1-isoindolinylidene)methyl pyridine (LI) (0.09g, 87%), m/e 413 (M⁺).
Attempted Condensation of Compound (LI) and 1,3-Diiminoisoindoline:

Compound (LI) (0.103g, 0.00025 mol) and 1,3-diiminoisindoline (0.036g, 0.00025 mol) were added to dry dimethyl formamide (20 ml). The reaction mixture was refluxed for 8 hours, during which time no ammonia was evolved. Dilution of the cooled solution with water (30 ml) caused a fine brown precipitate to separate out of solution. Filtration and drying yielded the starting material, 2,6-bis [cyano(3-imino-1-isoindolinylidene)methyl] pyridine (LI) (0.08g, 80%), m/e 413 (M⁺).
Synthesis of Aza-linked Macrocycle (LVIII):

1. To dry ethanol (50 ml) was added 1,3-diiminoisoindoline (1.45g, 0.01 mol) and oxydianiline (2.00g, 0.01 mol). The mixture was swirled at room temperature until the reactants had dissolved and was then refluxed for 20 minutes during which time ammonia was evolved. On cooling, an orange-coloured powder separated. Filtration and drying gave the aza-linked macrocycle (LVIII)m.p. 340°, m/e 622 (M⁺).

2. To a solution of sodium ethoxide from sodium (0.46g, 0.02 mol) in dry ethanol (50 ml), phthalonitrile (1.28g, 0.01 mol) and oxydianiline (2.00g, 0.01 mol) were added. The mixture was swirled until the reactants had dissolved and was then refluxed for 30 minutes. After cooling, the mixture was decanted into water (100 ml), Neutralization of the solution with 2N-hydrochloric acid caused the yellow-orange precipitate to coagulate. Filtration and drying gave the aza-linked macrocycle (LVIII), m.p. 340°, m/e 622 (M⁺).

4,4'-Di(bromomethyl)diphenyl Ether:

A mixture of N-bromosuccinimide (40g, 0.25 mol) and benzoyl peroxide (0.5g, 0.002 mol) was added in portions during 20 minutes to a refluxing solution of 4,4'-dimethyldiphenyl ether (20g, 0.101 mol) and benzoyl peroxide (0.25g, 0.001 mol) in benzene (100 ml). The cooled solution was filtered from succinimide (19.87g, m.p. 127°) washed with aqueous sodium hydroxide and water, dried (sodium sulphate : charcoal)
filtered and concentrated. Refrigeration of the concentrated filtrate gave a solid residue (27.3g, 76%) which recrystallised from light petroleum (b.p. 60° - 80°) to give colourless needles, m.p. 98°, (Lit. value 97 - 99°), m/e 356 (M⁺).

**Found:** C, 47.1; H, 3.3; Br, 45.0. C₁₄H₁₂Br₂O requires C, 47.2; H, 3.4; Br, 44.9%.

**4,4'-Di(cyanomethyl)diphenyl Ether**

A mixture of 4,4'-di(bromomethyl)diphenyl ether (14.2g, 0.04 mol), sodium cyanide (4.21g, 0.086 mol) and sodium iodide (0.2g, 0.001 mol) was refluxed in acetone (200 ml) for 36 hours. The solvent was evaporated and the residue was diluted with water (50 ml) and extracted with ether (3 x 100 ml) portions. The combined ether extracts were dried over sodium sulphate and evaporated. On cooling the residual oil, it solidified to give 4,4'-di(cyanomethyl)diphenyl ether (5.16g, 52%). Recrystallisation from ethanol gave white crystals, m.p. 68° (Lit. value 68°), m/e 248 (M⁺).

**Found:** C, 77.3; H, 5.0; N, 11.4. C₁₆H₁₂N₂O requires C, 77.4; H, 4.9; N, 11.3%.

**1-(4-Cyanomethyl-4'-cyanomethylene-diphenyl ether)-3-iminoisonoindoline (LX)**

To a solution of sodium ethoxide, from sodium (0.115g, 0.005 mol) in dry ethanol (50 ml) was added 4,4'-di(cyanomethyl)diphenyl ether (1.24g, 0.005 mol) and phthalonitrile (0.64g, 0.005 mol). The reaction mixture was refluxed for 2 hours.
The initial yellow colour of the solution changed to reddish-brown during the refluxing period. The cooled reaction mixture was decanted into water (100 ml) with vigorous stirring. A slight excess of 2N-hydrochloric acid was added causing the finely divided precipitate to coagulate. Filtration and drying afforded 1-(4-cyanomethyl-4'-cyanomethylene-diphenyl ether)-3-iminoisoindoline (LX), (1.08g, 57.5%), m.p. 208°, m/e 376 (M+).

\[ \begin{align*} 
\nu_{\text{max.}} \text{(Nujol)}: & \quad \nu_{\text{max.}} \text{(Nujol)}: \quad 3450 \text{ (w) (N-H)}; \quad 2200 \text{ (s) (C=N)}; \quad 1610 \\
& \quad 1520 \text{ (s) amidine}; \quad 1250 \text{ (s) (C-O)} \text{ 1190 (s)}, \\
& \quad 1150 \text{ (w), 1110 (w), 770 (s) and 700 (s) cm}^{-1} \text{ (aryl C-H)} \\
\lambda_{\text{max.}} \text{(96% EtOH):} & \quad 385, 295, 245, 230 \text{ nm} \quad (\epsilon: 14420, 13280, 7560, 13660). 
\end{align*} \]

1-(4-Cyanomethyl-4'-Cyanomethylene-diphenyl-ether)-3-oxoisoindoline (LXI).

1-(4-Cyanomethyl-4'-Cyanomethylene-diphenyl ether)-3-iminoisoindoline (0.376g, 0.001 mol) was dissolved in ethanol (20 ml) and 3N-hydrochloric acid (5 ml) was added. The solution was refluxed for 4 hours. The hot solution was neutralized with 3N-sodium hydroxide. On cooling 1-(4-Cyanomethyl-4'-Cyanomethylene-diphenyl ether)-3-oxoisoindoline (LXI) separated as a pale yellow powder (0.273g, 72.4%), m.p. 180°, m/e 377 (M+).

\[ \begin{align*} 
\nu_{\text{max.}} \text{(Nujol)}: & \quad 3400 \text{ (w) (NH)}; \quad 2200 \text{ (s) (C=N)}; \quad 1720 \text{ (s) (C=O)}, \\
& \quad 1610 \text{ (w) (C=N)}; \quad 1250 \text{ (s) (C-O)}; \quad 1170 \text{ (w), 1110 (w)}, \text{ 770 (s) and 710 (s) cm}^{-1} \text{ (aryl C-H)}. 
\end{align*} \]

4,4'-Bis [cyano-(3-imino-1-isoindolinyldene)methyl] diphenyl Ether (LXII).

In a solution of sodium ethoxide from sodium (0.23g, 0.01 mol) in dry ethanol (30 ml), 4,4'-di(cyanomethyl)diphenyl ether (1.24g, 0.005 mol) was dissolved by swirling. Phthalonitrile (1.28g, 0.01 mol) was added to the solution and the mixture was refluxed for 3 hours. After being cooled, the mixture was decanted into an excess of water and neutralized with 3N-hydrochloric acid (5 ml). Filtration and drying of the yellow-brown precipitate yielded the 'two-unit' compound (LX), (0.96g, 78%). m.p. 209°, m/e 376 (M⁺).

2. To a solution of sodium butoxide (from sodium (0.23g, 0.01 mol) in dry n-butanol (30 ml), phthalonitrile (1.28g, 0.01 mol) and 4,4'-di(cyanomethyl)diphenyl)ether (1.24g, 0.001 mol) were added. The mixture was refluxed for 6 hours, after which the solvent was reduced in volume and the residue was taken up in ethanol (50 ml). Decanting into water with vigorous stirring, yielded a light brown precipitate of the two-unit compound (LX), m/e 376 (M⁺).

3. 4,4-Di(cyanomethyl)diphenyl ether (1.24g, 0.005 mol) and phthalonitrile (1.28g, 0.01 mol) were added to dry dimethylformamide (30 ml), containing sodium hydride (0.24g, 0.01 mol). The resulting mixture was refluxed under a
stream of nitrogen for 48 hours. On cooling phthalocyanine separated. Dilution of the filtrate with water gave the two unit compound (LX), m/e 376 (M+).

4. To molten 4,4'-di(cyanomethylphenyl) ether (2.48g, 0.01 mol) maintained at 200° under a nitrogen phthalonitrile (2.56g, 0.02 mol) and sodium hydride (0.48g, 0.02 mol) were added. The reaction mixture was maintained at 200° for 30 minutes. After being cooled, the black molten mass was extracted (Soxhlet) with dry dimethylformamide. Dilution of the extract with water gave a brown flocculent precipitate. Filtration and drying yielded 4,4'-bis[cyano-3-imino-1-isoindolinyldiene)methyl] diphenyl ether (1.26g, 25%), m.p. 292° (decomp.), m/e 504 (M+).

\[ \text{max. (Nujol): } 3450 \text{ (m) (NH); 2200 (s) (C=\text{N}); 1640 (w) (C=\text{N}); 1610 (w) (C=\text{C}); 1520 (s) amidine; 1250 (s) (C=\text{O}); 1190 (s), 1150 (w), 1110 (w), 790 (s) and 710 (s) (aryl C-H).} \]

**Attempted Condensation of 4,4'-Bis[cyano(3-imino-1-isoindolinyldiene)methyl] diphenyl ether (XLII) with 4,4'-Di(cyanomethylphenyl) ether:**

Compound (LXII)(0.504g, 0.001 mol) and 4,4'-di(cyanomethylphenyl) ether (0.248g, 0.001 mol) were added to dry dimethylformamide (20 ml) containing sodium hydride (0.048g, 0.002 mol). The mixture was refluxed for 48 hours under a stream of nitrogen. No emission of ammonia took place. Cooling
and diluting the solution with water gave a dark brown precipitate. Filtration and drying of the solid yielded compound (LXII), (0.4g, 80%), m/e 504 (M⁺).

**Attempted Condensation of 4,4'-Bis\[cyano-(3-imino-l-isoin-dolinylidene)methyl\] diphenyl ether with 4,4'-Diaminodiphenyl ether:**

Compound (LXII) (0.504g, 0.001 mol) and 4,4'-diaminodiphenyl ether (0.2g, 0.001 mol) were added to dry dimethylformamide (30 ml). The reaction mixture was refluxed for 48 hours. No detectable quantity of ammonia was evolved. Upon cooling the solution and diluting it with water, a brown flocculent precipitate was obtained. Filtration and drying yielded compound (LXII), (0.41g, 82%), m/e 504 (M⁺).

**Attempted Cyclisation of 4,4'-Bis\[cyano-(3-imino-l-isoin-dolinylidene)methyl\] diphenyl ether (LXII).**

Compound (LXII) (0.504g, 0.001 mol) was added to nitrobenzene (30 ml) and heated to 200° and maintained at this temperature for 20 minutes. Upon cooling and diluting with diethyl ether (50 ml) the starting compound (LXII) was recovered unchanged, m/e 504 (M⁺).
Cyanoacethydrazide

Ethylcyanoacetate (22.6g, 0.2 mol) was dissolved in ethanol (100 ml). Hydrazine hydrate (100%) (10g, 0.2 mol) was added and the mixture was refluxed on a steam-bath for 1 hour. When the reaction mixture was cooled, cyanoacethydrazide separated as white crystals (18g, 91%). Recrystallization from ethanol gave white flakes, m.p. 115° (Lit. m.p. 114.5°-115°).

Attempted Preparation of 3-Cyanomethyl-1,2,4-triazole (Klosa's Method).

Cyanoacethydrazide (2.26g, 0.02 mol) was added to formamide (5 ml, 0.13 mol) and heated under reflux for 3 hours on a steam-bath. The cooled solution was diluted with ethanol (10 ml) and the brick-red precipitate filtered. Recrystallization from a large volume of glacial acetic acid gave bright red crystals, m.p. 300° (decomp.) m/e 218 (M⁺).

Methyl Acetimidate Hydrochloride

Into a cooled mixture of anhydrous acetonitrile (135g, 3.3 mol), methanol (150 ml, 3.3 mol) and diethyl ether (120 ml), there was introduced a slight molar excess of dry hydrogen chloride. The mixture was refrigerated overnight during which time a hard cake of shiny white crystals was formed. The diethyl ether was decanted, and the hydrochloride salt was dried in a vacuum over soda lime to remove the excess hydrogen chloride. A total of 89.8g (82%) of methyl acetimidate hydrochloride was obtained.
Methyl benzimidate hydrochloride

Into a cooled mixture of anhydrous benzonitrile (51.5g, 0.01 mol) dried methanol (22.8 ml, 0.5 mol) and anhydrous diethyl ether (80 ml) was introduced a slight molar excess of hydrogen chloride. The mixture, after standing in the refrigerator overnight, gave a precipitate of white shiny plates. Drying of the filtered product in a vacuum over soda lime gave 53.3g (79%) of methyl benzimidate hydrochloride.

3-Cyanomethyl-5-phenyl-1,2,4-triazole

Methyl benzimidate hydrochloride (8.56g, 0.05 mol) and sodium hydroxide (2.0g, 0.05 mol) were added to dry methanol (40 ml). The precipitated sodium chloride was filtered and the filtrate immediately added to a solution of cyanoacethydrazide (4.95g, 0.05 mol) in boiling methanol (20 ml). The solution was refluxed on a steam-bath for 40 minutes, and then evaporated to small volume and treated with diethyl ether (10 ml), whereupon a white powder was precipitated. Further evaporation of the methanol-ether filtrate gave the bulk of the product. Repeated crystallisation from ether-light petroleum containing a few drops of methanol gave white needles (6.3g, 68%) of 3-cyanomethyl-5-phenyl-1,2,4-triazole, m.p. 162° (Lit. 161-163°), m/e (M+) 184. P.m.r. (DMSO) 2.5 $\gamma$ (s), 1 proton; 1.9 $\gamma$ (m) 2 protons; 2.5 $\gamma$ (m), 3 protons; 5.8 $\gamma$ (s), 2 protons.

$\nu$ max. (Nujol): 3300 (s) (NH); 2200 (s) (C=N); 1610 (w) (C=N); 1580 (s) (C=C); 1260 (s), 1160 (s), 1130 (s) (aryl c-H); 790 (s), 720 (s) and 690 (s) cm$^{-1}$ (aryl C-H).

Found: C, 65.0; H, 4.5; N, 30.3,
3-Cyanomethyl-5-methyl-1,2,4-triazole:

Methyl acetimidate hydrochloride (11g, 0.1 mol) and sodium hydroxide (4.0g 0.1 mol) were added to dry methanol (80 ml). The sodium chloride formed was filtered and the filtrate was immediately added to a boiling methanolic solution of cyanoacethydrazide (9.9g 0.1 mol). The solution was refluxed for 20 minutes. On cooling a white flocculent precipitate was formed. Filtration and drying yielded the intermediate Amidrazone. (LXIV: R = C\textsubscript{2}H\textsubscript{3}CN, R' = CH\textsubscript{3}), m.p. 130°, m/e 140 (M\textsuperscript{+}). Cyclisation was achieved by heating the intermediate to 130° for 3 minutes. The product was recrystallised from benzene to give 3-cyanomethyl-5-methyl-1,2,4-triazole (4.4g, 36%), m.p. 135° (Lit. 134°, m.p. 134°), m/e 122 (M\textsuperscript{+}).

Condensation of 3-Cyanomethyl-5-phenyl-1,2,4-triazole with Phthalonitrile.

3-Cyanomethyl-5-phenyl-1,2,4-triazole (2.78g, 0.02 mol) and phthalonitrile (2.56g, 0.02 mol) were added with vigorous stirring to a solution of sodium ethoxide (from sodium (0.46g, 0.02 mol) in dry ethanol (50 ml)). When the reactants had dissolved, the solution was refluxed for 6 hours. The colour of the reaction mixture changed from a light yellow to a deep red. The cooled solution was neutralized with 2N-hydrochloric acid whereupon a yellow flocculent precipitate was formed. Filtration and drying yielded the crude
'two-unit' compound (LXIX) (5.1g, 8%) m.p. 240° m/e 312 (M').

νmax. (Nujol): 4500 (w), 3300 (s) (NH); 2200 (s) (C≡N); 1640 (w) (C=N); 1580 (w) (C=C); 1520 (s) amidine); 1860 (w), 1290 (w), 1220 (w), 1190 (w), 1140 (s), 790 (s), 710 (s) and 690 (s) cm⁻¹ (aryl C-H).

λmax. (96% EtOH): 236, 342, 420 nm. (ε: 32480, 24200, 28600).

Ethyl Cyanacetimidate hydrochloride

To an ice-cold mixture of diethyl ether (300 ml) and dry absolute ethanol (23g, 0.5 mol) malonitrile (33g, 0.5 mol) was added. A stream of dry hydrogen chloride was passed into the stirred solution. After 30 minutes the imino-ether hydrochloride began to precipitate. The mixture was refrigerated for 24 hours, filtered and washed with diethyl ether. The product yield after drying under vacuum was 58.7g (79%).

Ethyl Cyanocetimidate

To an ice-cold mixture of 40% aqueous potassium carbonate (200 ml) and diethyl ether (200 ml) in a separating funnel was added ethyl cyanacetimidate hydrochloride (26.5g, 0.178 mol). The mixture was shaken for 1 minute and the ether layer was separated and poured over anhydrous potassium carbonate. Cold diethyl ether (100 ml) was added to the aqueous layer and the extraction procedure was repeated. After two additional extractions, the combined extracts
were decanted into a fresh portion of drying agent and allowed to stand for 3 hours. The ether was carefully evaporated on the steam bath and the residue dried to constant weight in a vacuum dessicator. The yield of slightly impure, yellowish ethyl cyanacetimidate (m.p. 76°) was 18.4g, (92%). Recrystallisation from diethyl ether gave shiny white plates, m.p. 78°. (Lit. 69 m.p. 78-79°) m/e 112 (M+).

Condensation of Cyanoacethydrazide and Ethyl Cyanacetimidate

Cyanoacethydrazide (2.97g, 0.03 mol) and ethyl cyanacetimidate (3.36g, 0.03 mol) were added to absolute ethanol (50 ml) and refluxed on a steam bath. After 15 minutes refluxing a white flocculent precipitate was formed. Filtration and drying yielded 3.5g, of a white crystalline compound, m.p. 160°. Recrystallisation from water gave white shiny plates of compound (LXXI), m.p. 164°, m/e 165 (M+).

V max. (Nujol): 3400 (s); 3200 (s); 2250 (s); 1620 (s); 1530 (w); 1100 (s); 1120 (w).

Found: C, 43.78; H, 4.39; N, 42.48. C6H7N5O requires C, 43.64; H, 4.27; N, 42.4%.

Condensation of Compound (LXXI) with Phthalonitrile

Phthalonitrile (1.28g, 0.01 mol) and compound (LXXI) (0.83g, 0.005 mol) were added to 2-ethoxyethanol containing sodium (0.23g, 0.01 mol). The mixture was refluxed for 20 minutes during which time the colour of the solution changed from bright yellow to dark brown. On cooling a red brown product separated. Filtration and drying
yielded a light brown powder (1.8g), m.p. 350° (decomp), m/e 717 (M⁺).

ν\text{max. (Nujol)}: 3500 (w) (NH); 2200 (s) (C≡N); 1710 (s) (C=O); 1620 (s) (C=N); 1590 (w) (C=C); 1520 (s) (amidine); 1380 (s), 1340 (w), 1260 (w), 1100 (s), 1010 (s), 740 (s) and 710 (s) cm⁻¹ (aryl C-H).

**Attempted condensation of Cyanoacetamidine and Cyanoacethydrazide:**

In a 1-litre, 3-necked, round bottomed flask equipped with a stirrer and a soda-lime tube was placed a cold saturated solution of ammonia in anhydrous ethanol (500 ml). To the ice cold solution was added with stirring ethyl cyanacetimidate hydrochloride (14.8g, 0.1 mol). The mixture was stirred for 10 minutes and the precipitated ammonium chloride filtered. Cyanoacethydrazide (9.9g 0.1 mol) was added to the filtrate and the mixture refluxed until the evolution of ammonia ceased. When cooled, a white crystalline solid separated (5.6g). Repeated crystallisation from water gave brilliant white crystals of compound (LXXIII), m.p. 240° (Lit. m.p. 238-240°), m/e 149 (M⁺).

ν\text{max. (Nujol)}: 3450 (s), 3350 (s) (NH); 2200 (s) (C≡N); 1600 (w) (C=N); 1570 (w) (C=C).

Deuterated Compound: 2600 (s), 2500 (s) (ND).

λ\text{max. (96% EtOH)}: 295nm. (ε: 12200).

*Found:* C, 48.47; H, 4.91; N, 47.14. *Calc. for C₆H₇N₅:* C, 48.32; H, 4.73; N, 46.95%.
Attempted Condensation of Compound (LXXIII) and Phthalonitrile

Compound (LXXIII) (1.49g, 0.01mol) and phthalonitrile (1.28g, 0.01 mol) were added to 2-ethoxyethanol (20 ml) containing sodium (0.23g, 0.01 mol). The mixture was stirred at room temperature until the reactants had dissolved. It was then refluxed for 8 hours. After neutralization of the cooled reaction mixture with 2N-hydrochloric acid and dilution with water, phthalonitrile (0.92g, 72%) was recovered.
Condensation of Phthalonitrile and 2-Cyanomethyl-thiophene

(1:1 Ratio):

To a solution of sodium ethoxide from sodium (0.46g, 0.02 mol) in dry ethanol (100 ml) phthalonitrile (2.56g, 0.02 mol) and 2-cyanomethylthiophene (2.46g, 0.02 mol) were added. The mixture was stirred at room temperature until the phthalonitrile had dissolved and then refluxed for 4 hours. The cooled reaction mixture was neutralised with 2N-hydrochloric acid and the yellow orange precipitate filtered (3.97g, 79%). The product was taken up in dimethylformamide and chromatographed on an alumina column. Elution with benzene/ethylacetate (10:1) gave the non-crystalline yellow 1-α-cyanothienylidene-3-iminoisoindoline (LXXVI), m.p. 184°, m/e (M+) 251. P.m.r. (DMSO): 1.3 γ(s), 2 protons; 1.7 γ (m), 1 proton; 2 γ(m), 1 proton; 2.4 γ(m), 2 protons; 2.5 γ(m), 2 protons; 2.9 γ(m), 1 proton.

υ max. (Nujol): 3450 (w) 3380 (s) (NH); 2220 (s), (C≡N); 1660 (s) (C≡N); 1540 (s) (NH deformation); 1390 (s) 1370 (w), 128 (m) 1220 (m), 1170 (w), 1150 (w) (aryl & thienyl C-H); 770 (s), 770 (s), 700 (s) (aryl C-H).


Found: C 66.76; H 3.76; N 16.62; S 12.60; Calc. for C14H9N3S: C 66.92; H 3.61; N 16.72; S 12.76%.

Condensation of Phthalonitrile and 2-Cyanomethylthiophene

(1:2 Ratio):

(i) To a solution of sodium propoxide from sodium (0.46g,
0.02 mol) in dry n-propanol (50 ml), phthalonitrile (1.28g, 0.01 mol) and 2-cyanomethylthiophene (1.23g, 0.01 mol) were added. The mixture was refluxed for 12 hours. No emission of ammonia was detected during the refluxing period. On dilution of the cooled solution (100 ml) and neutralization with 2N-hydrochloric acid a yellow precipitate of 1-α-cyanothienylidene-3-iminoisoindoline (LXXVI) was obtained, m.p. 183°, m/e 251 (M⁺). λ max. (EtOH) 416 nm.

(ii) To a solution of sodium butoxide from sodium (0.23g, 0.01 mol) in dry n-butanol (50 ml), phthalonitrile (0.46g, 0.005 mol) and 2-cyanomethylthiophene (1.23g, 0.01 mol) were added. The mixture was stirred at room temperature to dissolve the phthalonitrile and then refluxed for 48 hours. The solvent was decanted into water (150 ml) and neutralised with 2N-hydrochloric acid. Filtration of the fine light brown precipitate gave 1.1g. (62%) of crude 1,3-Bis-α-cyanothienylidene-isoiindoline (LXXVII), m.p. 272°, m/e 357 (M⁺). λ max. (EtOH) 424 nm.

Preparation of 2,5-Bis-cyanomethylthiophene

A stream of dry hydrogen chloride was passed into a stirred solution of formalin (37%) (204 ml, 2.8 mol) and concentrated hydrochloric acid (50 ml), allowing the temperature to rise to 50-60° until the solution was saturated. The mixture was then cooled to 30° whereupon thiophene (70g, 0.833 mol) was added dropwise with stirring. When the mixture had been stirred for 20 minutes, the oily lower layer was siphoned off and washed with 3 portions (500 ml) of cold water.
The crude 2,5-bis-chloromethylthiophene (21.6g, 0.12 mol) was added portionwise over 10 minutes to a stirred mixture of sodium cyanide (11.76g, 0.24 mol) in anhydrous dimethylformamide (200 ml). There was an immediate increase in temperature and the solution darkened; cooling was applied to maintain the temperature below 90°. The mixture was then stirred at room temperature for 2 hours. Chloroform (90 ml) was added and the mixture poured into saturated sodium chloride solution (200 ml). Water was added to dissolve the precipitated sodium chloride and the chloroform layer separated. The aqueous layer was extracted with chloroform and the combined chloroform extracts were washed with saturated sodium chloride solution and dried with magnesium sulphate. Evaporation of the solvent gave a yellow oil which on being refrigerated yielded the crude 2,5-biscyanomethylthiophene (4.48g, 23%), m.p. 43° (lit. m.p. 39-40°).

Attempted Condensation of 2,5-Bis-cyanomethylthiophene and Phthalonitrile.

To a solution of sodium ethoxide from sodium (0.46g, 0.02 mol) in dry 2-ethoxyethanol (50 ml), phthalonitrile (1.28g, 0.01 mol) and 2,5-bis-cyanomethylthiophene (1.26g, 0.01 mol) were added. The solution was swirled at room temperature to dissolve the phthalonitrile. The reaction mixture immediately turned brown. It was then refluxed for 4 hours during which time ammonia was evolved. On cooling a brown-black solid separated. Filtration and drying gave a highly insoluble product (2.1g), m.p. > 350°.
18. Deutsches Patentamt, 879,100, 1953.
60. W Wolf, Deutsches Patentamt, 945,782, 1953.
67. S Rothenburg, Ber., 27, 687.
69. S M McElvain and B E Tate, J. Amer. Chem. Soc., 1949, 71, 40
70. S M McElvain and B E Tate, J. Amer. Chem. Soc., 1951, 73, 2762.