SYNTHETIC AND SPECTROSCOPIC STUDIES OF CYANOBIPHENYLS AND RELATED COMPOUNDS

A thesis submitted to the University of London
for the degree of Doctor of Philosophy

by

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CONTENTS

4. Discussion of results (continued)

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Abstract

2, 2'-, 3,3'- and 4,4'-dicyanobiphenyl have been prepared from the corresponding dihalogenobiphenyls and their nuclear magnetic resonance and ultraviolet absorption spectra observed. 2,2'-dicyanobenzidine has also been prepared from 2,2'-dibromobiphenyl and its NMR spectrum studied in concentrated and dilute sulphuric acid. The optical resolution of this compound was also attempted but the attempt proved unsuccessful.

Two possible routes to 6-nitro-2,2'-dicyanobiphenyl have been investigated, both starting from 6-nitrodiphenic acid. One route involved the conversion of this acid or one of its derivatives into 6-nitro-2,2'-diaminobiphenyl followed by tetrazotisation and reaction with cuprous cyanide. The diamine was successfully prepared and characterised but conversion into the dinitrile proved impossible by any of the methods attempted. The other route was by dehydration of 6-nitrobiphenyl-2,2'-dicarboxamide. Several dehydrating agents were tested on

biphenyl-2,2'-dicarboxamide, but the product, where identifiable, was always 4-cyanofluorenone. Similarly, the dehydration of 6-nitrobiphenyl-2,2'-dicarboxamide with thionyl chloride yielded 5-nitro-4-cyanofluorenone.

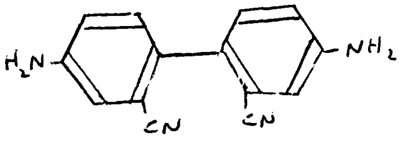
The ultraviolet and optical rotatory dispersion spectra of (+)-6-nitrodiphenic acid have been studied both in ethanol and in aqueous alkali. These spectra are discussed and the optical configuration of the acid is suggested.

1-cyanobenzo[c]cinnoline has also been prepared and its UV spectrum observed and compared with those of 1-nitrobenzo[c]cinnoline and benzo[c]cinnoline itself. Both benzo[c]cinnoline and 1-cyanobenzo[c]cinnoline are photochromic in ethanolic solution, and possible reasons for this are suggested.

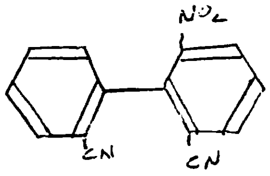
INTRODUCTION

Aims of the present investigation

Little work has previously been carried out on the steric effect of a 2-cyano group on the conformations of biphenyls. In order to study such an effect, possible routes were sought to 2,2'-dicyanobiphenyls with a view to obtaining a compound of this type in an optically active form. 2,2'-dicyanobenzidine and 6-nitro-2,2'-dicyanobiphenyl, both previously unknown compounds, were selected as being of special interest, the former because it might prove optically resolvable and the latter because of its relationship to the readily resolvable 6-nitrodiphenic acid.



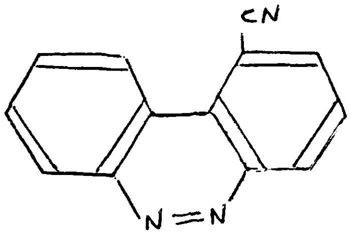
2,2'-dicyanobenzidine



6-nitro-2,2'-dicyanobiphenyl

Attempts to prepare 6-nitro-2,2'dicyanobiphenyl from 6-nitrodiphenic acid led to investigation of the Hofmann, Curtius and Schmidt reactions as applied to this acid and of the dehydration of its amide. Optical rotatory dispersion (O.R.D.) studies were carried out on the dextrorotatory form of the acid to determine, if possible, its absolute configuration.

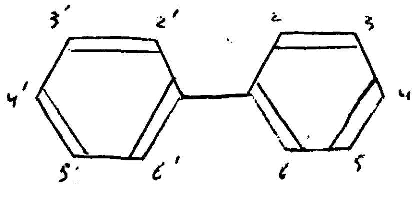
Finally, in order to study the steric effect of a 2-cyano group in a planar biphenyl, 1-cyanobenzo[c]-cinnoline was prepared and its ultraviolet spectrum observed and compared with those of 1-nitrobenzo[c]-cinnoline and benzo[c]cinnoline itself.



1-cyanobenzo[c]cinnoline

Conformations and spectroscopic properties of biphenyls

The biphenyl molecule has been shown by X-ray diffraction[1,2] to be planar in the solid state. In the gas phase, however, electron diffraction[3] shows that the two benzene rings are set at an angle of 45±10° to one another. This can be attributed to repulsion between protons in the 2,2', 6,6'-positions.



The preference of crystalline biphenyl for the planar conformation is probably due to intermolecular interactions.

In biphenyls carrying substituents at the sterically crowded 2,2', 6,6'-positions, the dihedral angle is increased. Littlejohn and Smith[4] have measured the dipole moments of a number of _ortho_-substituted biphenyls and have compared them with theoretical values calculated for the planar and orthogonal conformations on the basis of data for benzene derivatives. In all cases the observed moment accords better with the orthogonal conformation, although that of 2-bromobiphenyl is anomalously high.

Compound	for $\theta=0°$	for $\theta=90°$	observed
2-flurobiphenyl	1.26D	1.34D	1.30D
2-chlorobiphenyl	1.34D	1.43D	1.42D
2-bromobiphenyl	1.32D	1.41D	1.50D
2-iodobiphenyl	1.19D	1.27D	1.27D

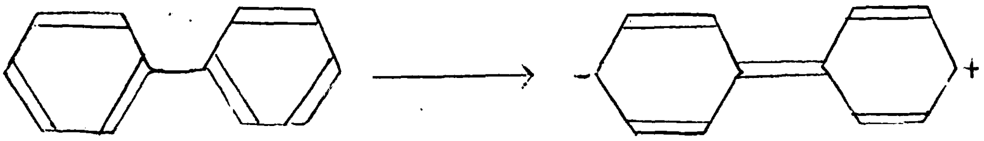
Littlejohn and Smith also measured the moments of 2,2'-disubstituted compounds[5] and calculated the corresponding dihedral angles. In determining the effect of one substituent on the other, it is necessary to guess the exact position of the centre of the substituent dipole and this introduces an uncertainty in the value of the angle.

Compound	Dihedral angle
2,2'-difluorobiphenyl	71-79°
2,2'-dichlorobiphenyl	69-82
2,2'-dibromobiphenyl	68-85
2,2'-diiodobiphenyl	50-84

In all cases the angle is less than 90°, indicating a cis orientation of substituents. Similar results are found by Bastiansen[6] using electron diffraction in the gas phase: 2,2'-dichlorobiphenyl, 2,2'-dibromobiphenyl and 2,2'-diiodobiphenyl all have a non-planar cis conformation with dihedral angles 74±5°, 75±5°, and 79±5° respectively. Some of these compounds are known to remain non-planar even in the solid state: X-ray diffraction work on 2,2'-dichlorobenzidine[7] and 2,2'-dimethylbenzidine dihydrochloride[8] shows the dihedral angles to be 72° and 70.6° respectively, with the substituents cis-oriented in both cases.

I. Fischer-Hjalmars[9] has calculated the resonance energy and the non-bonding interactions in biphenyl as a function of the dihedral angle using a self-consistent field method. The additional resonance energy due to conjugation between the rings is given approximately by the equation $M_\theta = M_0\cos^2\theta$ where M_θ is the value at dihedral angle θ and M_0 is the value for the planar conformation. Small angles of twist (up to 25°) do not therefore decrease the conjugation to a very great extent. A graph of the sum of the conjugation energy and the repulsive interaction between the ortho protons shows a minimum at θ 40° in excellent agreement with the electron diffraction results.

The size of the dihedral angle has a pronounced effect on the ultraviolet spectrum of biphenyls. That of biphenyl itself[10] shows a broad band at λ_{max}249 nm (ϵ_{max}=17000 in 96% ethanol) which is attributed to a $\pi \rightarrow \pi^*$ transition involving intramolecular charge transfer.

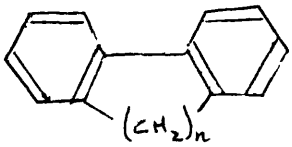


In the spectra of 2-substituted biphenyls, this band is hypsochromically shifted and reduced in intensity while in those of most 2,2'-disubstituted biphenyls it is absent or occurs only as an inflection on the long-wave side of the high frequency band centred at 200 nm.

Compound	λ_{max} (nm)	ϵ_{max}	ref.
2-methylbiphenyl	235	10500	10
2,2'-difluorobiphenyl	233.5	13300	11
2,2'-dimethylbiphenyl	227(infl.)	6800	10
2,2'-di-tert-butylbiphenyl	-	-	12

All spectra in 96% ethanol.

Spectroscopic studies have also been carried out on biphenyls having the 2,2'-positions joined by a saturated bridge[13]. Such compounds with 2-, 3- or 4-membered bridges have rigid structures and in consequence the dihedral angle has a fixed value which can be calculated or measured on an accurate scale model. The conjugation band is quite persistant and has been found for fairly large values of the dihedral angle.



n	θ	λ_{max} (nm)	ϵ_{max}
2	15	264	17000
3	49	247	15700
4	59	235	9680

All spectra in ethanol

It is remarkable that a separate conjugation band is found even for the compound with a four-membered bridge. According to Fischer-Hjalmars' approximate equation, this compound has only 25% of the conjugation energy of planar biphenyl. The appearance of the band may be due to the bathochromic effect of the methylene groups without which it would possibly appear as an inflection at higher frequency.

Substituents in the 3,3' positions buttress the effect of a 2-substituent by preventing it from bending away from the overcrowded centre of the molecule. Dieteren and Koningsberger[14] measured the ultraviolet spectra of biphenyl and a number of aminobiphenyls in 18N sulphuric acid and discovered such an effect in the spectrum of 2,2', 3,3'-tetraminobiphenyl. The conjugation band which still appears in the spectrum of 2,2'-diaminobiphenyl is reduced to an inflection at the same wavelength.

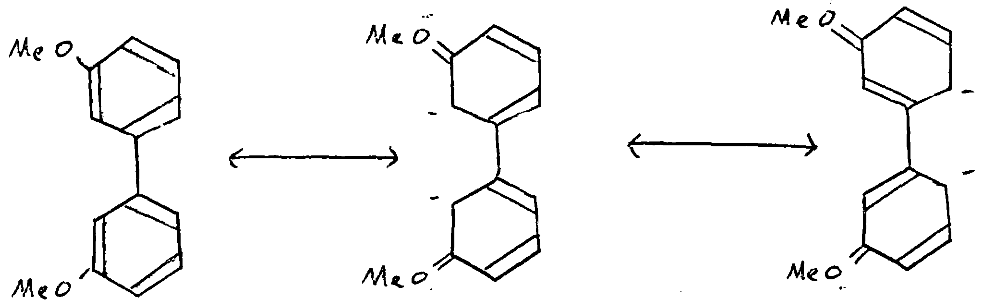
Compound	λ_{max} (nm)	ϵ_{max}
Biphenyl	249	17000
3-aminobiphenyl	249	17600
3,3'-diaminobiphenyl	249	18200
2,2'-diaminobiphenyl	225	8200
2,2', 3,3'-tetraminobiphenyl	(225)	7000

Spectra in 18N H_2SO_4

Braude and Forbes[10] claim to have observed a similar buttressing of hydrogen in spectra collected by Rodebush and Williamson[15]. These workers recorded their spectra photographically and their intensities are not very reliable but there is no mistaking the low-frequency absorption due to the isolated phenyl chromophores.

Compound	λ_{max}	ϵ_{max}	solvent
3,3'-dimethoxybiphenyl	250 285	12000 6000	hexane
3,3'-dihydroxybiphenyl	255 295	12000 6000	ethanol
3,3'-dimethylbiphenyl	255	16500	ethanol

It can be seen that 3,3'-dimethylbiphenyl does not show this effect. Nor does the salt of 3,3'-diaminobiphenyl investigated by Dieteren and Koningsberger. These substituents are sterically equivalent to a hydroxy group but do not show the same mesomeric properties. It seems probable that the apparent buttressing of hydrogen is really mesomeric in character as suggested by Beaven <u>et al</u>.[16]

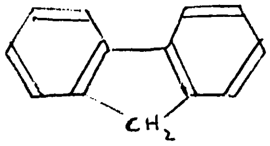


Partial charges are produced on the 2,2' and 6,6' carbon atoms and the repulsive interaction of these charges destabilises the planar state. It is possible however that the relevant band does appear in the spectrum, but is masked by the conjugation band.

Substitution in the 4,4'-positions of the biphenyl nucleus usually shifts the conjugation band to longer wavelengths due to the extension of conjugation and consequent stabilisation of the polar excited state. Fluorine however causes a small shift to shorter wavelengths.

Compound	λ_{max}	ϵ_{max}	Ref.
4,4'-diethylbiphenyl	256.5	22500	17
4-aminobiphenyl	280.5	19000	18
4-hydroxybiphenyl	297	23000	18
4-fluorobiphenyl	247	16900	11
4,4'-difluorobiphenyl	245	15000	11

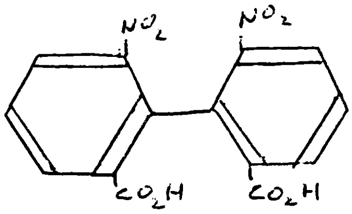
Attempts have been made to determine the dihedral angle in biphenyl and its derivatives from the characteristics of the ultraviolet spectra. Braude and Forbes[10] used the relationship $\epsilon = \epsilon_o \cos^2\theta$ where ϵ is the maximum extinction coefficient of the conjugation band, presumed to occur at constant wavelength, and ϵ_o is the corresponding extinction coefficient for fluorene which is necessarily planar.



However, fluorene is an untypical biphenyl in that the two benzene rings are not collinear[19]. Moreover, this method does not allow for frequency shifts in the conjugation band, which are often considerable, nor for the auxochromic effect of substituents. A better method is that of Suzuki[20], who has used a LCAO molecular orbital approximation to calculate the $\pi \rightarrow \pi^*$ transition energy in terms of the dihedral angle and has related this to the conjugation band frequency using two standard compounds. His planar standard is solid biphenyl whose spectrum he has corrected to take account of the red shift common in the spectra of solid aromatic compounds. For the orthogonal standard he uses the 200 nm band of benzene since the spectra of sterically hindered biphenyls closely resemble those of the corresponding benzene derivatives. The identification of the 200 nm band of benzene with the conjugation band of biphenyl is due to Platt[21]. Using this method, Suzuki has calculated the dihedral angle in biphenyl in solution to be 20° and that of gaseous biphenyl to be 40-43° in good agreement with Bastiansen's electron diffraction measurements.

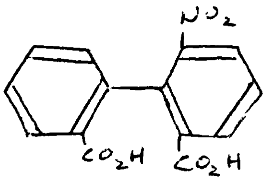
Optical activity of biphenyls

Biphenyls in which neither ring has a plane of symmetry perpendicular to the plane of the ring are dissymmetric in the non-planar conformation. If in addition the interconversion of enantiomeric conformations by rotation about the phenyl-phenyl bond is hindered by substituents in the 2,2', 6,6'-positions, the compound may be optically resolvable. Christie and Kenner[22] first resolved 6,6'-dinitrodiphenic acid in 1922.

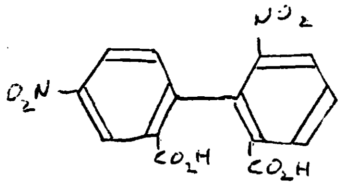


Since then many other biphenyls have been resolved. In 6,6'-dinitrodiphenic acid internal rotation is hindered by four substituent groups but two are sufficient to give labile optical activity if they are large enough. Searle and Adams[23] resolved 2,2'-diiodo-4,4'-dicarboxybiphenyl through the brucine salt and found its half-life for racemisation at 25° to be 91.3 minutes in dioxane, 125.4 minutes in ethyl acetate and 143.4 minutes in decinormal sodium hydroxide. Lesslie and Turner[24] resolved biphenyl-2,2'-disulphonic acid through the strychnine hydrogen salt and found that a solution of the active acid in dilute ammonia had an unchanged rotation after standing for three days at room temperature. However when the solution was heated to 100°, the acid racemised completely in ten minutes. In the same year, 1932, Turner and Shaw[25] resolved the monomethiodide of 2,2'-bis(dimethylamino)-biphenyl and found it to be optically stable at room temperature. In boiling water it has a half-life for racemisation of two hours.

More recent workers have studied the kinetics of racemisation in more detail. Brooks, Harris and Howlett[26] compared the racemisation rates of 6-nitrodiphenic acid, 6,4'-dinitrodiphenic acid and 4,6,4'-trinitrodiphenic acid, all in 2N aqueous sodium carbonate.

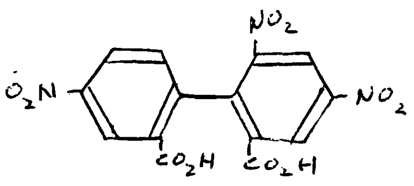


6-nitrodiphenic acid



6,4'-dinitrodiphenic acid

4,6,4'-trinitrodiphenic acid

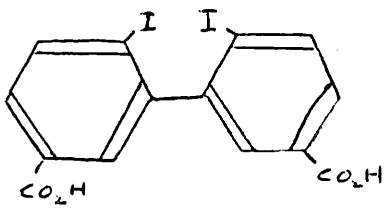


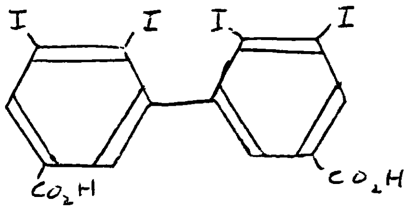
The acids containing additional nitro groups in the 4,4'-positions were optically more stable than 6-nitrodiphenic acid itself; this was found to be due not to any change in the activation energy for racemisation but to an increase in the Arrhenius parameter A.

Compound	Temp.(°C)	$10^4k(sec^{-1})$
6-nitrodiphenic acid	87.6	8.05
	80.6	4.24
	67.55	1.26
	57.0	0.435
4', 6-dinitrodiphenic acid	91.0	3.42
	83.4	1.69
	74.4	0.769
	70.0	0.515
4,4', 6-trinitrodiphenic acid	94.0	1.90
	84.6	0.85
	82.0	0.66
	72.4	0.275

Compound	E(kcal.mole^{-1})	$\log_{10}A(sec^{-1})$
6-nitrodiphenic acid	22.6	10.6
4', 6-dinitrodiphenic acid	22.6	10.1
4,4', 6-trinitrodiphenic acid	22.6	9.7

On the other hand, additional substituents in the 3,3'-positions increase the activation energy for racemisation by a buttressing effect. Rieger and Westheimer[27] measured the racemisation rates of the sodium salts of 2,2'-diiodo-5,5'-dicarboxybiphenyl and 2,2',3,3'-tetraiodo-5,5'-dicarboxybiphenyl in water and found activation energies of 21.6±0.1 kcal.mole^{-1} and 28.05±0.15 kcal.mole^{-1} respectively.





Little work has been done on the optical rotatory dispersion curves of unbridged biphenyls. Mislow and his co-workers[28] studied the O.R.D. spectra of six different 2,2'-dinitrobiphenyls symmetrically substituted in the 6,6'-positions using dioxane as solvent. All showed two Cotton effects of opposite sign centred at about 260 and 330 nm respectively. A positive Cotton effect at 330 nm was found to be characteristic of the R configuration. Mislow[29] has also found that functional derivatives of (R)-6,6'-dinitrodiphenic acid show a positive optical rotation at 546 nm. However this work has not been extended to unsymmetrically substituted diphenic acids.

The introduction of cyano groups into aromatic nuclei

Aryl cyanides or nitriles can be prepared from a variety of starting materials: aryl halides, amines, acids and acid derivatives and compounds in which hydrogen is replaced directly by the incoming cyanide group.

Aryl bromides, unlike aliphatic bromides, do not react with the cyanides of the alkali metals; they do however react with cuprous cyanide at temperatures above 150°.

$$\mathrm{ArBr + CuCN = ArCN + CuBr}$$

Von Braun, who discovered this reaction in 1931[30] used it to prepare 4-cyanofluoranthene. He heated 4-bromofluoranthene with a 10% excess of cuprous cyanide and kept the mixture at 260° for six hours. The nitrile was extracted from the cooled melt with dichloromethane in 80% yield. Subsequently the von Braun reaction was used to prepare a number of other nitriles[31], often with the addition of pyridine as solvent[32,33]. In 1941, Koelsch and Whitney[34] investigated the dry reaction and found that it was autocatalytic. They attributed this to the formation of a CuCN-ArCN complex soluble in the molten reaction mixture. The addition of preformed nitriles such as p-tolunitrile had a similar catalytic effect and so did cupric ions, possibly by forming a reactive complex with the aryl bromide. The reaction was carried out on a number of brominated benzenes, including the sterically crowded 2,4,6-trimethylbromobenzene and went substantially to completion in two hours without a catalyst. The reaction time could be shortened to 10-30 minutes by addition of a few drops of p-tolunitrile and a spatulafull of copper sulphate. The von Braun reaction is also applicable to aryl chlorides[32] provided that more vigorous conditions are used. 1-bromonaphthalene gives 1-naphthonitrile in 93% yield when heated with cuprous cyanide in pyridine to 220° for 15 hours; 1-chloronaphthalene, when subjected to the same reagents requires a temperature of 250° and a reaction time of 24 hours to give the same yield of 1-naphthonitrile.

Two new variations of the von Braun synthesis involve the use of dimethylformamide[35] or N-methylpyrrolidone[36] as a solvent. A number of brominated benzene derivatives have been converted into nitriles in refluxing dimethylformamide in yields of 80-100%. Only 2-6 hours are required for the reaction, which can also be used for activated aryl chlorides. The use of N-methylpyrrolidone gives similar results, with yields of 67-90%. 1-chloronaphthalene will also react in this solvent, giving 85%

of 1-naphthonitrile but the investigators carried out only one run on this compound with the very long reaction time of 24 hours. It is not known whether such a long period is needed or whether other non-activated chlorides are equally amenable.

Organic nitriles form complexes with cuprous cyanide and the free nitriles are best obtained from the reaction mixtures by decomposing the complexes with ammonia or ethylenediamine, both of which form sufficiently stable complexes with the cupric ion to cause cuprous compounds to disproportionate.

$$2ArCN.CuCN + 4NH_3 + 2H_2O = 2ArCN + Cu(NH_3)_4(OH)_2 + Cu + 2HCN$$

Alternatively the cuprous cyanide can be oxidised by a solution of ferric chloride in concentrated hydrochloric acid. This method is better for nitriles which are solid at room temperature, and which can therefore be removed from the solution by filtration without contamination by precipitated copper.

$$ArCN.CuCN + FeCl_3 + HCl = ArCN + CuCl_2 + FeCl_2 + HCN$$

In 1877, Merz[37] investigated the reaction of aryl halides with various metal cyanides in the absence of solvents. He found that lead cyanide is largely inactive: both chloro- and bromobenzene give only 6.5% yields of benzonitrile with this reagent. Silver cyanide is similarly inactive with chlorides and bromides but reacts with aryl iodides to give a 20-30% yield of the nitrile. A mixture of potassium ferrocyanide and quartz sand reacted with both chloro- and bromobenzene to give 20% yields of benzonitrile. Merz carried out his reactions in sealed tubes at 350-400° and distilled the products. The yield of nitrile was estimated by the amount of acid formed by saponification of the distillate.

An industrial variant of the von Braun reaction is to pass the vapour of an aryl halide mixed with hydrogen cyanide over copper powder at 450-1000°. By this method, 60-70% of the nitrile can be prepared.

The preparation of nitriles from aryl amines was first carried out by Sandmeyer in 1884[39]. The amine is diazotised and the diazonium salt solution is poured into one containing potassium cyanide and cuprous cyanide. The reaction is believed to proceed by a free radical mechanism:

$$ArN_2Cl + KCu^{I}(CN)_2 = ArN_2Cu^{I}(CN)_2 + KCL$$
$$ArN_2Cu^{I}(CN)_2 = Ar + N_2 + Cu^{II}(CN)_2$$
$$Ar + Cu^{II}(CN)_2 = ArCN + Cu^{I}CN$$

In harmony with this, it is found that when a solution of potassium cuprocyanide is poured into one of benzene-diazonium chloride instead of vice versa, the benzonitrile formed contains appreciable amounts of biphenyl[40].

The diazotisation is usually carried out in aqueous solution containing 2½ equivalents of a mineral acid: one equivalent to form the salt of the amine, one to generate nitrous acid from the sodium nitrite which is subsequently added and the remaining half-equivalent to maintain proper acidity. Sodium nitrite is added as a concentrated aqueous solution until the reaction mixture gives a positive test for free nitrous acid: a permanent blue colour on starch-iodide paper. A large excess of sodium nitrite should not be used, as it encourages decomposition of the diazonium salt. Weakly basic amines can be diazotised in concentrated sulphuric acid using solid sodium nitrite[41] or nitrosyl sulphuric acid[42]. The latter is obtained by dissolving sodium nitrite in sulphuric acid. Water is required to make the reaction go but for very weak bases, water may be replaced by phosphoric acid[43]. Weak bases may also be diazotised with nitrosylsulphuric acid in glacial acetic acid solution[42] or by nitrous acid in concentrated nitric acid: the nitrous acid is generated by the addition of a reducing agent such as sodium metabisulphite[44]. The last method is of rather limited application as it tends to cause nitration in *ortho* and *para* positions as well as oxidation of sensitive amines.

In the classic Sandmeyer procedure, the acid solution of the diazonium salt is poured directly into one of potassium cuprocyanide and the mixture warmed to 70° to complete the reaction. Aniline derivatives usually give yields of 60-70% in this reaction but this is not always the case with amino derivatives of polynuclear hydrocarbons[45].

In 1890, Gatterman[46] discovered a convenient modification of the Sandmeyer reaction: the diazonium salt solution is mixed with aqueous potassium cyanide and freshly precipitated copper powder is added in large excess. Gatterman used this reaction to prepare halides rather than cyanides and obtained yields of about 70% in most cases but could obtain only 30% of 2-chloronaphthalene from 2-naphthylamine, together with much resinous material.

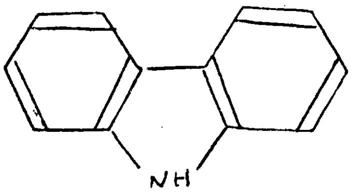
In 1920 a further modification was discovered by Korczynski *et al.*[40] who substituted nickel cyanide for cuprous cyanide and obtained good yields of benzonitrile, *p*-bromobenzonitrile and *p*-tolunitrile. They found cobalt cyanide a poor catalyst for the reaction, although excellent yields of aryl thiocyanates could be obtained using a solution of potassium cobalt thiocyanate.

All these procedures have one great disadvantage: the acid used in diazotisation liberates hydrogen cyanide when the two solutions are mixed and this not only makes the reaction potentially dangerous but wastes part of the cyanide solution. In 1924 therefore Clarke and Read[47] developed a method for conducting the Sandmeyer reaction in neutral solution. The solution of the diazonium salt is carefully neutralised with sodium carbonate and added in small portions with vigorous stirring to the cyanide solution, which is covered with a layer of benzene, to disperse the intermediate addition compound. The reaction is vigorous even at 0° and in the absence of benzene, it takes place with almost explosive violence, liberating a cloud of smoke which smells strongly of isocyanide. The reaction mixture is allowed to stand for five hours, after which the reaction is substantially complete, usually with a yield of 60-70% Warming to 50° increases the yield only slightly.

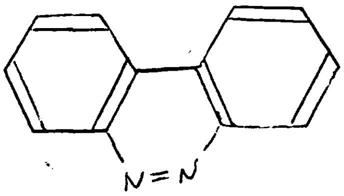
These results are strikingly at variance with those of Hodgson and Heyworth[48] who state that the reaction proceeds only slowly at 0° and that temperatures of 78-80° are necessary to obtain good yields. Both teams carried out their experiments on a range of compounds including some compounds common to both; it is difficult to account for the discrepancy unless it lies in the method of neutralisation: Hodgson and Heyworth neutralised with powdered chalk whereas Clarke and Read used sodium carbonate. It is difficult to avoid adding a slight excess and as sodium carbonate is readily soluble in water the result may have been an alkaline rather than a neutral solution.

Hodgson and Heyworth also compared the relative efficiency of potassium cuprocyanide and potassium nickel cyanide in this variation of the Sandmeyer reaction. In most cases the copper compound gave the better yield; indeed, m-nitroaniline and m-chloroaniline, which gave only 28% of the corresponding nitriles with neutral potassium cuprocyanide, gave hardly any yield at all with neutral potassium nickel cyanide. 2-naphthylamine is an exception in that the nickel compound gives better yields of 2-naphthonitrile than the copper compound: 25% as against 14.5% McRae[45] found that the same was true of 1-naphthylamine which could be converted into 1-naphthonitrile in 58-65% yield by pouring the acid solution of the diazonium salt into one of potassium nickel cyanide containing enough alkali for immediate neutralisation. Under the same conditions, potassium cuprocyanide gave only a low yield. This method of neutralisation does not seem to be applicable to diazotisations carried out in concentrated sulphuric acid.

2,2'-diaminobiphenyls often yield cyclic products when submitted to the Sandmeyer reaction. Dobbie _et_ _al_. in 1911[49] obtained carbazole and benzo[c]cinnoline from the reaction



carbazole



benzo[c]cinnoline

of tetrazotised 2,2'-diaminobiphenyl with cuprous bromide, the relative yields depending on the reaction conditions. Some 2,2'-dibromobiphenyl was also formed when the tetrazotisation was carried out in the presence of cuprous bromide but the yields were never higher than 15% and often less than 10% Similarly von Niementowski[50], who treated biphenyl-2,2'-bisdiazonium chloride with copper powder in 1901, expecting to obtain either biphenyl or 2,2'-dichlorobiphenyl, found carbazole to be the only identifiable product. Holt <u>et</u> <u>al</u>.[51] repeated Dobbie's experiment and claim to have isolated only 2,2'-dibromobiphenyl but they give no experimental details. Mislow and his co-workers[52] prepared 6,6'-dimethyl-2,2'-dicyanobiphenyl from 6,6'-dimethyl-2,2'-diaminobiphenyl but the crude yield was only 8% and the purified product amounted to only 2% of the theoretical yield. In some cases there are complications in the diazotisation itself. Schmidt and Schall[53] report that they were unable to diazotise 6-aminodiphenic acid at all. These results may be due to the formation of a lactam.

Nitriles can be prepared from acid amides or ammonium salts by the action of standard dehydrating agents such as phosphorus oxychloride[54], thionyl chloride[55] or the double salt of sodium chloride and aluminum chloride[56]. Thionyl chloride was first used by Michaelis and Siebert[55] in 1893. They obtained aliphatic nitriles in 50% yield and simple aromatic nitriles in over 80% yield.

$$ArCONH_2 + SOCl_2 = ArCN + SO_2 + HCl$$

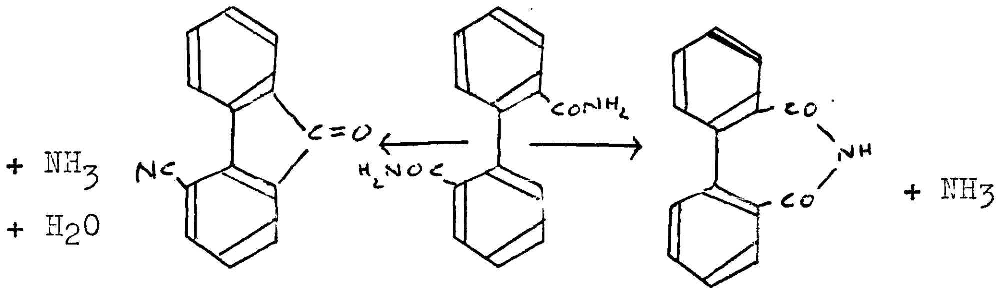
The thionyl chloride is used in a large excess and subsequently distilled off. The nitrile, with some resinous impurities, remains behind. The method cannot be used with amides containing aromatic amino groups, as these yield intractable violet dyes with the reagent.

The use of phosphorus oxychloride dates from 1934[54]. It gives yields of more than 90% with aliphatic and simple aromatic amides. Only one half or even one quarter of the equimolar amount is needed. The nitrile is removed by distillation. The double salt $NaCl.AlCl_3$ was first used to dehydrate amides in 1940[56] but has not found much application since. The nitrile is distilled from the mixture as fast as it is formed. Aryl amides usually give over 90% of the nitrile but 2,6-dichlorobenzamide gives only 67%, indicating that the reaction is sensitive to steric hindrance. The authors report that diamides give poor yields of dinitriles, although no examples are given.

Amides can also be dehydrated thermally at temperatures above 400° in the presence of catalysts such as alumina, pummice or graphite[57]. Pummice is the best catalyst. The nitrile is distilled off. The method dates from 1916 but is less often used than chemical dehydration. Using pummice as catalyst, 90% yields of nitrile can be obtained from aliphatic amides. Benzamide gives equally good yields but the method is unsuitable for aromatic amides of higher molecular weight, as it requires a high degree of volatility in the amide.

A variant of this method is the dehydration of carboxylic acids in the presence of certain nitrogen compounds. Benzonitrile can be obtained in yields of 80% by pyrolysing a mixture of zinc benzoate and lead thiocyanate[58]. The same reaction can be carried out with halogenated benzoic acids, but nitrobenzoic acids explode under these conditions and aminobenzoic acids yield only a small amount of volatile material consisting mainly of aniline. The reaction of an aromatic acid with an aryl sulphonamide (usually p-toluenesulphonamide)[59] in the presence of phosphorus pentachloride at 200° is compatible with the presence of nitro groups elsewhere in the molecule and usually gives the nitrile in 60-80% yield. The reaction mixture is decomposed with ice and the precipitated nitrile washed with alkali to remove excess sulphonamide. This method is especially useful for involatile nitriles.

Little work has been done on the dehydration of diphenic acid and its derivatives. 2,2'-Dicyanobiphenyl has been prepared from biphenyl-2,2'-dicarboxamide by the action of acetic anhydride in glacial acetic acid[60] but the yield is only 22% and the product is much contaminated and difficult to purify. The difficulty in preparing nitriles by this route lies in the possibilities for intramolecular cyclisation which can lead to two distinct products.



Fluorenone-
4-carbonitrile

Diphenimide

The formation of the cyclic imide seems to be the main side reaction when acetic anhydride is used as the dehydrating agent: diphenamic acid, the monoamide of diphenic acid, gives diphenimide in 66% yield when heated with this reagent in glacial acetic acid solution[60]. Diphenic acid mononitrile is formed in only 13% yield. With thionyl chloride, however, diphenamic acid gives a 63% yield of 2-cyanobiphenyl-2'-carbonyl chloride[61]. No reference could be found to the reaction of biphenyl-2,2'-dicarboxamide with the halides and oxyhalides of phosphorus but diphenic acid itself is dehydrated to fluorenone-4-carboxylic acid by excess of phosphorus oxychloride[62] or by phosphoric acid[63]. 6,6'-Dimethyldiphenic acid has been converted into 6,6'-dimethyl-2,2'-dicyanobiphenyl by heating with p-toluenesulphonamide and phosphorus pentachloride but in this case cyclisation to a fluorenone derivative is prevented by the methyl groups. Even so the yield of nitrile is only 39%[52]

Nitriles can also be prepared from the alkali metal salts of arylsulphonic acids by fusion with sodium cyanide[64], potassium cyanide[65] or potassium ferrocyanide[66]. Yields are usually 20-30% but may be higher when the sulphonic acid group is activated towards nucleophilic displacement by an electron-withdrawing group in an *ortho* or *para* position. For example, sodium 4-cyanobiphenyl-3-sulphonate gives 3,4-dicyanobiphenyl in 80% yield when fused with a mixture of sodium cyanide and potassium ferrocyanide[67].

The aminomethyl group can be converted into a cyanide group by dehydrogenation over powdered copper at 450° or powdered nickel at 320°[68].

$$C_6H_5CH_2NH_2 = C_6H_5CN + 2H_2$$

The main side reaction is hydrogenolysis.

$$C_6H_5CH_2NH_2 + H_2 = C_6H_5CH_3 + NH_3$$

Under appropriate conditions this hydrogenolysis reaction can be reversed and benzonitrile can be prepared directly from toluene and ammonia. In an industrial method[69] a mixture of toluene vapour and ammonia is heated to 524-530° and passed over molybdic oxide supported on activated alumina. The yield of nitrile per pass is only 8-10%, but by recycling the unchanged toluene high overall yields can be obtained.

Methods less often used for the preparation of nitriles include the dehydration of oximes with thionyl chloride[70], the action of cyanogen chloride on an aryl grignard reagent[71] and the thermal rearrangement of isonitriles and their precursors, arylformamides[72].

$$ArNHCHO = ArNC + H_2O = ArCN + H_2O$$

There are also a series of reactions in which a cyanide group replaces hydrogen directly. Cyanogen bromide reacts with many hydrocarbons in the presence of Al_2Cl_6 to give ketimides of the form $ArC{=}NH.CCl_3$ which yield nitriles when treated with dry sodium hydroxide in ether[74]. Overall yields vary between 50% and 70% Both these processes are electrophilic substitutions and orientation of the incoming group is similar to that in Friedel-Crafts reactions. Nucleophilic replacement of hydrogen is also possible: alcoholic potassium cyanide attacks the ortho position of aromatic nitro compounds but in the process the nitro group is expelled as a nitrate ion and replaced by hydrogen[75]. When nitrophenols are subjected to the same conditions, the entry of the cyanide group may be accompanied by partial reduction of the nitro groups or by the replacement of one or more nitro groups by alkoxy groups derived from the solvent[76]. Consequently this reaction is not suitable as a preparative method.

The application of the Hofmann and related reactions to diphenic acids

The Hofmann[77], Curtius[78] and Schmidt[79] reactions furnish methods for converting a carboxylic acid or one of its derivatives into an amine containing one less carbon atom. When carried out on dibasic acids they yield diamines containing two less carbon atoms. These methods are particularly interesting in the biphenyl series as they have been found to occur without change of configuration[80,81]. This opens a possible path to optically active 2,2'-dicyanobiphenyl starting from a derivative of an optically resolved diphenic acid. The product of the Hofmann, Curtius or Schmidt reactions should be an optically active biphenyl containing amino groups in the 2,2'-positions and these could be converted into cyano groups <u>via</u> the Sandmeyer reaction, which is also known to proceed without racemisation [82].

The Hofmann reaction involves the formation and subsequent decomposition of an N-bromoamide. Hofmann himself dissolved the acid amide in bromine and added alkali but higher yields are obtained by the modification of Hoogewerff and van Dorp[83]: bromine is dissolved in ice-cold caustic soda and the amide is added gradually to the sodium hypobromite solution so prepared.

$RCONH_2 + NaOBr = RCONHBr + NaOH$

The reaction is completed by warming the mixture.

$RCONHBr + NaOH = RNCO + NaBr$

$RNCO + H_2O = RNH_2 + CO_2 \uparrow$

An electron-deficient nitrogen compound is formed and this rearranges to an isocyanate. Basic hydrolysis of the isocyanate yields the amine.

In the Curtius reaction the same electron-deficient intermediate is formed by the thermal decomposition of an acid azide. In the classical Curtius method[78] the starting material is an ester.

$RCOOCH_3 + N_2H_4H_2O = RCONH.NH_2 + CH_3OH + H_2O$

$RCONH.NH_2 + HONO = RCON_3 + 2H_2O$

$RCON_3 = RNCO + N_2$

Alternatively, the azide can be formed directly from the acid chloride by shaking a solution of the latter with solid sodium azide[84] or with saturated aqueous sodium azide[85].

$RCOCl + NaN_3 = RCON_3 + NaCl$

Curtius decomposed the azides by heating with absolute alcohol and the product was a urethane which was subsequently hydrolysed with aqueous acid.

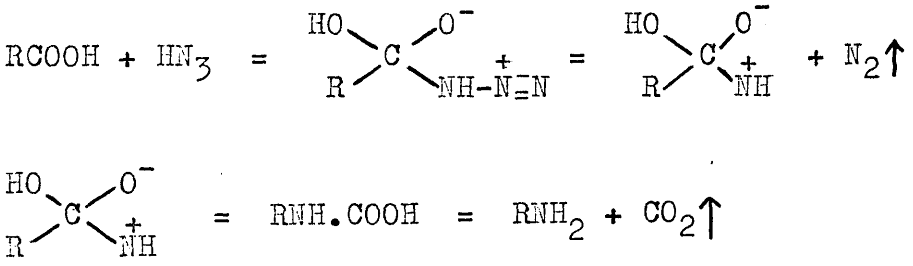
$$RCON_3 = RNCO + N_2\uparrow$$

$$RNCO + C_2H_5OH = RNH.COOC_2H_5$$

$$RNH.COOC_2H_5 + H_2O = RNH_2 + C_2H_5OH + CO_2\uparrow$$

The azide may also be treated directly with dilute acid[84] or rearranged to the isocyanate[86] by heating in an inert solvent and subsequently hydrolysed with acid.

In the Schmidt reaction, an acid is allowed to react with hydrazoic acid in concentrated sulphuric acid. The initial step is the formation of an addition compound which immediately breaks down to give an electron-deficient intermediate similar to but not identical with that of the Hofmann and Curtius reactions.

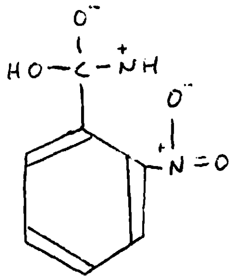


The hydrazoic acid may be generated *in situ* from sodium azide[87].

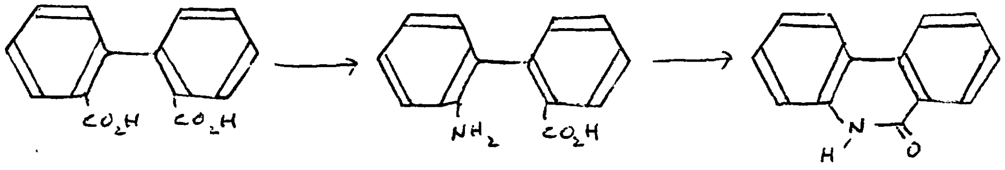
When these rearrangements are carried out on aromatic acids they are found to be inhibited by the presence of electron-withdrawing substituents in the aromatic nucleus. Hauser and Renfrew[38] carried out the Hofmann reaction on _m_- and _p_-nitrobenzamide and recovered 25% and 46% respectively of the corresponding benzoic acids. Benzamide itself gives only 5% of benzoic acid. The hydrolytic reaction leading to the acid apparently has a lower temperature cooefficient than the rearrangement, for carrying out the reaction at a higher temperature leads to an increased yield of amine and a correspondingly lower yield of recovered acid. Briggs and Lyttleton[79] have carried out similar studies on the Schmidt reaction and have found the following results.

Compound	Acid recovered	Yield of amine
Benzoic acid	25%	69%
_m_-nitrobenzoic acid	32%	63%
_p_-nitrobenzoic acid	54%	41%

Curiously, _o_-nitrobenzoic acid gave almost the same results as benzoic acid itself, apparently because the electron-withdrawing effect of the nitro group is countered by a favorable _ortho_ interaction. (See figure overleaf)

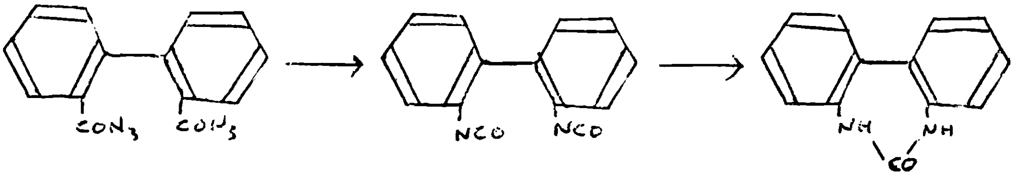


Although these reactions have been carried out successfully on substituted 2-carboxybiphenyls[81,82], complications often arise in the case of diphenic acid and its derivatives owing to competing cyclisation reactions. Thus when Carrona carried out the Schmidt reaction on diphenic acid in 1941[89] he obtained phenanthridone as well as the expected 2,2'-diaminobiphenyl. Unfortunately he does not quote the relative yields of the two products. Stephenson[90] reports that the yield of phenanthridone is much reduced if the reaction is carried out in a large excess of concentrated sulphuric acid. Under these conditions the diamine can be obtained in 66% yield. The cyclisation probably proceeds via an amino acid intermediate.



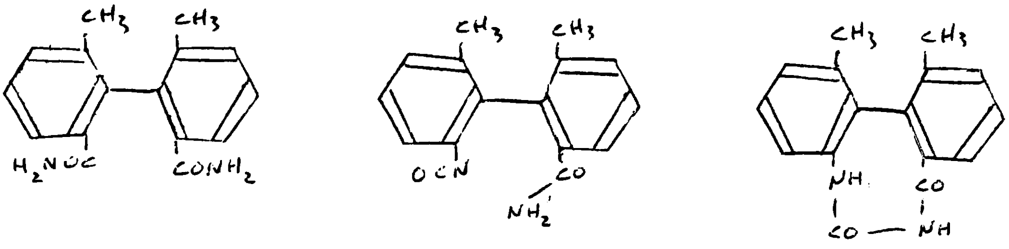
phenanthridone

Cyclisation to phenanthridone is prevented if the diazide is preformed as in the Curtius reaction. In this case rearrangement of both azide groups proceeds simultaneously. However an alternative mode of cyclisation can still occur leading to a cyclic urea.

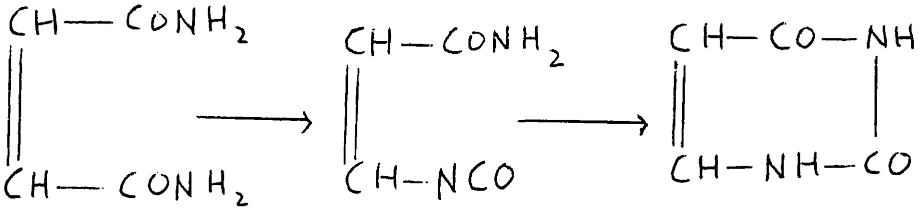


In 1941 Labriola[91] prepared the diazide of diphenic acid from the dimethyl ester via the dihydrazide, the classical Curtius procedure. The diazide decomposed spontaneously at room temperature in ether/benzene solution to give a mixture of the cyclic urea and the diamine. The same mixture was obtained when the decomposition was carried out in ether/ethanol and the resultant urethane subjected to basic hydrolysis. No yields are quoted in either case.

Bell[82] reports that no 6,6'-dimethyl-2,2'-diaminobiphenyl can be prepared from 6,6'-dimethyldiphenic acid by either the Hofmann or the Curtius reaction. The products of the Curtius reaction are not specified but the Hofmann reaction yields a red acidic solid for which analytical figures are given. They are consistent with the formula $C_{16}H_{14}N_2O_2$. It is possible that this represents yet a third mode of cyclisation:

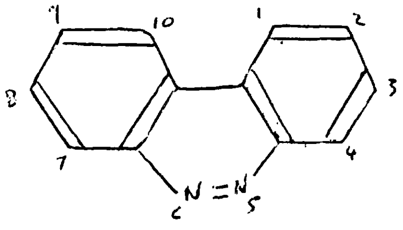


A similar cyclisation occurs when the diamide of maleic acid is treated with sodium hypochlorite; the product is uracil[92].



On the other hand, Holt and Hughes[93] converted the diamide of 6,6'-dinitrodiphenic acid into 6,6'-dinitro-2,2'-diaminobiphenyl in 48% yield by means of the Hofmann reaction. They used 2.3 molar equivalents of bromine and ten molar equivalents of sodium hydroxide in a 10% aqueous solution. The addition of the amide was carried out at ice-bath temperature and the mixture heated for ten minutes. They report that any deviation from these conditions seriously lowers the yield.

Benzo[c]cinnoline and substituted benzo[c]cinnolines



Benzo[c] cinnoline has been reported to be formed when 2,2'-dinitrobiphenyl is reduced with a variety of agents such as zinc and alkali[94], reduced iron[95], ferrous oxalate[96], triethyl phosphite[97] or sodium amalgam[98] but yields are usually less than 60% Two more effective methods, which have also been used to prepare substituted benzo[c]cinnolines, are electrolytic reduction of the corresponding 2,2'-dinitrobiphenyl and reduction of the latter with lithium aluminium hydride. The electrolytic method is the older of the two and was used by Ullman and Dieterle in 1904[99] to prepare 3,8-diaminobenzo[c] cinnoline and its tetramethyl and tetraethyl derivatives. The parent compound was prepared in 80% yield, the derivatives in 50-60% yield. 3,8-Dimethylbenzo[c]cinnoline was prepared by the same method but the yield is not given. Lithium aluminium hydride reduces 2,2'-dinitrobiphenyl to benzo[c]cinnoline in over 90% yield[100] and can be used to prepare substituted benzo[c]cinnolines in 70-80% yield providing that no amino groups are present[101], but 2,2'-dinitrobenzidines are reduced to the corresponding benzo[c]cinnolines in only 20% yield and 6,6'-dinitro-2,2'-diaminobiphenyl gives only a 42% yield of 1,10-diaminobenzo[c]cinnoline[93]. Nuclear chlorine and bromine are unaffected by lithium aluminium hydride but iodine is eliminated[101].

Benzo[c]cinnoline has several times been reported as a product of the catalytic hydrogenation of 2,2'-dinitrobiphenyl. Everett and Ross[102] obtained benzo[c]cinnoline as the only product when the hydrogenation was carried out over Raney nickel but Stetter and Schwartz[103] report that the course of the reaction is pH-dependent: in neutral solution the product is 2,2'-diaminobiphenyl but in the presence of alkali benzo[c] cinnoline is formed in 50% yield. The substitution of palladised charcoal for Raney nickel increases the yield to 90% Small amounts of alkali do not have this effect; according to Blood and Noller[104] the effect of a few drops of 6N caustic soda on the hydrogenation of 2,2'-dinitrobiphenyl over Raney nickel is to increase the rate of reduction to the diamine without encouraging the formation of benzo[c]cinnoline. The use of Adams' platinum oxide catalyst leads to the formation of 2,2'-diaminobiphenyl in 96% yield[104,105]. Benzo[c]cinnoline is not reduced under the same reaction conditions and so does not appear to be an intermediate in the reduction[105]. However Radell et al.[94] report that benzo c cinnoline is reduced to 2,2'-diaminobiphenyl by hydrogenation over Raney nickel at 34° and 100 p.s.i. Some light is shed on this by the work of Moore and Furst[106] on the reduction of 2,2'-dinitrobiphenyl with hydrazine hydrate in the presence of Raney nickel. They discovered that 2,2'-diaminobiphenyl is the only product when freshly prepared catalyst of a type low in aluminium is used but that the use of aged, high-aluminium catalysts leads to cyclic products. By suitable variation of the reaction conditions, benzo[c]cinnoline-5,6-dioxide, benzo[c]cinnoline-5-oxide and benzo[c]cinnoline itself can all be prepared in good yield. The reduction of benzo[c]cinnoline to 2,2'-diaminobiphenyl is difficult and requires a large excess of hydrazine, confirming the conclusion of Ross et al.[105] that benzo[c]cinnoline is not a normal intermediate in the formation of this compound.

Benzo[c]cinnoline has also been prepared by the oxidation of 2,2'-diaminobiphenyl. Oxidation with perboric acid[107] gives only a 50% yield but the same reagent converts 3,3'-dibromo-2,2'-diaminobiphenyl into the corresponding benzo[c]cinnoline in 70% yield and a similar oxidation of 3,5,3', 5'-tetrabromo-2,2'diaminobiphenyl with peracetic acid[107] proceeds in 92% yield. Phenyl iodosoacetate converts 3-, 4- and 5-nitro-2,2'-diaminobiphenyls into the corresponding nitrobenzo c cinnolines in 50-70% yield[108].

The ultraviolet spectrum of benzo[c]cinnoline resembles that of phenanthrene[109]. There are three main regions of absorption, termed groups I, II and III and centred at *ca* 250, 300 and 350 nm respectively. In ethanol their approximate molar extinction coefficients are 50,000, 9000 and 1500. The group II and group III bands are broad and show some vibrational structure. The group III band tails off slowly above 380 nm and this is attributed to an $n \rightarrow \pi^*$ transition involving one of the nitrogen lone pairs. In non-polar solvents such as *cyclo*hexane, the intensity of the group III band is reduced and the lone pair absorption appears as a separate band at 410 nm. At the same time the vibrational structure of the group II and III bands is partly resolved.

The effect on the spectrum of substitution has been studied only in n-hexane[110]. Saturated hydrocarbon substituents at C-1 cause large red shifts in the group II bands but the same substituents at other positions in the molecule cause only small red shifts or none. When both C-1 and C-10 are substituted, the red shift in the group II bands is ca 20 nm. The shift appears to be due to a loss of planarity in the molecule due to steric strain: 4,7-diamino-1,10-dimethylbenzo[c]cinnoline shows labile optical activity and has been resolved[111]. With unsaturated substituents and with those able to donate lone pairs the picture is more confusing. Bromine and chlorine cause red shifts of ca 11 nm when situated at C-1 but they have a similar effect at C-4. The nitro group on the other hand is said to have little effect on the spectrum when at C-1 or C-4.

Electrophilic substitution in the benzo[c]cinnoline nucleus takes place mainly at position 1. Nitration with nitric/sulphuric acid (1:3) at 0°[112] gives 58% of 1-nitrobenzo[c]cinnoline and 12% of an isomer subsequently identified as 4-nitrobenzo[c]cinnoline[113]. Bromination in sulphuric acid in the presence of silver sulphate gives 27% of 1-bromobenzo[c]cinnoline and 4% of a dibromo compound thought to be 1,7-dibromobenzo[c]cinnoline; in organic solvents such as carbon tetrachloride bromination does not take place and the sole product is a molecular complex of bromine and benzo[c]cinnoline. Theilacker and Baxmann[111] obtained 4,7-dinitro-1,10-dimethylbenzo[c]cinnoline by nitration of 1,10-dimethylbenzo[c]cinnoline. From all these experiments it seems clear that the most reactive positions in the nucleus are 1 (and 10) followed by 4 (and 7). This contrasts with the theoretical prediction of Dewar and Maitlis[114], who, on the basis of molecular orbital calculations place the positions in the following decreasing order of reactivity: 1, 3, 4, 2. Their calculation takes no account of the effect of protonation at one of the nitrogen atoms but this would be expected to decrease the reactivity of position 4 still further by generating a positive charge immediately adjacent to it. The observed order of reactivity ($4>3$) is not explained.

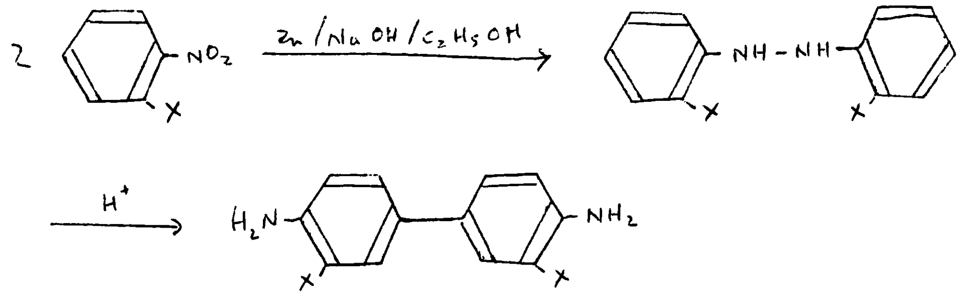
DISCUSSION OF RESULTS

Preparation of 4,4'-3,3'- and 2,2'-dicyanobiphenyl

The three symmetrical dicyanobiphenyls were prepared from the corresponding halides in order to compare their ultraviolet spectra and also to test the efficiency of the von Braun reaction (see p. [illegible]) when applied to different positions of the biphenyl nucleus.

4,4'-Dibromobiphenyl was readily obtained by the direct bromination of biphenyl with molecular bromine in carbon tetrachloride solution in the presence of iron filings. When the hot solution was filtered and cooled, the product crystallised out in substantially pure condition in over 60% yield. 4,4'-Dicyanobiphenyl was obtained from the dibromo compound by reaction with cuprous cyanide in boiling dimethylformamide (the method of Friedman and Schechter. See p. 23 and ref. 35). Friedman and Schechter suggest the use of 150 ml. of solvent per mole of aryl bromide but this proved insufficient to dissolve the reactants and the reaction failed to take place. The use of a much larger volume of dimethylformamide (50 ml. for 10 moles of 4,4'-dibromobiphenyl) brought about the reaction conveniently. The yield of 4,4'-dicyanobiphenyl was usually about 60% when ethylenediamine was used in the working up of the reaction mixture (see p. 24) but rose to 90% when ferric chloride solution was substituted in this step. Friedman and Schechter report a quantitative yield irrespective of the nature of the working up.

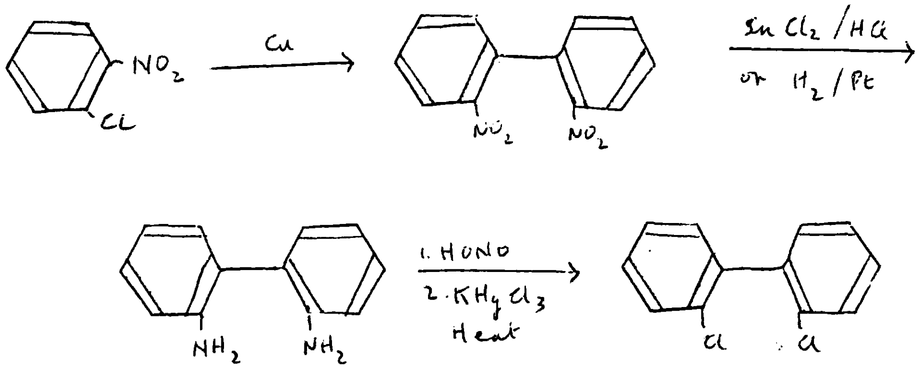
3,3'-Dihalogenobiphenyls are best prepared by deamination of 3,3'-dihalogenobenzidines which can be obtained by the following reaction sequence:



X=Cl, Br, I.

o-Chloronitrobenzene was the most accessible starting material. It was reduced to 2,2'-dichlorohydrazobenzene as shown above but no attempt was made to isolate this product. Instead the reaction mixture was filtered from excess zinc and poured into moderately concentrated hydrochloric acid to bring about the final rearrangement into 3,3'-dichlorobenzidine which precipitates from solution in the form of a sparingly soluble dihydrochloride. The salt was deaminated by tetrazotisation in acid solution followed by treatment with ice cold 30% hypophosphorous acid. The yield of 3,3'-dichlorobiphenyl is good but the value of the sequence as a whole is limited by the low yield of 3,3'-dichlorobenzidine from *o*-chloronitrobenzene.

2,2'-Dichlorobiphenyl was prepared by a similar reaction sequence from *m*-chloronitrobenzene. An alternative path was also investigated starting from *o*-chloronitrobenzene.



o-Chloronitrobenzene was converted into 2,2'-dinitrobiphenyl by the action of copper bronze (the Ullmann reaction) and the product reduced to 2,2'-diaminobiphenyl. This reduction was more difficult than expected. When stannous chloride was used as the reducing agent the yields were very variable and never higher than 60% and the amine was deeply coloured and hard to purify. Catalytic hydrogenation over platinum gave, on one occasion, a 99% yield of substantially pure 2,2'-diaminobiphenyl, but repetition of the experiment produced only a yellow solid of m.p. 150-160° and some impure starting material. The yellow material was not investigated further but was presumed to consist mainly of benzo[c]cinnoline (Lit. m.p. 156°) which is known as a product of the hydrogenation of 2,2'-dinitrobiphenyl over Raney nickel, though it has never before been reported in hydrogenations conducted over platinum (see p. 46). Once formed, benzo[c]cinnoline cannot be further reduced under these conditions[105]. It is not known what caused this capricious behavior as the reaction conditions were as far as possible the same in both experiments.

The difficulties of the Sandmeyer reaction of 2,2'-diaminobiphenyl have already been described (p. 30 f.). The diamine was therefore converted into the dichloride by the method of Schwechter[115]. Tetrazotised 2,2'-diaminobiphenyl was allowed to react with an aqueous solution of potassium mercuric chloride and the precipitated complex salt filtered off, dried and pyrolysed. However, the yield of 2,2'-dichlorobiphenyl was only 20% and in view of this and of the unforeseen difficulties in the reduction of 2,2'-dinitrobiphenyl, this path was not pursued further.

2,2'- and 3,3'-Dichlorobiphenyl did not react with cuprous cyanide in boiling dimethylformamide or N-methylpyrrolidone. Only unchanged starting material could be extracted from these mixtures. However, the reaction took place successfully when the reactants were mixed with pyridine sufficient to cover them without dissolving them completely and heated to 200° for a prolonged period. 3,3'-Dichlorobiphenyl gave a 31% yield of the corresponding dinitrile after 24 hours and 2,2'-dichlorobiphenyl an 8% yield after 40 hours. The pronounced difference in the reactivity of the two compounds is probably due to steric factors, the 2-position being relatively inaccessible to the reagent.

4,4'- and 3,3'-Dicyanobiphenyl are white crystalline solids which separate from alcoholic solution as prisms, changing to needles above 190°. 2,2'-Dicyanobiphenyl crystallises as white needles from methanol but the prism form can be obtained from benzene solution and undergoes the usual crystal change on heating to 150°. In both 3,3'- and 2,2'-dicyanobiphenyl this crystal change is accompanied by partial melting and resolidification. The infrared spectra of all three compounds show an absorption band due to $C\equiv N$ stretching as shown below.

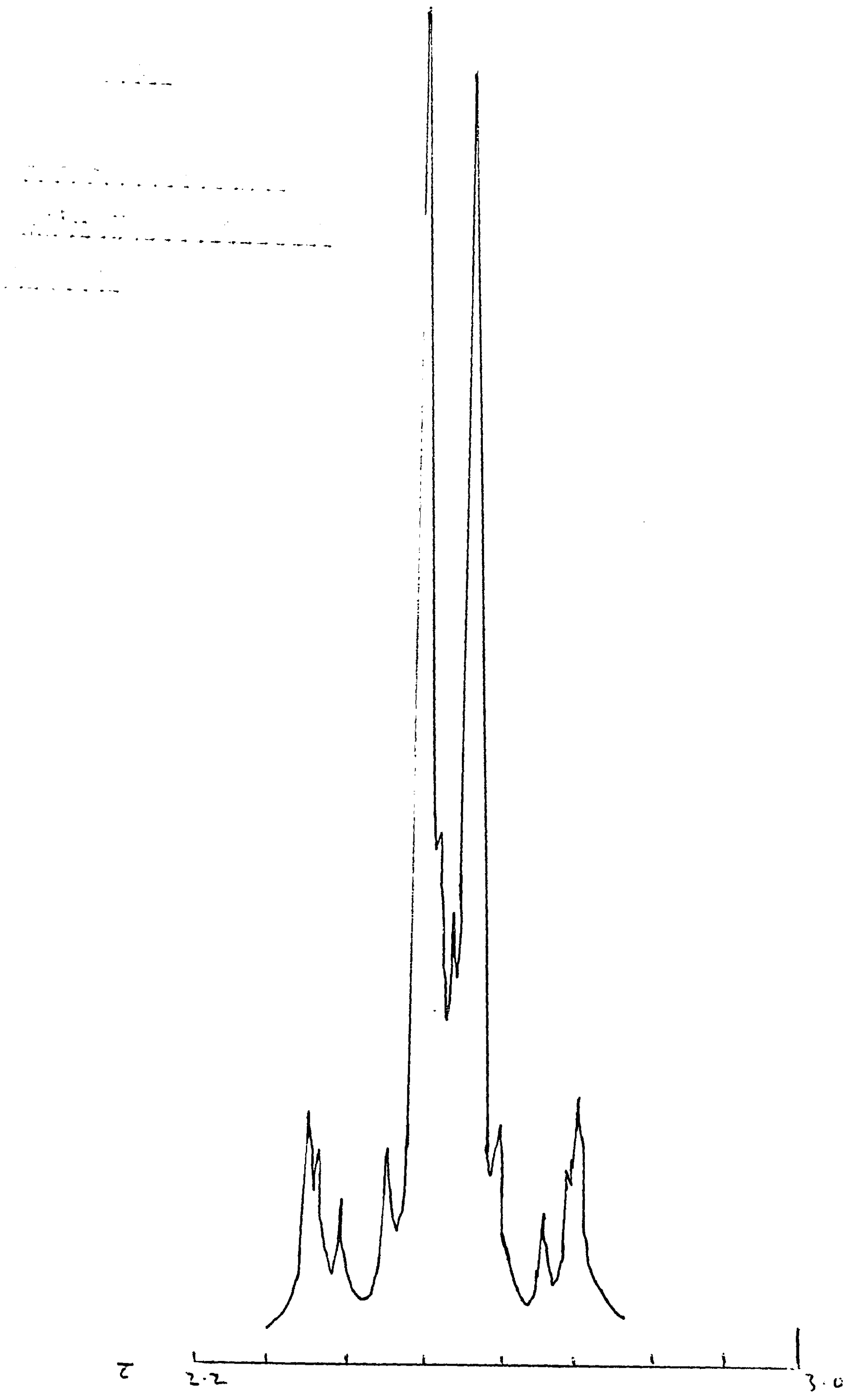
Compound	Frequency of band (cm^{-1})
2,2'-dicyanobiphenyl	2227
3,3'-dicyanobiphenyl	2230
4,4'-dicyanobiphenyl	2222

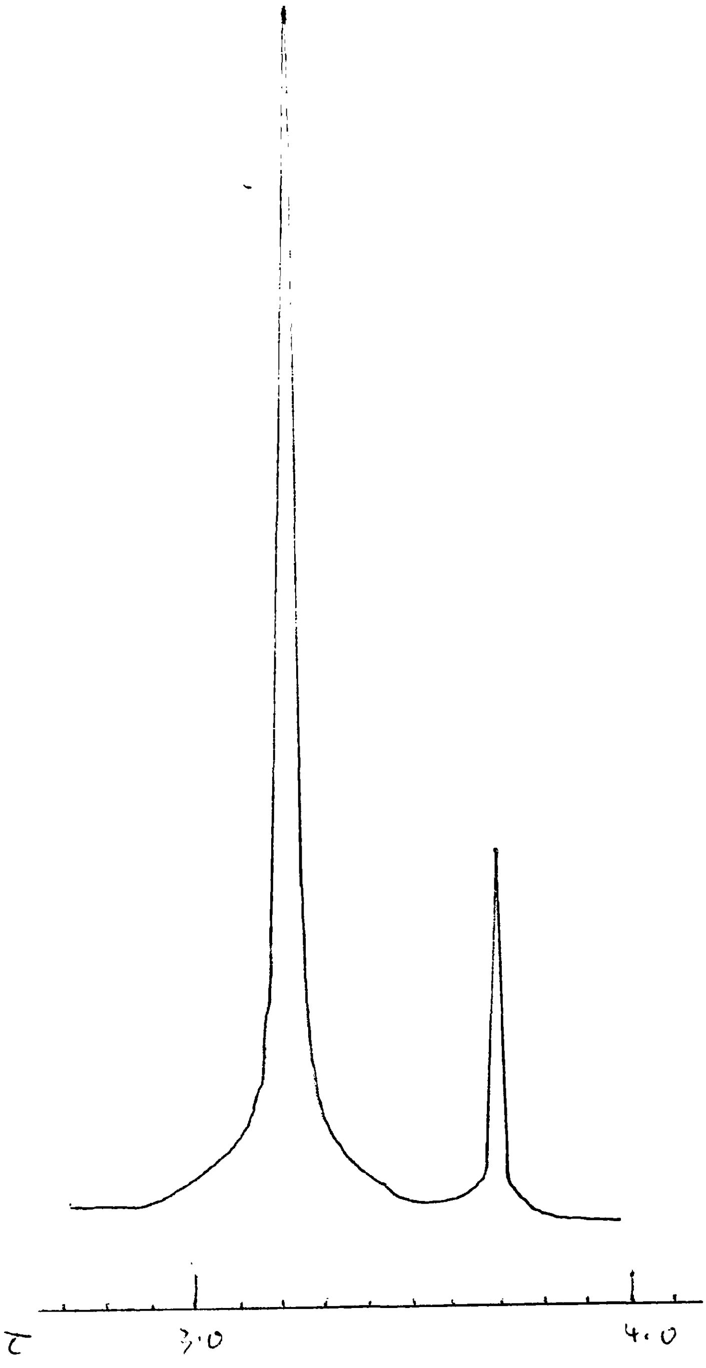
The three values are quite close and do not suggest any distortion of the cyano groups in 2,2'-dicyanobiphenyl despite their crowded environment.

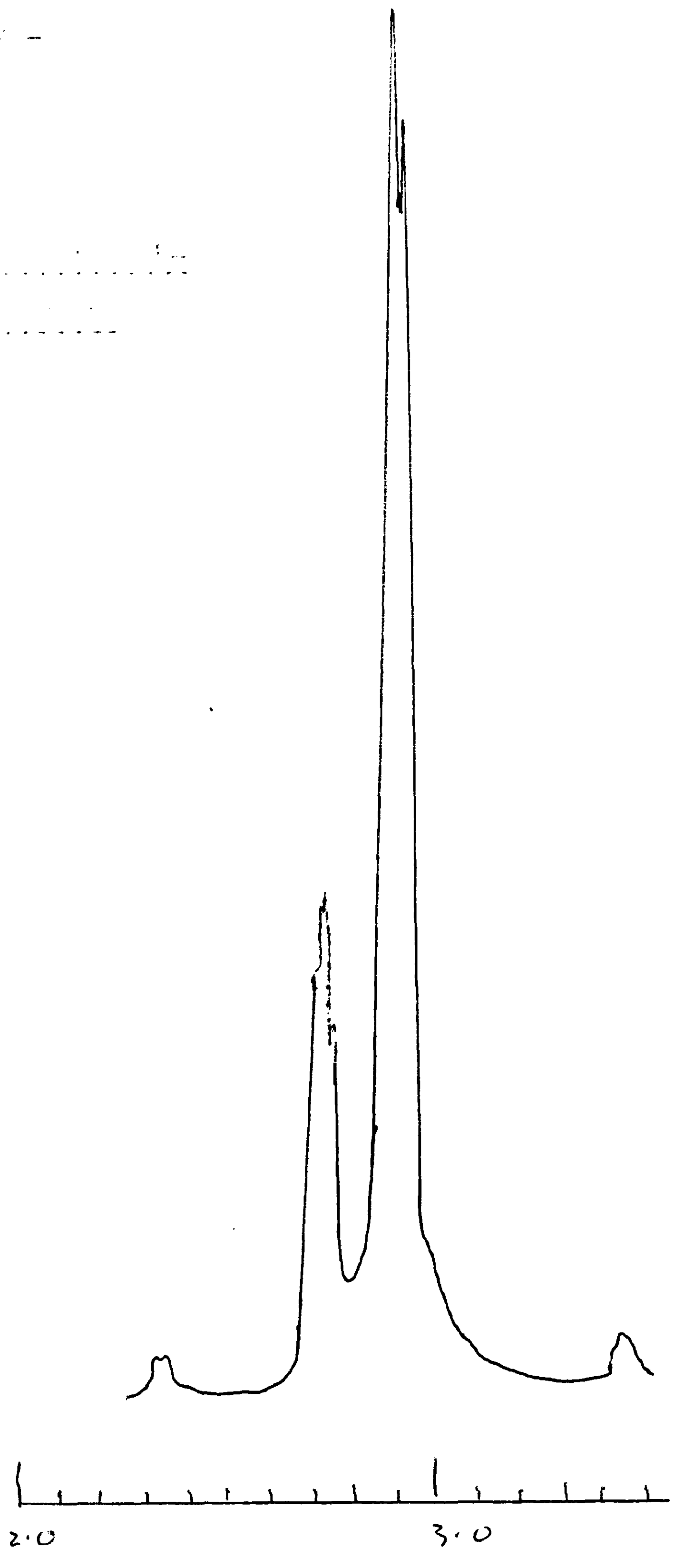
The ultraviolet spectra of these compounds were measured in 95% ethanol and are shown in Figs. 1-3. They show, in addition to the conjugation band, a moderately strong band near 280 nm which probably corresponds to the 265 nm band of benzonitrile. The positions and intensities of these bands are shown in the table below.

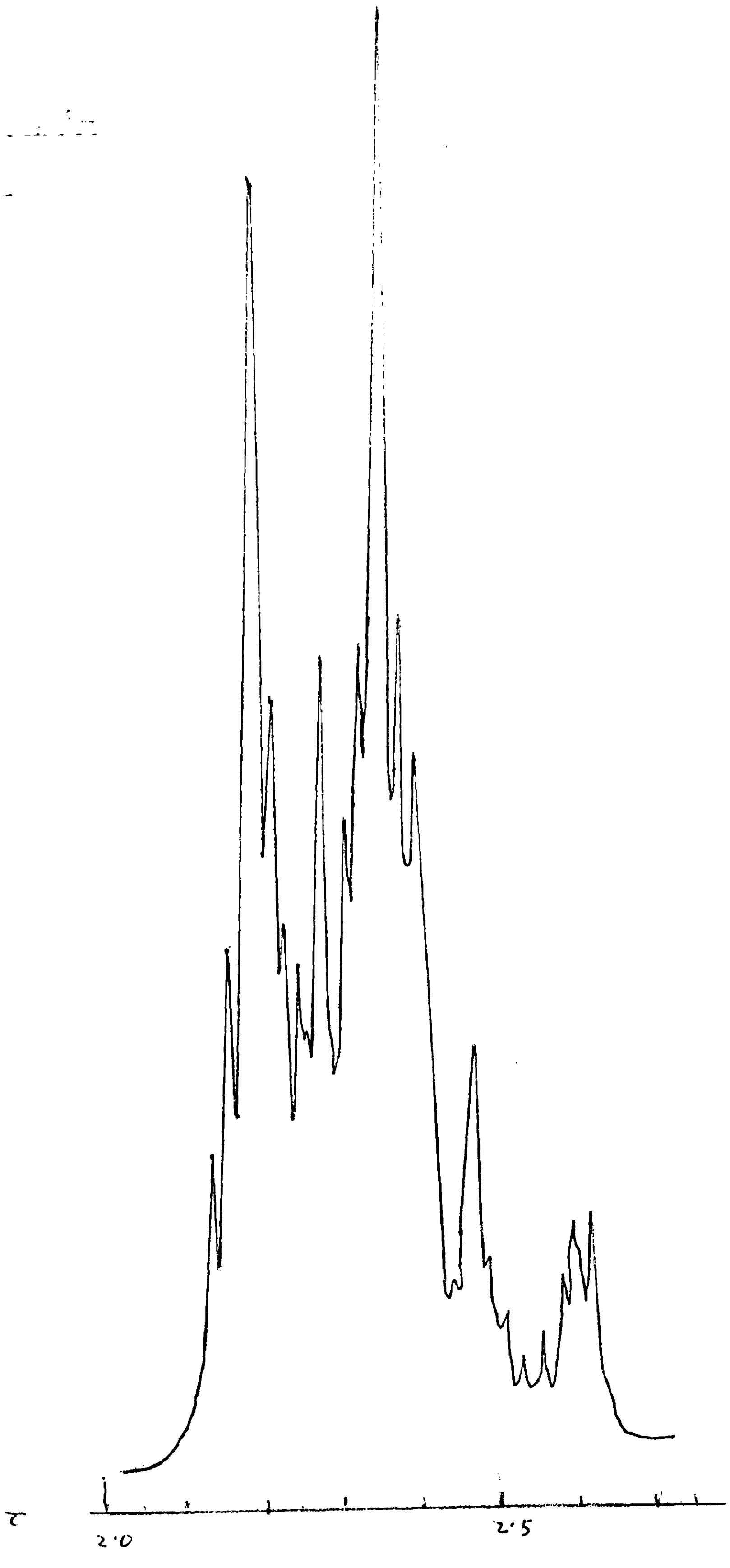
Compound	Conjugation band		Long-wave band	
Biphenyl	249	17,000	-	-
2,2'-dicyanobiphenyl	(248)	6,200	283	3,400
3,3'-dicyanobiphenyl	252	16,500	(282)	3,700
4,4'-dicyanobiphenyl	275	36,500	-	-

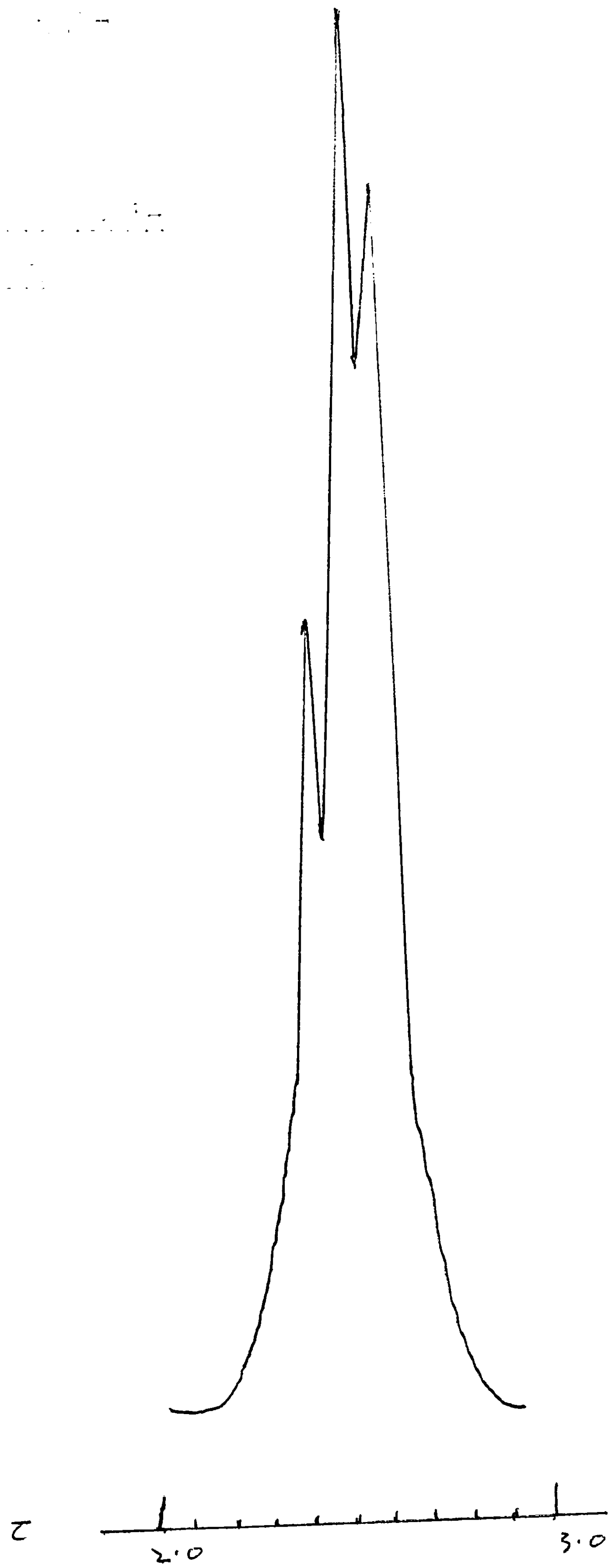
The figures for biphenyl itself are taken from Ref. 10. Wavelengths in brackets are those of inflections.

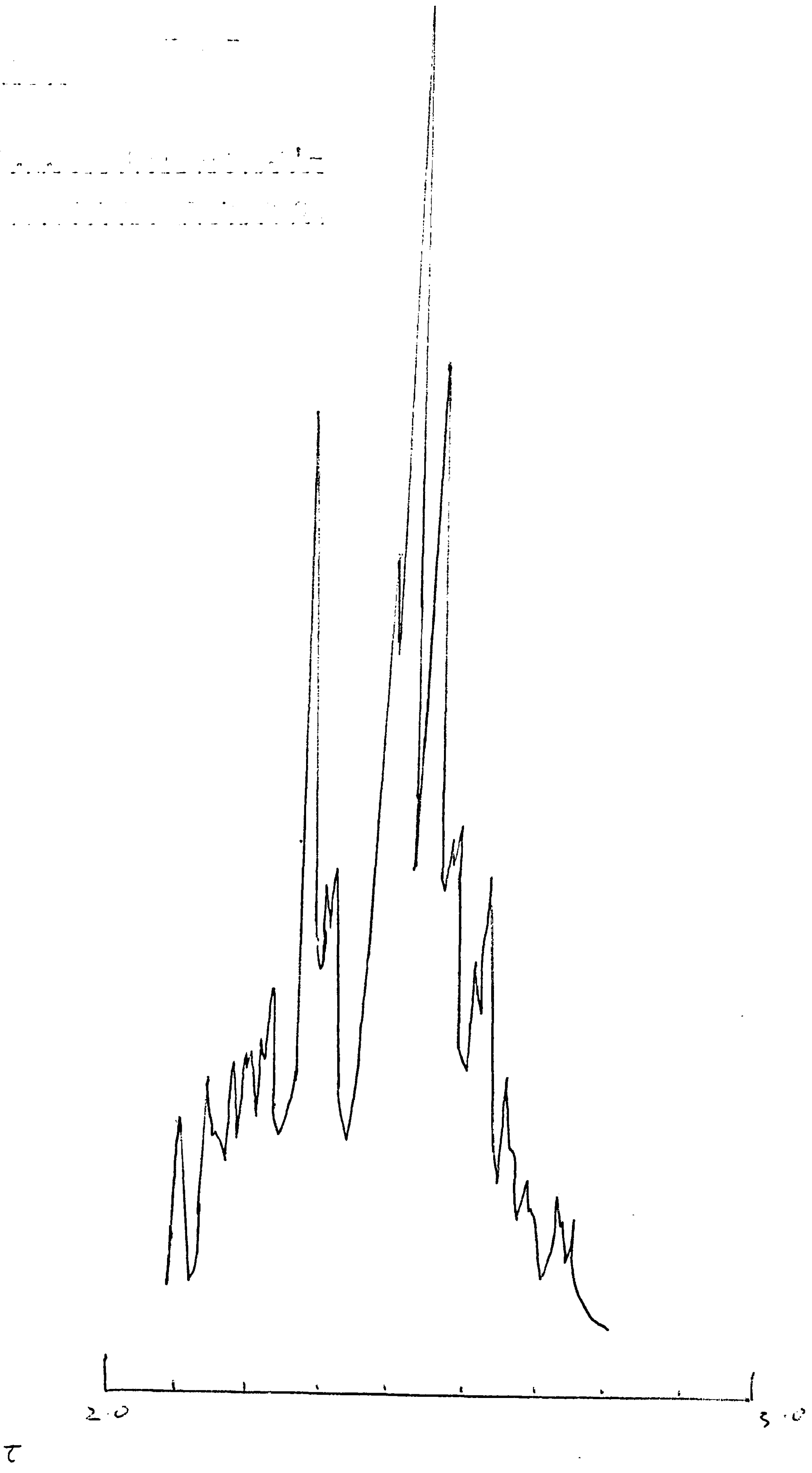

τ
2.2
3.0

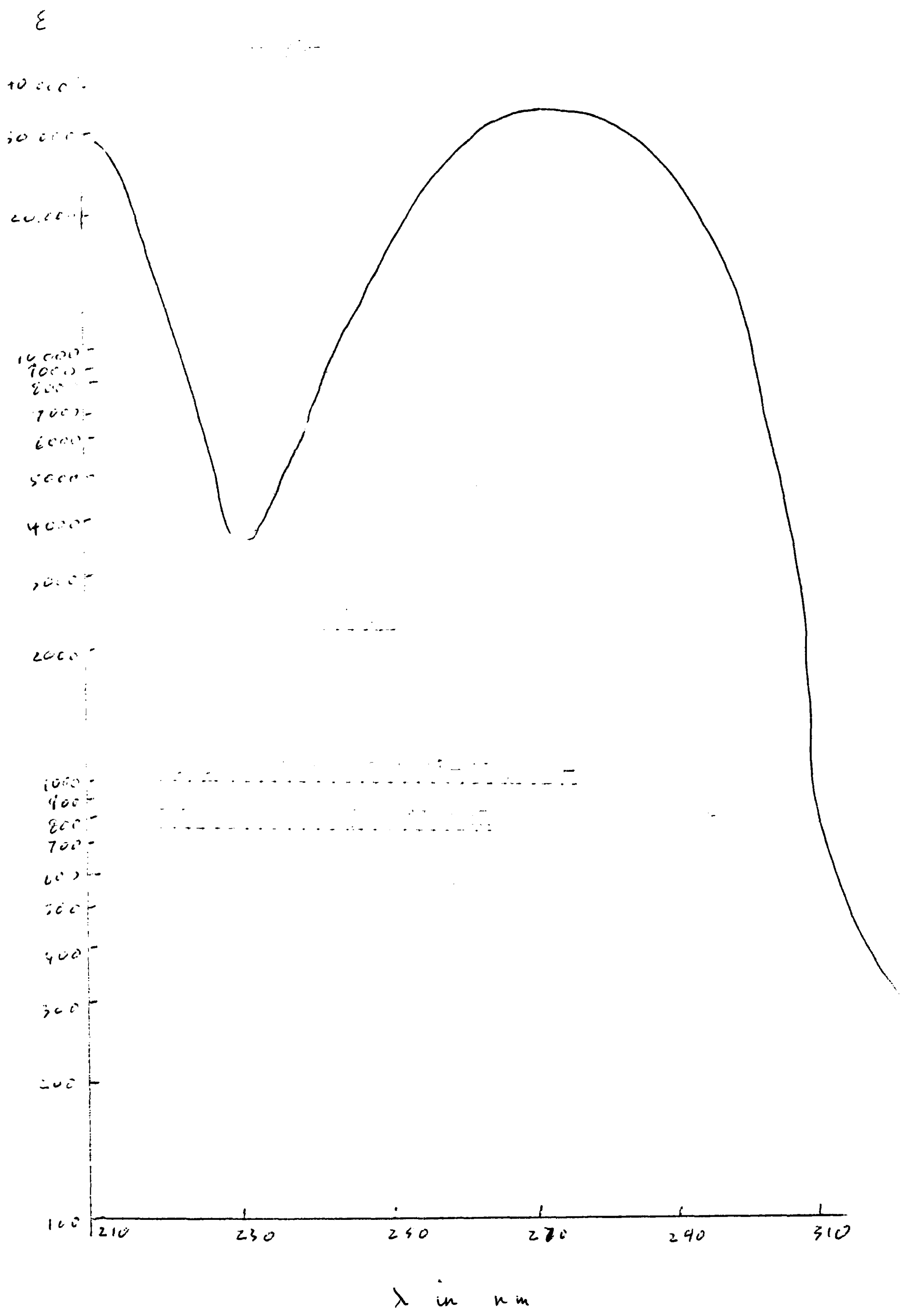

τ
3.0
4.0

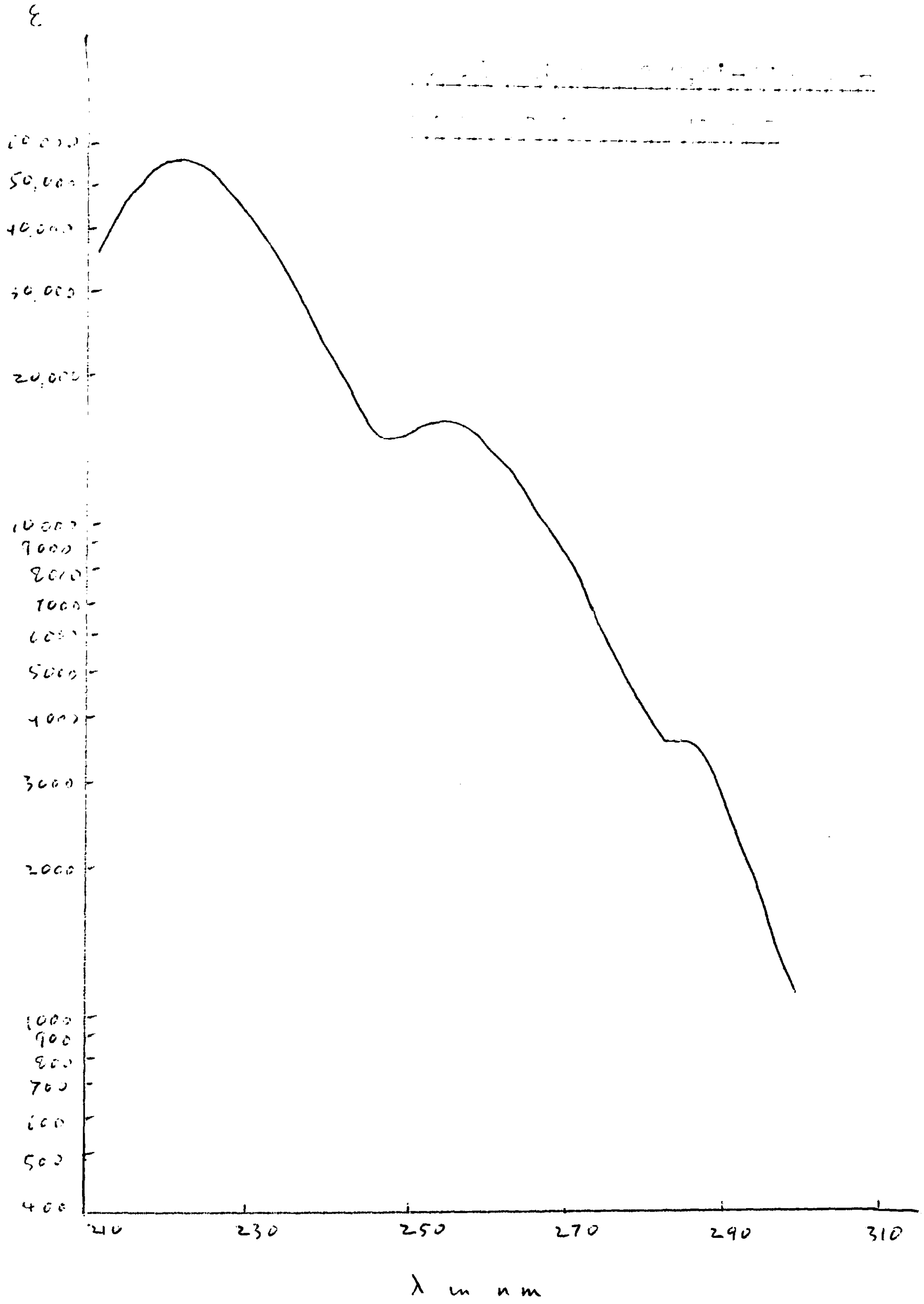

2·0
3·0
τ

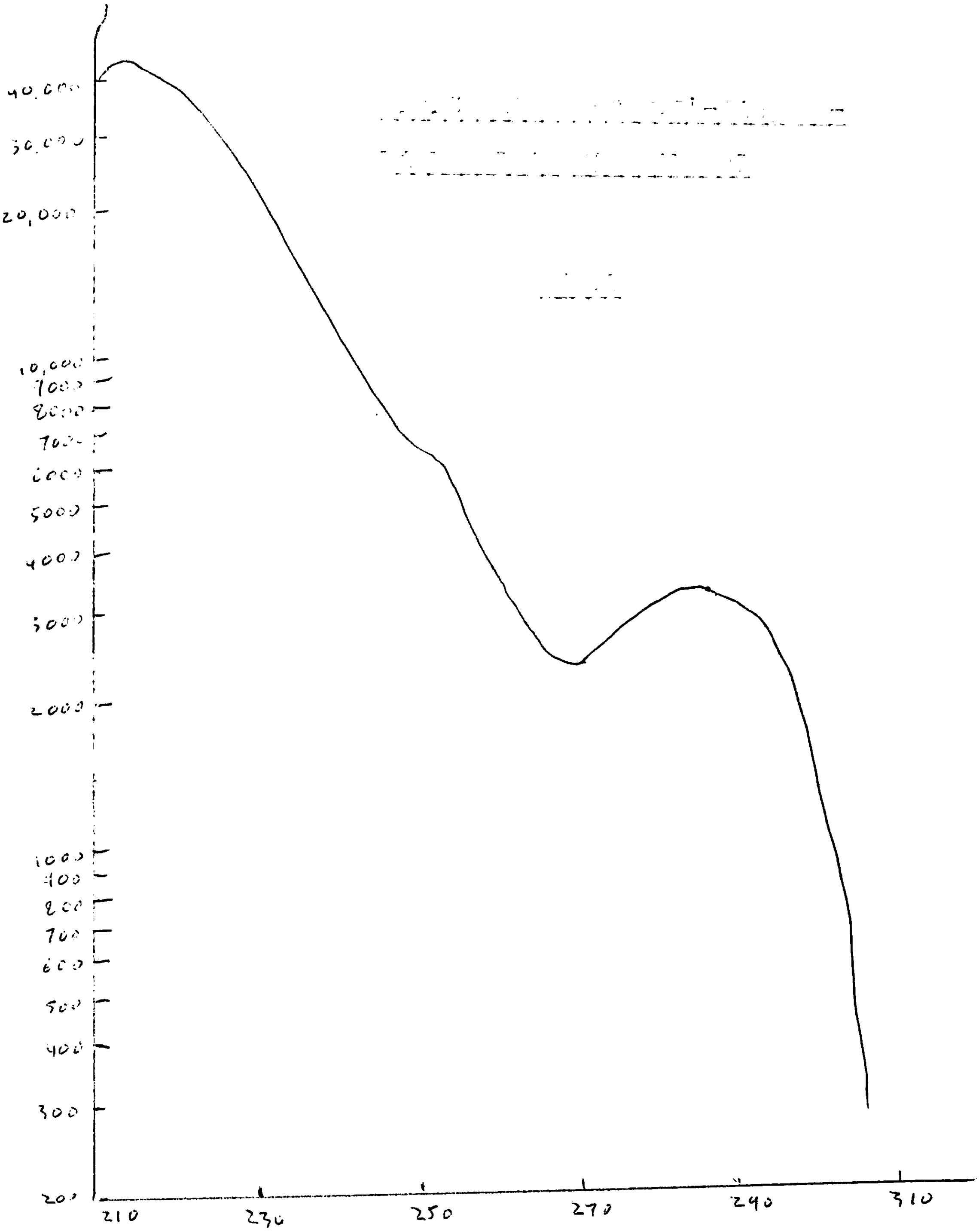

τ
2·0
2·5


τ
2·0
3·0


2.0
3.0
τ


ε
40 000
30 000
20 000
10 000
9000
8000
7000
6000
5000
4000
3000
2000
1000
900
800
700
600
500
400
300
200
100
210
230
250
270
290
310
λ in nm


ε
60,000
50,000
40,000
30,000
20,000
10,000
9000
8000
7000
6000
5000
4000
3000
2000
1000
900
800
700
600
500
400
210
230
250
270
290
310
λ in nm


[illegible]
40,000
30,000
20,000
10,000
9000
8000
7000
6000
5000
4000
3000
2000
1000
900
800
700
600
500
400
300
200
210
230
250
270
290
310

The effects shown are in line with those discussed on p. 12 ff. A cyano group in the 4-position causes a smaller bathochromic shift in the conjugation band than an amino or hydroxy group in the same position (see table on p.). In the 2-position the cyano groups have the expected effect of suppressing the conjugation band. The spectrum of 3,3'-dicyanobiphenyl is comparable with that of 3,3'-dihydroxybiphenyl (p. 15) in that a band begins to appear at long wavelengths corresponding to the isolated phenyl chromophore.

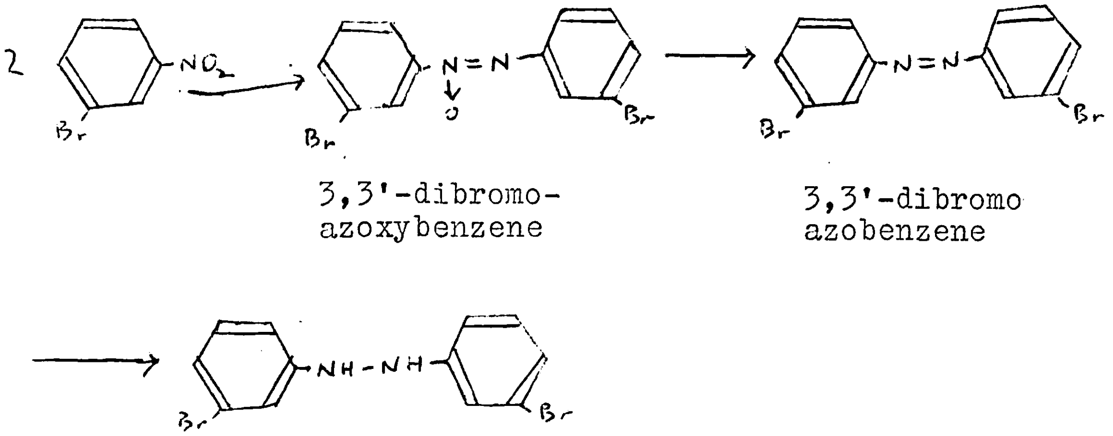
N.M.R. spectra have also been measured and compared with those of the corresponding halides. The splitting pattern is too complicated to be analysed by inspection but is clearly dependent on the nature as well as the orientation of substituents. The halides and the nitriles have quite different spectra.

Preparation of 2,2'-dicyanobenzidine

As described on pp. 18 f , the presence of bulky groups in the 2,2'-positions of the biphenyl nucleus may give rise to labile optical activity. In order to determine whether 2,2'-dicyanobiphenyls can be obtained in optically active condition, it is necessary either to prepare them from optically resolved precursors by a path which will not involve racemisation or to find some means of resolving their racemic forms. 2,2'-Dicyanobenzidine, a previously unknown compound, should form salts with chiral acids and this provides a possible means of optical resolution.

The most obvious path to 2,2'-dicyanobenzidine involves the action of cuprous cyanide on a 2,2'-dihalogenobenzidine. 2,2'-Dichlorobenzidine was already available from previous work but attempts to convert it into 2,2'-dicyanobenzidine under the conditions used for 2,2'-dicyanobiphenyl above were unsuccessful. The amine decomposed even when the reaction was carried out under nitrogen and only an intractable tar was obtained. Clearly less vigorous conditions are required and this suggests the use of 2,2'-dibromobenzidine as the starting material.

2,2'-Dibromobenzidine was prepared from m-bromonitrobenzene by a path similar to that outlined on p.. for 3,3'-dichlorobiphenyl. The reduction of m-bromonitrobenzene to the hydrazo stage proved unexpectedly difficult. Zinc and alkali carried the reduction only to the azo stage or to a mixture of azo- and azoxybenzenes.



3,3'-dibromo-azoxybenzene

3,3'-dibromo azobenzene

3,3'-dibromohydrazobenzene

This mixture was further reduced with zinc and glacial acetic acid and the product treated with concentrated acid to bring about the rearrangement to 2,2'-dibromobenzidine. Yields were variable, never more than 20%; sometimes the reaction failed altogether. Attempts were made to reduce the mixture with alkaline formalin solution in the presence of 2,3-dichloro-1,4-naphthoquinone, a method discovered by A.W. Sogn[116], but these too terminated at the stage of 3,3'-dibromo-azobenzene. Once again, further reduction with zinc and acetic acid was only occasionally successful. *m*-Bromonitrobenzene itself proved inert to reduction with formalin.

2,2'-Dibromobenzidine precipitated from acid solution as a sparingly soluble dihydrochloride which was converted into the free base by dissolving it in hot water and adding an excess of solium hydroxide solution. The free base was filtered off, dried in air and converted into the nitrile by reaction with cuprous cyanide in dimethylformamide in an atmosphere of nitrogen.

2,2'Dicyanobenzidine is a cream-coloured crystalline solid which decomposes without melting above 260°. It resembles the dicyanobiphenyls in undergoing a change from prismatic crystals to needles at <u>ca</u>. 200°. Although it is stable at room temperature in the solid state, its solutions darken rapidly and only brown crystals can be recovered. This, together with its low solubility in common solvents, makes it hard to purify. The method adopted was to dissolve the compound in dilute hydrochloric acid and allow the solution to stand over charcoal for some time in order to remove coloured impurities. The purified base could then be reprecipitated by alkali.

The infrared spectrum of 2,2'-dicyanobenzidine shows an absorption band at 2227 cm^{-1} due to $C\equiv N$ stretching. The wavelength is exactly the same as for the corresponding absorption in 2,2'-dicyanobiphenyl (see p. 57).

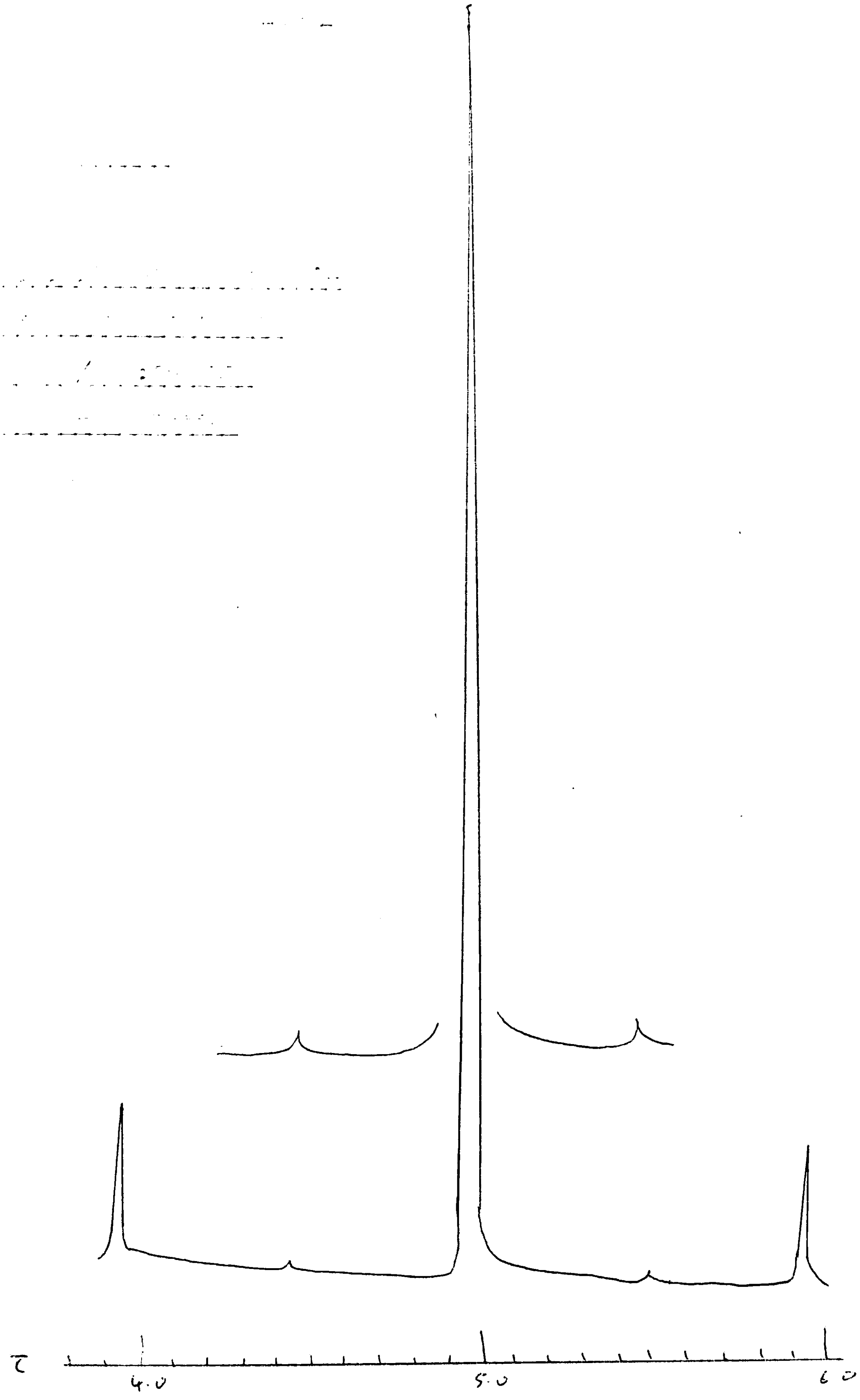
An attempt was made to resolve 2,2'-dicyanobenzidine into enantiomeric forms. The compound gave no crystalline salts with D-(+)-tartaric acid but with (+)-camphor-10-sulphonic acid it yielded a white, crystalline camphorsulphonate which charred without melting at <u>ca</u> 220°. The actual temperature at which decomposition began depended on the crop.

1st crop	228°
2nd crop	225°
3rd crop	220°

This seems to indicate an inhomogeneity in the salt, caused either by contamination with unchanged starting materials or by partial optical resolution. Unfortunately, the salt proved insoluble in all common solvents. It dissolved slightly in dimethyformamide but the solution was colloidal and scattered light so strongly that polarimetric examination was impossible.

The nuclear magnetic resonance spectrum of 2,2'-dicyanobenzidine was examined in deuterated sulphuric acid. In this solvent, exchange of the amino protons is suppressed and the peaks due to these protons are reduced to low humps by the powerful relaxing effect of the nitrogen quadrupole moment. It was hoped however that the aromatic proton spectrum would not be affected significantly by the solvent. In fact the spectrum presented a remarkable appearance. Three sharp widely spaced peaks were found in the region 4-6τ. In anhydrous deuterosulphuric acid, these were at τ 3.8, 4.35 and 4.9, the peak ratios being approximately 1:4:1. The distance between the peaks, 35 Hz, seems too large for a normal coupling constant and yet the pattern is clearly symmetrical about the centre. When the compound was dissolved in D_2SO_4 diluted with D_2O (pD 2.14), the spectrum was similar but centred at lower field and more widely spaced. The peaks were initially at τ 4.0, 4.95 and 5.95 but the two outer peaks moved out slowly with time remaining equal in size and equally spaced about the centre. The peak ratio varied more strikingly with time. Initially it was approximately 1:12:1 but after 24 hours it was reduced to 1:9:1. Another feature of the spectrum in dilute acid was the appearance of additional small peaks arranged in pairs about the centre. These also became more clearly marked with time. The spectrum in concentrated acid showed no time dependence.


4.0
5.0
τ


τ
4.0
5.0
6.0

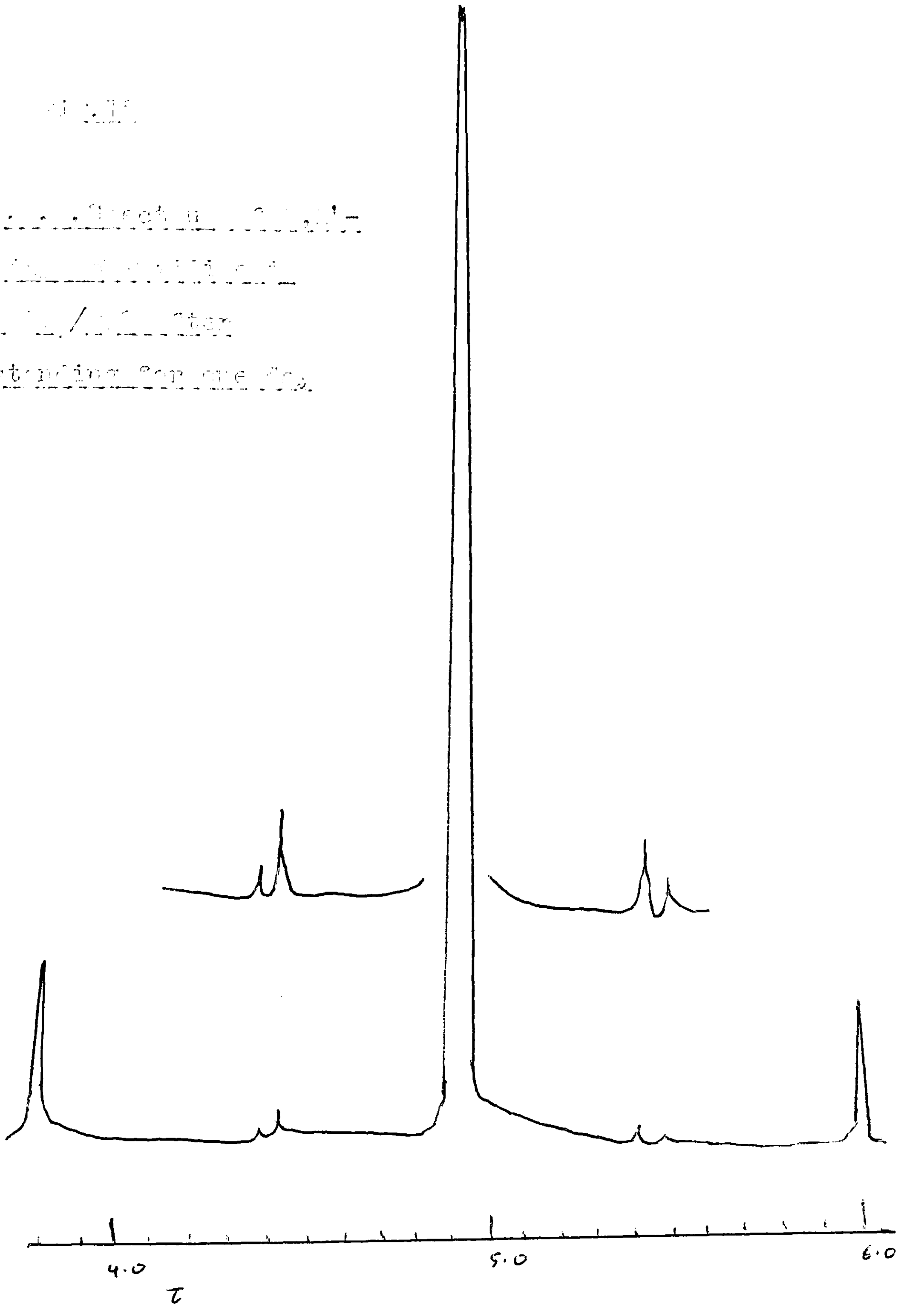
N.M.R.

[illegible] acetone [illegible]

[illegible]

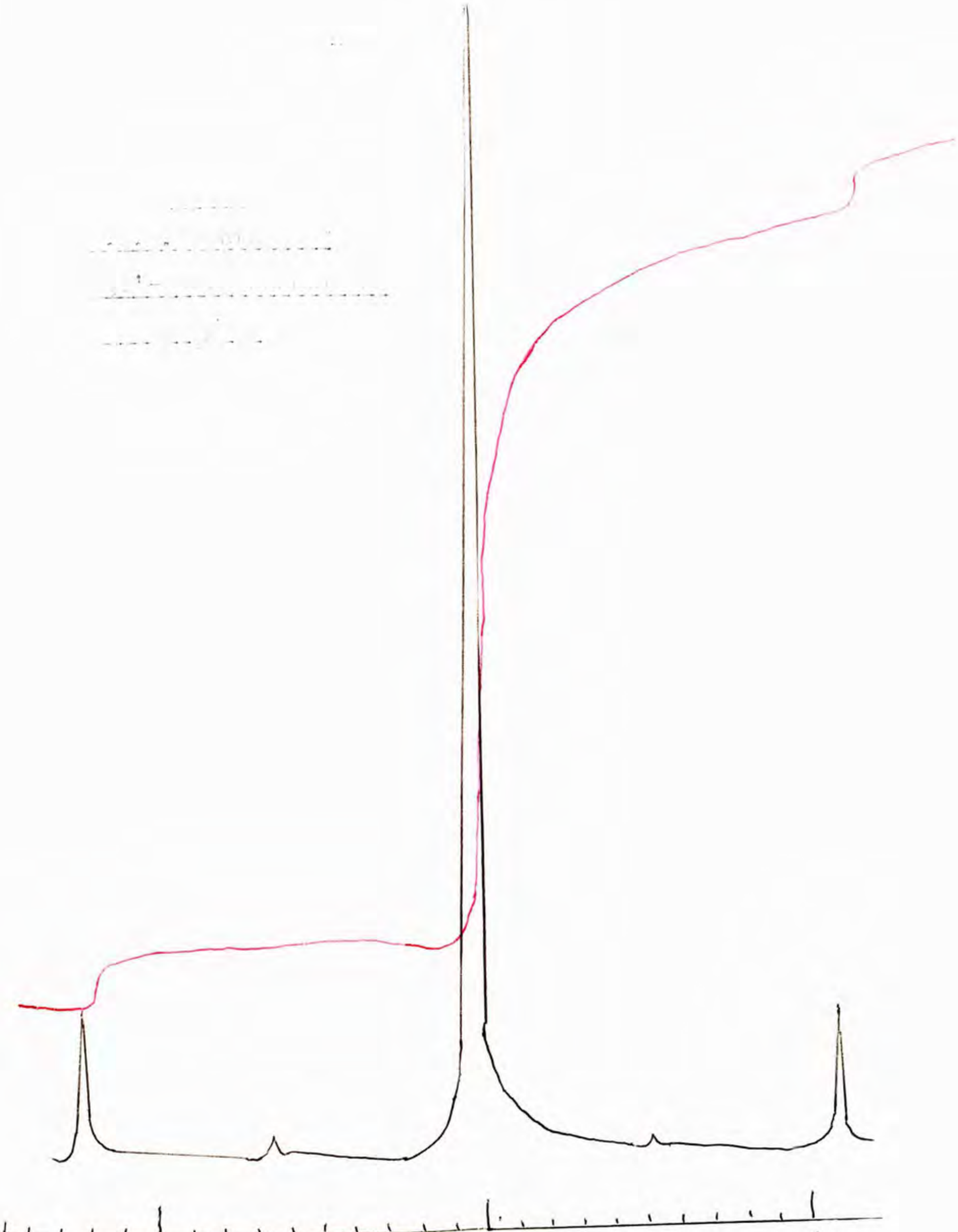
[illegible] after

standing for one day.

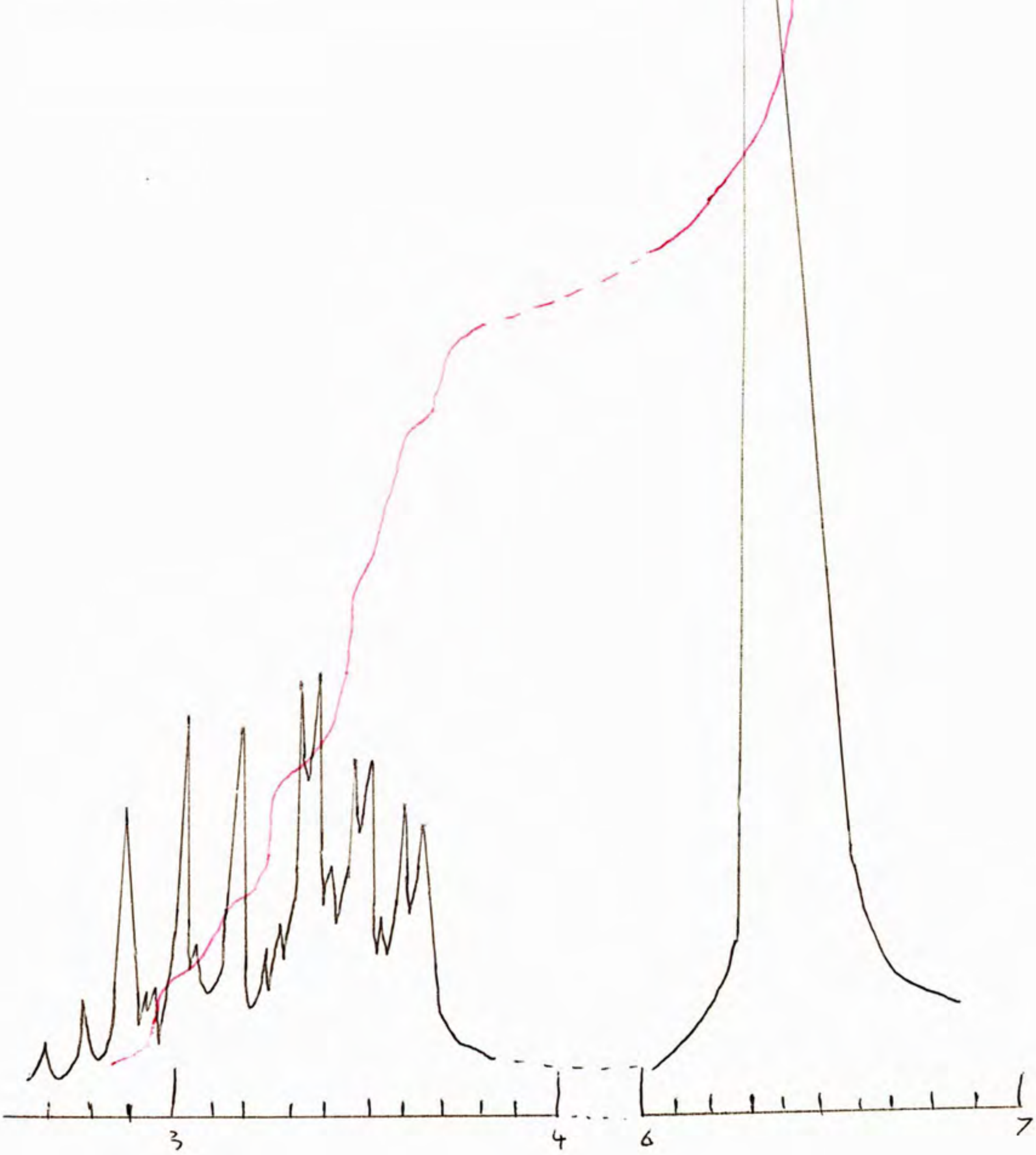


For comparison, the spectrum of 2,2'-dibromobenzidine was also examined in dilute D_2SO_4. The pattern of peaks was very similar to that for 2,2'-dicyanobenzidine in the same solvent, the peaks being at τ 3.8, 4.95 and 6.1 and the peak ratios about 1:12:1. No explanation could be found for these spectra but they are clearly characteristic of 2,2'-disubstituted benzidines in acid solution and do not depend on the presence of cyano groups. The narrowness and sharpness of the peaks suggests that the patterns are due to aromatic and not to amino protons, although the centre of the pattern is far from the normal aromatic region of τ 3-4. In neutral organic solvents, the 2,2'-disubstituted benzidines show the expected complex aromatic multiplet at τ 2.8-4 and a single peak due to amino protons at τ 6.4: a spectrum of 2,2'-dichlorobenzidine is appended.

In the mass spectrum of 2,2'-dicyanobenzidine, the strongest line was at m/e 234 corresponding to the molecular ion $C_{14}H_{10}N_4$. There were smaller peaks at m/e 206 and 179 (9% each) corresponding to sequential loss of 2(HCN + H). The loss of HCN from an aromatic amine is a well-known splitting mode; the <u>cyclo</u>pentadiene residue which is formed can then stabilise itself by loss of an additional proton to give a <u>cyclo</u>pentadienyl radical



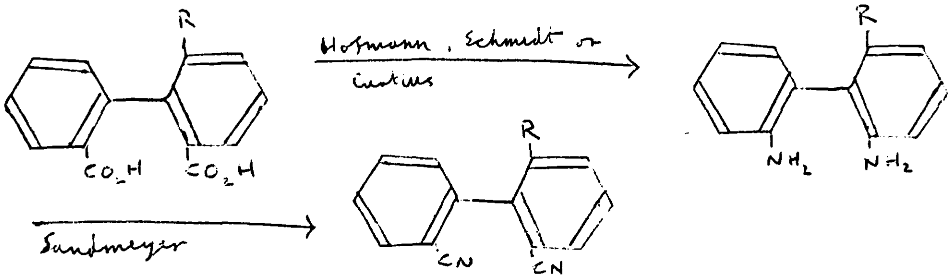
τ
4.0
5.0
6.0


3
4
6
7

with fully delocalised π-type orbitals. The spectrum also showed small amounts of 2-cyano-2'-bromobenzidine (M.W. 287) and 2,2'-dibromobenzidine (M.W. 300) to the extent of 6% and 1% respectively. However, organic halides are considerably more volatile than the corresponding nitriles and hence show up disproportionately in the mass spectra of mixtures. The concentration of the brominated compounds in the original solid mixture is probably very small indeed.

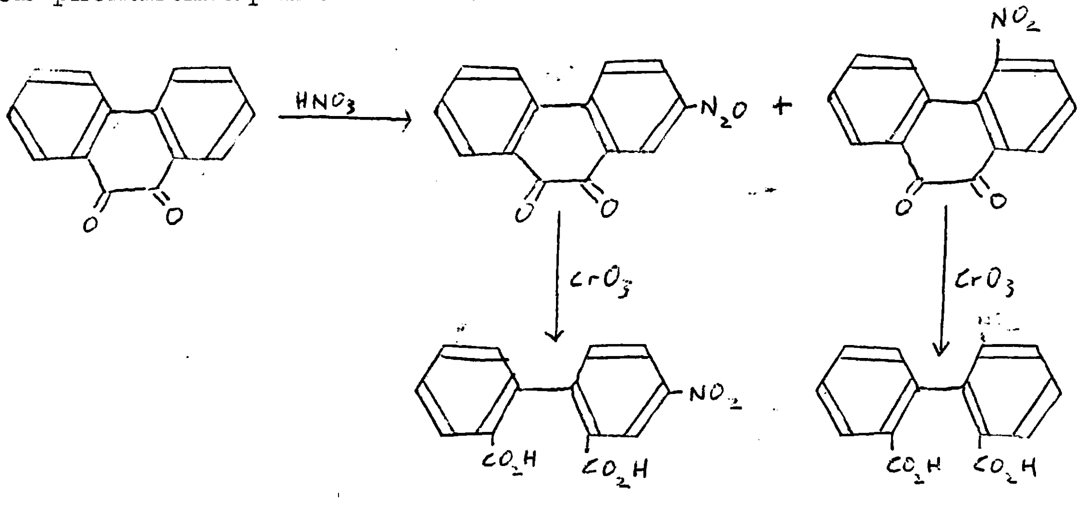
Studies towards the preparation of 6-nitro-2,2'-dicyano biphenyl

The most promising path to optically active 2,2'-dicyanobiphenyls is to prepare them from optically active substituted diphenic acids *via* the diamines.



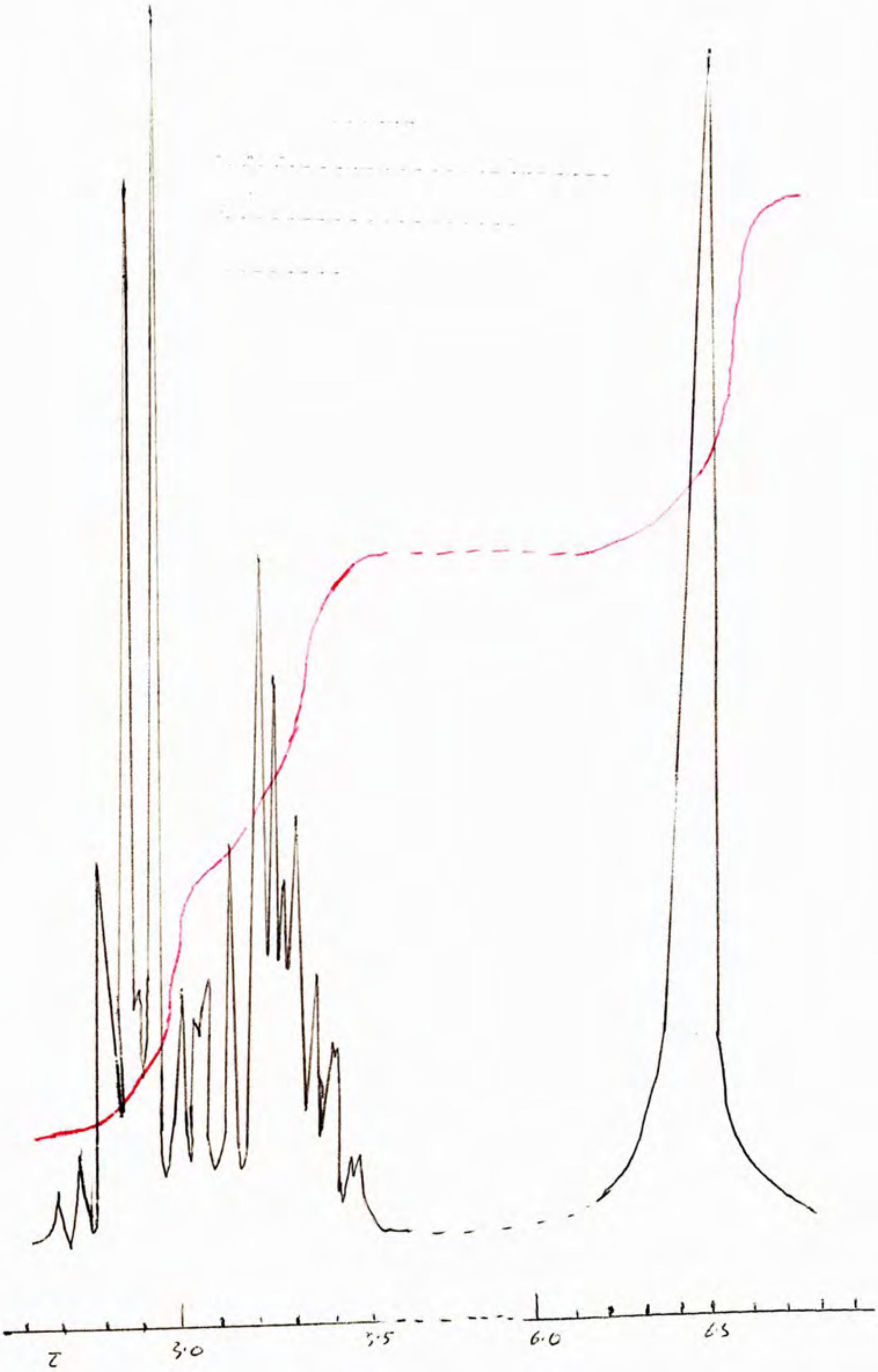
The reactions shown above are known to proceed without racemisation[80,81,82] although the Sandmeyer reaction is often accompanied by cyclisations leading to carbazole or benzo[c]cinnoline (see pp. 30 f.).

6-Nitrodiphenic acid is readily resolvable and was therefore chosen as the starting material. Together with its isomer, 4-nitrodiphenic acid, it was prepared from phenanthraquinone as follows:



The Hofmann, Schmidt and Curtius reactions were tested on racemic acids. These acids are formally related to 2,2'-dicyanobiphenyl and their reactions have an intrinsic interest as well as possibly leading to optically active 2,2'-diaminobiphenyls.

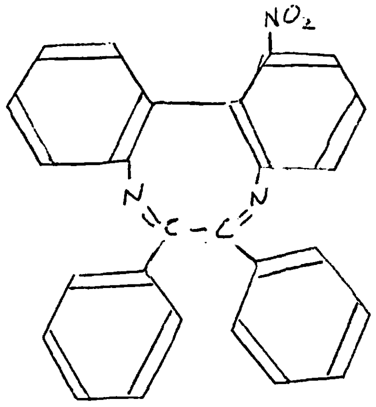
Racemic 6-nitrodiphenic acid was converted first into its di-acid chloride by treatment with thionyl chloride and then into its diamide by the action of ammonia. The diamide was subjected to the Hofmann reaction under the conditions specified by Holt and Hughes[93] for the diamide of 6,6'-dinitrodiphenic acid. 6-Nitro-2,2'-diaminobiphenyl was obtained as a yellow oil which rapidly turned red in air; the red colour could be removed by chromatography on alumina using diethyl ether as eluant. 2,2'-Diaminobiphenyl itself is sometimes obtained as a similar red oil but can be crystallised from alcohol whereas 6-nitro-2,2'-diaminobiphenyl has not so far been obtained in crystalline form. The compound is only weakly basic. When gaseous hydrogen chloride is passed into its ethereal solution a white hydrochloride separates but reverts to the free amine on exposure to atmospheric moisture. The infrared spectrum shows the expected bands at 3500 and 3400 cm^{-1} due to symmetric and antisymmetric NH_2 stretches and at 1530 and 1360 cm^{-1} due to symmetric and antisymmetric NO_2 stretches together with a strong NH_2 deformation band at 1620 cm^{-1}. The nuclear magnetic resonance (N.M.R.) spectrum, measured in deuterochloroform shows a complex aromatic multiplet at τ2.5-3.5 and an NH peak at τ3.53. The ratio of aromatic to amino protons is 1.7:1 in good agreement with the theoretical value of 1.75:1. In the mass spectrum, however, the species of highest molecular weight was shown by accurate measurements to have the formula $C_{12}H_5N_3Br_2O_2$ corresponding to a mononitro-dibromo-benzo[c]cinnoline and no peak was shown corresponding to 6-nitro-2,2'-diaminobiphenyl. In view of the I.R. and N.M.R. data, the dibromobenzo[c]cinnoline must be regarded as an artifact formed during the vaporisation of the sample. The presence of molecular bromine either free or in complex form could account both for bromination of the amine and for oxidative cyclisation to a benzo[c]cinnoline. It seems likely that bromination is the first step since, according to the work of Corbett and Holt[107], the presence of bromine <u>ortho</u> or <u>para</u> to the amino groups encourages cyclisation. The alternative order of reaction is also precluded by the unwillingness of benzo[c]cinnoline itself to react with bromine (see p. 50). Nor can the



2
3·0
3·5
6·0
6·5

peak be due to the molecular complex of bromine and benzo[c]cinnoline since the immediate breakdown product of that would be benzo[c]cinnoline itself and no such peak appears on the spectrum.

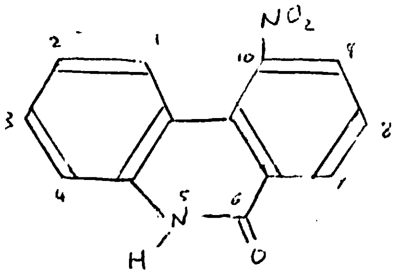
The presence of nuclear bromine in the original compound is inconsistent with the N.M.R. spectrum: if two nuclear protons were substituted by bromine, the ratio of aromatic to amino protons would be 1.25:1 instead of the observed 1.7:1. Furthermore, a sodium fusion test carried out on the compound gives only a negligible positive result for halogens. No reliable quantitative analysis could be carried out owing to the readiness with which the compound oxidised in air, and attempts to prepare a crystalline diacetyl derivative produced only mixtures. However, condensation with benzil produced a crystalline solid whose analysis was consistent with the expected product, 4'-nitro-2,3-diphenyl-5,6:7,8-dibenzo-1,4-diazocine.

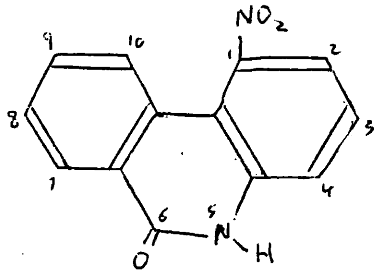


This confirms the identity of the initial amine as 6-nitro-2,2'-diaminobiphenyl.

The Schmidt reaction furnishes a means of preparing 2,2'-diaminobiphenyls direct from the corresponding diphenic acids. Both 4- and 6-nitrodiphenic acids were treated with solid sodium azide in concentrated sulphuric acid; in both cases the product was a neutral solid of high melting point which appeared to be a phenanthridone. The formation of phenanthridone in the Schmidt reaction of diphenic acid itself has been described on p~~p~~. 42 Such a cyclisation should be encouraged by any factor that inhibits the Schmidt reaction on one carboxyl group while allowing it to proceed on the other. In 4- and 6-nitrodiphenic acids a nitro group is situated _meta_ to one of the two carboxy groups and, as shown by the work of Briggs and Lyttleton[79], _meta_-nitro groups have a significant inhibiting effect on the Schmidt arrangement although their electron-withdrawing power can be exercised by induction only.

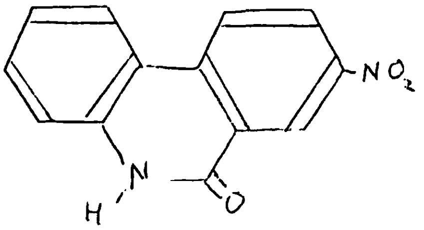
On this basis one would expect 6-nitrodiphenic acid to give rise to 10-nitro- rather than 1-nitro-(5H)-6-phenanthridone

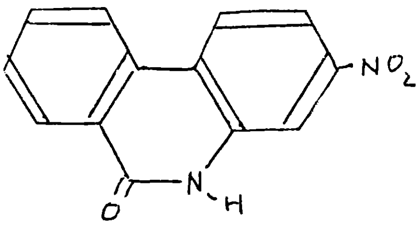




m.p.[118] 316-318°   m.p.[118] 325-327°

and 4-nitrodiphenic acid to give 8-nitro- rather than 3-nitrophenanthridone



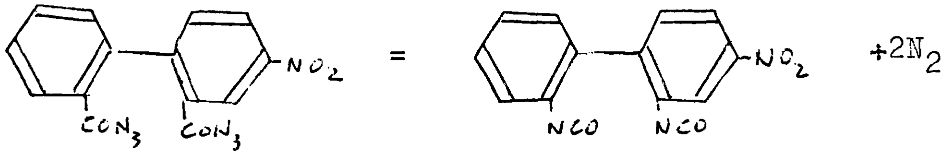


m.p.[117] 324-326°   m.p.[117] 357-358°

In fact the melting points found in the present work were 312-314° for the product from 6-nitrodiphenic acid and 318-321° for the product from 4-nitrodiphenic acid. The product of the Curtius reaction of 4-nitrodiphenic acid melted at 320-323°. Although this does not identify the products unambiguously as 10- and 8-nitrophenanthridone, it provides good evidence for the identification; accurate melting points above 310°

are difficult to obtain on an ordinary Koffler hot-stage. The infrared spectra of both compounds resemble an authentic spectrum of phenanthridone itself given in the catalogue of the American Petroleum Institute (no. 2331). The percentage yield, calculated as nitrophenanthridone, is close to 80% in both cases and this is interesting in view of the steric properties of the two acids; the average angle between the rings and the distance between the carboxyl groups would be expected to be different, yet cyclisation apparently takes place with equal ease.

The Curtius reaction was carried out on 4-nitrodiphenic acid only. The acid chloride was dissolved in acetone and treated with an aqueous solution of sodium azide. The di-acid azide which precipitated was heated in benzene under reflux to effect its decomposition and rearrangement into the di-isocyanate.



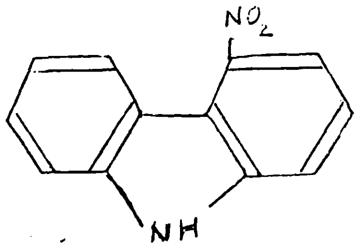
Concentrated hydrochloric acid was then added and the mixture vigorously boiled to hydrolyse the isocyanate groups. This hydrolysis was ineffective; no basic material was obtained by basification and extraction of the acid layer. Instead, the product was a yellow solid insoluble in acid and only sparingly soluble in benzene. The infrared spectrum showed a band at 2300 cm^{-1}, the characteristic stretching frequency for the N=C=O group. This compound, presumably 4-nitro-2,2'-di-<u>iso</u>cyanatobiphenyl, was not characterised further but was suspended in concentrated hydrochloric acid and boiled for a further two hours in the hope of effecting the final hydrolysis to 4-nitro-2,2'-diaminobiphenyl. Once again a yellow crystalline non-basic solid was obtained but its infrared spectrum was now rather different. The band at 2300 cm^{-1} had disappeared but a much stronger band had appeared at 2130 cm^{-1}, a frequency characteristic of polymeric isocyanates such as cyanurates. When recrystallised from ethyl acetate/light petroleum it had a melting point of 315-319° - and its analysis approximated to that for 4-nitro-2,2'-diisocyanatobiphenyl. An attempt was made to determine the degree of polymerisation by molecular weight measurement using a Mechrolab vapour pressure osmometer. The molar concentrations obtainable were very low owing to the high molecular weight of the compound and its low solubility in common organic solvents. The highest solubility was in chloroform but a saturated solution at room temperature contained only 10.13 g./litre and its molar concentration as measured on the machine was no more than 0.01 M. This is too small to be reliable. The theoretical molar concentrations are

Monomer	0.036
Dimer	0.018
Trimer	0.012
Tetramer	0.009

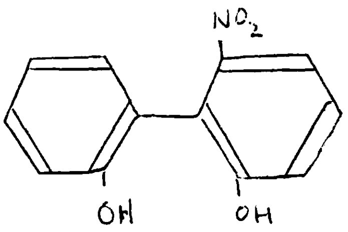
This definitely excludes the monomer and virtually excludes the dimer. A trimer or tetramer seems most likely.

In order to prevent polymerisation, a specimen of the diazide was subjected to rearrangement in the form of a suspension in concentrated hydrochloric acid without the addition of an organic solvent. This procedure is somewhat hazardous but ensures that any isocyanate formed is rapidly hydrolysed. In fact, partial hydrolysis of the azide occurred and the main product was 8-nitro-(5H)-6-phenanthridone in over 70% yield. In one small-scale experiment some 4-nitrodiphenic acid was also recovered. The Curtius reaction carried out under these conditions therefore resembles the Schmidt reaction. It is however more explosive; on one occasion a loud report was heard during the rearrangement and a glass stopper, placed in one neck of the two-necked reaction vessel, was blown out with some force. No explosions occurred during the Schmidt reactions of either 6- or 4-nitro-diphenic acids.

Unfortunately all attempts to convert 6-nitro-2,2'-diaminobiphenyl into 6-nitro-2,2'-dicyanobiphenyl by the Sandmeyer reaction were unsuccessful. Diazotisation was carried out both in dilute and concentrated sulphuric acid and the bisdiazonium salt solution neutralised and treated with potassium cupro-cyanide in accordance with the instructions of Clarke and Read[47]. When dilute acid was used the oily amine was recovered unchanged, showing that tetrazotisation had not taken place. This is a not unexpected result considering the very weak basicity of the amine. In concentrated sulphuric acid tetrazotisation proceeded normally as shown by a test with alkaline β -naphthol but the final product, an acidic solid, did not show in its infrared spectrum the characteristic 2200 cm^{-1} band of organic nitriles. Thin layer chromatography showed this solid to be a mixture of several compounds; probably the main constituents are 4-nitrocarbazole and 6-nitro-2,2'-dihydroxybiphenyl.



4-nitrocarbazole



6-nitro-2,2'-dihydroxybiphenyl

Both are to be expected as products of the decomposition of 6-nitrobiphenyl-2,2'-bisdiazonium sulphate and the latter would account for the partial solubility of the mixture in aqueous alkali.

It was not thought practicable to omit the neutralisation step since the addition of concentrated sulphuric acid to an aqueous cyanide solution would lead to the evolution of considerable heat as well as toxic gases and any diazonium salt present would certainly be hydrolysed. Dilution of the acid with ice chips in order to keep the temperature down was found to be as lengthy a procedure as neutralisation and left enough time for the carbazole to form. The work of Dobbie et al.[49] on the Sandmeyer reaction of 2,2'-diaminobiphenyl itself with cuprous bromide showed that carbazole formation proceeded readily in acid solution. 2,2'-dibromobiphenyl was obtainable only by carrying out the tetrazotisation in the presence of cuprous bromide so that the bisdiazonium salt could react before it broke down into carbazole. This is clearly inapplicable to reactions with cyanides, which are unstable in acid solution.

The dehydration of a 6-substituted biphenyl-2,2'-dicarboxamide provides a further possible route to 6-substituted 2,2'-dicyanobiphenyls. The vigorous conditions required preclude the preparation of optically pure products but subsequent optical resolution may be possible given the presence of acidic or basic groups elsewhere in the molecule. In order to investigate this route, several dehydration experiments were carried out on the parent compound, biphenyl-2,2'-dicarboxamide or diphenic acid diamide.

The diamide was prepared from diphenic acid via the dichloride. Thionyl chloride, which converts 4-

and 6-nitrodiphenic acids into their acid chlorides, causes cyclisation of diphenic acid itself to the anhydride; however, the use of phosphorus pentachloride avoided this complication. The crude chloride was treated immediately with aqueous ammonia to convert it into the diamide.

Of the various methods listed on pp. 31 ff for converting aromatic amides into nitriles, the simplest to carry out is dehydration with thionyl chloride. The reagent is liquid and hence needs no solvent, it is easily removed by distillation and the products of its hydration are gaseous and escape at once from the reaction vessel.

$$SOCl_2 + H_2O = 2HCl + SO_2$$

However the reaction of thionyl chloride with diphenic acid diamide yielded only 4-cyanofluorenone which sublimed from the reaction mixture in bright yellow needles. It was identified by its melting point and by its infrared spectrum which showed $C\equiv N$ stretching at 2250 cm^{-1} and ketonic $C=O$ stretching at 1710 cm^{-1}. The same product was obtained when phosphorus oxychloride was used for the dehydration; as mentioned on p. 35 , phosphorus oxychloride causes cyclisation of diphenic acid itself to 4-carboxyfluorenone. The action of phosphorus pentoxide on biphenyl-2,2'-dicarboxamide under dry mesitylene is similar to that of the oxychloride: once again the product is 4-cyanofluorenone. Without a solvent to protect the reagent from atmospheric moisture no simple product could be obtained.

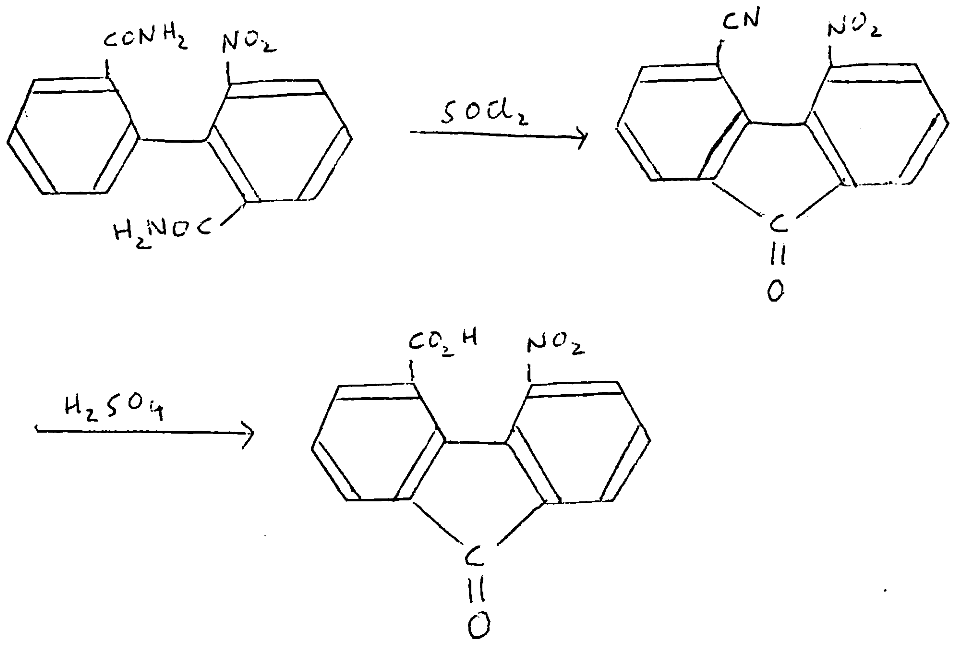
In view of these results it was not thought worthwhile to try the method described on p. 33 which involves heating an aromatic carboxylic acid with phosphorus pentachloride and p-toluenesulphonamide. The mechanism of this reaction is not known but probably involves the intermediate formation of the carboxylic acid amide and cyclisation of this by PCl_5 seems highly probable. That the amide cyclises to a fluorenone derivative more readily than the acid is shown by its behavior with thionyl chloride.

The action of lead thiocyanate on the zinc salt of diphenic acid as described on p. 33 might well yield 2,2'-dicyanobiphenyl but the reaction was not investigated as it could not safely be used on 6-nitrodiphenic acid. E.E. Reid[58] who developed this method reports that the presence of the nitro group in the molecule leads to explosions.

Dehydration of biphenyl-2,2'-dicarboxamide with the mixed salt $NaCl.AlCl_3$ (see p. 32) is very likely to cause cyclisation since this reaction can be seen as an internal Friedel-Crafts acylation and Al_2Cl_6 is a well-known Friedel-Crafts catalyst. Moreover, the method is said[56] to be unsuitable for the dehydration of diamides. Hence the reaction was not investigated. Catalytic dehydration was also rejected as it must be carried out in the gas phase for good results and the derivatives and substitution products of diphenic acid are not very volatile.

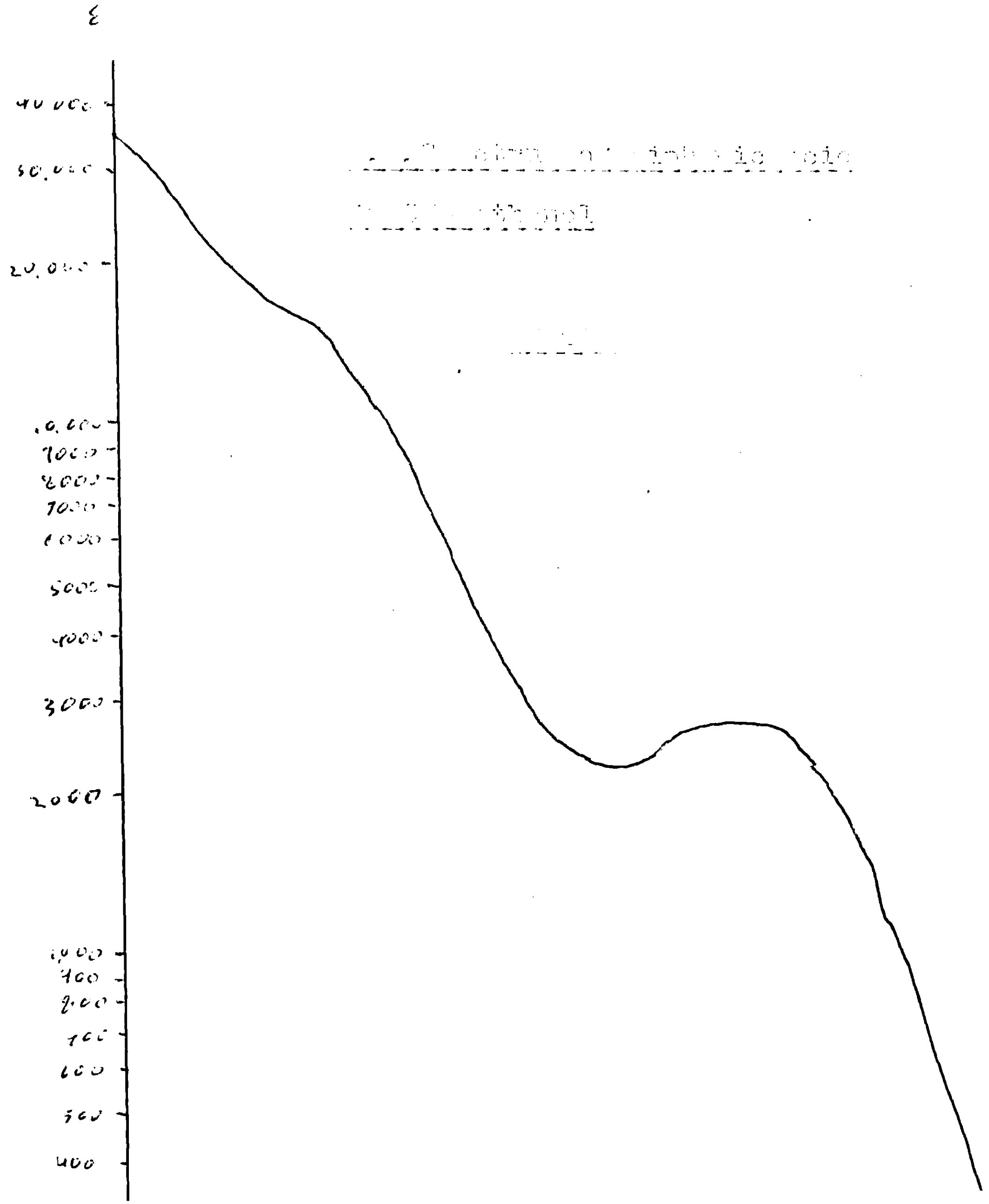
The presence of an additional group in the 6-position of biphenyl-2,2'-dicarboxamide should discourage cyclisation to a fluorenone derivative; for this reason an attempt was made to dehydrate 6-nitrodiphenic acic diamide to 6-nitro-2,2"-dicyanobiphenyl using thionyl chloride. However cyclisation took place as before; the infrared spectrum of the product, the typical 1720 cm^{-1} band of a ketone together with bands at 1360 and 1540 cm^{-1} corresponding to the stretching frequencies of the nitro group and a band at 2250 cm^{-1} due to a cyano group. The spectrum is fully consistent with the structure of 5-nitro-4-

cyanofluorenone. Since the compound was an intractable yellow oil which could not be induced to crystallise, attempts were made to convert it to the known 5-nitrofluorenone-4-carboxylic acid. Hydrolysis with warm concentrated sulphuric acid yielded an off-white crystalline solid with the chemical properties of an acid. Unfortunately it turned out to be a mixture of indeterminate melting point. Purification by crystallisation failed and more elaborate methods were excluded by the very small quantity available. Once again the infrared spectrum is fully consistent with the structure proposed and it seems almost certain that cyclisation has in fact taken place.



Spectroscopic studies of 6-nitrodiphenic acid

The ultraviolet spectrum of diphenic acid in ethanol closely resembles that of its dinitrile, 2,2'-dicyanobiphenyl. The conjugation band appears only as an inflection at 230 nm ($\epsilon_{max} \sim 16,000$) and there is a band due to the carboxyphenyl chromophore at 281 nm ($\epsilon_{max} = 2710$). However the spectrum of 6-nitrodiphenic acid is less clearcut owing to the overlapping of the various bands and no definite peaks can be observed; instead absorption falls fairly steadily with increasing wavelength. At a temperature of 21°, two definite inflections can be traced; one at 228 nm ($\epsilon_{max} \sim 23000$) and the other at 280 nm ($\epsilon_{max} \sim 3400$). These correspond to the conjugation band and the carboxyphenyl band respectively. The nitrophenyl band can just be distinguished as a small inflection at 265 nm ($\epsilon_{max} \sim 4800$); in 2,2'-dinitrobiphenyl spectrum in ethanol measured for comparison this band appears at 260 nm ($\epsilon_{max} \sim 12,000$). There seems also to be an inflection at 310 nm ($\epsilon_{max} \sim 1400$). Finally, long-wave nitro absorption covers the region 330-384 nm. This spectrum, unlike that of diphenic acid, shows a definite variation with temperature: at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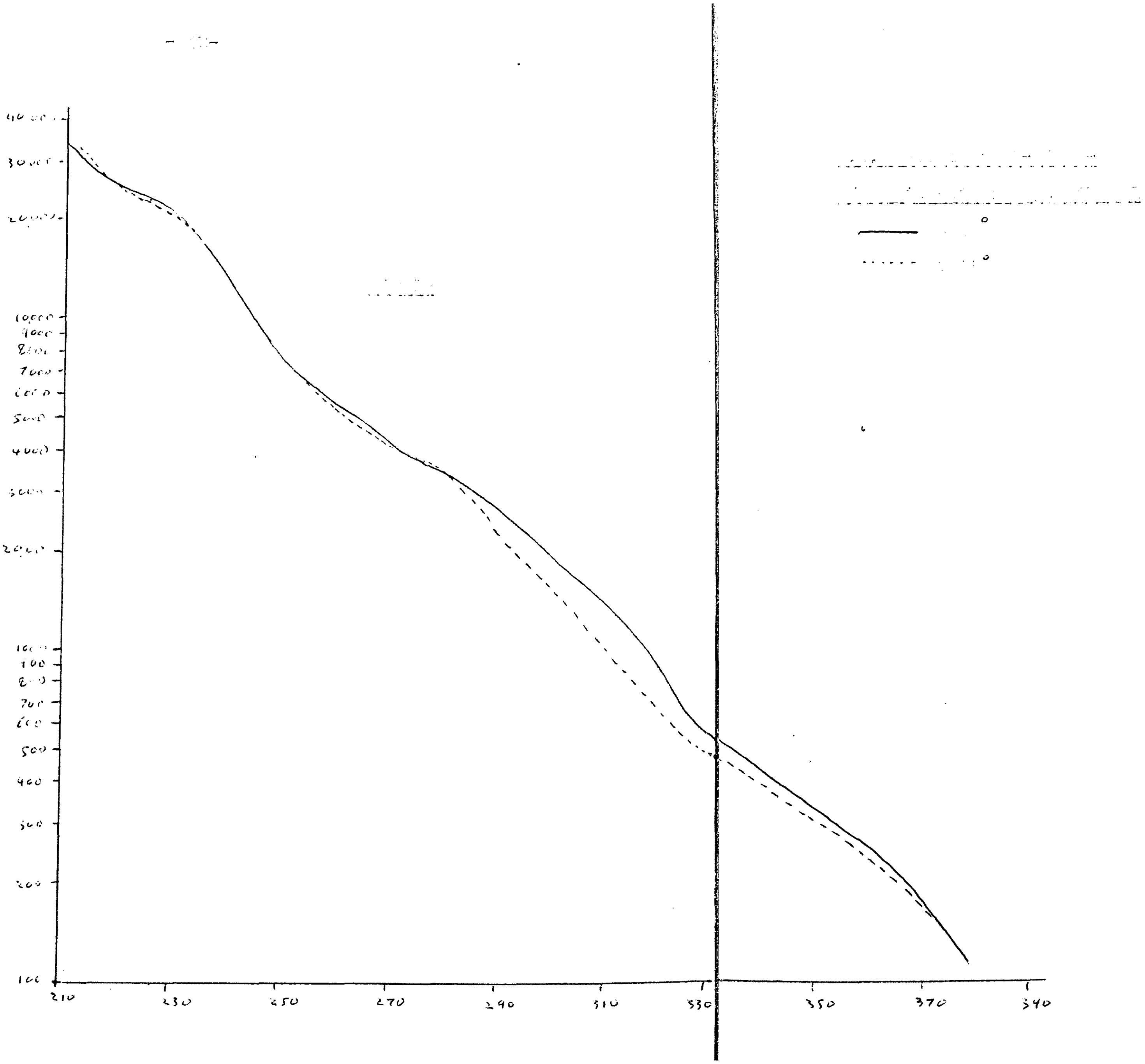
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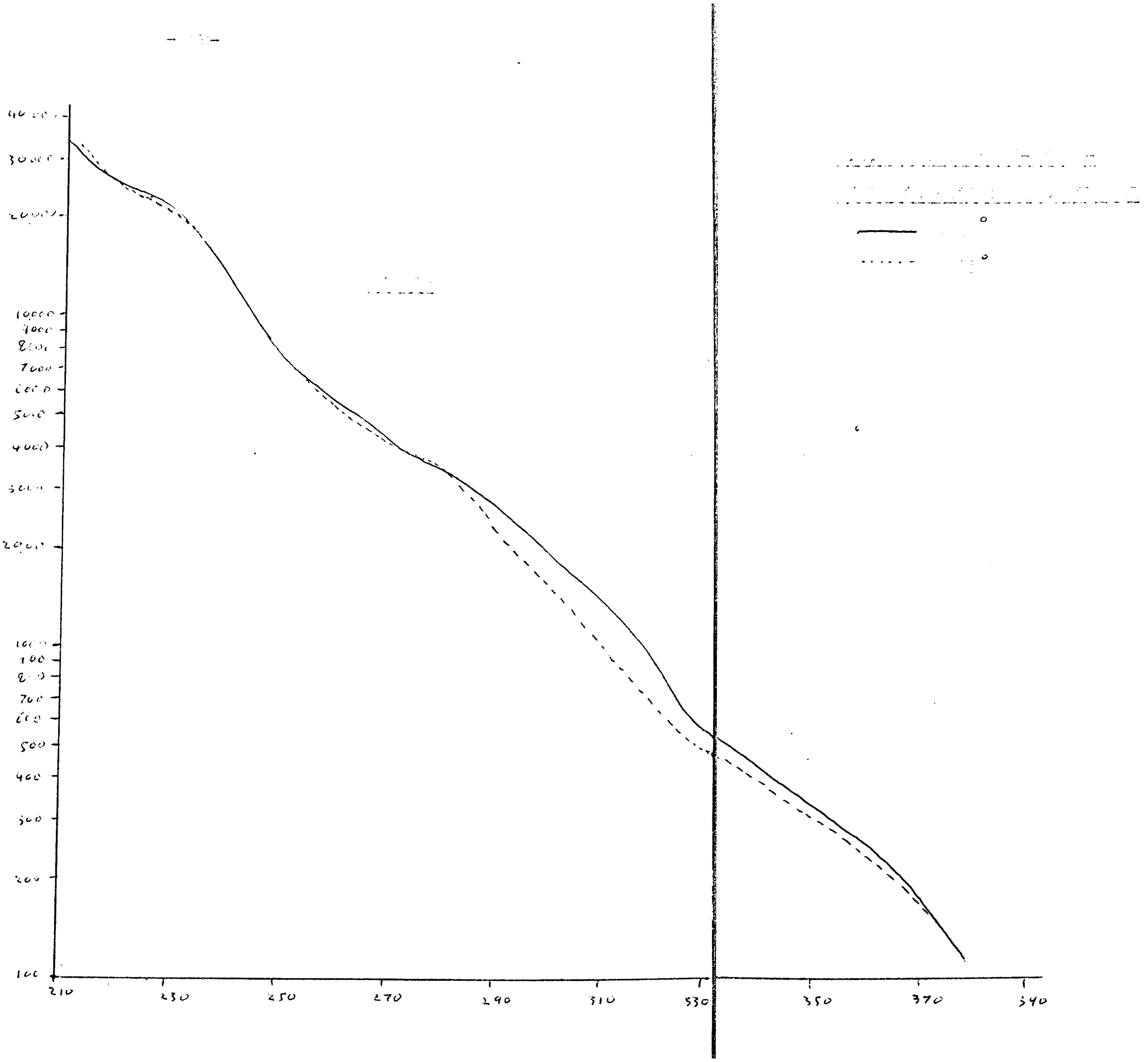
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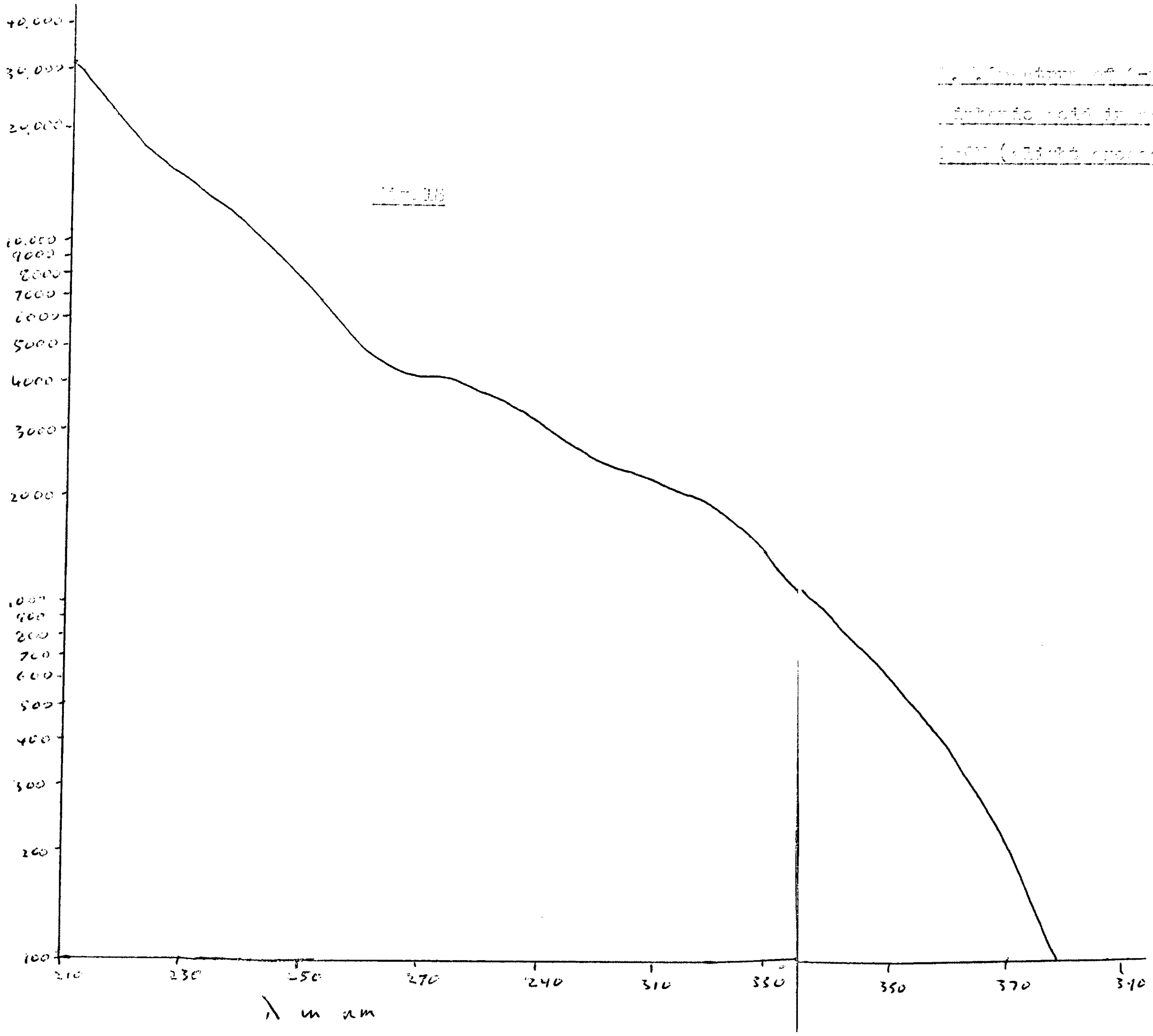
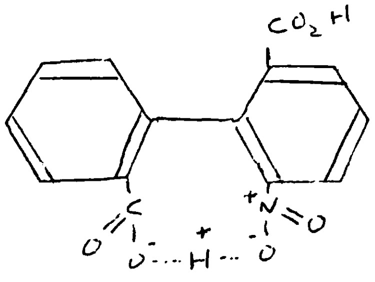


Fig. 18

[illegible]
[illegible] acid in [illegible]
[illegible] ([illegible])

45° the 265 and 310 nm inflections disappear completely and absorption falls much faster between 290 and 330 nm. Clearly there is an underlying band at 310 which disappears when the temperature is raised.

In alkaline solution 6-nitrodiphenic acid exists as its dianion. Again there are no definite peaks in the spectrum but inflections are more strongly marked. The conjugation band is now a very broad inflection at 230 nm ($\epsilon_{max} \sim 15{,}000$). A broad shoulder at 270 nm ($\epsilon_{max} \sim 4500$) seems to represent the nitrophenyl absorption while the inflection due to the carboxyphenyl absorption has shifted to 310 nm. The minor inflections in the spectrum of the acid in ethanol at 21° are thus seen to be characteristic of the anion. It is possible that some dissociation takes place under these conditions but it is hard to see why the effect should be suppressed at higher temperatures. Moreover the same effect would be expected in diphenic acid itself where it is not in fact observed. A more probable explanation is that hydrogen bonding takes place between the nitro group and the carboxy group on the other ring, mimicking the effect of dissociation. Such a weak bond might be expected to be broken by a rise in temperature. (See overleaf)



Unfortunately the optical rotatory dispersion curves of the acid and its anion shed little light on the problem. They are difficult to interpret owing to considerable overlapping of the various Cotton effects. The amplitudes of these effects are only apparent and of little significance.

In the ORD spectrum of (+)-6-nitrodiphenic acid in 95% ethanol at 23° two Cotton effects are clearly visible: a positive one at 350 nm corresponding to the low frequency nitro band and a negative one at 263 nm corresponding to the nitrophenyl band. The specific amplitudes are +22,990° and -5,330° respectively. The trough at 322 nm seems too deep to be merely the second extremum of the 350 nm effect; it may also contain the first extremum of a negative Cotton effect at 312 nm of which the peak at 292 nm is the second extremum. This would correspond to the anionic carboxyphenyl band whose appearance in the spectrum is discussed above. However the 292 nm peak could also be associated with another Cotton effect due to the normal carboxyphenyl band at 281 nm which does not otherwise show on this spectrum.

In the ORD spectrum of (+)-6-nitrodiphenic acid in dilute alkali, the nitrophenyl band again gives rise to a negative Cotton effect centred at 267 nm. The very wide curve between 300 and 380 nm probably represents a superimposition of two negative Cotton effects: one at 350 nm corresponding to the low frequency nitro band and one at 310 nm corresponding to the anionic carboxyphenyl band. The trough at 230 nm is associated with the conjugation band whose exact position is difficult to determine from the ultraviolet spectrum; it may lie anywhere between 225 and 240 nm. The ORD spectrum might give more information on this point if it were possible to penetrate further into the ultraviolet but unfortunately the absorption is too great. An interesting feature of the spectrum is that the Cotton effect due to the low frequency nitro band is reversed in sign when the acid is ionised whereas that due to the nitrophenyl band remains constant

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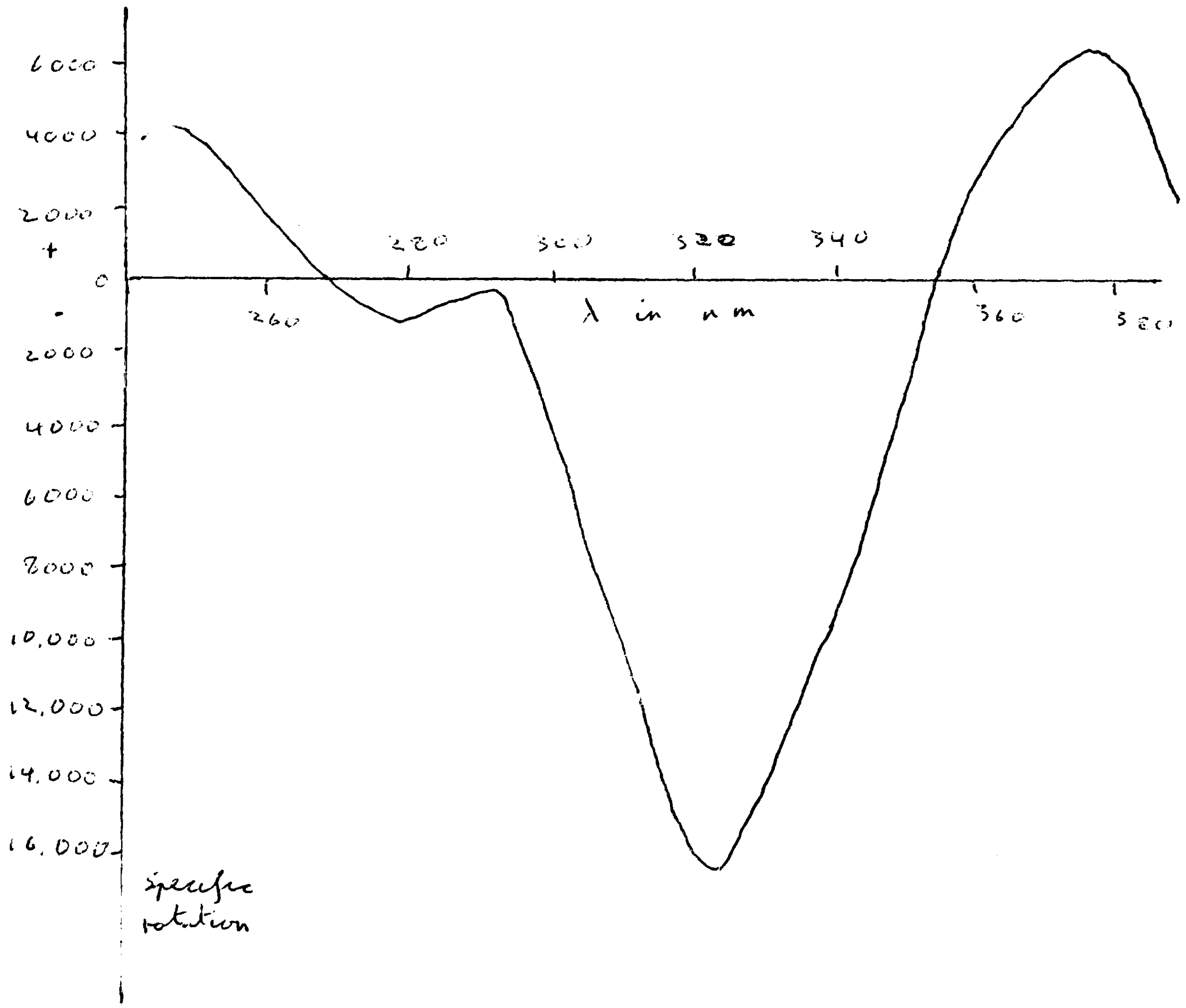
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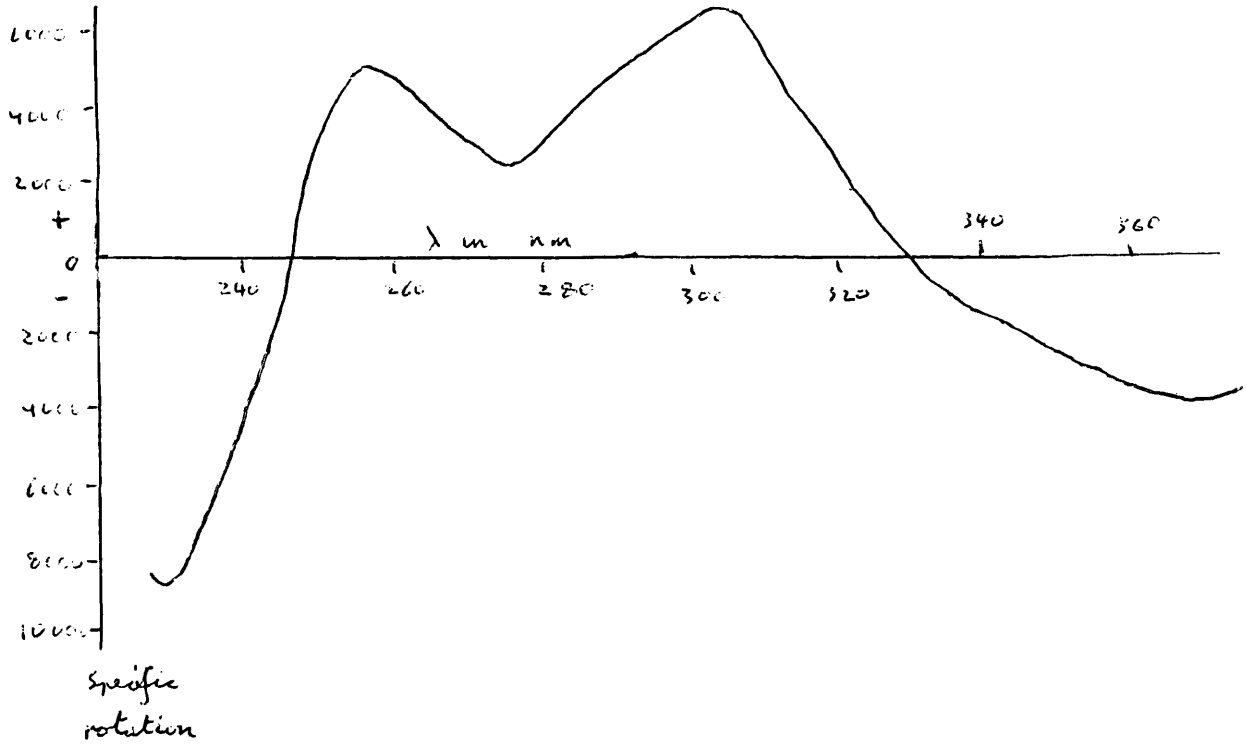
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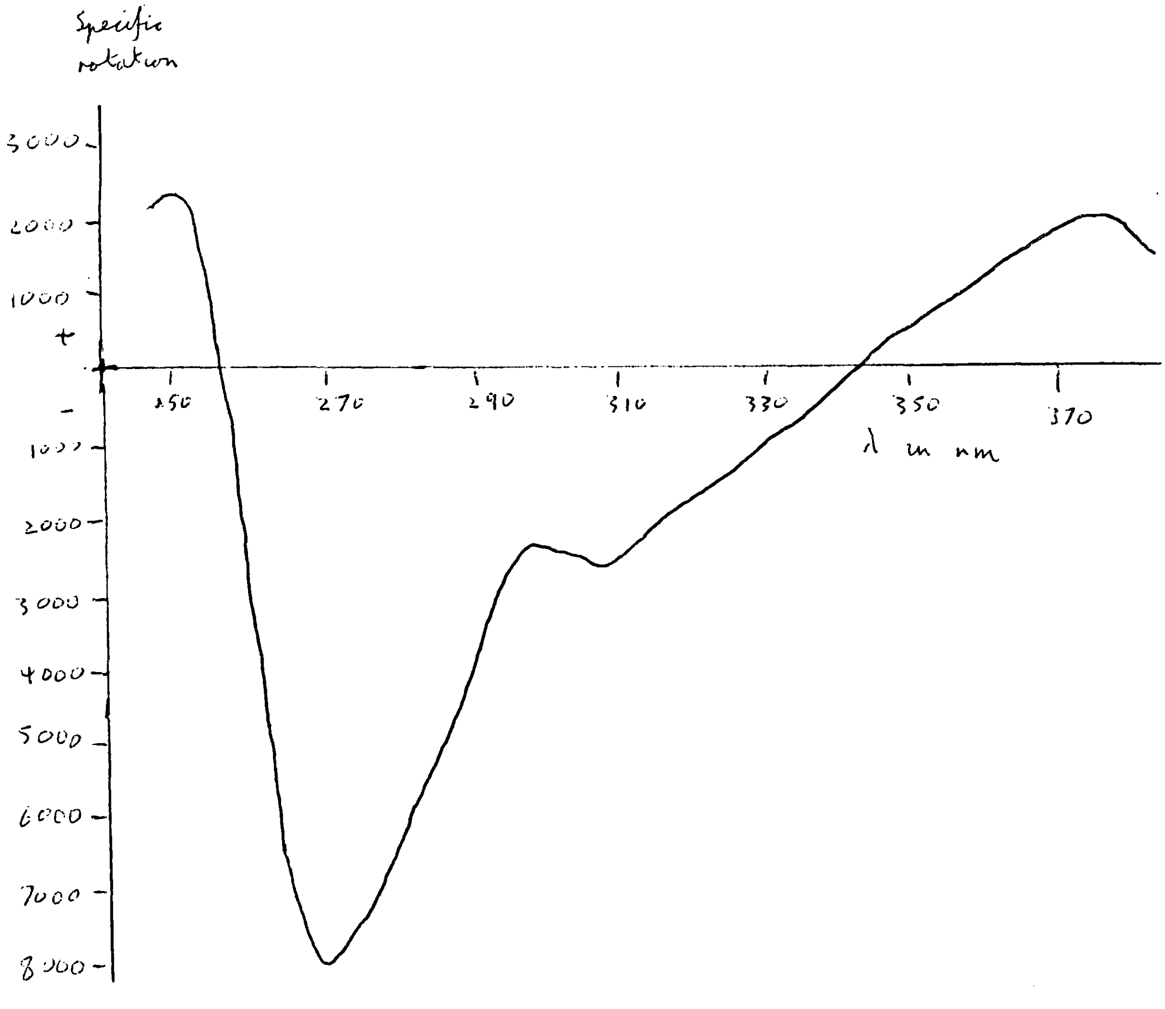
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in sign although it is reduced in width and amplitude. A table showing the various bands with their ultraviolet absorption intensities and the specific amplitudes of the associated Cotton effects is appended.

Out of the various ORD spectra observed by Mislow and his coworkers[52] the most relevant to this enquiry is that of (R)-6,6'-dinotrodiphenic acid in dioxane. The nitrophenyl band appears as a large negative Cotton effect centred at 260 nm and the low frequency nitro band as a positive Cotton effect centred at 340 nm. A small peak at 297 nm may be associated either with the carboxyphenyl band near 280 nm or with an anionic type carboxyphenyl band near 310 nm. The signs of the Cotton effects identified are the same as in (+)-6-nitrodiphenic acid and suggest that this compound has a similar configuration. Models and diagrams show that the configuration of 6-nitrodiphenic acid which corresponds to (R)-6,6'-dinitrodiphenic acid is the (S) one.

Absorption bands of (+)-6-nitrodiphenic acid in 95% ethanol

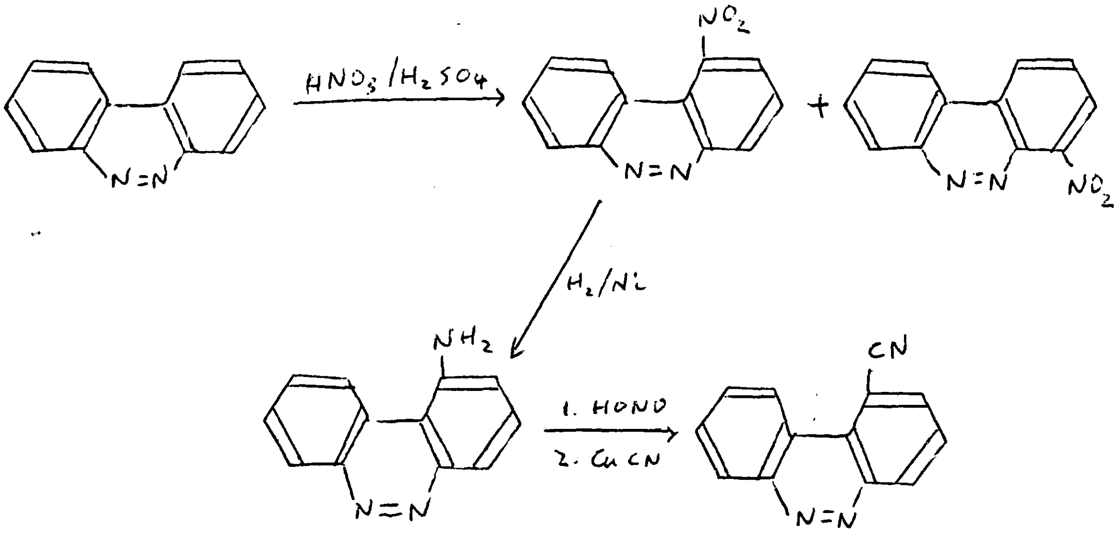
Band	Nitrophenyl	Carboxyphenyl	"Anionic"	Long-wave nitro
(UV)	265 (sh.)	280 (sh.)	310 (sh.)	masked
Intensity	4800	3400	1400	-
(ORD)	263	282	312 ?	350
Specific amplitude	-5330	+ 884	-16600 ?	+ 2300

Absorption bands of (+)-6-nitrodiphenic acid in dilute alkali

Band	Nitrophenyl	Anionic carboxyphenyl	Long-wave nitro
(UV)	270 (sh.)	310 (sh.)	masked
Intensity	4500	2200	-
(ORD)	267	338	
Specific amplitude	- 2500	- 10500	

Preparation and properties of 1-cyanobenzo[c]cinnoline

The preparation of benzo[c]cinnoline from 2,2'-dinitrobiphenyl has already been discussed on p. 45 f. The same methods are available for the preparation of symmetrically substituted benzo[c]cinnolines. However unsymmetrically substituted benzo[c]cinnolines must be prepared from the parent compound as the corresponding unsymmetrically substituted 2,2'-dinitrobiphenyls are not usually available as starting materials. In the present work benzo[c]cinnoline was prepared in 94% yield by the reduction of 2,2'-dinitrobiphenyl with an ethereal suspension of lithium aluminium hydride. Various derivatives of benzo[c]cinnoline were prepared as follows:



The two products of nitration of benzo[c]cinnoline were separated by continuous extraction with light petroleum in which only the 1-isomer was soluble. The by-product, identified by Corbett and Holt[113] as the 4-isomer, was not further investigated since the aim of this series of experiments was to compare the spectroscopic properties of 1-substituted benzo[c]cinnolines with particular emphasis on 1-cyanobenzo[c]cinnoline.

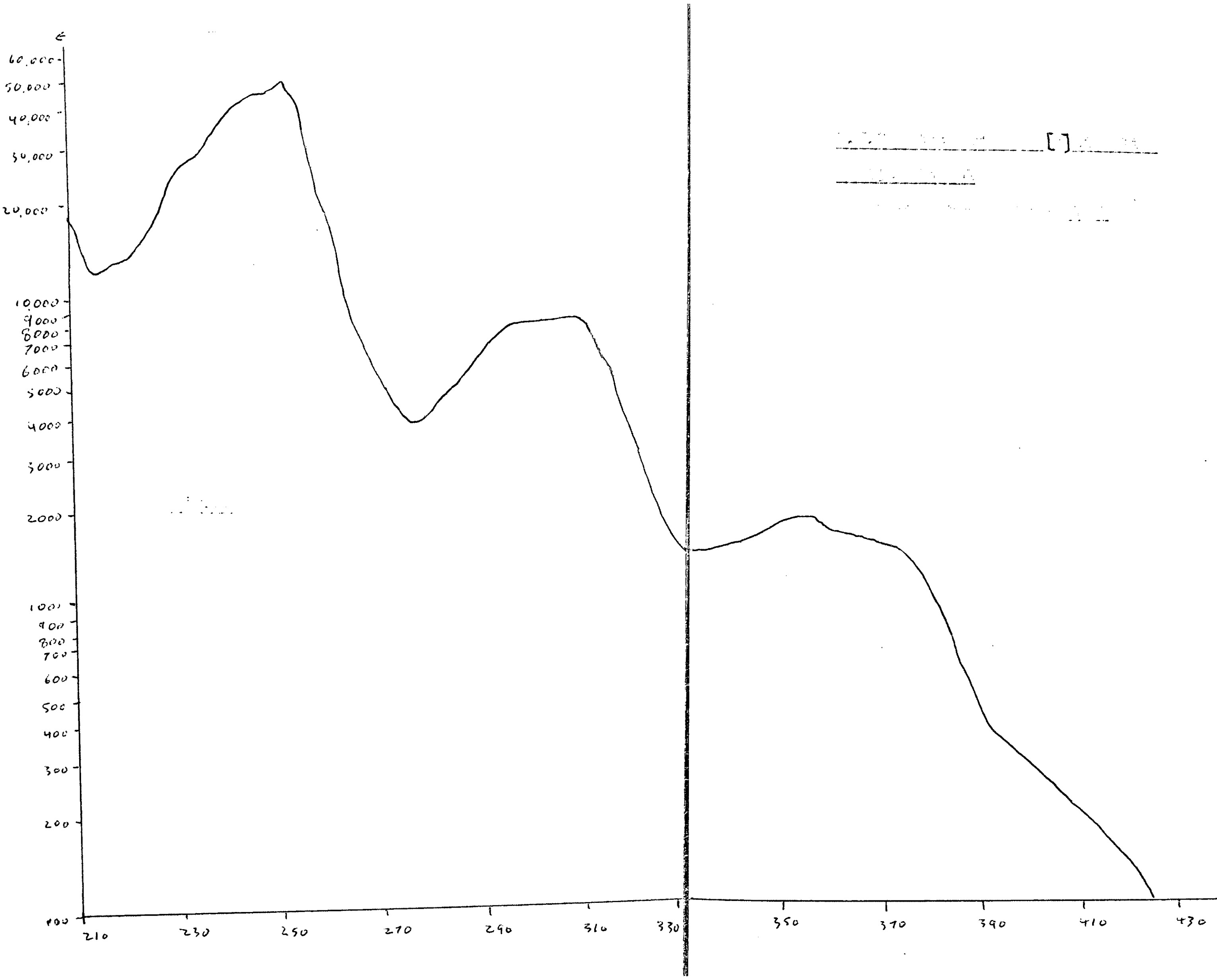
The hydrogenation of 1-nitrobenzo[c]cinnoline was carried out according to the method of Smith and Ruby[112] although the compound was found to be less soluble in methanol than these investigators report. They recommend a solution of 2g. in 100 ml.; in fact the highest concentration attainable at room temperature in this investigation was 0.75 g. per 100 ml. Hydrogenation was carried out over W2 Raney nickel at room temperature and 45-50 p.s.i. but results were erratic and often the product was mixed with unchanged starting material. The latter could be removed by placing the solid product on top of a column of alumina, with a pad of filter paper interposed, and eluting with benzene. The eluted 1-nitrobenzo[c]cinnoline was used again and the 1-aminobenzo[c]cinnoline was recovered from the top of the column. The compound purified in this way was a brown solid whose infrared spectrum showed no nitro bands at 1340 and 1520 cm^{-1}. Its chemical properties were those of a weak base, soluble in concentrated acids and sparingly soluble in dilute acids to give violet-red solutions. On basification the solutions turned yellow and the amine separated as a brown precipitate. When solutions of the amine in organic solvents were heated they darkened in colour and the solid recovered from them was almost black; for this reason the product of the hydrogenation was not recrystallised but was used directly for the next stage after removal of unchanged 1-nitro-benzo[c]cinnoline. The amine was diazotised in dilute sulphuric acid, the progress of the reaction being shown by the discharge of the red colour from the solution; the conversion into 1-cyano-benzo[c]cinnoline was carried out, as usual, in basic solution. The yield of 1-cyano-benzo[c]cinnoline was low, either because of steric factors or because of the low basicity of the amine. The nitrile was separated from by-products by rapid chromatography on alumina using benzene/ether as eluant; it was important not to allow the compound to remain adsorbed on alumina for more than ca. 24 hours as hydrolysis then set in. This was shown clearly by the infrared spectrum: the C≡N stretching absorption at 2200 cm^{-1} disappeared and new bands appeared at 1630 cm^{-1} and at 3200 and 3300 cm^{-1} corresponding respectively at C=O stretching in an amide and primary NH_2 stretching.

Among the by-products of the Sandmeyer reaction was a dark brown copper compound appreciably soluble in methanol and showing in its infrared spectrum the 2100 cm^{-1} band of inorganic nitriles. This compound had a molecular weight of 105 as measured by the Mechrolab osmometer in methanolic solution. It gave no positive tests for cupric ions but pyrolysis yielded a solid with the properties of cupric oxide. Possibly the original solid was $Cu^{I}_2\ Cu^{II}(CN)_4$ which, when ionised would have an average molecular weight of 102.5.

Pure 1-cyanobenzo[c]cinnoline sublimes readily above 200° and melts at 238°. It is very soluble in benzene from which it can be precipitated by light petroleum, and sparingly soluble in alcohol. The readiness with which it undergoes hydrolysis when adsorbed on alumina has already been noted; the water involved is no doubt adsorbed by the alumina from moist solvents. Sterically crowded nitriles such as 1-cyanobenzo[c]cinnoline are usually very inert to hydrolysis in homogenous solution but the reaction might take place more easily when both reactants are adsorbed on an inert supporting material. Thus a number of esters are known to undergo spontaneous hydrolysis on alumina. Moreover the same overcrowding which renders the cyano group relatively inaccessible in solution may encourage hydrolysis in the adsorbed compound since the carboxamide group which is formed juts out less than the original cyano group.

Spectroscopic study of benzo[c]cinnolines

The ultraviolet spectrum of benzo[c]cinnoline in ethanol was copied from a published spectrum by Badger, Pearce and Pettit[119]. The general appearance of the spectrum is described on p. 48. The group I band has its maximum at 252 nm (ϵ = 50,000), the group II band at 308 nm (ϵ = 9,000) and the group III band at 354 nm (ϵ = 1800). The spectrum of 1-nitrobenzo[c]cinnoline is said by Corbett _et al._[110] to be "similar"; whether this refers to the positions of the main bands or to the general appearance of the spectrum is not certain. In the present investigation, the spectrum of 1-nitrobenzo[c]cinnoline was found to be distinctly different from that of the parent compound. The group I band has shifted considerably towards shorter wavelengths, the new maximum being at 236 nm (ϵ = 40,000). A broad plateau (ϵ = 9,400) extends from 280 to 312 nm where a sudden fall in absorption marks the long-wave side of the group II band. The plateau may be due to the overlapping of the nitrophenyl absorption with the $\pi \longrightarrow \pi^*$ absorptions of the benzo[c]cinnoline nucleus. In 2,2'-dinitrobiphenyl this chromophore has its maximum absorption at 260 nm but the fall on the long-wave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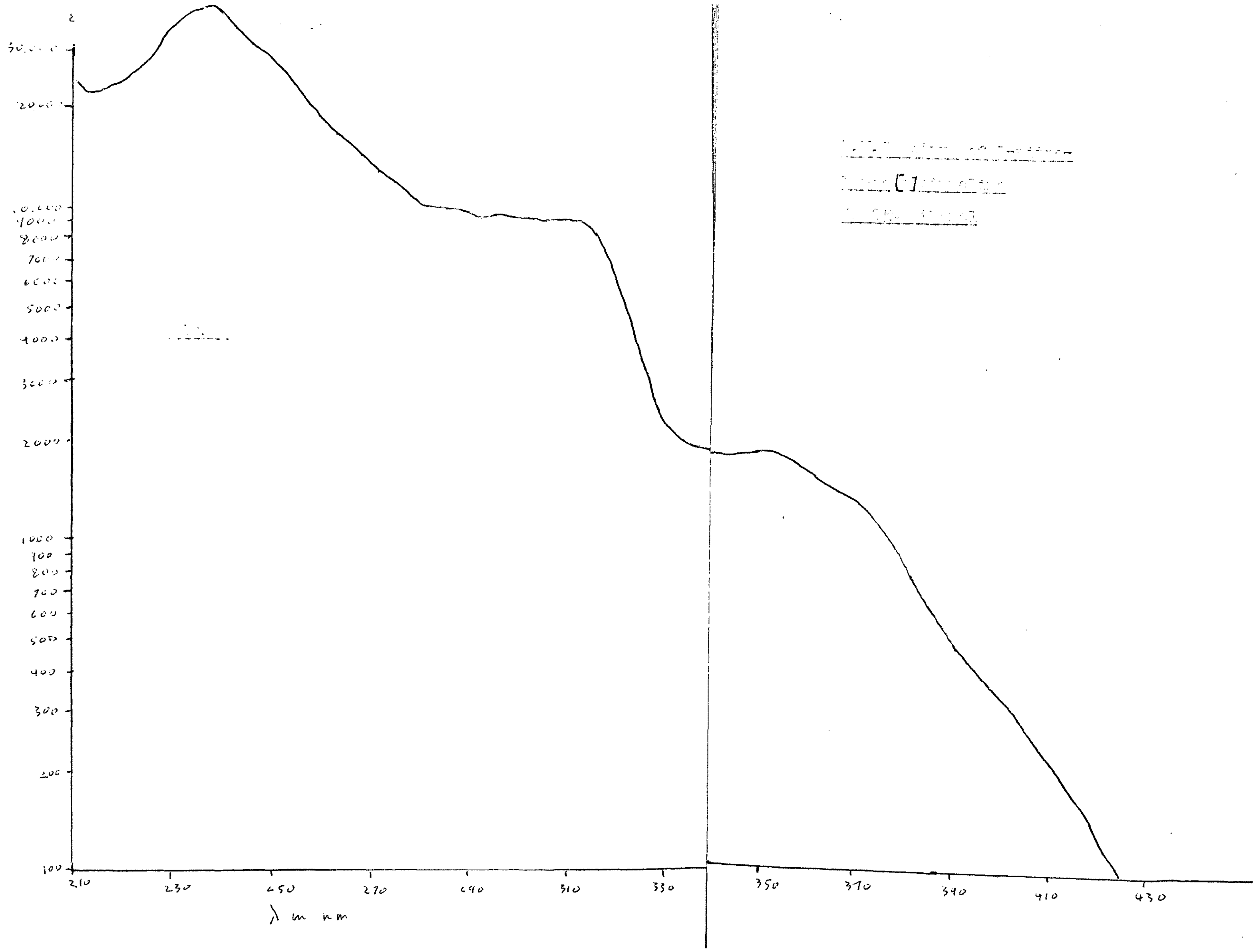
side is slow below 310 nm. As expected, the spectrum of 1-nitrobenzo[c]cinnoline shows considerable absorption at long wavelengths due to the superimposition of the group III band, lone pair absorption and low frequency nitro absorption, although the group III maximum at 352 nm (ϵ = 1900) is still close to that of the unsubstituted compound.

The spectrum of 1-cyanobenzo[c]cinnoline is very different. The group I band is shifted to longer wavelengths, the new maximum being at 265 nm (ϵ = 34,000) and there is no sign of the cyanophenyl chromophore which in 2,2'-dicyanobiphenyl absorbs at 283 nm (see p.). The group II band is at 310 nm (ϵ = 8100) and the group III bands at 352 and 367 nm (ϵ = 1520 and 1330 respectively). Thus the spectrum resembles that of the parent compound apart from the red shift in the group I band and the appearance at 216 nm of another band (ϵ_{max} = 32100) which has clearly shifted up from below 210 nm.

These results are difficult to interpret; their most striking feature is the considerable variability in the position and intensity of the group I band which Corbett et al.[110] describe as relatively insensitive to the effects of substitution.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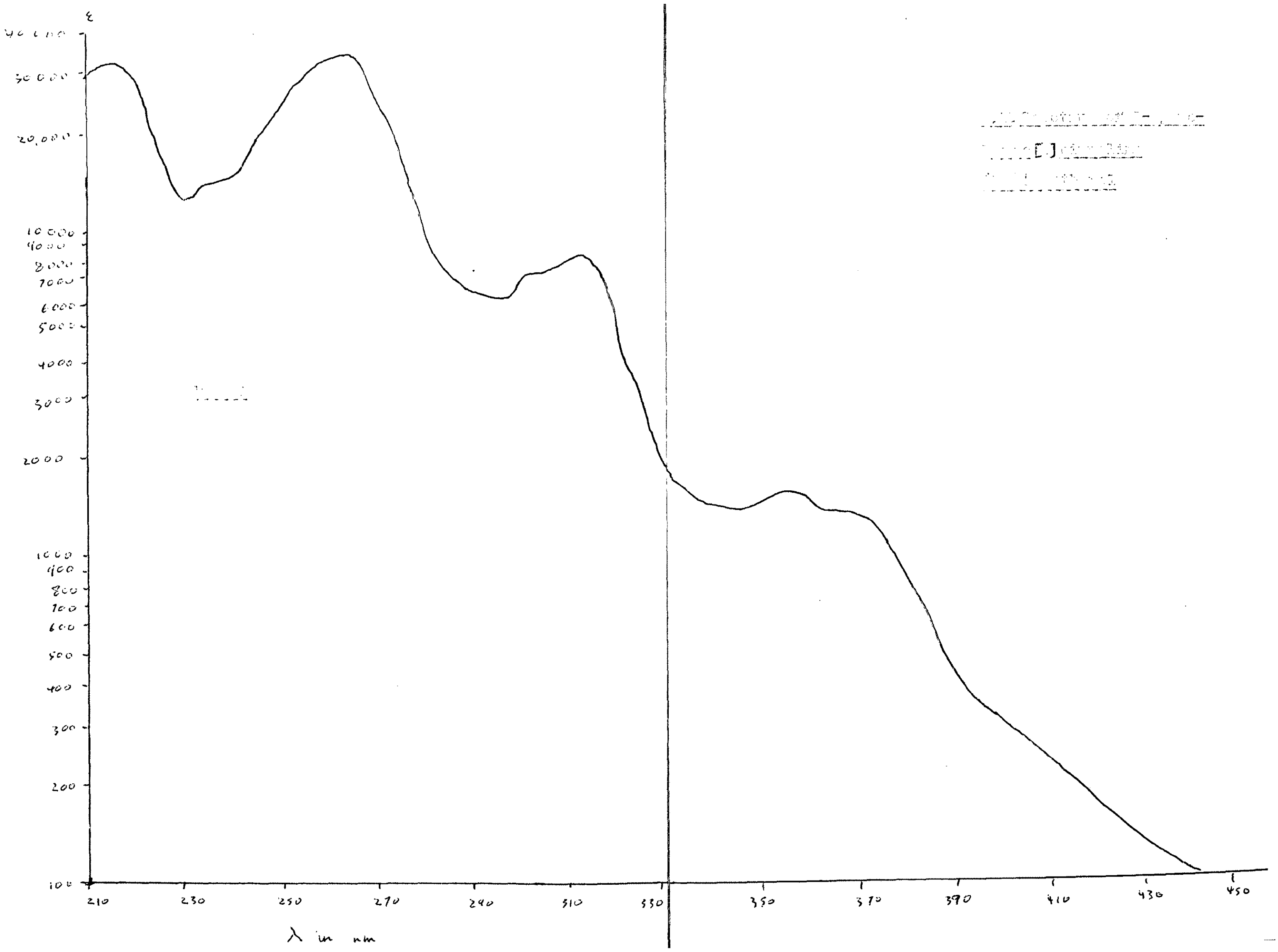
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Compound	λ_{max}	ϵ_{max}
Benzo[c]cinnoline	252	50,000
1-Nitrobenzo[c]cinnoline	237	40,000
1-Cyanobenzo[c]cinnoline	264	33,900

The appearance of an isolated phenyl chromophore in 1-nitrobenzo[c]cinnoline is also significant in view of the similar phenomenon observed in twisted 2,2'-disubstituted biphenyls. If this is truly the result of a loss of planarity in the benzo[c]cinnoline nucleus it is necessary to ask why the same thing does not happen with 1-cyanobenzo[c]cinnoline.

On p. 96 the ready hydrolysis of 1-cyanobenzo[c]cinnoline on alumina was explained on the basis of steric factors; the amido group formed is broader than the original cyano group but also shorter and it can neutralise its extra breadth by taking up a conformation perpendicular to the plane of the ring system. The nitro group is similar in its geometry to the amido group: both are trigonal-planar with the central atom sp^2 hybridised. But the nitro group is more strongly conjugated with the ring as shown by its greater efficiency in inducing exclusive <u>meta</u> substitution in the benzene series[120]; consequently it is less likely than

$CONH_2$ to take up a perpendicular conformation and its breadth makes its steric effect greater than that of the linear cyano group.

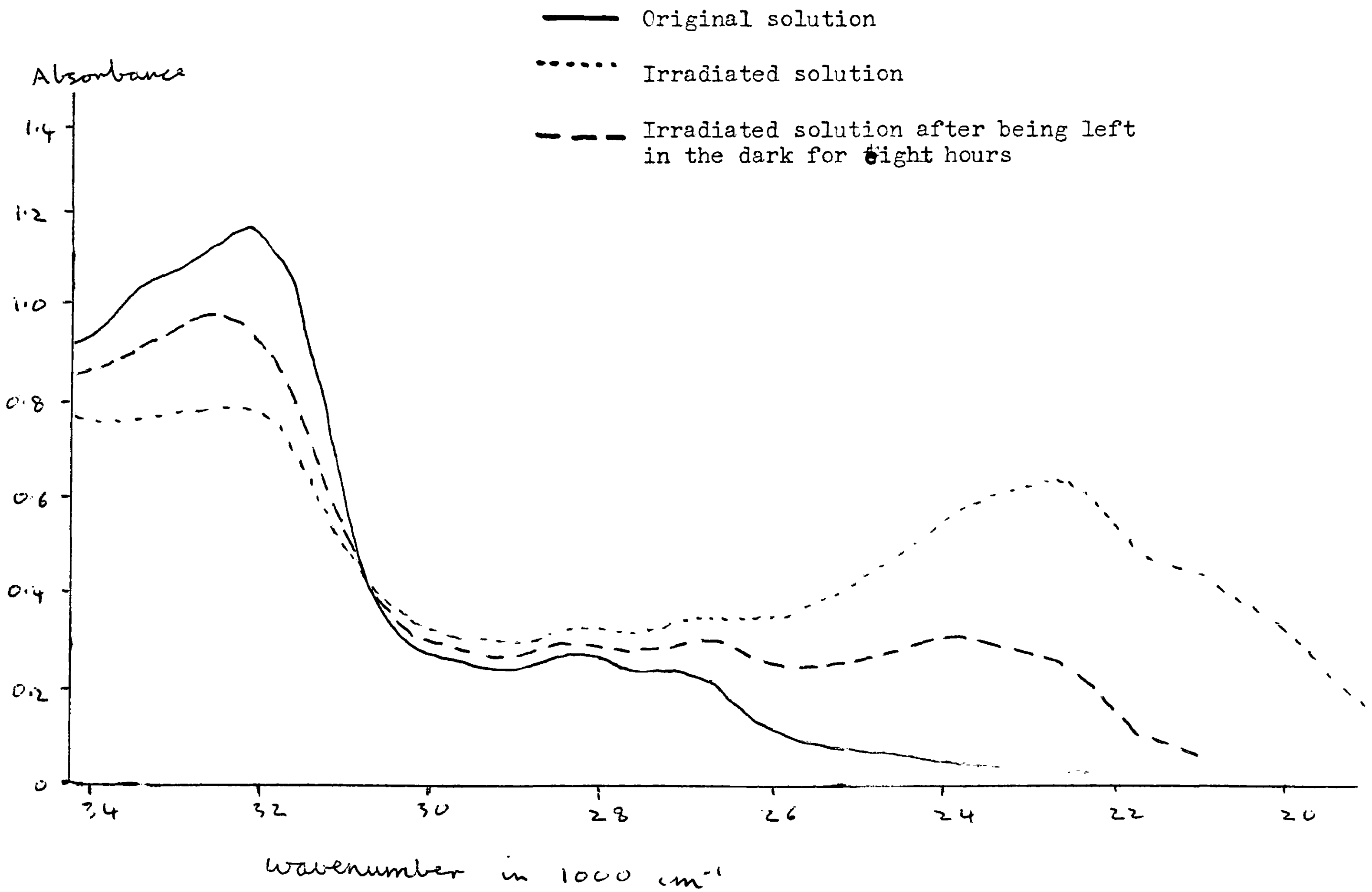
A curious property of the benzo[c]cinnolines which has not previously been reported is that some of them are photochromic in alcoholic solution. The effect is most clearly seen in 1-cyanobenzo[c]cinnoline whose solutions in ethanol change visibly in colour when exposed for an hour or two to sunlight or strong ultraviolet illumination. A solution of 0.035 g/litre changes from colourless to yellow and one of 0.35 g/litre from pale yellow to orange. In the visible spectrum a new band appears at 444 nm. Its intensity cannot be calculated as the concentration of the coloured form is not known; however in a 1 cm thickness of an irradiated solution initially containing 0.349 g/litre of 1-cyanobenzo[c]cinnoline, the new band appeared with an optical density D_{max} of 0.62. The maximum possible concentration of the absorbing species is 0.349 g/litre corresponding to complete conversion and this supplies the lower limit for the molar extinction coefficient: $\frac{0.62 \times 205}{0.349}$ or 364. The upper limit is probably of the order of 10,000. The ultraviolet spectrum also shows some changes; the group I and group II bands are reduced in intensity but extend further towards the blue end of the spectrum. The effect is easily explicable if the corresponding bands in the coloured form are at slightly higher frequencies so that the absorptions of the two compounds overlap in the mixture. The group III band appears as a plateau on the short-wave side of the new band in the visible; the intensity is somewhat higher than before (ϵ_{max} at 352 nm = 1880).

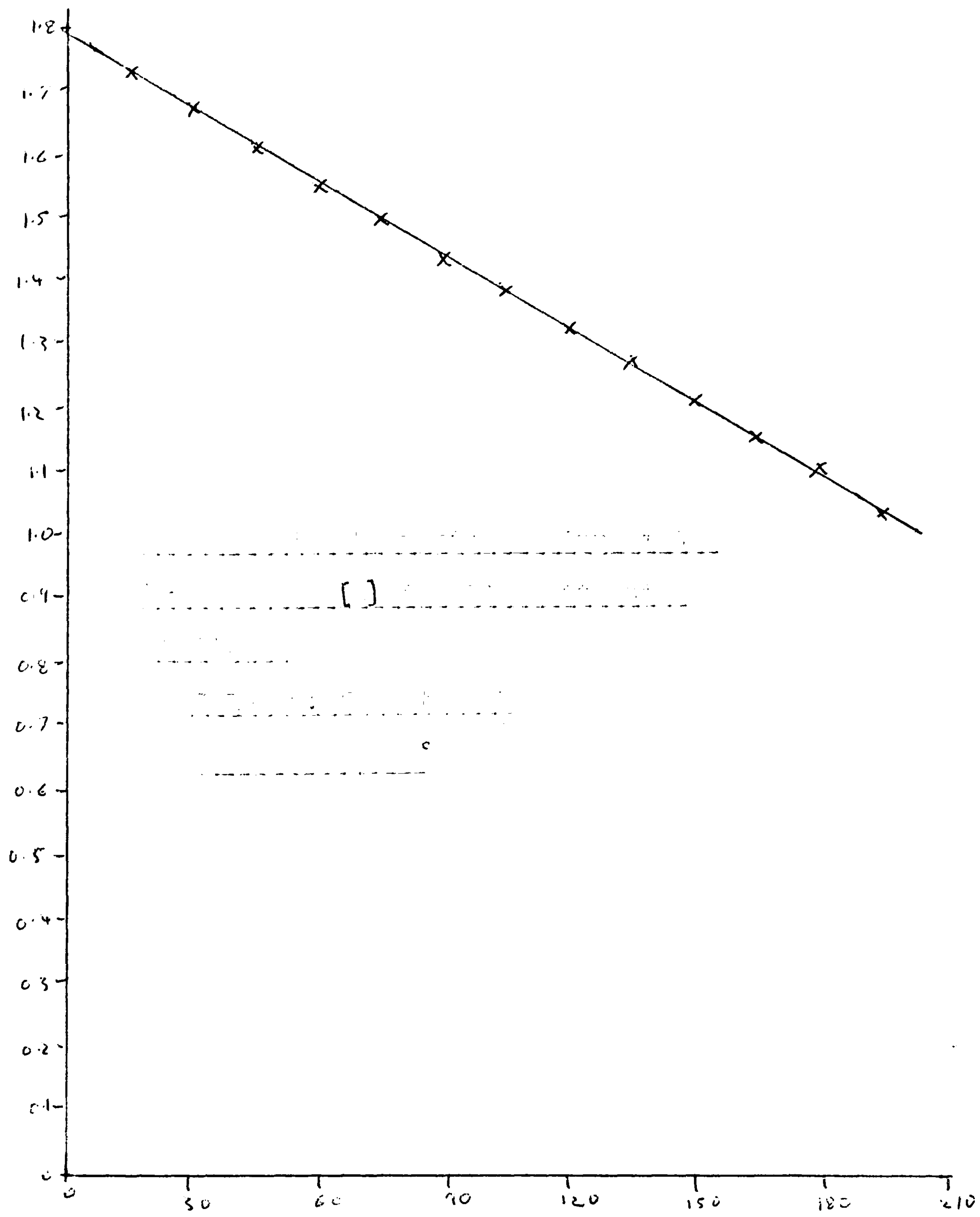
When the irradiated solution is allowed to remain in the dark for some hours the change is reversed but only partially, the system gradually reaching equilibrium. The intensity of the visible band diminishes according to a first-order law with a rate of 1.51×10^{-4} sec^{-1} and a half-life of 74.5 minutes at 30°. The equilibrium mixture can be restored to the highly coloured state by further irradiation. When the solution is evaporated to dryness the reaction is completely reversed; the solid obtained has the normal melting point of 1-cyanobenzo[c]cinnoline and, when freshly redissolved in ethanol, shows the original ultraviolet/visible spectrum. This is the case whether the evaporation is carried out with warming or at room temperature. Clearly

Fig.25

Automatically recorded U.V. spectrum of 1-cyanobenzo[c]cinnoline in 95% ethanol

Path length 1 cm. Conc. 6.349 mg./10 ml.

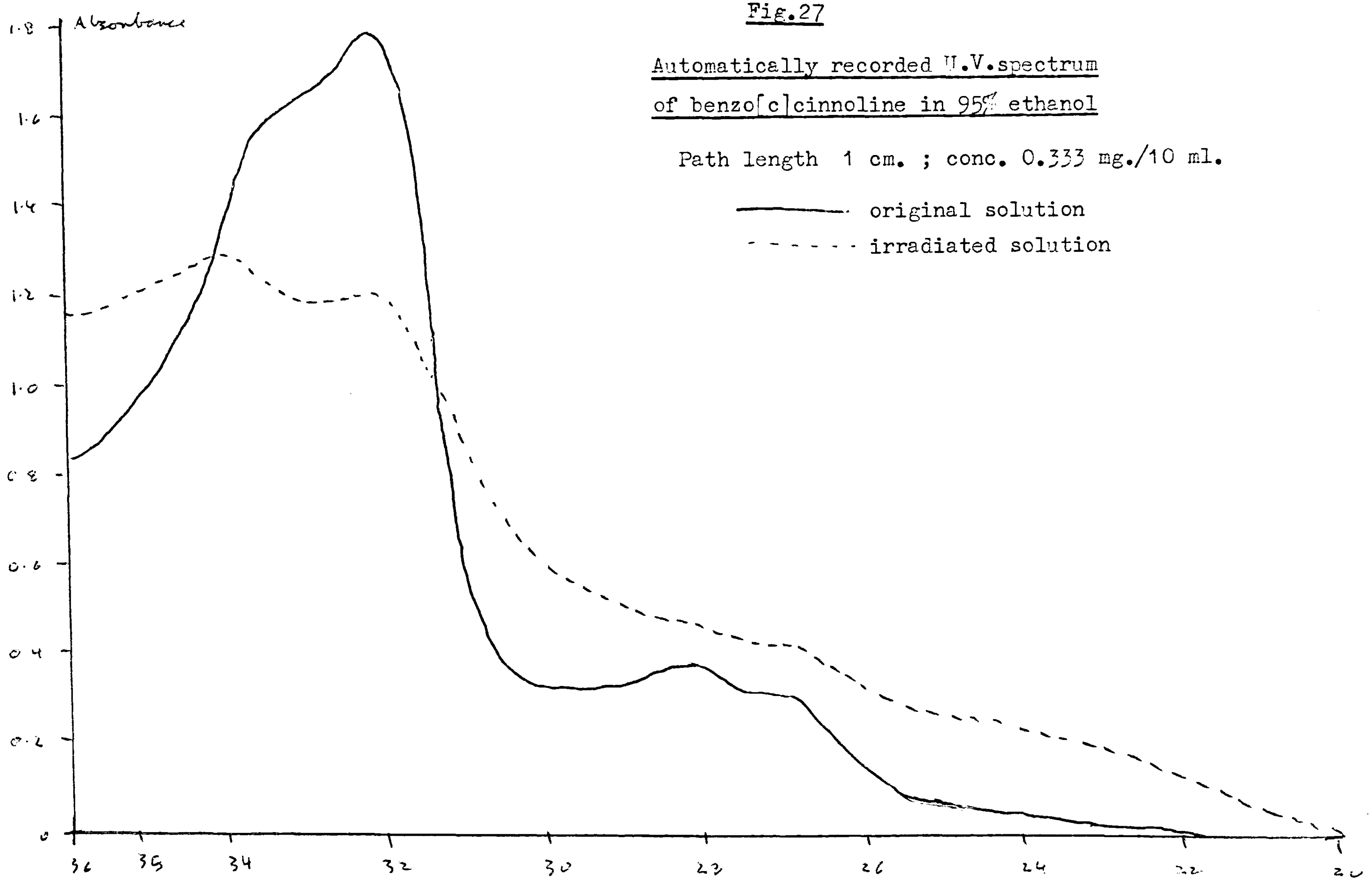



1·8
1·7
1·6
1·5
1·4
1·3
1·2
1·1
1·0
0·9
0·8
0·7
0·6
0·5
0·4
0·3
0·2
0·1
0
0
30
60
90
120
150
180
210

the solvent plays some part in the photochromic reaction. This is borne out by the absence of any change when a solution of the compound in benzene is strongly irradiated.

1-Nitrobenzo[c]cinnoline is not photochromic but benzo[c]cinnoline itself in ethanolic solution undergoes a change on irradiation which cannot be reversed merely by allowing the solution to stand in the dark. A new band appears between 330 and 360 nm and fills the gap between the group II and III bands; it shows no clear maximum because of overlapping. There is sufficient absorption below 400 nm to cause a deepening of the colour of the solution perceptible to the naked eye although it is not so dramatic as in the case of 1-cyano benzo[c]cinnoline. The blue shift in the group II band is more striking: in the irradiated solution two bands are visible, one at 308 nm (the original position) and one at 296 nm. The two maxima have almost the same optical density. As in the case of 1-cyanobenzo[c]cinnoline the spectral changes are completely reversed by evaporation of the solution. However, as mentioned above, there is no change when the solution is allowed to stand in the dark.

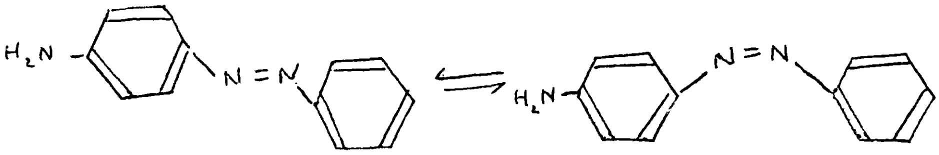
Fig.27



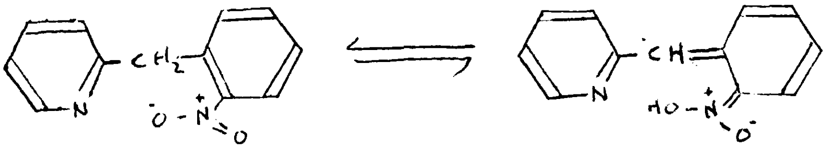
Automatically recorded U.V.spectrum of benzo[c]cinnoline in 95% ethanol

Path length 1 cm. ; conc. 0.333 mg./10 ml.

The phenomenon of photochromism is due to a reversible photochemical reaction of the type A⇋B where B is of higher energy than A. When the source of light energy is withdrawn, the reaction is reversed. A number of different reactions have been associated with photochromism. The photochromism of p-aminoazobenzene is due to cis-trans isomerism[121]:

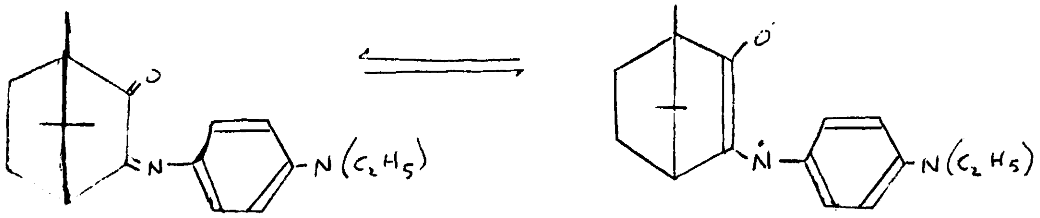


In the case of benzo[c]cinnoline this is clearly impossible. -(2-Pyridyl)-*o*-nitrotoluene owes its photochromism to a tautomeric change involving a shift of hydrogen[122]:



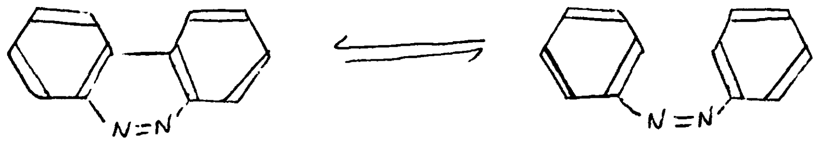
This too is inapplicable to the benzo[c]cinnoline system.

Certain camphor derivatives become paramagnetic on irradiation and this is associated with a colour change[123]:



However, irradiated solutions of benzo[c]cinnolines show no sign of paramagnetism. An irradiated and deeply coloured solution of 1-cyanobenzo[c]cinnoline in ethanol (o,5g./litre) gave no detectable E.S.R. signal. If any paramagnetic compounds are present their total concentration must be less than 10^{-7} molar, far too little to account for the colour change.

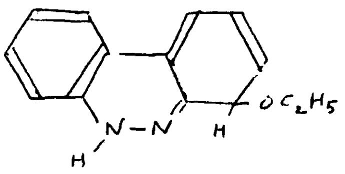
Another possibility which must be discounted is reversible photoreduction to cis-azobenzene. If this

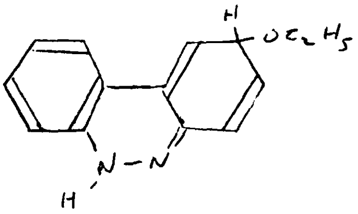


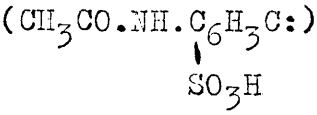
reaction in fact took place it would be strictly irreversible as the product would isomerise at once to the stable trans-azobenzene.

Two possibilities remain. The coloured form may be a solvent complex or a complex with oxygen.

Any solvent complex formed would have to be σ rather than π-bonded since the phenomenon appears only in ethanolic and not in benzene solutions; such a complex might have one of the formulae shown below.





A complex with oxygen or an organic peroxide would have parallels elsewhere: the photochromism of the styrene derivative  $(CH_3CO.NH.\underset{\substack{|\\ SO_3H}}{C_6H_3}C:)_2$ is believed to be due to a similar phenomenon[124]. Moreover benzo c cinnoline itself is known to form molecular complexes with the halogens although the formation of these is not dependent on irradiation (see p.). Unlike the product of the photochromic reaction they can be isolated in the solid state although they decompose rapidly on warming. Their structure is not known.

Of the two possibilities described above, a reaction with oxygen seems the more probable. The inability of the product to survive evaporation of the solution suggests that the solvent plays some part but this may be the indirect one of stabilising the complex by solvation. There is no immediately apparent reason why 1-nitrobenzo c cinnoline should not show a photochromic change in ethanolic solution or why such a change should be reversible in the dark in the case of 1-cyanobenzo c cinnoline but not in the case of benzo c cinnoline itself; in order to elucidate the phenomenon it would be necessary to carry out experiments with a variety of substituted benzo c cinnolines in different solvents, some in the absence of oxygen. This would be outside the scope of the present inquiry.

Melting points below 200° were taken in an oil bath. Melting points above 200° and those involving decomposition were taken on a Koffler hot-stage and are marked with an asterisk. All melting points are uncorrected.

Routine infrared spectra were recorded on a Unicam SP200 spectrophotometer and more accurate spectra on a Grubb-Parsons GS2A spectrophotometer. Oils were studied as thin films, solids as mulls in "Nujol" or as pressed KBr discs containing 1% of the substance.

Automatically recorded ultraviolet spectra were measured on a Unicam SP800 spectrophotometer and all other ultraviolet spectra on a Unicam SP500 manual spectrophotometer. Quartz cells were used throughout.

Optical rotations at 546 nm were measured with a Bellingham and Stanley visual polarimeter using a mercury lamp. Optical rotatory dispersion curves were recorded on a Perkin-Elmer P23 spectropolarimeter.

Microanalyses were carried out by Dr. A. Bernhardt in West Germany and mass spectra by the Physico-chemical Measurement Unit at Harwell.

N.M.R. Spectra were measured on a Varian A60 instrument at 60 MHertz.

4,4'-Dibromobiphenyl

Biphenyl (15.4 g.1 mol) was dissolved in CCl_4 (100 ml.) in a three-necked flask fitted with a reflux condenser and a dropping funnel. Iron filings (0.5 g.) were added and the mixture was heated to boiling point. Bromine (10.2 ml., 2 mol) was added dropwise through the funnel at such a rate that no bromine escaped through the condenser. Heating was continued after addition until testing at the mouth of the condenser with ammonia showed no further emission of HBr. The solution was filtered hot and the flask and filter funnel were washed with small quantities of hot CCl_4. On cooling, 4,4'-dibromobiphenyl (20.7 g., 66%) separated as white needles, m.p. 164.5-165.5° (Lit[125]. 164°)

The experiment was repeated and altogether 62 g. of 4,4'-dibromobiphenyl were prepared.

4,4'-Dicyanobiphenyl

Modified from L. Friedman and H. Schechter[35]

a) 4,4'-Dibromobiphenyl (3 g.1 mol) was heated with cuprous cyanide (4 g., 4.4 mol) in dimethylforma-

4,4'-Dicyanobiphenyl (continued)

mide (50 ml.) for 4½ hours. The mixture was poured into water (200 ml.) and ethylenediamine (35 ml.). The resultant suspension was filtered and the filtrate extracted with benzene. The extract, evaporated to dryness, was combined with the residue and recrystallised from ethanol. 4,4'-Dicyanobiphenyl (1.3 g., 64%) was obtained as white crystals, m.p.* 226-228°. One recrystallisation from ethanol raised the melting point to* 232-235°(Lit.[126] 235°. Friedman and Schechter give 242-244°).

The experiment was repeated and altogether 6.2 g. of 4,4'-dicyanobiphenyl were prepared by this method.

b) 4,4'-Dibromobiphenyl (3 g., 1 mol) was heated with cuprous cyanide (4 g., 4.4 mol) in dimethylformamide (50 ml.) for 4½ hours as before. Ferric chloride (8 g., anhydrous) was dissolved in water (20 ml.) and concentrated HCl (2 ml.). The reaction mixture was poured into this solution and the suspension left to stand at room temperature for thirty minutes. The precipitate was then filtered off and dried *in vacuo* to yield 4,4'-dicyanobiphenyl (1.8 g., 92%) as a white solid of m.p.* 219-221°. Two recrystallisations from

4,4'-Dicyanobiphenyl (continued)

ethanol raised the melting point to* 230-232.

The experiment was repeated and altogether 5.4 g. of 4,4'-dicyanobiphenyl were prepared.

In some of the above experiments, azeotropically dried D.M.F. was used as solvent. The yield was not improved. When the solvent contained 5% of pyridine, only starting material was recovered.

2,2'-Dinitrobiphenyl

F.R. Shaw and E.E. Turner[127]

a) o-Chloronitrobenzene (60 g., 1 mol) was melted in a wide hard-glass tube immersed in a Wood's metal bath at 250° and copper bronze (40 g., 1.65 atoms) was slowly added over a period of one hour. The reaction mixture was extracted with an equal volume of o-dichlorobenzene and filtered hot through a pre-heated Buchner funnel. The residue was washed with more o-dichlorobenzene. Light petroleum (b.p. 40-60°) was added to the solution until a slight cloudiness was produced. On cooling, 2,2'-dinitrobiphenyl (17.6 g., 38%) separated

2,2'-Dinitrobiphenyl (continued)

as dark green needles, m.p. 121-122.5°. The product was dissolved in benzene and treated with charcoal then reprecipitated with light petroleum (b.p. 60-80°) as golden brown crystals, m.p. 122-124° (Lit.[128] 124°).

The experiment was repeated and altogether 92.3 g. of 2,2'-dinitrobiphenyl were prepared by this method.

b) The addition of copper was carried out as above and the pasty reaction mixture was poured onto a thick wad of filter paper and allowed to cool and solidify. The solid was then powdered in a mortar and well extracted with boiling benzene. The extract was treated with charcoal, filtered and evaporated to yield 2,2'-dinitrobiphenyl (20.7 g., 45%) as golden crystals, m.p. 123-124°.

2,2'-Diaminobiphenyl

a) 2,2'-Dinitrobiphenyl (12.2 g., 1 mol) was added to a solution of $SnCl_2.2H_2O$ (74.5 g., 6.6 mol) in concentrated HCl (32.8 g., 18 mol) over a period of 20 minutes. The mixture was heated under reflux for half an hour, cooled and basified with 30% caustic soda. The resultant colloidal solution was extracted five times with ether and the combined ethereal extracts washed with saturated brine and dried over Na_2SO_4. The ether was distilled off and the residue distilled in vacuo to yield 2,2'-diaminobiphenyl (5.6 g., 61%) as a yellow oil (b.p. 190-195° at 10 mm.). The amine crystallised from ethanol as almost white needles, m.p. 76-77° (Lit.[102] 77-78°).

The experiment was repeated and altogether 10 g. of 2,2'-diaminobiphenyl were prepared by this method. Attempts to shorten the period of heating led to incomplete reduction and the product was a yellow solid, melting with decomposition above 210°. This was not investigated further but was presumed to be a mixture of benzocinnoline-N-oxide and benzocinnoline-N,N-dioxide.

b) A.F. Blood and C.R. Noller[104]

2,2'-Dinitrobiphenyl (20 g.) was dissolved in ethyl acetate (250 ml.) and ethanol (80 ml.) and hydrogenated over Adams' catalyst at 60° and 2-3 atmospheres for three hours. The catalyst was filtered off and the

2,2'-Diaminobiphenyl (continued)

solvent removed under reduced pressure to yield 2,2'-diaminobiphenyl (15 g., 99%) as a brown crystalline mass. Two recrystallisations from ethanol gave almost white crystals, m.p. 77-78°.

2,2'-Dichlorobiphenyl from 2,2'-Diaminobiphenyl

H.W. Schwechter[115]

2,2'-Diaminobiphenyl (12.2 g., 1 mol) was tetrazotised in water (100 ml.) containing sulphuric acid (7 ml.) with a solution of $NaNO_2$ (10 g., 2.2 mol) in water. KCl (8 g., 1.9 mol) was dissolved in the minimum amount of water and $HgCl_2$ (30 g., 1.7 mol) was added. The two solutions were mixed and the yellow precipitate filtered off, washed with acetone and dried _in vacuo_. The complex salt was mixed in a mortar with NH_4Cl (80 g.) and pyrolysed cautiously in a round-bottomed flask fitted with a reflux air condenser and immersed in a Wood's metal bath at 200°. Heating continued for 3¾ hours during which the mixture shrank and coagulated. The cooled solid was powdered and

2,2'-Dichlorobiphenyl from 2,2'-Diaminobiphenyl (continued)

extracted with light petroleum (b.p. 40-60°) until the extracts were colourless. Evaporation of the combined extracts yielded 2,2'-dichlorobiphenyl (3.3g., 22%) as yellow crystals, m.p. 53-56°(Lit.[115] 59°). It recrystallised from methanol as off-white needles, m.p. 56-58°.

3,3'-Dichlorobenzidine dihydrochloride

o-Chloronitrobenzene (100 g., 2 mol) was warmed with ethanol (128 ml.) in a 2-litre 3-necked flask fitted with two double-surface reflux condensers and a powerful stirrer. A solution of NaOH (152 g., 10 mol) in water (255 ml.) was added and the mixture allowed to reflux. Zinc dust (152 g., 5 atom) was then added gradually over a period of one hour. The mixture was boiled for one hour more and poured into 75% v/v HCl (640 ml.) cooled in an ice bath. The residue in the reaction flask was washed several times with ethanol and the washings added to the acid. After one hour, the precipitate was filtered off, treated with charcoal in water and reprecipitated with concentrated HCl. The product was a pale grey solid (29.7 g., 29%) whose

3,3'-Dichlorobenzidine dihydrochloride (continued)

solution showed the expected properties of an amine salt.

The experiment was repeated once and altogether 43 g. of 3,3'-dichlorobenzidine dihydrochloride were prepared.

3,3'-Dichlorobiphenyl

3,3'-Dichlorobenzidine dihydrochloride (5 g., 1 mol) was suspended in water (50 ml.) and concentrated HCl (4 mol) and tetrazotised with a solution of $NaNO_2$ (2.4 g., 2.2 mol) in the minimum amount of water. The deep red solution was poured into 30% hypophosphorous acid (50 ml.), kept in the refrigerator for 17 hours and at room temperature for 4 hours and filtered. The filtrate and the residue were separately extracted with light petroleum (b.p. 40-60) and the combined extracts washed with 20% sodium hydroxide(2 x 20 ml.) and chromatographed on alumina. 3,3'-Dichlorobiphenyl (2.3 g., 62%) was obtained as a white crystalline solid, m.p. 25-27° (Lit.[129] 29°).

3,3'-Dichlorobiphenyl (continued)

The experiment was repeated on a larger scale and altogether 15 g. of 3,3'-dichlorobiphenyl were prepared.

2,2'-Dichlorobenzidine dihydrochloride

This was prepared analogously to 3,3'-dichlorobenzidine dihydrochloride, starting from *m*-chloronitrobenzene. The salt (28.8 g., 22%) was obtained as glistening yellow plates. The experiment was repeated and altogether 44.8 g. of 2,2'-dichlorobenzidine dihydrochloride were prepared.

2,2'-Dichlorobiphenyl from 2,2'-Dichlorobenzidine

This was prepared analogously to 3,3'-dichlorobiphenyl starting from 2,2'-dichlorobenzidine dihydrochloride. The product (4.5 g., 65%) was obtained as white crystals, m.p. 58-59°(Lit.[49] 59°). The experiment was repeated and altogether 8.5 g. of 2,2'-dichlorobiphenyl were prepared by this method.

3,3'-Dicyanobiphenyl

3,3'-Dichlorobiphenyl (3 g., 1 mol) was heated at 160° for 24 hours with cuprous cyanide (4 g., 3.3 mol) and pyridine (ca. 20 ml.). The black, tarry mixture was washed into dilute aqueous ammonia with a little dimethylformamide. The precipitate was filtered off and extracted thoroughly with boiling methylated spirit. On cooling, straw-coloured crystals (560 mg., m.p. 188-192°) separated. The ammoniacal solution was extracted with ether, the extract evaporated and the residue recrystallised from ethanol to give a further 350 mg. of the same material. The crops were combined and chromatographed on silica gel, using benzene as eluant. 3,3'-Dicyanobiphenyl (850 mg., 31%) was obtained as white prisms, m.p.* 207-211° with change of crystal form to needles above 190°. Recrystallisation from ethanol raised the melting point to * 211-212°.

(Found: C, 82.1; H, 4.1; N, 13.7% $C_{14}H_8N_2$ requires C, 82.3; H, 4.0; N, 13.7%)

The mother liquors from which the crude, coloured crops were obtained were concentrated to give 490 mg. of an off-white, crystalline solid which melted below

3,3'-Dicyanobiphenyl (continued)

120°. The infrared spectrum of this solid showed a CN stretch and qualitative analysis showed the presence of nitrogen and chlorine. The material was not investigated further but was assumed to be 3-chloro-3'-cyanobiphenyl.

2,2'-Dicyanobiphenyl

A mixture of 2,2'-dichlorobiphenyl (3 g., 1 mol), cuprous cyanide (4 g., 3.3 mol) and pyridine (c. 20 ml.) was heated at 200° for 40 hours. The mixture was worked up as described for 3,3'-dicyanobiphenyl. Chromatography with benzene on silica gel yielded 2,2'-dicyanobiphenyl (224 mg., 8%) as pale yellow prisms. It crystallised from methanol as white needles, m.p. 176.5-178°(Lit.[60] 172°).

2,2'-Dibromobenzidine

m-Bromonitrobenzene (100 g.) was reduced with zinc in alkaline solution in a manner exactly analogous to that of *m*-chloronitrobenzene. After heating for one

2,2'-Dibromobenzidine (continued)

hour, the solution was poured into 75% HCl. The precipitate (36.5 g.) melted below 100° and was probably a mixture of 3,3'-dibromoazoxybenzene and the corresponding azobenzene. The mixture was covered with ether (500 ml.) and zinc (100 g.) was added. Glacial acetic acid (30-40 ml.) was added dropwise through a funnel. After heating for ten hours, the solution turned from red to yellow. It was decanted from residual zinc, concentrated to c. 80 ml. and added slowly to concentrated HCl (140 ml.). After one hour the precipitate of 2,2'-dibromobenzidine dihydrochloride (19.6 g., 19%) was filtered off.

Subsequent reductions led to mixtures of azo- and azoxy- compounds which proved inert to further reduction by zinc and glacial acetic acid.

Attempted further reduction of 3,3'-dibromoazobenzene

A.W. Sogn[116]

Crude 3,3'-dibromoazobenzene (7 g.) was suspended in 76% aqueous sodium hydroxide solution (5 ml.) and

Attempted further reduction of 3,3'-dibromoazobenzene (continued)

methanol (10 ml.) together with 2,3-dichloro-1,4-naphthoquinone (1 g.) as catalyst. The mixture was warmed to 60° and aqueous formaldehyde ("formalin" 9 ml.) was added dropwise with magnetic stirring over 30 minutes. The mixture was stirred at 40° for five hours more and poured into concentrated hydrochloric acid. The product was a red-brown non-basic solid, m.p. 117-121° (Lit.[130] for 3,3'-dibromoazobenzene 125.5°). Recovery 92%.

Attempted reduction of m-bromonitrobenzene

m-Bromonitrobenzene (6 g.) was reduced as above using the same amounts of reagents. The product was an orange solid non-homogeneous under the microscope, m.p. 35-45°. This is clearly unchanged starting material (m.p. 56°) mixed with some 3,3'-dibromoazo- or 3,3'-dibromoazoxybenzene.

2,2'-Dicyanobenzidine

2,2'-Dibromobenzidine (7.0 g., 1 mol) was heated under nitrogen with cuprous cyanide (8.0 g., 4.4 mol)

2,2'-Dicyanobenzidine (continued)

and dimethylformamide (100 ml.) and the mixture was allowed to reflux for seven hours. The viscous black solution was then poured into aqueous ammonia (*d*. 0.88), the precipitate filtered off under suction and thoroughly extracted with hot methanol and the product reprecipitated from the methanolic extract with water. 2,2'-Dicyanobenzidine separated as a soft brown crystalline mass containing much occluded water. The compound was further purified by dissolving it in dilute HCl, treating the solution with charcoal at room temperature and reprecipitating with ammonia. The purified 2,2'-dicyanobenzidine was in the form of cream prisms which changed to needles at *200° and charred rapidly above *260°. The yield was 1.1 g., 23%

No satisfactory analysis could be obtained owing to the extreme sensitivity of the compound to aerial oxidation. However, mass spectroscopy showed a base peak at m/e 234 corresponding to the expected product and lesser peaks at m/e 206 and 178 corresponding to loss of HCN + H^+ twice over. This mode of splitting is characteristic of aromatic amines[131].

Attempted optical resolution of 2,2'-Dicyanobenzidine

a) 2,2'-Dicyanobenzidine (100 mg., 1 mol) and D-(+)-tartaric acid (106 mg., 2 mol) were dissolved separately in alcohol and the solutions mixed. There was no precipitate after five days. The solution was concentrated and left in the refrigerator for two days. A yellow solid slowly separated but this did not appear to be crystalline. The yield was 59 mg., only 29% reckoned as di-hydrogen tartrate.

b) 2,2'-Dicyanobenzidine (400 mg., 1 mol) and (+)-camphor-10-sulphonic acid (790 mg., 2 mol) were dissolved separately in methanol and the solutions mixed. There was no immediate precipitate but, after concentrating the solution somewhat, colourless crystals began to separate. The following crops were obtained:

I 497 mg. decomp. above* 228°
II 102 mg. decomp. above* 225°
III 110 mg. decomp. above* 220°
Evaporated mother liquor 245 mg. decomp. above 104°

Attempted optical resolution of 2,2'-Dicyanobenzidine (continued)

200 mg. of the first crop were dissolved in ice-cold dimethylformamide but the solution, though filterable, was opalescent and scattered light too strongly for a reading of the optical rotation to be taken.

2- and 4-Nitrophenanthraquinone

Schmidt and Spoun[132]
T.M. Poole[133]

Phenanthraquinone (60 g., 1 mol) was nitrated in batches by boiling with concentrated nitric acid (d. 1.42, 1800 ml.) for twenty minutes. The cooled reaction mixture was poured into cold water (5 litres). The product was filtered off, washed with water, thoroughly dried in air and boiled with alcohol (1 litre). The insoluble 2-nitrophenanthraquinone was filtered off (41 g., 56%, crude m.p.* 260-265°). The filtrate was cooled, filtered from the mixture of 2- and 4-nitrophenanthraquinones which separated, and concentrated to ca. 400 ml. On cooling the solution, 4-nitrophenanthraquinone (20 g., 27%, crude m.p. 168-170°), crystallised out.

2- and 4-Nitrophenanthraquinone (continued)

The nitrophenanthraquinones were separately recrystallised from glacial acetic acid giving 2-nitrophenanthraquinone of m.p. 263-265° (Lit.[i] 262-264°) and 4-nitrophenanthraquinone of m.p. 172-173° (Lit.[133] 172-175°).

The experiment was repeated twice and altogether 69 g. of 4-nitrophenanthraquinone and 126 g. of 2-nitrophenanthraquinone were prepared.

4-Nitrodiphenic acid

Moore and Huntress[134]

T.M. Poole, loc. cit.

2-Nitrophenanthraquinone (10 g., 1 mol) was dissolved in concentrated sulphuric acid (30 ml.) and reprecipitated as a fine powder by cautious addition of water (100 ml.) with ice cooling and swirling. A solution of potassium dichromate (40 g., 3.3 mol) in water (400 ml.) was added and the mixture heated under reflux for 2.5 hours. The reaction mixture was cooled and filtered and the acid washed with water until the washings were

4-Nitrodiphenic acid (continued)

colourless. The crude acid was covered with water and solid sodium bicarbonate was added until effervescence ceased. The residual quinone was filtered off and the filtrate gradually acidified with dilute H_2SO_4. 4-Nitrodiphenic acid (9.6 g., 85%) separated as almost white crystals, m.p.* 215-217° (Lit.[133] 214-215°).

6-Nitrodiphenic acid

Schmidt and Kampf[135]

T.M. Poole, loc. cit.

4.-Nitrophenanthraquinone (12 g., 1 mol) was boiled under reflux for one hour with a solution of $K_2Cr_2O_7$ (33 g., 2.36 mol) in water (450 ml.) and concentrated H_2SO_4 (30 ml.). The reaction mixture was cooled, the product filtered off and washed well with water. It was purified by dissolving in dilute ammonium hydroxide, filtering and acidifying with dilute sulphuric acid. 6-Nitrodiphenic acid separated as s white crystalline solid (10.7 g., 79%). On recrystallisation from alcohol, it yielded white plates, m.p.* 248.5-250° (Lit.[135] 248-250°)

6-Nitrobiphenyl-2,2'-dicarboxamide

6-Nitrodiphenic acid (4 g., 1 mol) was covered with thionyl chloride (10 ml., 10 mol) and the mixture was heated under reflux for 72 hours. Excess thionyl chloride was removed at the pump. The resultant oil was added dropwise to a large excess of aqueous ammonia (d. 0.88). There was immediate evolution of white fumes and a yellow, plastic solid separated. The mixture was left at room temperature for twenty minutes. During this time the product hardened and became crystalline. It was filtered off and recrystallised from ethanol to yield 6-nitrobiphenyl-2,2'-dicarboxamide (3 g., 76%) as pale yellow needles, m.p. 235-236° with gas evolution.

(Found: C, 59.0; H, 4.0; N, 14.9. $C_{14}H_{11}N_3O_4$ requires C, 59.0; H, 3.9; N, 14.7%)

6-Nitro-2,2'-diaminobiphenyl

After P.F. Holt and A.N. Hughes[93]

6-Nitrobiphenyl-2,2'-dicarboxamide (580 mg., 1 mol) was added slowly to an ice-cold solution of bromine (0.25 ml., 2.3 mol) in 10% aqueous sodium hydroxide

6-Nitro-2,2'-diaminobiphenyl (continued)

(8 ml., 10 mol). The mixture was magnetically stirred for ten minutes during which the amide dissolved to give a viscous greenish solution. The solution was filtered, heated rapidly to 80° and kept at 80-90° for a further ten minutes. It was then filtered into an excess of saturated aqueous ammonium chloride and the resultant brown colloidal solution thoroughly extracted with ether. Evaporation of the ether extract yielded 6-nitro-2,2'-diaminobiphenyl (183 mg., 40%) as a yellow oil which rapidly turned red in air.

No satisfactory analysis could be obtained as the compound was very readily oxidised. It was therefore characterised as the benzil derivative, prepared as follows:

4-Nitro-2,3-diphenyl-5,6:7,8-dibenzo-1,4-diazocine

6-Nitro-2,2'-diaminobiphenyl (100 mg., 1 mol) and benzil (120 mg., 1 mol) were heated together for six hours in propionic acid (2 ml.) under reflux. The dark

4-Nitro-2,3-diphenyl-5,6:7,8-dibenzo-1,4diazocine (continued)

red solution was cooled and water was added dropwise until crystallisation began. The product (104 mg., 59%) was filtered off and recrystallised from ethanol to give almost white needles, m.p. 272-273°.

(Found: N, 10.4; O, 8.1% $C_{26}H_{17}N_3O_2$ requires N, 10.4; O, 7.9%)

The preparation of the amine was repeated and altogether 4.9 g. of 6-nitro-2,2'-diaminobiphenyl were prepared.

Schmidt reaction on 6-nitrodiphenic acid

After E.M. Stephenson[90]

6-Nitrodiphenic acid (0.7 g., 1 mol) was suspended in concentrated sulphuric acid (5.8 ml.) and sodium azide (0.8 g., 5 mol) was added gradually over ten minutes. After a further five minutes, the mixture was cautiously warmed on a hot-plate. There was vigourous effervescence and the acid dissolved to give a deep red solution. After thirty minutes the solution was diluted with water until precipitation of the pro-

Schmidt reaction on 6-nitrodiphenic acid (continued)

duct was complete. 10-Nitrophenanthridone (0.46 g., 79%) was obtained as a pale buff powder. It crystallised readily from glacial acetic acid as yellow needles, m.p. 312-314° (Lit.[118] 316-318°).

Schmidt reaction on 4-nitrodiphenic acid

The reaction was carried out in an analogous way to the above. The product was 8-nitrophenanthridone (0.45 g., 77%) which crystallised from glacial acetic acid as pale yellow needles, m.p. 318-321°. (Lit.[117] 326-327°).

Curtius reaction on 4-nitrodiphenic acid

1.) 4-Nitrodiphenic acid (3 g., 1 mol) was covered with thionyl chloride (7.5 ml., 10 mol) and heated under gentle reflux for 72 hours. The solution was evaporated to dryness under reduced pressure. Half of the acid chloride produced was dissolved in acetone and shaken with a saturated aqueous solution of sodium azide (1.5 g.). After five minutes, 4-nitrobiphenyl diazide separated as a heavy flocculent precipitate. The azide was filtered off under suction, dried *in vacuo* and

Curtius reaction on 4-nitrodiphenic acid (continued)

heated under reflux for two hours in dry benzene. During this time there was steady evolution of gas. Concentrated hydrochloric acid was added and the mixture allowed to boil vigourously under reflux for a further 90 minutes. The product was a yellow solid, insoluble in acid and almost insoluble in benzene. Its infrared spectrum showed pronounced N=C=O stretching at 2300 cm^{-1}. The solid was suspended in concentrated hydrochloric acid and allowed to reflux for two hours. The compound now showed a strong infrared band at 2350 cm^{-1} together with bands at 1700 and 1770 cm^{-1}. This combination is characteristic of a polymeric isocyanate as is the inertness to further hydrolysis. Recrystallisation from ethyl acetate/light petroleum gave material m.p. 315-319°.

(Found: C, 57.3; H, 3.0; N, 15.1% ($C_{14}H_7N_3O_4$) requires C, 59.7; H, 2.5; N, 15.0%)

An attempt was made to measure the molecular weight using a Mechrolab vapour pressure osmometer. Owing to the low solubility of the compound in all solvents, no satisfactory reading could be obtained, but the results suggest either a trimer or a tetramer, more probably the former.

Curtius reaction on 4-nitrodiphenic acid (continued)

2.) The remainder of the acid chloride was converted into the azide as above. The azide was suspended in concentrated hydrochloric acid and the mixture allowed to boil under reflux. A vigourous reaction took place and at one point there was a loud report. When effervescence had ceased, the mixture was filtered and the filtrate neutralised and extracted with ether. This produced a very small amount of a brown gum, possibly 4-nitro-2,2'-diaminobiphenyl. The residual solid was recrystallised from glacial acetic acid to yield 8-nitro-(5H)-6-phenanthridone, m.p. 320-323°. The yield of nitrophenanthridone was not known accurately but was clearly over 70%

Attempted Sandmeyer reaction on 6-nitro-2,2'-diaminobiphenyl

Clarke and Read, *loc. cit.*[47]

a) 6-Nitro-2,2'-diaminobiphenyl (183 mg., 1 mol) was suspended in water containing sulphuric acid (5 equiv.) and diazotised with a solution of sodium nitrite (128 mg., 2.2 mol). The solution was neutralised with

Attempted Sandmeyer reaction on 6-nitro-2,2'-diaminobiphenyl (continued)

solid sodium carbonate and added slowly to one containing potassium cyanide (200 mg., 4 mol) and cuprous cyanide (179 mg., 2.5 mol). The cyanide solution was covered throughout by a layer of benzene. The mixture was left at room temperature overnight and filtered. The solid obtained (107 mg.) was shown by its infrared spectrum to be a mixture of reclaimed amine and cuprous cyanide. Extraction of the aqueous solution yielded an additional 54 mg. of the amine. Neither fraction showed the characteristic 2200 cm^{-1} band of organic nitriles.

b) 6-Nitro-2,2'-diaminobiphenyl (276 mg., 1 mol) was dissolved in concentrated sulphuric acid and diazotised with aqueous sodium nitrite (183 mg., 2.2 mol). The solution was neutralized as above and poured into one of KCN (400 mg., 5 mol) and CuCN (270 mg., 2.5 mol), covered as before with benzene. The mixture was left to stand overnight at room temperature but no nitrile could be isolated from it.

c) 6-Nitro-2,2'-diaminobiphenyl (1.4 g.) was diazotised in concentrated sulphuric acid with a solution

Attempted Sandmeyer reaction on 6-nitro-2,2'-diaminobiphenyl (continued)

of sodium nitrite (0.9 g., 2.2 mol) in the same solvent. A few drops of the resultant solution gave a red precipitate with alkaline β-naphthol indicating that diazotisation had proceeded normally. The solution was poured onto ice and neutralised with solid sodium carbonate. It was then poured into a solution of cuprous cyanide (1.4 g.) and potassium cyanide (2.8 g.) covered with benzene as before. The mixture was allowed to stand at room temperature overnight and filtered. The aqueous solution was thoroughly extracted with benzene and the extract evaporated to dryness. The residue was combined with the material removed by filtration and chromatographed on alumina. Methanol eluted a brown resinous solid (635 mg.) which showed acidic properties. The infrared spectrum showed no band due to a cyano group. This material was not investigated further but was assumed to contain 4-nitrocarbazole as its main constituent.

Biphenyl-2,2'-dicarboxamide

Underwood and Kochmann[136]

Diphenic acid (15 g., 1 mol) was heated with phosphorus pentachloride (27 g., 2 mol) in a Woods metal bath. The bath temperature was kept at 190-195° for thirty minutes and at 150° for one hour. The reaction mixture was cooled and poured into aqueous ammonia (d. 0.88). Biphenyl-2,2'-dicarboxamide (10.4 g., 69%) precipitated as a white solid. Recrystallisation from ethanol yielded white crystals, m.p.* 212-214° dec. (Lit.[137] 212°).

Note: Underwood and Kochman prepared the dichloride by the above method but did not convert it into the diamide. They prepared the latter from the imide and ammonia.

Dehydration of Biphenyl-2,2'-dicarboxamide

1.) Biphenyl-2,2'-dicarboxamide (1 g., 1 mol) was covered with thionyl chloride (3 ml., 10 mol) and heated under reflux until evolution of HCl was complete (75 minutes). Excess thionyl chloride was decomposed

Dehydration of Biphenyl-2,2'-dicarboxamide (continued)

with ice and the precipitated product (705 mg.) was chromatographed on silica gel. Benzene eluted 4-cyanofluorenone (583 mg., 68%) as a yellow crystalline solid. It crystallised from ethanol as long yellow needles, m.p.* 242-244° with sublimation (Lit.[138] 244°).

2.) Biphenyl-2,2'-dicarboxamide (2 g., 1 mol) was heated with phosphorus pentoxide (2 g., 2.5 mol) for $1\frac{3}{4}$ hours in a Wood's metal bath at 240-250°. The mixture was then cooled, water added and the product filtered off, dried and chromatographed on silica gel. The chief product was a red, acidic solid (468 mg.) which was not investigated further.

3.) Biphenyl-2,2'-dicarboxamide (1 g., 1 mol) and phosphorus pentoxide (1 g., 2.5 mol) were covered with dry mesitylene (20 ml.) and the mixture was boiled under reflux for nine hours. The solution was filtered from phosphoric acid and cooled. Addition of light petroleum (b.p. 80-100) precipitated crude 4-cyanofluorenone (530 mg., 62%), m.p.* 238-240°.

Dehydration of biphenyl-2,2'-dicarboxamide (continued)

4.) Diphenyl-2,2'-dicarboxamide (1.5 g., 1 mol) was covered with redistilled phosphorus oxychloride (0.6 ml., 1 mol) and benzene (20 ml.) and the mixture was boiled under reflux for twelve hours. The solution was filtered and evaporated to yield crude 4-cyanofluorenone (850 mg., 66%), m.p.* 239-242°.

Dehydration of 6-nitrobiphenyl-2,2'-dicarboxamide

The amide (0.6 g.) was covered with a large excess of thionyl chloride (4 ml.) and the mixture was boiled under reflux for 72 hours. The product obtained by evaporation of the excess thionyl chloride was a brown viscous oil whose infrared spectrum was consistent with the structure of 5-nitro-4-cyanofluorenone. The yield was 241 mg., 46% calculated as 5-nitro-4-cyanofluorenone. The oil was covered with concentrated sulphuric acid and warmed without boiling for three hours. The mixture was poured onto ice and filtered. The product was a cream-coloured solid which dissolved with effervescence in aqueous sodium carbonate solution and could be reprecipitated by acidification of the solution. However

Dehydration of 6-nitrobiphenyl-2,2'-dicarboxamide (continued)

this process was more difficult than expected and much of the solid refused to go into solution. The precipitated solid weighed only 50 mg., 19% calculated as 5-nitrofluorenone-4-carboxylic acid. The solid showed the expected features in its infrared spectrum but melted indeterminately 190-200°. (Lit.[134] 238-239°).

Optical resolution of 6-nitrodiphenic acid

J.W. Brook[139]
F. Bell and Robinson[140]

Racemic 6-nitrodiphenic acid (4 g.) and anhydrous quinine (9 g.) were dissolved separately in absolute ethanol (2 x 100 ml.) and the solutions were mixed. Fractional crystallisation afforded the quinine salt of (+)-6-nitrodiphenic acid, $_{546}$ = +275° in $CHCl_3$ (c. = 1.0 g./100 ml., l = 1 dm.) at a temperature of 21°. (Lit.[139] +273°). The salt (5.47 g.) was suspended in water and decomposed by the addition of dilute hydrochloric acid. The active acid was extracted into ether and the extract washed with dilute HCl, dried

Optical resolution of 6-nitrodiphenic acid (continued)

over anhydrous calcium chloride and evaporated in vacuo to yield (+)-6-nitrodiphenic acid (1.8 g., $_{546}$ = +78° in ethanol) (Lit.[140] +65.2°). The alcoholic mother liquor was treated similarly and afforded (-)-6-nitrodiphenic acid (20 g., $_{546}$ = -50°)

Benzo[c]cinnoline

Modified from G.M. Badger, J.H. Seidler and B. Thompson[100]

Lithium aluminium hydride (15.5 g., 5 mol) was suspended in dry ether (85 ml.) in a three-necked 250 ml. flask fitted with two double-surface reflux condensers and a dropping funnel. The suspension was magnetically stirred while a solution of 2,2'-dinitrobiphenyl (20.7 g., 1 mol) in dry benzene (180 ml.) was added dropwise through the funnel. Each addition was followed by a vigorous reaction. The mixture was heated under reflux for a further 3½ hours, cooled and cautiously decomposed with water. The precipitated hydroxides were filtered off under suction, the organic layer

Benzo[c]cinnoline (continued)

separated from the filtrate and the aqueous layer and solid residue separately extracted with ether until the extracts were colourless. The combined organic layers were evaporated to yield crude benzo [c] cinnoline (14.2 g., 94%) as tarry brown crystals. Recrystallisation from benzene yielded golden-brown crystals, m.p. 153-155° (Lit.^{100} 156°). The experiment was repeated and altogether 30 g. of benzo c cinnoline were prepared.

W2 Raney nickel

R. Mozingo^{141}

Sodium hydroxide (12.6 g.) was dissolved in water (50 ml.) in a 150 ml. beaker and cooled to 10°. Raney nickel-aluminium alloy (10 g.) was added in small portions with mechanical stirring and without allowing the temperature to rise above 25°. Addition took 1½-2 hours. The mixture was allowed to come to room temperature and warmed gently until evolution of hydrogen had become slow (8-12 hours). The alkali was decanted off and the precipitated nickel washed once with dis-

W2 Raney nickel (continued)

tilled water and once with 10% sodium hydroxide solution. It was then washed by decantation with water until the washings were neutral to litmus and ten times more. Finally it was washed three times with 95% ethanol and three times with absolute ethanol and stored under absolute ethanol in a stoppered bottle.

1-Nitrobenzo[c]cinnoline

W.T. Smith, Jr. and P.R. Ruby[112]

Solid benzo[c]cinnoline (12.6 g.) was added slowly to a magnetically stirred mixture of colourless concentrated nitric acid (20 ml.) and concentrated sulphuric acid (60 ml.) contained in a 250 ml. beaker. Addition took thirty minutes. Stirring was continued for a further six hours and the mixture was then poured onto ice (*ca*. 120 g.). Aqueous ammonia (*d*- 0.88) was added until precipitation was complete, the solid product was filtered off, thoroughly air-dried and extracted continuously with light petroleum (b.p. 60-80) until the extract was only faintly coloured. Evaporation of

1-Nitrobenzo[c]cinnoline (continued)

the resultant solution yielded 1-nitrobenzo[c]cinnoline (8.2 g., 52%) as a green solid. Recrystallisation from ethanol yielded long pale-green needles, m.p. 159-162° (Lit.[112] 160-162°). The experiment was repeated and altogether 19 g. of 1-nitrobenzo c cinnoline were prepared.

1-Aminobenzo[c]cinnoline

W.T. Smith, Jr. and P.R. Ruby, *loc.cit.*

1-Nitrobenzo[c]cinnoline (1.5 g.) was dissolved in methanol (200 ml.) and hydrogenated at 45-50 p.s.i. and room temperature over Raney nickel. The pressure of hydrogen dropped by 14 p.s.i. in two hours. The solution was filtered and evaporated to yield 1-aminobenzo[c]cinnoline (1.3 g., almost theoretical yield) as a red-brown solid. Nitro bands were absent from the infrared spectrum.

Some subsequent preparations were contaminated with unreduced 1-nitrobenzo[c]cinnoline. This could be removed easily by placing the solid amine on top of a column of type H alumina in benzene and eluting with

1-Aminobenzo[c]cinnoline (continued)

benzene until no further solid could be obtained. The eluted 1-nitrobenzo[c]cinnoline could be used again and the residual 1-amino[c]cinnoline recovered from the top of the column.

The experiment was repeated and altogether 6.3 g. of 1-aminobenzo[c]cinnoline were prepared. In order to avoid oxidation the compound was not recrystallised but was used directly for the next step.

1-Cyanobenzo[c]cinnoline

1-Aminobenzo[c]cinnoline (3.0 g., 1 mol) was suspended in dilute sulphuric acid (solution at pH3) and diazotised with a solution of sodium nitrite (1.2 g., 1.1 mol). The solution was carefully neutralised with solid sodium carbonate and poured into one containing cuprous cyanide (2.3 g., 1.5 mol) and potassium cyanide (4.6 g., 2.5 mol) covered with a layer of benzene. The mixture was left overnight at room temperature and filtered. The residue was extracted continuously with hot benzene until the extract was colourless. The filtrate was also thoroughly extracted with benzene. The

1-Cyanobenzo[c]cinnoline (continued)

combined extracts were chromatographed on alumina. A 1:1 mixture of benzene and ether eluted the product (250 mg., 8%) as a yellow solid. It crystallised from benzene as long golden needles, m.p.* 238° with sublimation.

(Found: C,76.6; H. 3.6; N, 20.1% $C_{13}H_7N_3$ requires C,76.1; H, 3.5; N, 20.5%)

In chromatographing this compound it is important not to leave it on the column for more than ca. 24 hours. If this precaution is not taken, the eluate has the infrared spectrum of an amide and not of a nitrile.

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