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THE ISOCYANO GROUP AS A CARBENOID FUNCTION
CYCLIZATION OF ORTHO-ISOCYANOBIPHENYL AND DERIVATIVES

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J. DE JONG

RIJKSUNIVERSITEIT TE GRONINGEN

**THE ISOCYANO GROUP AS A CARBENOID FUNCTION
CYCLIZATION OF ORTHO-ISOCYANOBIPHENYL AND DERIVATIVES**

PROEFSCHRIFT

TER VERKRIJGING VAN HET DOCTORAAT IN DE
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OP GEZAG VAN DE RECTOR MAGNIFICUS DR. W.F. DANKBAAR
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COREFERENT: PROF. DR. J.H. BOYER

The study described in this thesis was carried out at the University of Illinois, Chicago Circle Campus, under the supervision of Prof. Dr. J.H. Boyer.

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RECEPTIE NA AFLOOP DER PROMOTIE
IN HET UNIVERSITEITSGEBOUW

STELLINGEN

I

Matteson en Bailey hebben niet bewezen dat biphenyldiazomethaan op dezelfde wijze addeert aan vinylisocyanide als aan acrylonitril.

D.S. Matteson, R.A. Bailey, *J. Amer. Chem. Soc.*, 90, 3761 (1968)

II

De theoretische beschouwingen door Freeman en Johnson aangevoerd om hun belangstelling in het photochemisch gedrag van de di-p-tolyldiazonen van biacetyl en benzyl kenbaar te maken zijn overbodig.

P.K. Freeman, R.C. Johnson, *J. Org. Chem.*, 34, 1746 (1969).

III

De verklaring die Faucher en Robert geven aan het discontinue gedrag van kalium tetracyanochinomethaan (TCNQ) bij 130°C is onjuist.

J.P. Faucher, H. Robert, *Comptes rendus*, 270 série B, 174 (1970).

IV

Het mechanisme dat Tsuchihaschi en Iriuchijima voorstellen voor de chlorering van sulfoxiden geeft geen verklaring voor de stereospecificiteit van de reactie.

G. Tsuchihaschi, S. Iriuchijima, *Bull. Chem. Soc. Japan*, 43, 2271 (1970).

V

De resultaten van Schubert en Ke verkregen bij γ -bestraling van Busycon Hemocyanine zijn moeilijk te rijmen met het door Konings gevonden lineaire verband tussen het kwadraat van het koper gehalte en de zuurstofbindingscapaciteit van Helix Pomatia Hemocyanine.

J. Schubert, C.H. Ke, *J. Amer. Chem. Soc.*, 93, 1282 (1971); W.N. Konings, R. van Driel, E.F.J. van Bruggen, M. Gruber, *Biochem. Biophys. Acta*, 194, 55 (1969).

VI

De methode die Schröder gebruikt om de oplosbaarheid van een reagerend gas in een electroliet oplossing te berekenen is aanvechtbaar.

Compt. Rend. Congr. Intern. Chim. Ind. 36^e, p. 248, Brussel (1967).

VII

Ryhänen heeft niet volledig aangetoond, dat de heterotrofe afbraak van humus verbindingen door toevoeging van fosfaat en nitraat aan Fins oppervlakte water wordt bevorderd.

R. Ryhänen, Mitt. Internat. Verein. Limnol., 14, 168 (1968).

VIII

Ferstandig geeft een onjuiste voorstelling van waterstofbrug vorming van een alcohol met het eindstandige koolstofatoom van een isocyanide groep.

L.L. Ferstandig, J. Amer. Chem. Soc., 84, 3555 (1962).

IX

De toelichting op de aftrek voor dieetkosten van diabetici in de Nederlandse Staatscourant is aanvechtbaar.

Nederlandse Staatscourant 252, 11 (1970).

X

Het is alleszins het overwegen waard de verkoop van schoenen in paren te vervangen door de verkoop van losse exemplaren.

Aan mijn ouders

Aan Ciska

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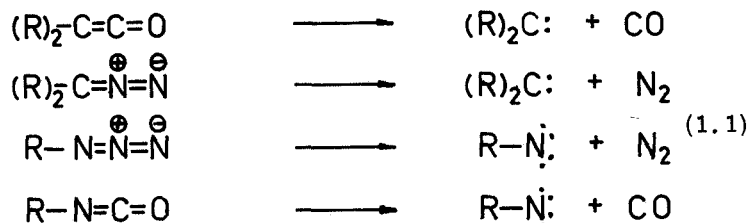
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CHAPTER I

INTRODUCTION.

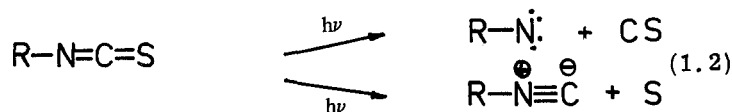
During the past decades considerable interest has grown in the chemistry of carbenes and nitrenes. Both represent abnormal valence states of carbon and nitrogen and are found to be highly reactive. The generation of these species and their reactions have been extensively reviewed.²

Among the various methods to produce carbenes or nitrenes, homolysis of cumulated systems has been successfully explored. Cleavage may be brought about thermally or through electronic excitation. Thus, photolysis of ketenes⁴ or diazomethanes⁵ leads to carbenes. Azides⁶ and isocyanates⁷ have been shown to produce nitrenes.



In this view a photochemical study of isothiocyanates seemed to be attractive for two reasons.

1. Cleavage of the nitrogen-carbon double bond would produce a nitrene and carbonmonosulfide.
2. Cleavage of the sulfur-carbon double bond would lead to an isocyanide and sulfur.



The latter cleavage pattern is not new and has been reported for some alkylisothiocyanates upon excitation. However, it was hoped that arylisocyanides from arylisothiocyanates would give subsequent reactions under the irradiation conditions. Very little is known about the excited state behavior of isocyanides, which makes it difficult to predict any subsequent reaction course.

1.1. Isothiocyanates.

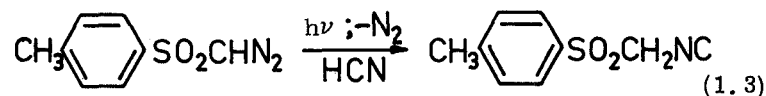
Schmidt et al.⁸ reported the formation of aliphatic isonitriles by the photolysis of the corresponding isothiocyanates, i.e., only methyl- and ethylisothiocyanate produced isocyanides, although no such photolysis products were found upon irradiation of n-butyl- and cyclohexylisothiocyanate. A similar photolytic cleavage has been observed for NCS^\ominus in which the cyanide ion and sulfur are the products.⁹ But flash photolysis of ethylisothiocyanate and thiocyanate in the gaseous phase produced thiocyanogene radicals¹⁰, which were also formed upon irradiation of thiocyanogene.¹¹ In the reversible photoisomerization of benzylthiocyanate and isothiocyanate in solution also homolytic bond cleavage is involved.¹²

Finally the pyrolysis of methylated ethylisothiocyanates in the gaseous phase produced HNCS and C_nH_{2n} .¹³

These literature data would predict the formation of arylisonitriles and sulfur upon irradiation of the corresponding isothiocyanates. However, it seemed to us that an alternative cleavage into a nitrene and carbonmonosulfide might be tracked down by a proper choice of the model compound.

1.2. Isonitriles.

A study of the excited state behavior of isonitriles appears to have been neglected. Only data for the simplest member of this family are available. Thus, the irradiation of methylisocyanide in the gaseous phase resulted in the rearrangement to methylcyanide.¹⁴ Recently cyclohexylisocyanide has been irradiated together with diphenyldiazomethane producing a ketimine.¹⁵ Further, the photolysis of p-tolylsulfonyldiazomethane in liquid hydrogen cyanide afforded p-tolylsulfonylmethylisocyanide.

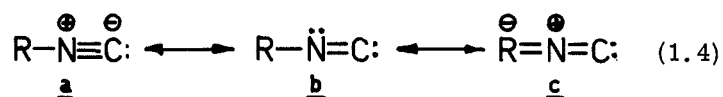


No indication was found for the "subsequent" formation of p-tolylsulfonylmethylcyanide.¹⁶

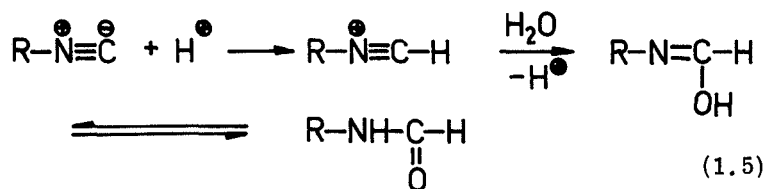
Recently, all the aspects of isonitrile chemistry have been reviewed in a book edited by I. Ugi.¹⁷ Ground state reactions of the isonitriles have been more extensively studied, especially since a general procedure was developed for the preparation of isonitriles.¹⁸

The isocyanide group takes in fact its very own place among

the various functional groups. The terminal carbon atom is formally divalent and resembles to this respect carbenes. In general, however, its reactivity has not been found to parallel that of carbenes at all. Carbenes show electrophilic properties, whereas isonitriles reveal more or less nucleophilic properties.¹⁹ Moreover, isonitriles are stable compounds. This has been satisfactorily explained by considering the lone pair electrons on the nitrogen atom. By sharing this lone pair the terminal carbon atom obtains a formally negative charge and has no longer the sextet of electrons characteristic of carbenes. An isonitrile is considered as a hybrid of the following resonance structures

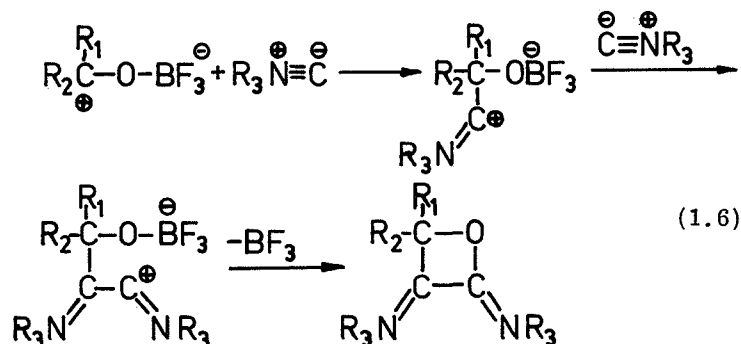


Structure a makes the greatest contribution. The triple bond character has been very well established by extensive microwave studies²⁰, by dipole moment studies²¹, by analysis of infrared²² and Raman spectra²³, etc.²⁴ Most reactions of isonitriles have been satisfactorily explained in terms of nucleophilic character. E.g., formamides may be prepared by the acid-catalyzed addition of water to isonitriles. The mechanism is probably as follows²⁵



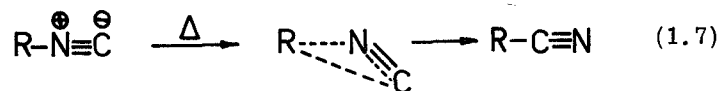
A wide variety of compounds is known to react with an isonitrile in this fashion (α -addition) either with or without a catalyst.²⁹

A carbonyl group activated by electron withdrawing substituents reacts with isonitriles.²⁷ Activation of a carbonyl function may be obtained with strong Lewis acids.



(The well-known Passerini reaction²⁶ is another example).

Isonitriles form stronger hydrogen bonds with alcohols than do nitriles,³⁰ which has been confirmed theoretically.³¹ But not all reactions of isonitriles can be explained by taking into account its nucleophilic properties. This has been shown by reactions involving an isonitrile in neutral media at various temperatures. The very well-known rearrangement of isonitriles into nitriles is an example. Experimental evidence has been obtained against ionization in the transition state.



Casanova et al.³² studied the rearrangement of cyclobutyl isocyanide. When a cationic carbon is involved, one would expect carbon skeleton rearrangement (a demonstrated propensity of the cyclobutyl cation). This conclusion is supported by the work of Rabinowitch et al.³³ who found no electronic effect on the rates of isomerization of *para*-substituted arylisocyanides (*p*-chlorophenyl, *p*-tolyl, and *p*-methoxyphenyl isocyanide). The observed retention of configuration in the rearrangement of optically active *sec*-butylisocyanide points in the same direction. These experimental findings are not in good agreement with extended Hückel calculations of Van Dine and Hoffmann³⁴ who found in every isocyanide studied an increase in positive charge at the migrating carbon atom in the transition state.

Further the reaction with sulfur is illustrative. Either in boiling benzene or ethanol high yields of the corresponding isothiocyanates are found,³⁵ and isolated as the thiourea derivatives.

1.3. Scope of the thesis.

The formation of cyclohept[b]indole by irradiation of *ortho*-isocyanobiphenyl is a new reaction which reveals electrophilic carbenoid properties of the aromatic isocyanide group. This appears to be the first example of an aromatic ring expansion brought about by an insertion of an isocyanide carbon atom. The reaction was discovered upon irradiation of *ortho*-isothiocyanatobiphenyl. Both *ortho*-isocyanobiphenyl and cyclohept[b]indole were found to be produced (Chapter II). This subject has been extended with the irradiation of 2,X'-diisocyanobiphenyls (Chapter III). Some physico-chemical data of the produced isocyanocyclohept[b]indoles are discussed in Chapter IV. The last Chapter, V, describes an apparent different reaction course by irradiation of *ortho*-isocyanobiphenyl in methanol, i. e., the formation of another isomer, phenanthridine. Evidence has been found against a direct insertion reaction in the formation of the latter.

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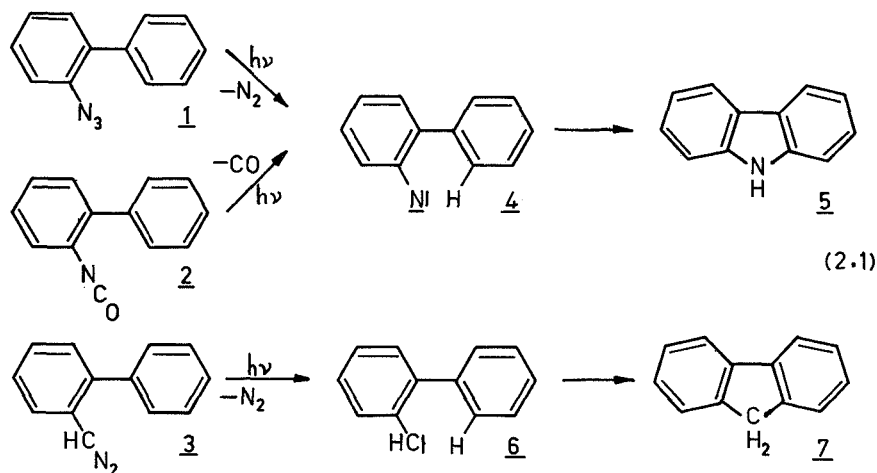
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CHAPTER II

IRRADIATION OF *ORTHO* ISOTHIOCYANATO- AND *ORTHO* ISOCYANOBIPHENYL.

2.1 Introduction

Photolysis of *ortho*-azido-(1)¹ and *ortho*-isocyanato-biphenyl² 2 yields carbazole. The reaction apparently proceeds by formation of an intermediate nitrene 4 which inserts into the *ortho* C-H bond of the adjacent phenyl ring. Similarly a carbene 6 can be generated upon photolysis of 2-biphenyldiazomethane³ 3 giving fluorene 7.



In view of these results *ortho*-isothiocyanatobiphenyl 9 was anticipated to yield carbazole 5 when homolytic cleavage of the nitrogen-carbon bond would occur upon excitation under appropriate conditions.

2.2 Results and discussion

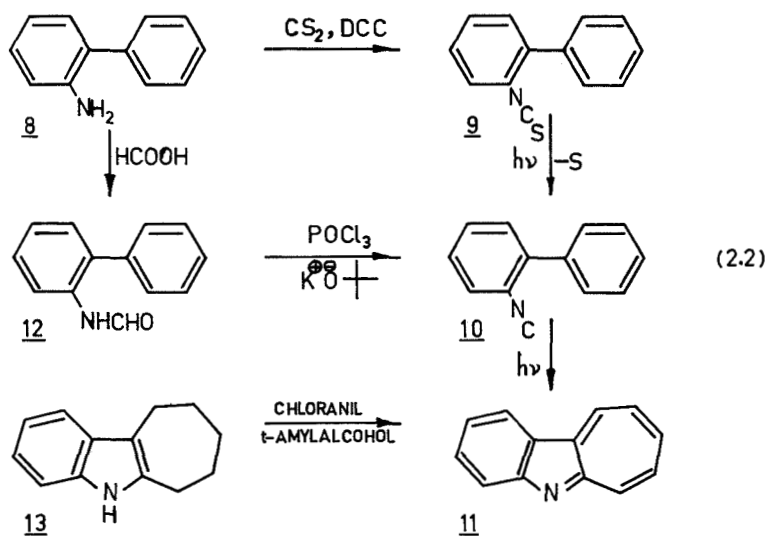
The *o*-isothiocyanatobiphenyl 9 was prepared according to a general procedure described by Jochims⁴ from *o*-aminobiphenyl 8, dicyclohexyl carbodiimide (DCC) and carbondisulfide and obtained in a yield of 75 percent.

The isothiocyanate **9** was irradiated in cyclohexane at 254 nm for 64 hrs under nitrogen. Column chromatographic separation on silica afforded 25 percent *o*-isocyanobiphenyl, 28 percent cyclohept[b]indole and 24 percent sulfur. All yields are corrected for recovered starting material (83 percent). Product identification was achieved by comparison of spectral data and tlc plates with those obtained from authentic compounds. The sulfur was identified by mixture melting point (undepressed).

Ortho-isocyanobiphenyl⁵ **10** was obtained by treatment of **8** with formic acid, which afforded *ortho*-*N*-formylaminobiphenyl⁶, and subsequent dehydration of the latter with phosphorus oxychloride⁷ in basic medium.

It was obtained as a colorless liquid bp 113-114° (1.5 mm) in contrast to the reported solid mp 116-118°, apparently in error.⁵

Dehydrogenation of 5,6,7,8,9,10-hexahydrocyclohept[b]indole afforded cyclohept[b]indole (1 percent).⁸



The formation of *o*-isocyanobiphenyl and sulfur upon irradiation of **9** is apparently the result of homolytic cleavage of the carbon-sulfur bond.¹⁰

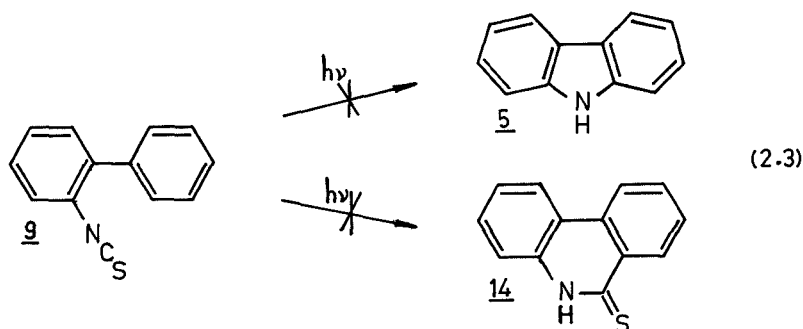
Schmidt et al.¹⁰ isolated 5-10 percent of ethylisocyanide after 12 hrs of irradiation of ethylisothiocyanate. Upon prolonged irradiation no higher yields were obtained. A high conversion of methylisothiocyanate could be reached, when the methylisocya-

nide was allowed to undergo a subsequent reaction as soon as it formed¹⁰ (Passerini reaction). The low conversion of *o*-isothiocyanatobiphenyl 9 may be ascribed to efficient cage recombination of *o*-isocyanobiphenyl and sulfur pairs.

The crude reaction mixture from *o*-isothiocyanatobiphenyl 9, was carefully examined for the presence of carbazole 5 with thin layer chromatography (authentic material supplied by Aldrich Chemical Company) and so were the fractions obtained upon column chromatography. But formation of 5 could not be tracked down. It is concluded that either homolytic cleavage of the nitrogen-carbon bond does not occur at all, or the generated nitrene scavenges very fast the carbonmonosulfide within the solvent cage. (Carbonmonosulfide is known in transitory existence when produced in a high frequency discharge through carbondisulfide, or by photolysis of carbondisulfide.⁹)

Thus, if cleavage occurs at all, recombination of two very reactive species (a nitrene and CS) apparently prevails over intramolecular insertion of the nitrene into the C-H bond of the adjacent phenylring.

Although Swenton² isolated upon irradiation of *ortho*-isocyanatobiphenyl besides phenanthridine, phenanthridine-6(5H)-one, we have not found phenanthridine-6(5H)-thione 14.



The cyclohept[b]indole 11 isolated from the photolysis mixture of *ortho*-isothiocyanatobiphenyl 9 was apparently formed upon subsequent excitation of the initial product *ortho*-isocyanobiphenyl 10, because it was also obtained upon independent irradiation of 10. Irradiation of 10 in cyclohexane (7.5 mM) for 19 hrs gave 62 percent of 11, corrected for recovered 10 (69 percent).

Prolonged irradiation (57 hrs) of 10 in cyclohexane (21.0 mM) afforded besides cyclohept[b]indole 11, a trace of phenanthridine (less than 1 percent) upon fractionation of the crude reaction mixture on silica. IR spectrum, glc and tlc retention times

were identical with those from authentic phenanthridine (see experimental, Chapter V). Cyclohept[b]indole was isolated in a yield of 42 percent, after correction for recovered starting material (62.8 percent). In an independent experiment cyclohept[b]indole was found to be photosensitive. While products were not identified, no phenanthridine could be detected by glc even at low attenuation of the recorder.

The latter experiments were initiated from the results depicted in Chapter V (Irradiation of *o*-isocyanobiphenyl in methanol afforded phenanthridine). In those experiments evidence was obtained against a direct insertion of the isocyanocarbon producing phenanthridine.

It is therefore quite well possible, that the traces of phenanthridine obtained as described above, were formed by catalytic action of a trace of water.

The formation of cyclohept[b]indole was monitored by UV spectroscopy for the irradiation of 20.0 mM solutions of *o*-isocyanobiphenyl in cyclohexane under nitrogen as well as under oxygen (figure 2.1).

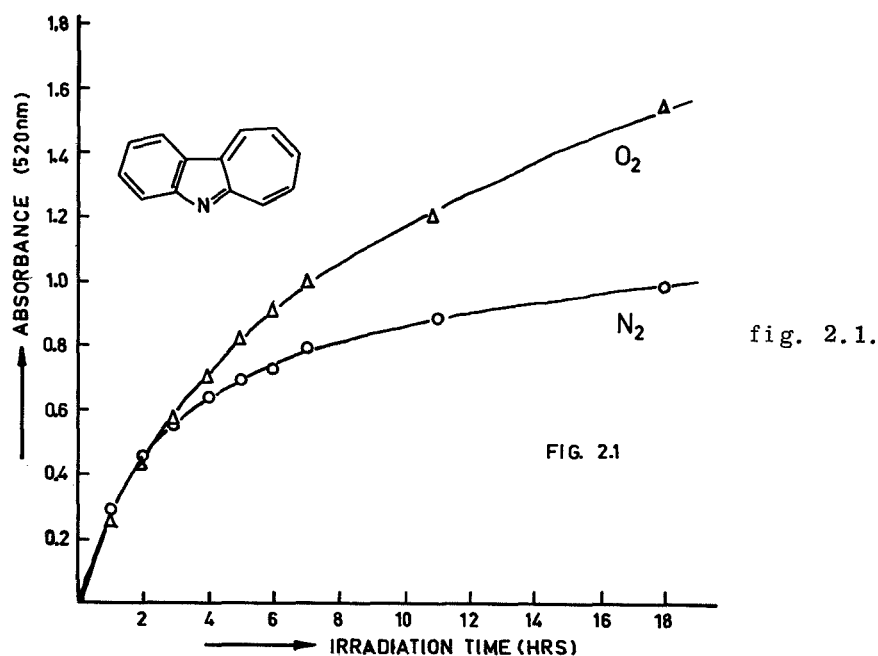


Fig. 2.1. Formation of cyclohept[b]indole upon irradiation of *o*-isocyanobiphenyl in cyclohexane at 254 nm under oxygen and nitrogen monitored by UV spectroscopy.

Because oxygen is known as a triplet quencher¹¹ the results suggest that in this isomerization no triplet is involved, or that a possible involved triplet has a very short lifetime.¹¹

That more product was formed under oxygen may be ascribed to the heavy coating of the glasswall observed by irradiation under nitrogen, while the photolysis tube remained remarkably clean under oxygen. Through coating with tarry materials much light will be filtered away. Some support was found upon irradiation of a similar solution of 10 under oxygen in which the photolysis tube was previously coated by irradiation of a solution of 10 under nitrogen. After six to seven hours no cyclohept[b]-indole was found. Then most of the coating tar was oxidized away and production of 11 started.

IR analysis of the crude reaction mixture (irradiation under O₂) did not detect the formation of *ortho*-isocyanatobiphenyl. Nor could its possible subsequent cyclization product², phenanthridine-6(5H)-one be detected by tlc.

The observed insertion revealed carbenoid* properties¹² of the terminal isocyanocarbon. The reaction might serve as a useful route to cyclohept[b]indole substituted in the seven-membered ring by irradiation of 2-isocyano-X'-substituted biphenyls.

*A carbenoid is a reactive intermediate which behaves in some but not all reactions like a carbene. In general carbenoids react more selective than do carbenes. They rarely show C-H insertion.¹³

Experimental part.

The irradiations were carried out in a Rayonet RPR 100 photochemical chamber reactor (Southern New England Ultraviolet Co.) equipped with 16 low pressure mercury 254 nm lamps. Solutions, when irradiated under nitrogen (Matheson, high purity grade) were degassed with a heavy stream of nitrogen previous to irradiation. The nitrogen was dried over Molecular Sieves and Drierite. Cyclohexane (Baker, spectro grade) used as an irradiation medium, was always distilled from lithiumaluminum hydride straight into the quartz irradiation tube.

UV spectra were recorded on a Cary 14 spectrophotometer.

IR spectra were obtained on a Perkin Elmer 237B grating infrared spectrophotometer, NMR spectra were obtained on a Varian A 60, a spectrometer working at 60 Mc/sec, with tetramethylsilane as an internal standard. The chemical shifts are reported in ppm in the δ scale, the tetramethylsilane peak is defined as $\delta=0$. Mass spectra were obtained on a Perkin Elmer 270 mass spectrometer.

Gaschromatographic analysis were carried out on a Barber Coleman Flame Ionization Gas-chromatograph model 5320 using a 8 x $\frac{1}{4}$ stainless steel coil packed with 5% Ge-Xe-60 Chromasorb-G, 60-80 AW DMGS (supplied by Nuclear Chicago), with nitrogen as carrier gas. The column temperature was 210-220°C. A flow rate of 60-70 ml min⁻¹ was used. The temperature of the injection port was about 250°C and of the detector about 280°C.

For column chromatography silicagel (Baker analyzed, J.T. Baker Chemical Co.) was used. Melting points and boiling points are uncorrected. Melting points were determined in a silicone oil bath unless otherwise stated. Elemental analysis were carried out by Micro-Tech Laboratories Inc., Skokie, Illinois U.S.A.

o-ISOTHIOCYANATOBIPHENYL (9)⁴

A solution of 20.60 g (0.10 mole) dicyclohexylcarbodiimide (DCC) (Aldrich Chemical Co.) in 20 ml pyridine and 40 ml carbon disulfide was cooled to -10°C with stirring a solution of 16.9 g (0.10 mole) of o-aminobiphenyl in 20 ml of pyridine was added dropwise. The solution was stirred for three hrs at -10° to 0°C and subsequently stirring was continued for 18 hrs at room temperature. The suspension of 1,3- dicyclohexylthiourea was filtered off and washed with cold ether. The solvents were removed under reduced pressure and the liquid residue was again treated with ether affording another crop of 1,3-dicyclohexylthiourea which was filtered off. The total yield of the thiourea, was 92.2 percent, mp 178-181°C. Distillation of the residue, after removal of the ether, gave always some N,N'-di(o-biphenyl) thiourea in all the fractions.*

Initial purification by chromatography on silica (eluted with n-hexane) and subsequent distillation under reduced pressure afforded o-isothiocyanatobiphenyl as a colorless viscous liquid (15.8 g, 75.0 percent), bp 130-132°C (0.25 mm), n_D^{26} -1.6805; uv (cyclohexane) 285 (ϵ 11,000), 249 nm (ϵ 18,400); uv (ethanol) 281 (11,400), 249 (17,900); ir (neat) 2100 cm⁻¹ (broad and strong, ν NCS); nmr (CDCl₃) δ 7.35 (m); mass spectrum (70 eV) m/e (rel intensity) 211 (100), 210 (17.5), 179 (31), 178 (100), 177 (25), 167 (21), 152 (60), 151 (56).

*Apparently some N,N'-di-(o-biphenyl) thiourea was present in the crude reaction mixture, which decomposed¹⁴ under the conditions for the distillation into ortho-aminobiphenyl and ortho-isothiocyanatobiphenyl. Codistillation of both and recombination to the thiourea explains the observed impurity.

Anal. Calcd for $C_{13}H_9NS$: C, 73.90; H, 4.29; N, 6.63; S, 15.18; mol wt 211.29.
Found: C, 74.25; H, 4.49; N, 6.75; S, 15.00.

N,N'-DI-(o-BIPHENYLYL)THIOUREA.¹⁵

A solution of 1.0 g (4.74 mmole) of o-isothiocyanatobiphenyl and 0.80 g (4.72 mmole) of o-aminobiphenyl in 10 ml of alcohol was slightly heated for 15 min. Scratching on the glasswall (cooled solution) caused a copious white precipitate. Filtration and recrystallization from alcohol gave 1.06 g (59.0 percent) of colorless needles, mp 150-151°.

Anal. Calcd for $C_{25}H_{20}N_2S$: C, 78.91; H, 5.30; N, 7.36; S, 8.43; mol wt 380.51.
Found: C, 78.70; H, 5.25; N, 7.30; S, 8.32.

o-ISOCYANOBIPHENYL⁷ (10).

To a stirred solution of 7.50 g (67.0 mmole) of commercial potassium t-butoxide in 30 ml of tert-butylalcohol, at 50-60°C, was added in 15 min a solution of 3.74 g (20 mmole) of o-(N-formyl)aminobiphenyl in 60 ml of dry tetrahydrofuran (distilled from lithiumaluminum hydride).

Stirring was continued for an hour. Then 1.8 ml of phosphorus oxychloride (19 mmole) was added slowly (25 min). Stirring was continued for another 2 hrs at 50-60°. Soon a white precipitate separated. Dry ice (1 g) was added. The solvents were removed under reduced pressure at 30°C.

The residue, dissolved in ether, was extracted with water (total 30 ml). The ether solution was dried ($CaCl_2$), filtered, concentrated, and chromatographed on neutral Al_2O_3 (Baker analyzed). o-Isocyanobiphenyl eluted with benzene was distilled under reduced pressure, 2.35 g (65.0 percent), bp 113-114° (1.5 mm), $n_D^{21.5}$ 1.6115; η_{sp}/c (cyclohexane) 247 mm (ϵ 11750); uv (methanol) 244 (ϵ 10500); ir (neat) 2130 cm^{-1} ($\nu_{N\equiv C}$); nmr ($CDCl_3$) δ 7.38 (m); mass spectrum (70 eV) m/e (rel intensity) 180 (16), 179 (100), 178 (28), 152 (28), 151 (24), 89.5 (6), 89 (8).

Anal. Calcd for $C_{13}H_9N$: C, 87.12; H, 5.06; N, 7.82; mol wt 179.22.
Found: C, 87.17; H, 5.32; N, 7.88.

o-(N-FORMYL)-AMINOBIPHENYL.⁶

A solution of 16.0 g (96.0 mmole) of o-aminobiphenyl in 160 ml of 90 percent formic acid was refluxed for 5 hrs. The formic acid was distilled off. The residue was dissolved in 100 ml of ether and filtered.

o-N-formylaminobiphenyl, crystallized from the solution, 12.0 g (67.5 percent) mp 73-75° (lit.⁶ 75°).

CYCLOHEPT[b]INDOLE⁸

To a stirred refluxing solution of 5.0 g (27.0 mmole) of 5,6,7,8,9,10-hexahydrocyclohept[b]indole (mp 142-143.05°C, lit.¹⁸ mp 140-141°) in 100 ml of tert-amylalcohol was added with small portions 15 g (61.0 mmole) of powdered chloranil (Aldrich Chemical Co., recrystallized from acetic acid, mp 290°). After addition was completed refluxing was continued for another 6 hrs. The cooled solution was diluted with ether and was extracted with

2N sodiumhydroxide to remove tetrachlorohydroquinone. The ether solution was then extracted with 2N hydrochloric acid and the yellow aqueous layer was washed with ether and cyclohexane. Basifying, extracting with cyclohexane, drying (Na_2SO_4), filtering and concentrating afforded 55 mg (1.0 percent) of cyclohept[b]indole. The uv spectrum and the ir spectrum were superimposable upon those from the cyclohept[b]indole obtained upon irradiation of o-isocyanobiphenyl.

IRRADIATION OF o-ISOTHIOCYANATOBIPHENYL.

A solution of 1.240 g (5.90 mmole) of o-isothiocyanatobiphenyl in 400 ml of cyclohexane was flushed with nitrogen for three hrs and then irradiated at 254 nm for 64 hrs under a slow stream of nitrogen.

The cyclohexane was evaporated and the residue, chromatographed on silica (Merck 0,2-0.5 mm), afforded 9 mg of sulfur (24 percent), mp 117-119°C, mixture mp 117-119°C.¹⁷ (eluted with n-hexane); 1.030 g of starting material (83.0 percent), eluted with n-hexane-benzene (10:1) and identified by ir and tlc; 44.5 mg (25 percent) of o-isocyanobiphenyl, eluted with n-hexane-benzene (3:2) and identified by ir and tlc; 50 mg (28 percent) of cyclohept[b]indole, eluted with chloroform-ether (4:1), mp 134.5-136°C (sealed tube) (lit.⁸ 143°C): methiodide mp 232° (lit.⁸ mp 232°). UV and ir spectra of cyclohept[b]indole were identical with those reported by Anderson and Tazuma;¹⁸ mass spectrum (70 eV) m/e (rel intensity) 180 (23), 179 (100), 178 (29), 152 (17), 151 (15), 89.5 (15), 89 (29), M^{\oplus} (12 eV) m/e 179.

Anal. Calcd for $\text{C}_{13}\text{H}_9\text{N}$: C, 87.12; H, 5.06; N, 7.82; mol wt 179.22.
Found: C, 86.91; H, 5.16; N, 7.61.

Several other fractions were obtained on eluting with solvent mixtures of n-hexane-benzene, benzene-chloroform and chloroform-ether. In none of them carbazole could be detected by thin layer chromatography. Neither has any trace of phenanthridine-6(5H)-one been found by using the same technique.

IRRADIATION OF o-ISOCYANOBIIPHENYL (9).

A solution of 540 mg (3.0 mmole) of o-isocyanobiphenyl in 400 ml of cyclohexane was irradiated under nitrogen at 254 nm for 19 hrs.

The irradiated mixture was chromatographed on silica (Baker analyzed). Starting material was eluted with n-hexane-benzene (3:2), 409 mg (75.7 percent). The precise yield was determined by gaschromatography with disc integration (69.5 percent). Calibration was carried out with a solution of known concentration of 9. With chloroform-ether (3:1), 103 mg (62.8 percent) of cyclohept[b]indole was eluted.

Both were identified by comparison of ir spectrum and tlc plate with those of authentic materials.

Similarly a solution of 1.50 g (8.4 mmole) of 9 in cyclohexane (400 ml) was irradiated. The progress of product formation (10) was monitored by uv spectroscopy from aliquots taken at intervals of 19 hrs. The amount of product did not increase and remained constant after 19 hrs of irradiation. Chromatography of the reaction mixture after 57 hrs of irradiation afforded 942 mg (62.8 percent) of starting material, eluted with n-hexane-benzene (3:2); less than 5 mg (1 percent) of phenanthridine, eluted with benzene-chloroform (1:3) and identified by comparing the ir spectrum, glc rt and tlc rt with authentic data; 230 mg of cyclohept[b]indole, eluted with chloroform and identified as before (42 percent after correction for recovered starting material).

Further, solutions of 2.0 mM of 9 (400 ml) in cyclohexane were irradiated under oxygen and nitrogen. The progress of product (10) formation was monitored by uv spectroscopy (520 nm). The results are depicted in figure 2.1.

Examination of an ir spectrum of the crude reaction mixture (oxygen experiment) did not detect the formation of o-isocyanatobiphenyl. Nor could any phenanthridine-~~(6,5H)~~-one be detected by tlc.

Finally 50 mg of 10 in 400 ml of cyclohexane were irradiated under nitrogen as before. After 19 hrs of irradiation all the cyclohept[b]indole was lost (uv spectroscopy). Phenanthridine could not be detected from the residue by glc or tlc.

References.

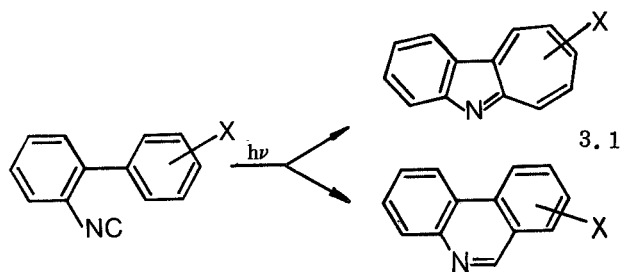
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CHAPTER III.

IRRADIATION OF 2, X'-DIISOCYANOBIPHENYLS

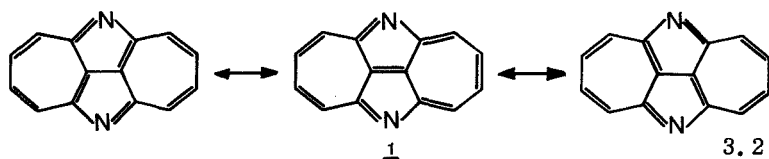
3.1. Introduction

The apparent carbenoid character of the terminal carbon of the isocyanofunction has been demonstrated upon excitation of 2-isocyanobiphenyl in the previous chapter. It seemed of interest to find out whether the reaction would be influenced by a substituent on the phenyl ring under attack, i. e., a substituent either in the 2', 3' or 4' position. An aromatic C-C as well as a C-H insertion should be taken into consideration (3.1).

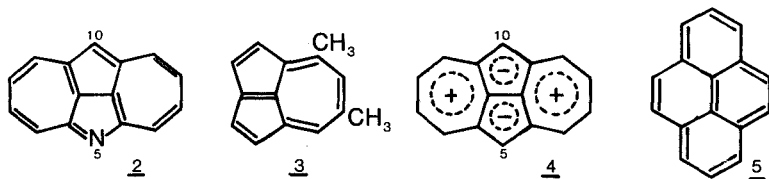


With a 2'- or 3'-substituent the reaction might take two different courses. Our attention was focussed on the 2, X'-diisocyanobiphenyls ($X = \overset{\oplus}{N} \equiv \overset{\ominus}{C}$) because of the easy accessibility and the expectation that the products would reveal interesting properties. Molecules with an isocyanide group attached to a seven-membered ring are unknown. The seven-membered ring in cyclohept[b]indole is expected - in analogy to azulene - to bear a positive charge, which may in the isocyanide-substituted derivatives increase the divalent character on the terminal carbon atom of the functional group.

Further, the possibility was considered that with the 2, 2'-diisocyanobiphenyl a double insertion might lead to the unknown 5, 10-diazadiphepentalene, 1.



The all carbon analog, dipleiapentalene 4 is also an unknown compound. The synthesis of pentalene¹ itself has not yet been accomplished. Few examples of pentalene derivatives have been reported e.g. the hydrocarbon¹ 3.



It should be noted that the seven-membered rings in dipleiapentalene are expected to be positively charged, whereas the two 5-membered rings are negatively polarized according to formula 4. Further, a simplified comparison of dipleiapentalene 1 with pyrene² 5 might be made. The two compounds are isoelectronic (16π -electrons). Pyrene has been reported to possess a resonance stabilization of 109 kcal/mole.³ This stabilization has been accounted for by regarding pyrene as concentric 14- and 2π -electron systems connected by cross links. In general, resonance stabilization is predicted for monocyclic systems containing $4n+2\pi$ -electrons (Hückel rule⁴). A first order approximation permits application of the rule to dipleiapentalene 4 by considering the 14π -electrons on the periphery of the molecule. In analogy with pyrene, resonance stabilization is expected for dipleiapentalene 4 or its 5,10-diaza analog 1. From a HMO calculation a delocalization energy (DE) of 6.029β and 6.506β has been calculated for resp. dipleiapentalene 4 and pyrene 5. Assuming $\beta \cong -16$ kcal³ a DE of ≈ 100 kcal can be calculated for 4 (compare with 109 kcal for 5). Due to ring strain effects this figure is likely too high.⁵

The same approximation (HMO) permits calculation of the electron density on carbon atom five and ten of dipleiapentalene, $q_5 = q_{10} = 1.166$. For 5-azadipleiapentalene 2 electron densities can be derived by using the first order approximation formulas (3.3 and 3.4) and substituting data as reported by Streitwieser and Brauman for dipleiapentalene.⁸

$$q_R' = q_R + \pi_{R,5} \Delta\alpha_5 \quad (3.3)$$

$$\Delta\alpha_5 = h_N \beta; \beta_{CN} = k_{CN} \beta_{CC} \quad (3.4)$$

q_R' = new electron densities

q_R = electron densities calculated for the all carbon analog⁸

$\pi_{R,5}$ = atom-atom polarizability

$\Delta\alpha_5$ = change in Coulomb integral on atom 5 by substituting carbon for nitrogen

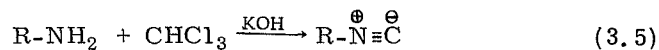
$h_N = 0.5$ (parameter); $k_{CN} = 1$ (parameter).⁶

Thus we obtained for the system 2, $q_5' = 1.406$ and $q_{10}' = 1.169$ and conclude that considerable negative charge flowed to the nitrogen. The influence upon carbon atom ten is negligible. For the 5,10-diaza analog 1 a similar figure $q_{10}' = q_5' = 1.4$ is estimated.

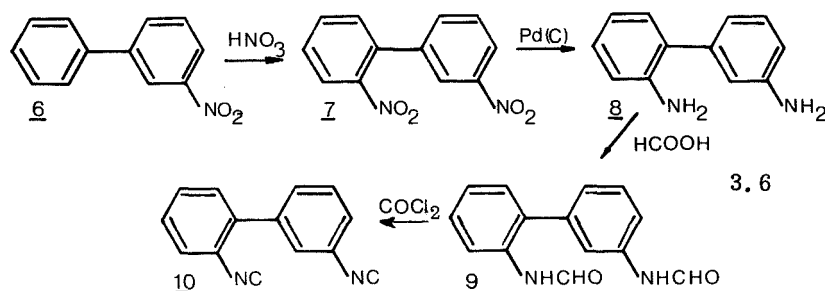
The figures predict a relatively high basicity of the nitrogens.⁷

3.1.2. PREPARATION OF 2,X'-DIISOCYANOBIPHENYLS (X¹=2,3 or 4)

Isocyanides have been known for more than a hundred years⁹. In the classical method for their preparation, amines in chloroform are treated with alkali (3.5). The yields are in general poor.



About fifteen years ago dehydration of the corresponding N-formylamines was introduced¹⁰. Ugi and coworkers¹¹ have systematically investigated the preparation of isocyanides by different dehydrating agents in combination with various bases. A general procedure using phosgene as dehydrant in combination with triethylamine is recommended. Hundreds of isocyanides have been prepared in this way, also two of the compounds we were interested in, i. e., 2,2'-diisocyanobiphenyl (11) and 2,4'-diisocyanobiphenyl 30. This method was also chosen for the preparation of 2,3'-diisocyanobiphenyl. The reaction scheme for the preparation of the 2,X'-diisocyanobiphenyls is outlined for the 2,3'-isomer as an example.



The 2, 3'- and 2, 4'-dinitrobiphenyls^{12,13} have been prepared from commercial available 3- and 2-nitrobiphenyl¹⁴, whereas 2,2'-dinitrobiphenyl was also commercial available¹⁴. Purification of the 2, 3'- and 2, 4'-dinitrobiphenyls facilitated the isolation and purification of the diisocyanides. In the catalytic reduction to the amines the calculated amount of hydrogen was required. IR analysis of the product mixture did not detect the presence of a remaining nitro compound. Satisfactory formylation with 90 percent formic acid was checked by ir absorption of CO and NH groups. Acid free formylamines were dehydrated with phosgene into the corresponding 2, X'-diisocyanobiphenyls, which were purified by chromatography over silica and eluted with benzenechloroform (1:1).

In the preparation of 2,2'-diisocyanobiphenyl 11, 2-isocyno-2'-diformamidobiphenyl 45 was obtained as a side-product and isolated. Partially dehydrated products from the reaction mixtures containing 2, 3'- and 2, 4'-diisocyanobiphenyl were not isolated because of the greater complexity of the reaction mixtures.

3.1.3. CHOICE OF THE SOLVENT.

The solvent may be of fundamental importance in photo reactions. Rate and (or) reaction course may change dramatically by changing the solvent. The solvent may be involved as an undesired reactant.

Photochemical reactions in solutions occur in general from the lowest excited states. While higher excited states may initially be reached, the molecules are rapidly deactivated by collision with solvent molecules¹⁵. Changing the polarity of the solvent may also change the relative positions of the excited states¹⁶. Consequently the chemical behavior of the

compound under study may change. The situation becomes more complex when both excited singlet and triplet states are reactive. Solvents may also participate in the reactions by trapping high energy intermediates. This method has been frequently used for tracing carbenes¹⁷.

To minimize side reactions cyclohexane was chosen as the solvent, in spite of the poor solubility of the 2,2'-diisocyanobiphenyls (2.5×10^{-3} M).

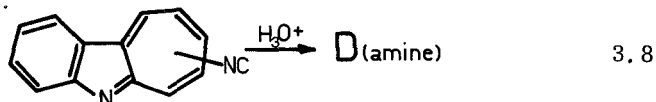
3.2. Results.

3.2.1. IRRADIATION OF 2,2'-DIISOCYANOBIIPHENYL 11.

Irradiation (254 nm, one hour) of 2,2'-diisocyanobiphenyl 11 (200 mg) in cyclohexane (400 ml) gave within a few minutes a violet solution. Separation from a column of silicagel gave starting material in 17.6 percent, a violet isocyanide *B* ($\nu_{\text{N=C}}$ 2109 cm^{-1}), an amine *C* ($\nu_{\text{N-H}}$ 3484 and 3355 cm^{-1}) and a trace of a deep red solid *E*.



An analysis of the ir spectrum (CHCl_3) from the crude reaction mixture before chromatography on silica did not detect the products *C* and *E*. The colored isocyanide *B* was isomeric with starting material 11 as was revealed by elemental analysis and the low voltage mass spectrum (12eV, $M^{\oplus}m/e$ 204). Fine structure for the longest wavelength band, λ_{max} 522 nm (ϵ 395), together with a low intensity may be diagnostic for azulenes¹⁸. The nmr spectrum showed only aromatic protons (δ 8.95-7.37). These data are consistent with an isocyanocyclohept[b]indole as the structure. It was obtained in a yield of 26.7 percent. A clear choice between the 10- or 6- position of the isocyano function could not be made.



The violet isocyanide *B* was dissolved in ether and shaken with aqueous 2N hydrochloric acid. The aqueous solution

becomes yellow, whereas the organic layer decolorizes instantaneously. Complete conversion to an amine *D* ($\nu_{\text{N-H}}$ 3509 and 3401 cm^{-1}) was found.

The mass spectrum (12eV, $M^{\oplus}m/e$ 194), the elemental analysis of the picrate derivative and the aromatic protons in the nmr spectrum of *D* indicated, that the isocyanide *B* was hydrolysed to the corresponding amine *D*. While the amine *C* possessed different properties, it was isomeric with the amine *D*, as shown by the elemental analysis and the low voltage mass spectrum (12 eV, $M^{\oplus}m/e$ 194). It was obtained in a yield of 42.9 percent. The nmr spectrum showed aromatic protons. These data support a proposed aminocyclohept[b]indole, as the structure for *C*. The uv spectrum in benzene (λ_{max} 480 nm (ϵ 4000)) was inconclusive for the presence of the azulene moiety¹⁸. Isomeric aminophenanthridines were considered as structures for *C* and *D*, but were excluded after comparing the reported melting points and colors (Table 3.3).

3.2.1.2. A precursor to an amine different from an isocyanide.

The presence of a not isolated compound *A* in the irradiated solution of 2,2'-diisocyanobiphenyl became evident after comparing an ir spectrum of the crude reaction mixture with similar data of isolated products (figure 3.1) 3.2). An attempt to isolate it was partly successful. The isocyanide *B* and starting material 11 were separated with small amounts of ether as was verified from ir spectra. An ir spectrum of the black shiny amorphous residue in chloroform indicated only a very weak band in the isocyanide region (2109 cm^{-1}), ascribed to *B*, and no absorption due to starting material. Most of the observed bands were also seen in the ir spectrum of the crude reaction mixture. Thus the residue can be considered as a fairly purified sample of *A*. Apparently *A* is not an isocyanide. When in an exploratory experiment this residue was dissolved in excess of ether and treated with aqueous 2N hydrochloric acid, the amine *C* was obtained along with tarry material insoluble in ether or aqueous acid.

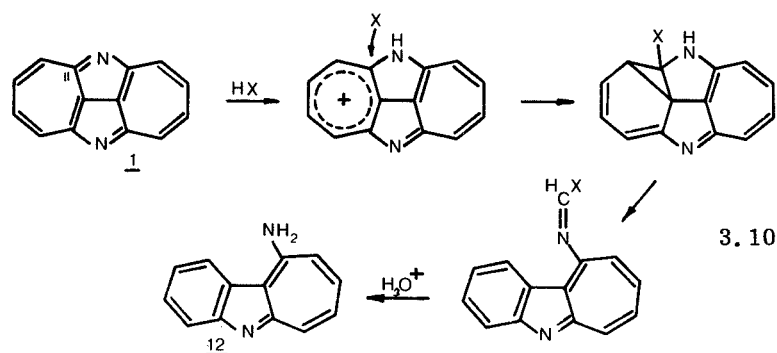
Another observation shed some light upon the properties of *A*. A dramatic color change from violet to ochre was observed on adding a few drops of absolute ethanol to the solution after irradiation. A uv spectrum of the ochre solution resembled the spectrum of the isocyanide *B* in the 500-700 nm region. Chromatography over silica did not

bring about isolation of new products. Again the isocyanide *B*, the amine *C* and starting material were obtained. Since the color change can not be attributed to *B*, (which is present before and after addition of ethanol) it must be caused by a reaction from *A*.

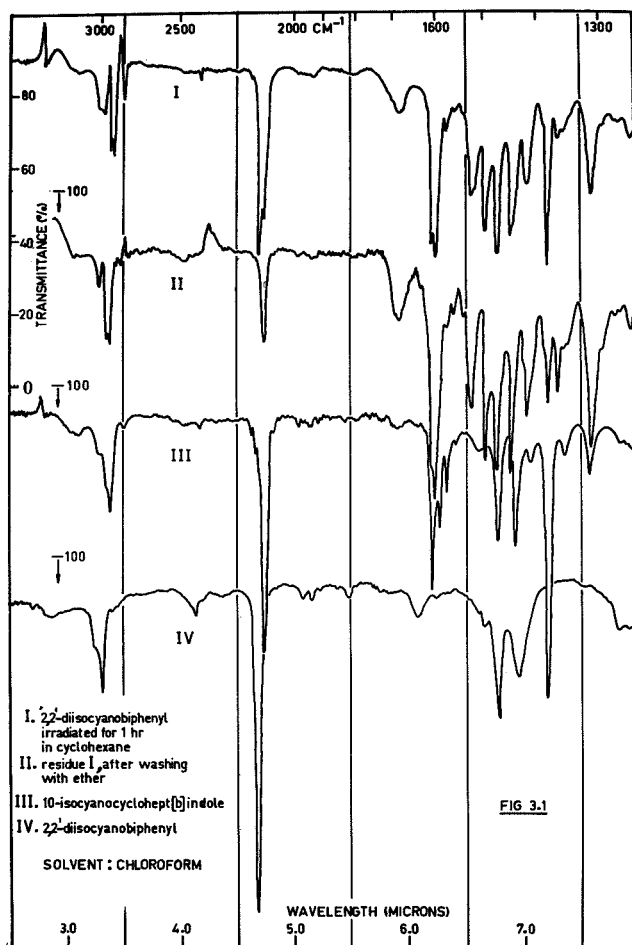
Summarizing we found:

1. evidence that insertions into both aromatic C-C bonds from the *ortho* isocyanide had taken place, i. e., in the 1'-2' or 1'-6' carbon-carbon bond of the adjacent phenyl ring.
2. that only one isocyanide *B* could be isolated.
3. that the precursor *A* to the amine *C* probably is not an isocyanide.
4. that the compound *A* is sensitive toward weak aqueous acidic conditions (silica).
5. that the compound *A* reacts instantaneously with ethanol under mild conditions.

Taking all these facts into account, the double insertion product 5,10-diazadiphepentalene 1 was considered as a likely candidate for the intermediate *A*. The observations 4 and 5 are readily explained recalling the predicted high basicity on the nitrogens in 1 (introduction 3.1). Protonation (aqueous acid) or strong hydrogen bonding (ethanol) on the nitrogen may facilitate nucleophilic attack at carbon atom 11. Ring contraction, bond breaking, subsequent reaction with or without solvent participation may lead to a 10-substituted cyclohept[b]indole. Hydrolysis on silica would give 10-aminocyclohept[b]indole (3.10).



Consequently the 6-isocyanocyclohept[b]indole would represent the always isolated violet isocyanide *B*. However, less in agreement with this preliminary assignment were the relative basicities of the amines *C* and *D*. When a



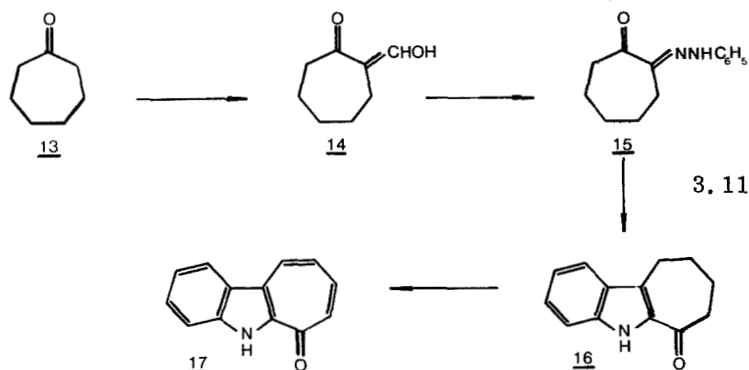
solution of the product mixture obtained by irradiation of 2,2'-diisocyanobiphenyl 11 was extracted with 2N hydrochloric acid, extraction of the aqueous layer with ether after adjusting to pH 6-7 afforded the amine *C* only. The isolation of the amine *D* from the aqueous solution required adjusting to pH 10-12. This would favor the amine *C* to be 6-aminocyclohept[b]indole, since intramolecular hydrogen bonding would lower the basicity.

To learn more about the intermediate *A* an independent synthesis of either 6-amino- or 10-aminocyclohept[b]indole was required.

3.2.1.3. Alternative preparative approach to 6-aminocyclohept[b]indole

The initial route chosen for the preparation of 6-aminocyclohept[b]indole was based on the amination of cyclohept[b]indole, since this material was available (Chapter II). Attempted reactions with 90 percent hydrazine hydrate¹⁹, or hydroxylamine²⁰ were unsuccessful.

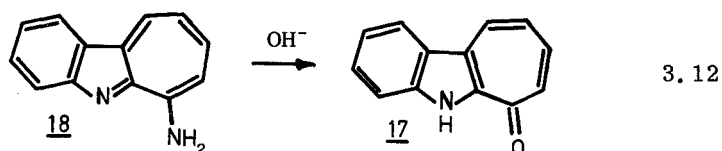
A second attempt consisted of the amination of cyclohept[b]indole-6(5H)-one 17. The ketone 17 was synthesized as outlined in scheme 3.11.



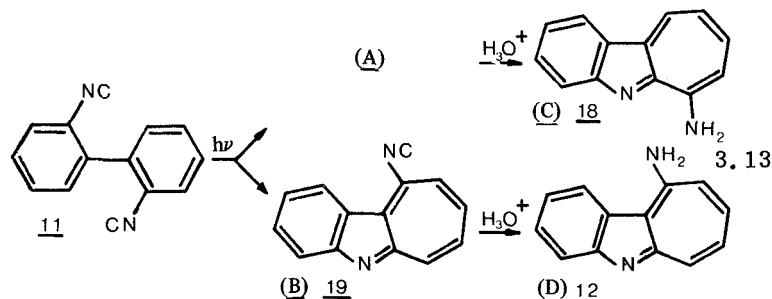
The condensation of cycloheptanone with ethylformate under basic conditions has been described by Prelog, Ruzicka and Metzler²¹. The preparation of the monohydrazone of cycloheptadione 15 followed by a Fisher indole reaction to 1-keto-2,3,4,5-tetrahydroheptindole 16 has been given by Treibs and Mühlstädt. Each reaction gave a satisfactory yield. Both Pd(C)²³ and chloranil²⁴ had been successful in dehydrogenating 5,6,7,8,9,10-hexahydrocyclohept[b]indole, but failed to transform 16 into 17 in sufficient quantities for isolation.

When sulfur²⁵ was used as a dehydrogenation agent, 17 could be obtained in a yield of 28 percent. Amination²⁶ of cyclohept[b]indole-6(5H)-one 17 with ammoniumacetate afforded a trace of a red solid ($\nu_{C=O}$ 1694 cm^{-1}). Probably an (acetyl) derivative. It was converted into an amine upon hydrolysis with aqueous 6N HCl, which proved to be C from its ir spectrum and a tlc plate. This was also an indication that C corresponds to 6-aminocyclohept[b]indole.

An indirect structure proof was found in the known conversion of aminotropolones²⁷ into tropolones. Treatment of the amine C with alkali in alcoholic solution gave 17 in a yield of 74.5 percent. (3.12).

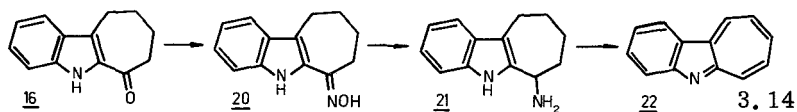


These results excluded firmly that A is 5,10-diazadipoleia-pentalene, since A was proved to be related to the amine C. The reaction sequence can now be assigned (3.13).



An attempted dehydrogenation of 6-amino-5,7,8,9,10-pentahydrocyclohept[b]indole 21 with 10% palladium on charcoal afforded a trace of cyclohept[b]indole 22, the deamination product²⁸, but 6-aminocyclohept[b]indole 18 was not detected.

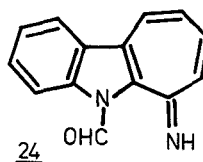
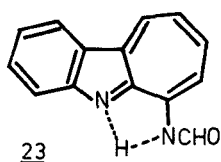
The introduction of the oxime function with hydroxyl amine hydrochloride⁵⁴ 20 followed by the reduction of the oxime with lithiumaluminium hydride⁵⁵ 21 has been reported.



3.2.1.4. Reactions with the cyclization product A

3.2.1.4.1. 6-Formamido-cyclohept[b]indole 23.

It was mentioned that work-up of the crude reaction mixture from irradiated 2, 2'-diisocyanobiphenyl on silicagel gave a trace of a red product *E*. This compound showed an ir absorption for a carbonyl group at 1704 cm^{-1} and an amine stretching vibration at 3279 cm^{-1} . Treatment with acid gave 6-aminocyclohept[b]indole, which was also isolated in large yield from the crude reaction mixture of irradiated 2, 2'-diisocyanobiphenyl by chromatography over silica. Considering the weak acidity of silica, it was assumed that 6-aminocyclohept[b]indole had been formed via *E* from *A*. Further attempts to detect *E* were carried out by extracting the crude reaction mixture of the irradiated 2, 2'-diisocyanobiphenyl with a weak acidic aqueous hydrochloric acid solution (pH 2-3). Starting material was recovered from the organic layer in 17.6 percent and careful work-up of the aqueous deep red solution afforded a mixture of 10-isocyanocyclohept[b]indole 19 (*B*) and the product *E*. None of 6- or 10-aminocyclohept[b]indole could be detected from the ir spectrum of the crude reaction mixture. The isocyanide 19 and the product *E* were separated by chromatography. All spectroscopic data support the product *E* to be 6-formamidocyclohept[b]indole 23; however repeated elemental analysis were not definitive. The mass spectrum (70 eV and 12 eV) indicated the proper molecular weight ($M^{\oplus} m/e$ 222). The low field protons observed in the nmr spectrum and the correct integration for N-H and O=C-H supported the assignment. The low intensity of the longest wavelength band seen in the uv spectrum is also consistent with the assignment¹⁸. The N-H frequency in the ir spectrum is



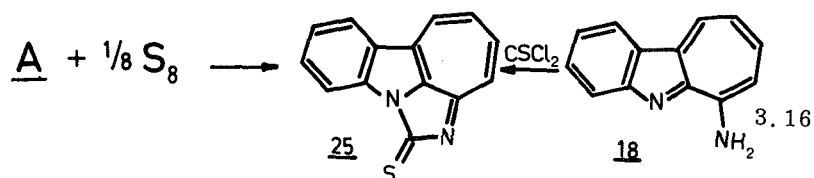
3. 15

broad and does not show a shift in going from chloroform to a potassium bromide pellet. This observation is also in agreement with the amide structure and tends to eliminate the conceivable isomeric structure 24.

The N-formylamine 23 was converted into the amine 18 by treatment with moderate acidic or basic aqueous solutions. On heating it decomposes also to the amine 18.²⁹

3.2.1.4.2. Reaction with sulfur.

Isocyanides are only slowly transformed into isothiocyanates on treatment with sulfur in refluxing benzene.³⁰ When sulfur was added to the reaction mixture of 2,2'-diisocyanobiphenyl, after the irradiation was stopped, a reaction occurred. Examination of an ir spectrum of the crude reaction mixture in the range 2200-2000 cm^{-1} , revealed the presence of both starting material 11, and 10-isocyanocyclohept[b]indole 19, which was later hydrolyzed and isolated as the 10-amino cyclohept[b]indole 12. But no absorptions could be ascribed to isothiocyanates. The sulfurization product appeared to be a cyclic thiourea 25, and was obtained in a yield of 37.3 percent, when corrected for recovered starting material. The thiourea 25 was independently obtained from 6-amino-cyclohept[b]indole and thiophosgene in a yield of 14.7 percent.



About 60 hrs were required to complete the apparent sulfurization of A at room temperature. The reaction of A with sulfur, under conditions for which the other isocyanides present in the solution are apparently not reactive, furnished additional evidence that A is not an isocyanide.

3.2.1.4.3. Reaction with aniline.

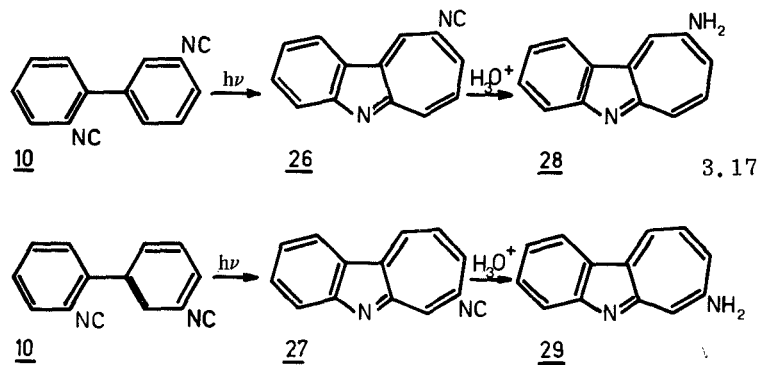
In contrast to the immediate color change observed when ethanol was added to the product mixture after irradiation, a reaction monitored by uv absorption occurred on similar treatment with aniline over a period of 60 hrs. The reaction mixture was chromatographed over silica. The amount of recovered starting material could not be determined precisely because of poor separation from aniline. The 10-isocyanocyclohept[b]indole was eluted with benzene-chloroform (1:1). Its resistance to react with aniline was verified in an inde-

pendent experiment under identical conditions. Benzene-chloroform (1:2) eluted 37 mg (30.6%) of formanilide, which was identified by comparison of an ir- and uv- spectrum with authentic data. Elution with ether-acetone (3:1) gave 68 mg (35.0%) of 6-aminocyclohept[b]indole 18, identified by comparison of an ir spectrum with authentic data. Chloroform-ether (2:1) eluted a new compound, which is tentatively assigned the structure of 6-anilinocyclohept[b]indole 50: 36 mg, mp 181-182°, $\nu_{\text{N-H}}$ 3437 cm^{-1} , M^{\oplus} (m/e) 270. Further support was found in the ms fragmentation by loss of $\text{C}_7\text{H}_5\text{N}$ to give F^{\oplus} 167 which corresponds to carbazole.

3.2.2. IRRADIATION OF 2,3' - AND 2,4' -DIISOCYANOBIHENYL

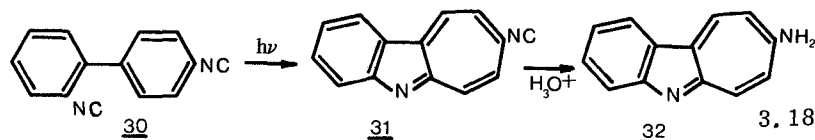
Irradiation (254 nm, one and a half hour) of a solution of either 2,3'-(10) or 2,4'-diisocyanobiphenyl 30 in cyclohexane gave within a few minutes a violet solution. The crude reaction mixtures were chromatographed on a column of silica.

The starting material 10 was recovered in 45.0 percent, while two violet isocyanides (both showing $\nu_{\text{N}\equiv\text{C}}$ 2119 cm^{-1}) were obtained in yields of 16.4 and 57.3 percent (corrected for recovered starting material). These products are isomeric with starting material as was revealed from an elemental analysis and a low voltage mass spectrum (M^{\oplus} m/e 204). The uv spectra (Chapter IV) support a structure assignment for isocyanocyclohept[b]indoles. Further evidence was found in the easy hydrolysis to the amines by dissolving each in benzene and shaking with 2N hydrochloric acid. These amines are blue (Chapter IV).



The amines were found to be insoluble in n-hexane, cyclohexane, benzene and chloroform. Violet methylenechloride solutions, when not degassed with nitrogen, turned dark brown after several hours. This betrays an apparent sensitivity toward air. We were not able to purify the amines sufficiently for an elemental analysis. The amine related to the major product was analyzed as the hydrochloric acid salt.

From the 2,4'-diisocyanobiphenyl 30 only one product could be obtained, that showed the characteristics of a C-C insertion product ($\nu_{\text{N}\equiv\text{C}}$ 2114 cm^{-1}). Starting material was recovered in 21.5 percent, while the product was obtained in a yield of 78.0 percent, when corrected for recovered starting material. Elemental analysis and a mass spectrum at low voltage (M^{\oplus} m/e 204) revealed the product to be isomeric with starting material. The uv spectrum supported again the cyclohept[b]indole structure.



The 8-isocyanocyclohept[b]indole 31 was quantitatively hydrolyzed to the amine. This yellow amine had poor solubility characteristics and could not be purified for elemental analysis; however, the yellow hydrochloric acid salt was analyzed. A trace of an isocyanide compound ($\nu_{\text{N}\equiv\text{C}}$ 2123 cm^{-1}) different from both starting material and 8-isocyanocyclohept[b]indole was obtained after elution with benzene-chloroform (1:1). Sufficient quantities for further characterization were not available; nevertheless it is tentatively considered to be 8-isocyanophenanthridine.

3.2.3. QUANTUM YIELDS

The product quantum yields were determined for isocyanocyclohept[b]indoles. Solutions of the corresponding *ortho* isocyanobiphenyls in cyclohexane (2.5×10^{-3} M) were irradiated at 254 nm under atmospheric conditions for 5 min after which a reproducible conversion to 15-28 percent product was found. The chemical yield was determined by measuring the optical density at a fixed wavelength in the visible region of the spectrum. Starting material does not

absorb in this region. No indication has been found for the presence of contaminants absorbing in the region 500-650 nm as was concluded from yield determinations at several wavelengths within this region. Neither was detected from the ir spectra of the crude reaction mixtures the presence of isocyanates (oxidation products from the isocyanides). Irradiation of 2,3'-diisocyanobiphenyl afforded a mixture of two products both absorbing in the visible region. The yields were obtained by solving two equations with two variables of the type,

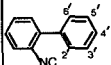
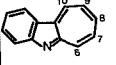
$$\epsilon_{x1} C_1 + \epsilon_{x2} C_2 = E_x$$

C_1 and C_2 concentrations; ϵ_{x1} and ϵ_{x2} extinction coefficients of products at λ_x ; E_x is the observed absorbance at λ_x

The output of the light source was determined by using potassium ferrioxalate as the actinometer (2.00×10^{16} quanta $\text{sec}^{-1} \text{cc}^{-1}$). Conditions for the actinometer were carefully chosen as recommended by Parker and Hatchard.³¹ The results are given in Table 3.1.

The loss of 2-isocyanobiphenyl was determined gaschromatographically and found to be 14.5 ± 0.4 percent. This figure is in agreement with the yield of cyclohept(b)indole, 14.9 percent as determined spectrophotometrically (λ , 527.5 nm; ϵ 366).

TABLE 3.1.

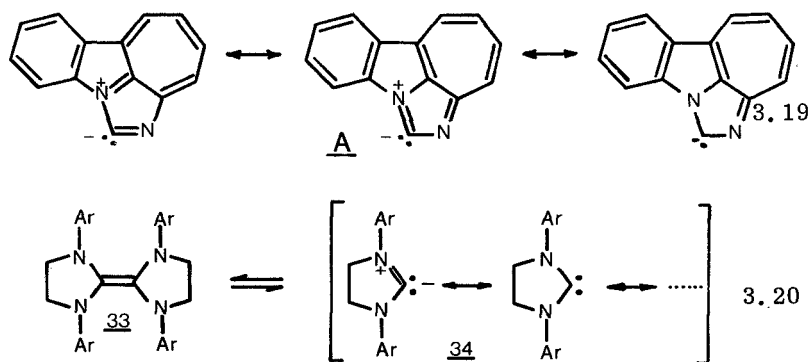
a. starting materials	t (min)	b. E (duplicate)	e. λ (μ) (nm; benzene)	f. $c \times 10^4$ (mol/l)	% product	% recovered	g. $\epsilon_{\lambda} \times 10^2$	h. $\epsilon_{\lambda} \times 10^2$	products
	5.0	0.275(0.275)	527.5(366)	3.77	14.9	85.5	3.77	1.84	
2,4'-diisocyanobiphenyl	5.0	0.460(0.440)	525 (326)	6.90	27.6		6.90	3.45	8-isocyanocyclohept(b)indole
2,3'-diisocyanobiphenyl	5.0	c. 0.390(0.390) d. 0.270(0.270)	515 (268)	1.75	7.0		1.75	1.75	9-isocyanocyclohept(b)indole
			600 (164)						
			515 (411)	3.78	15.1		3.78	3.78	7-isocyanocyclohept(b)indole
			600 (296)						

a. 10 ml of $2.5 \times 10^{-3} \text{M}$ solutions irradiated; b. E = absorbance, see text; c. E at 515 nm; d. E at 600 nm; e. wavelength at which E was read; f. concentration of product corrected to 10 ml; g. product quantum yield; h. product quantum yield per available side of attack.

3.3. Discussion.

3.3.1. IRRADIATION OF 2,2'-DIISOCYANOBIPHENYL.

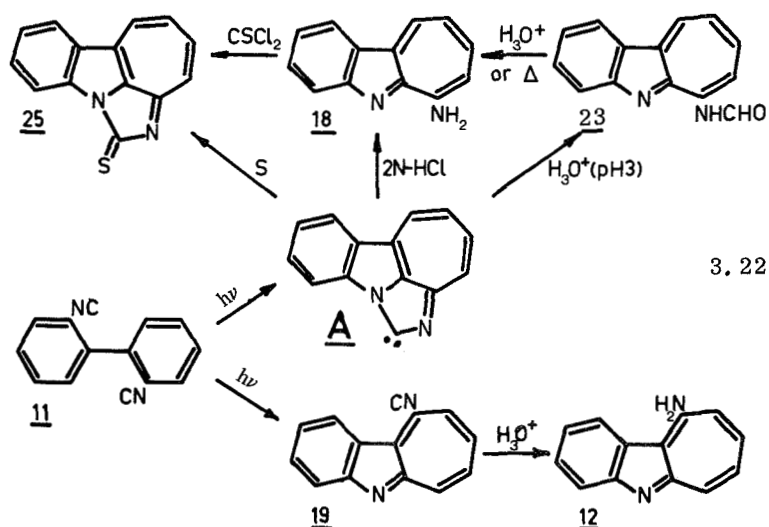
It has been shown that the isocyano-carbon in 2,2'-diisocyanobiphenyl inserts into an *ortho* carbon-carbon bond of the adjacent phenyl ring. The synthesis of cyclohept[b]indole-6(5H)-one 17 from 6-keto-5,7,8,9,10-pentahydro-cyclohept[b]indole 16 and from one of the aminocyclohept[b]indoles (C, 18), obtained upon hydrolysis of the insertion product, contributed to a structure assignment for an intermediate *A*. A cyclic thiourea 25 was produced in another reaction between *A* and sulfur. It was also prepared from the 6-aminocyclohept[b]indole 18 by treatment with thiophosgene. Evidence is against 6-isocyanocyclohept[b]indole as the structure for *A*; however, *A* is likely isomeric with it. In a preferred rationalization initially formed 6-isocyanocyclohept[b]indole produces a new isomer by cyclization conceivably stabilized by resonance (3.19).



The ylide is similar to 1,3-diaryl-imidazolidinylidene-2 known as nucleophilic carbenes 34. The latter were proposed by Wanzlick³² to explain reactions of the stable dimer 33. Moreover the reactivity of this dimer parallels the reactivity of *A* with sulfur and with water.

Thus Wanzlick found, e. g., that treatment of the dimer 33 (Ar = phenyl) with an excess of elemental sulfur at room temperature in pyridine for 12 days gave a high yield, 85 percent, of 1,3-diphenyl-imidazolidine-thione-2³³. In another experiment addition of water to the dimer (Ar = phenyl), dissolved in boiling pyridine, afforded N-formyl-N,N'-diphenylethylenediamine.³² From the dimer (Ar = α -naphthyl)³⁴ he

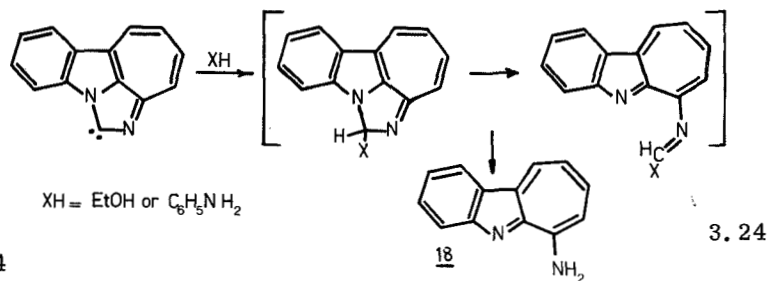
was able to isolate 1,3-di- α -naphthyl-imidazolidiniumchloride. Treatment with ammoniumhydroxide gave N-formyl-N,N'-di- α -naphthyl-ethylenediamine. These data support the reaction scheme outlined below for the irradiation of the diisocyanide and subsequent reactions of the products.



The presence of the proposed nucleophilic carbene **A** may account for other observations. The apparent instantaneous reaction with ethanol may proceed by 1,1-addition (3.24). Kirmse³⁵ has demonstrated that in the reaction of diphenylcarbene with ethanol initially a carbonium ion might be formed followed by attack of methanol (3.23).



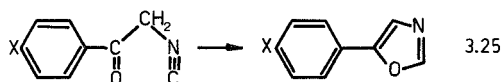
The nucleophilicity of the divalent carbon atom in **A** may have initiated a similar reaction sequence in which ring opening gave the isomeric formimidine (3.24). Considering the known sensitivity of formimidines³⁶ toward acid hydroly-



sis, it was not unexpected that addition product(s) with ethanol were not detected after chromatography on silica.

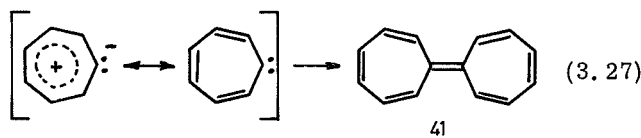
The much slower reaction with aniline (3.24) furnished more evidence for the apparent nucleophilic character of *A*. The isolation of formanilide supported an attack of aniline on *A*. Subsequently or simultaneously a proton shift and ring opening gave the formamidine. Here again unisolated product apparently hydrolyzed during chromatography on silica.³⁷ The formation of 6-anilinocyclohept[b]indole **50** is believed to proceed from the formamidine rather than from the corresponding 6-aminocyclohept[b]indole, since an independent attempt to prepare **50** from **18** and aniline failed.³⁸

Whether the cyclization, which produces *A*, is a ground state isomerization or a photon induced one is an open question. In this context it must be remembered that a similar ground state cyclization with an isocyano group in β position has been found.³⁹



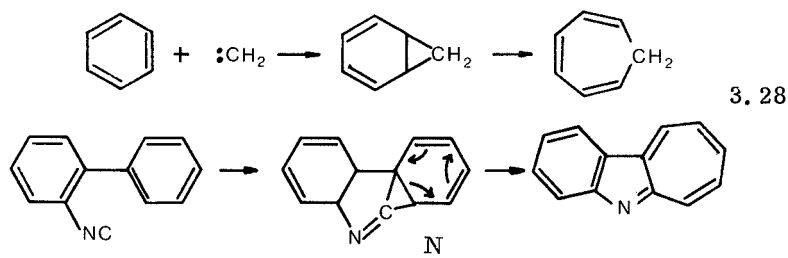
It should be noted that a proper overlap of the lone pair of the indolo-nitrogen with π -bonding of the isocyano group, perpendicular to the aromatic π -cloud in initially formed 6-isocyanocyclohept[b]indole is conceivable.

It was mentioned that Wanzlick generated his aminocarbene from a dimer. Some controversy has arisen concerning the reactivity of these nucleophilic carbenes, and reaction mechanisms have been proposed in terms of the free carbene.^{40,41} Lemal and co-workers⁴¹ found no evidence of any cross-over products by mixing **33A** (Ar=phenyl) and **33B** (Ar=p-tolyl) under various reaction conditions described by Wanzlick. They proposed, that the reactions ascribed to the carbene could be interpreted in terms of an electrophilic attack on the π -electron system of the dimer. This proposal was supported by Winberg and co-workers⁴², who could find no evidence of cross-over products using more reactive aliphatic peraminoethylenes. Many other reactions have been postulated as going via nucleophilic carbene intermediates and have been reviewed by Kirmse and Hine.^{43,44} An interesting intermediate has been recently postulated in which the vacant orbital of the carbene is *also* an integral part of an aromatic system (3.27). Cycloheptatrienyli dine readily dimerizes to heptafulvalene **41**.⁴⁵



3.3.2. ISOMERIZATION OF *ortho*-ISOCYANOBIPHENYLS; HYDROLYSIS OF THE ISOCYANOCYCLOHEPT[B]INDOLES

The isomerization of *ortho*-isocyanobiphenyl into cyclohept[b]indole upon irradiation in cyclohexane as described in Chapter II has been extended to 2, X'-diisocyanobiphenyls. The yields are high. The isomeric isocyanophenanthridines have not been found. Neither has the double insertion product 5,10-diazadiploapentalene been found upon irradiation of 2,2'-diisocyanobiphenyl. The mechanism of the reaction has not been studied. However, the reaction has been assumed to be analogous to the reaction of methylene with benzene, where a norcaradiene is an intermediate.⁴⁶ A similar intermediate *N* is presumably the result of the excitation and



subsequent attack of the isocyano group, in which the relevant orbitals of the terminal carbon are involved. The attack may be conformationally dependent, i.e., favorably initiated from an *ortho*-isocyanobiphenyl twisted around the pivotal bond. The results of an irradiation of *ortho*-isocyanobiphenyls in which the 6- and 6'-position are tied together by $(\text{CH}_2)_n$ could be helpful in elucidation of conformational dependence on intramolecular cyclization.

Some support might be found already in the reported twisting of *ortho*-alkylbiphenyls⁴⁷ (Table 3.2). A considerable twisting of the isocyanobiphenyls is anticipated by assuming that the isocyano group is as bulky as a methyl group. Unfortunately, the angle of twist in *ortho*-isocyanobiphenyls can not readily

be deduced from the uv spectra (Table 3.2). Nevertheless, the hypsochromic shift of 2,2'-diisocyanobiphenyl versus 2-isocyanobiphenyl suggests more twisting around the pivotal bond for the 2,2'-diisocyanobiphenyl.

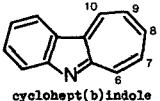
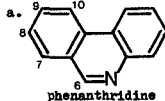
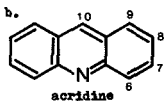
TABLE 3.2

biphenyls substituent	λ_{\max} (nm)	Θ , deg	ϵ
2 - methyl ^a	235	58	10000
2,2' - dimethyl ^a	227	70	6800 ^b
none ^a	252	23	18300
2 - isocyano	247		11750
2,2' - diisocyano	233		13900
2,3' - diisocyano	244		10350

- a. H.H.Jaffé and M.Orchin, "Theory and Applications of Ultraviolet Spectroscopy", John Wiley and Sons, New York, 1962, p 404.
 b. E.A.Braude and W.F.Forbes, J. Chem. Soc., 1955, 3777.

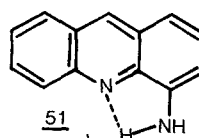
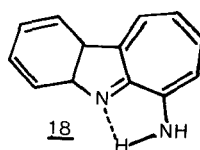
The isolated isocyanocyclohept[b]indoles can be dissolved in weak aqueous acid (pH 2-3) without undergoing rapid hydrolysis. However, the corresponding amines are readily obtained by dissolving the isocyanocyclohept[b]indoles in 2N HCl. Protonation of the indole-nitrogen is expected to assist in this hydrolysis. The color and melting points of the aminocyclohept[b]indoles and the aminophenanthridines are compared (Table 3.3). The color alternation for the amino-

TABLE 3.3

substituent	 cyclohept(b)indole		 phenanthridine		 acridine	
	color	mp	color	mp	color	mp
6 - amino -	orange	179 - 180	colorless	195.5	orange	105 - 106
7 - amino -	blue	> 220	pale yellow	208 - 210	yellow	218
8 - amino -	yellow	174 (dec)	pale yellow	203 - 204	orange	213 - 214
9 - amino -	blue	> 220	colorless	192 - 194	orange	180
10 - amino -	yellow	170 (dec)	pale yellow	143.5- 144.5	pale yellow	233

- a. A.G.Caldwell and L.P.Walls, J. Chem. Soc., 1952, 2156.
 b. R.C.Elderfield, "Heterocyclic Compounds", John Wiley and Sons, New York, 1952, Volume IV p 530.
 The given numbering is not generally accepted, but used for convenience.

cyclohept[b]indoles is not unusual for substituted azulene type molecules⁴⁸ (Chapter IV). Being aromatic amines a sensitivity towards air is not surprising. The poor solubility of the aminocyclohept[b]indoles in n-hexane, cyclohexane, benzene and chloroform reveals a tendency to associate. They are all soluble in ethanol or methanol. Only the 6-aminocyclohept[b]indole 18 has any appreciable solubility in cyclohexane. This property must be related to intramolecular hydrogen bonding. An exactly analogous behavior is demonstrated by the aminoacridines, which are all poorly soluble in apolar solvents, except 1-aminoacridine 51.⁴⁹



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3. 3. 3. QUANTUM YIELDS.

For the determination of the quantum yield a low conversion of starting material into product is advised to avoid secondary processes, e.g., absorbance of quanta by product with or without chemical consequences. Since the extinction coefficients in the detection region (500-700 mμ) for the products is low (ϵ 250-400), a rather high conversion into products was required. Alarmed by the photosensitivity of cyclohept[b]indole, apparently more pronounced under oxygen free conditions (Chapter II), solutions were irradiated under vacuum and under oxygen. Reproducible results were obtained under atmospheric conditions, without the exclusion of oxygen (Table 3.1). A complication might have arisen if each isocyanocyclohept[b]indole had been oxidized under these conditions to the corresponding isocyanate as has been found by Boyer and Ramakrishnan⁵⁰ in the irradiation of several substituted isocyanobenzenes under oxygen. No evidence for such a conversion was obtained upon examining the spectra (uv and ir) of the crude reaction mixtures.

Unfortunately an adequate method could not be developed for the determination of the quantum yields of the products from irradiated 2, 2'-diisocyanobiphenyl. However, our experiments consistently show a preferred attack of the *ortho* isocyano group at the 1', 2'-carbon-carbon bond. If similar, yet unknown, factors influence product formation from 2, 3'-

diisocyanobiphenyl we must conclude 7-isocyanocyclohept[b]-indole to be the major product. Because of the few lines of evidence for this assignment even a careful evaluation of the numerical values of the quantum yields per available side of attack (Table 3.1) in terms of a substituent effect would be unjustified.

The numerical values of these quantum yields indicate moderate efficiency, $0.01 < \Phi_0 < 0.1$. The easy spectrophotometric detection of product supports the proposed use of 2-isocyanobiphenyl as an actinometer.

Experimental Part.

SEE FOR GENERAL REMARKS THE EXPERIMENTAL PART OF CHAPTER 2.

2,2'-DIAMINOBIIPHENYL (43)

A solution of 10 g (54.4 mmole) of 2,2'-dinitrobiphenyl 46 (Aldrich Chemical Company) in 200 ml of absolute ethanol was shaken with 1 g of 5% palladium on powdered charcoal in Parr's hydrogenation apparatus under an initial pressure of 40 psi. After the calculated amount of hydrogen was taken up (15 min) shaking was continued for another hour, during which time no additional pressure drop was observed. The catalyst was filtered off and the alcoholic solution gave on concentrating in the rotary evaporator 7.5 g (95%) of 43: mp 75-77° (lit.⁵¹ mp 78-79°). The product is free from 46 as far as could be judged by comparing its spectra and tlc plates of product and 46.

2,2'-DIFORMIMODOBIIPHENYL (44)

A solution of 6.0 g (32.6 mmole) of 43 in 60 ml of 90% formic acid was kept at reflux temperature for 3 hrs. The formic acid was distilled off and the residue made free from acid by taking it up in chloroform and extracting with 2N sodium hydroxide. The chloroform solution, dried (Na₂SO₄), filtered and evaporated yielded a sticky residue: ir (CHCl₃) 3383 (N-H), 1695 cm⁻¹ (C=O). Colorless crystals of 44, 6.43 g (82%) were obtained from ethanol: mp 143-145° (lit.⁵² 145.8-146.4).

2,2'-DIISOCYANOBIIPHENYL (11)

To a solution of 4.12 g (16.7 mmole) of 44 in 100 ml of methylenechloride and 7 ml of triethylamine were added 46 drops of phosgene (33-38 mmole). The solution, in a three necked round bottomed flask (250 ml) fitted with a mechanical stirrer, a regular reflux condenser and a cold finger condenser (dry ice-acetone), was kept below 10°C by cooling in an ice-bath.

After addition of phosgene was completed, stirring was continued for another hour, then water was added. The layers were separated and the non-aqueous layer is dried (Na₂SO₄), filtered and after removing the methylene chloride, the residue was taken up in benzene. Starting material 44, 800 mg (19.4%), and identified from its ir spectrum, fell out. Silicagel (Baker analyzed) was added to the remaining solution and the residue, upon removing the solvent in the rotary evaporator, was put on top of a silicagel column packed in n-hexane (150 g of silicagel; column diameter 1.5 inch) and fractionated with solvent mixtures. Eluted with n-hexane-benzene (1:1) was 11. Upon concentrating the solutions 1.0 g (29%) of colorless needles were obtained: mp 110.5-112° (lit.¹¹ 101-104°); uv max (cyclohexane) 233 sh (ε 11900), 275 sh (ε 950); uv max (methanol) 233 sh (ε 14400), 270 sh nm (ε 1460); ir (CHCl₃) 2128 cm⁻¹ (N≡C); nmr (CDCl₃) δ 7.50 (narrow multiplet); mass spectrum (70 eV) m/e (rel intensity) 204 (100), 203 (39), 178 (16), 177 (40), 176 (16).

Anal. Calcd for C₁₄H₈N₂: 82.32; H, 3.95; N, 13.73. Found: C, 82.28; H, 3.95; N, 13.76.

With benzene-chloroform mixtures (1:1 to 1:3) was eluted 2-isocyano-2'-formamido-

biphenyl 45 in a total yield of 1.0 g (27%). An analytically pure sample was obtained upon recrystallization from ethanol mp 106-107.5°; ir (CHCl₃) 3378 w (N-H), 2119 m (N≡C), 1695 str (C=O).

Anal. Calcd for C₁₄H₁₀N₂O: C, 75.65; H, 4.54; N, 12.61; O, 7.19. Found: C, 75.39; H, 4.46; N, 12.61; O, 7.43.

IRRADIATION OF 2,2'-DIISOCYANOBIPHENYL (11) IN CYCLOHEXANE.

A. A solution of 250 mg (1.23 mmole) of 11 in 400 ml of cyclohexane was irradiated for 4 hrs under a slow stream of nitrogen at 254 nm. After the solvent was removed in the rotary evaporator, the residue, put on top of a column of silicagel packed in n-hexane (diameter 1", length 10") was fractionated by eluting with solvent mixtures. Starting material 11 was eluted with n-hexane-benzene (1:4) 44 mg (17.6%), and identified by comparing an ir spectrum (CHCl₃) and tlc plate with the authentic data. Upon elution with benzene-chloroform (4:1) 3 mg (1.2%) of the red formamido-cyclohept[b]indole 23 were obtained, followed by 55 mg (26.7%) of 10-isocyanocyclohept[b]indole 19 eluted with benzene-chloroform (1:1). An ir spectrum and tlc plate for 19 gave identical comparison with corresponding authentic data (Experimental C). Finally 6-aminocyclohept[b]indole 18 was eluted with ether-ethanol (4:1) in a yield of 84 mg (42.9%). The amine 18 was purified for analysis by dissolving in refluxing cyclohexane, filtering the hot solution (leaving some dark material on the filter) and recrystallizing the precipitate obtained upon cooling, from carbon-tetrachloride. The orange solid sublimed (temperature 160-180°, pressure about 15 mm) and showed a mp of 179-180° (sealed mp tube); uv max (benzene) 480 (ε 4000), 374 (ε 12800), 352 (ε 15000), 316 (ε 19800), 300 nm (ε 26000); uv max (2N HCl) 413 (ε 6700), 328 (ε 8000), 270 (ε 33000); ir (CHCl₃) 3484 str, 3355 str, 1600 str, 1580 str, 1524 w, 1468 m, 1458 str, 1414 w, 1385 str, 1344 str, 1316 m, 1307 cm⁻¹ m, nmr (CDCl₃) δ 8.60 (d, 1, J = 10 Hz), 8.27 (d, 1, J = 8 Hz), 8.01-6.93 (m, 6), 6.01 (s, 2, NH₂); mass spectrum (70 eV) m/e (rel intensity) 194 (84), 193 (7), 168 (18), 167 (100), 166 (30), 140 (23), 139 (17), 97 (13), 96.5 (<6), 83.5 (30), 83 (10), 69.5 (16), 63 (20).

Anal. Calcd for C₁₃H₁₀N₂: C, 80.37; H, 5.15; N, 14.43; mol wt 194.10. Found: C, 80.22 (80.48); H, 5.39 (5.14); N, 14.38 (14.59).

B. A solution of 200 mg (0.98 mmole) of 11 in 400 ml of cyclohexane was irradiated for 1 hr under conditions similar to those described in part A. The solvent was evaporated, the residue dissolved in diethylether and extracted with 2N hydrochloric acid. The ether solution gave, after drying (Na₂SO₄), filtering and removing the solvent, 33 mg (16.5%) of starting material. An ir spectrum and tlc plate showed a mixture of 11 and 45. The aqueous layer, cooled in an ice-bath, was neutralized with 2N sodium hydroxide (to pH 6-7, pHydron indicator paper). Extraction with ether, drying (Na₂SO₄), filtering and concentrating afforded 73 mg (46%) of the amine 18 (identified by ir and tlc comparison with data of 18 from experiment A). The still very yellow aqueous layer was further basified and again extracted with ether. After an identical work-up procedure 45 mg (28.4%) of 10-aminocyclohept[b]indole 12 was obtained. The material, insoluble in n-hexane, cyclohexane, benzene, slightly soluble in chloroform and soluble in methanol or ethanol, was not satisfactory recrystallized. The material appears to be too basic to allow elution from silicagel with regular organic solvents but it was eluted in a reasonably pure state with diethylether-methanol mixtures from basic aluminiumoxide (Merck): mp 200°C (turns dark from 170°)

uv max (CH_2Cl_2) 440 sh (ϵ 700), 403 (ϵ 2600), 325 (ϵ 32500); uv max (2N HCl) 394 (ϵ 4600), 305 (ϵ 22500), 272 (ϵ 20000); ir (CHCl_3) 3509 w, 3401 m, 1626 m, 1618 str, 1575 m, 1447 w, 1399 str, 1305 m, (dmso- d_6) δ 8.97 (d, 1, J = 8 Hz), 8.83-7.37 (m, 7); mass spectrum (70 eV) m/e (rel intensity) 194 (100), 193 (25), 167 (70), 166 (30), 140 (35), 139 (28), 97 (39), 96.5 (26), 83.5 (39), 83 (26), 69.5 (35). A picrate derivative was prepared and recrystallized from 10% aqueous acetic acid and from ethanol as yellow needles: mp 229-230°.

Anal. Calcd for $\text{C}_{19}\text{H}_{13}\text{N}_5\text{O}_7$: C, 53.91; H, 3.09; N, 16.55. Found: C, 53.33 (53.61); H, 2.93 (3.20); N, 16.23.

C. Two solutions of 204 mg (1 mmole) of 11 in 400 ml of cyclohexane were irradiated under conditions described in part A. The combined solutions were extracted with a weakly acidic hydrochloric acid solution (pH 2-3). The organic layer afforded only 72 mg (17.6%) of starting material 11 identified as before. The aqueous solution, deep orange, was treated carefully with a 2N aqueous sodiumhydroxide solution to cloudiness and extracted with ether. (Often a few more drops were required to leave a colorless aqueous solution). The ether layer, deep red, was dried (Na_2SO_4), filtered and concentrated. An ir spectrum of the residue revealed the presence of a mixture of 10-isocyano- (19) and 6-formamidocyclohept[b]indole 23. Benzene-chloroform (1:1) eluted 65 mg of 23 than 60 mg of 19 from a silicagel column (50 g, 1" column diameter). The separation was not satisfactory as shown by ir. On elution with ether-methanol (10:1) 80 mg (20.6%) of 18 were obtained (ir spectrum was identical with ir spectrum of 18 obtained in experiment A. Compounds 19 and 23 were then successfully separated by preparative thin layer chromatography (Chromar Sheet 1000, Mallinckrodt) using chloroform as eluent. The N-formylamine 23 recrystallized from n-hexane-benzene (1:1) as 20 mg (4.7%) of small deep red needles: mp 115-140° (decomposes, gas evolution); uv max (benzene) 500 (ϵ 1290), 380 (ϵ 9130), 343 (ϵ 17900), 308 nm (ϵ 25200); ir (CHCl_3) 3279 m, (N-H, broad), 1704 str (C=O), 1605 str, 1546 str, 1473 str, 1414 str, 1399 str, 1350 m, 1314 str, 1284 str, 1263 cm^{-1} m; ir (KBr) 3279 m (N-H, broad), 1681 str (C=O), the remaining part of the spectrum showed no significant absorption shifts in comparison with the absorptions from the spectrum taken in chloroform; nmr (CDCl_3) δ 9.87 (s, 1, N-H), 9.00 (s, 1, O=C-H), 9.30 (d, 1, J=11 Hz), 8.85 (d, 1, J=8 Hz), 8.6-7.3 (m, 6); mass spectrum (70 eV) m/e (rel intensity) 222 (14), 221 (14), 204 (13), 194 (95), 167 (100), 140 (17), 139 (14), 97 (14), 83.5 (23).

Anal. Calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}$: C, 75.67; H, 4.50; N, 12.61; O, 7.21. Found: C, 77.11 (77.01); H, 5.33 (5.02); N, 10.65 (11.11); O, 7.07. The formylamine 23 in a melting point tube was inserted for 10 minutes into an oilbath at 145°. Both an ir spectrum (CHCl_3) and a tlc plate of the remaining material revealed the presence of the corresponding amine 18 (tlc: Eastman Chromatogram Sheet 6060; eluens ethanol-chloroform (2:1), R_F 20: 0.72, R_F 13: 0.34). Compound 23 is easily hydrolyzed by acid or base. In shaking a solution of 23 in diethylether (7 mg in 15 ml) for 90 sec with 20 ml of an aqueous 0.25 N sodiumhydroxide solution, 23 was completely converted into 18 as was shown after the usual work-up from an ir spectrum and tlc plate, whereas shaking a basic aqueous solution (pH 10) for 10 min appeared to leave the material 23 unchanged. The 10-isocyanocyclohept[b]indole 19 (30 mg from prep tlc was obtained in long violet needles upon recrystallization from cyclohexane, 18 mg (4.3%): mp >300° on heating turning black, as was observed on a Koffler-Heizbank). uv max (benzene) 560 (ϵ 400), 520 (ϵ 380), 368 (ϵ 4900), 369 (ϵ 5600), 336 (ϵ 25500), 324 (ϵ 29500); ir (CHCl_3) 2941 m, 2109 str, (N \equiv C), 1613 str, 1592 m, 1577 m, 1475 m, 1443 m, 1385 str, 1319 cm^{-1} m; nmr (CDCl_3) δ 8.95 (d, 1, J=

8 Hz), 8.63 (m, 1), 8.30-7.37 (m, 6); mass spectrum (70 eV) m/e (rel intensity) 204 (100), 205 (28), 203 (41), 177 (33), 176 (18), 178 (18), 102 (15), 88.5 (15).

Anal. Calcd for $C_{14}H_8N_2$: C, 82.37; H, 3.95; N, 13.72; mol wt. 204.13. Found: C, 81.67 (81.80); H, 3.93 (3.97); N, 13.47 (13.65). The material 19 withstands hydrolysis in weakly acidic solution (pH 2-3). Shaking with a strong basic solution also produced no change as determined by the ir spectra of recovered material.

D. To the deep red-violet solution obtained after irradiation of 200 mg (1.0 mmole) of 11 (part A) was added 100 mg (3.1 mmole) of sulfur. The solution was stirred for 60 hrs under nitrogen. A red precipitate was filtered off. Its ir spectrum ($CHCl_3$) indicated mainly the cyclic thiourea of 6-aminocyclohept[b]indole 25, confirmed by tlc. Similar data obtained from the residue of the filtrate revealed the presence of 10-isocyanocyclohept[b]indole 19 and 11. The excess sulfur was removed by combining the isolated mixtures and dissolving in ether, followed by extraction with an aqueous 2N hydrochloric acid solution. The ether solution yielded 90 mg of solid material (starting material as shown by ir and very likely sulfur). Crude 25, 71 mg (30.7%) was obtained from the aqueous layer after neutralizing the solution with aqueous sodium hydroxide to pH 5 (pHydron indicator paper), extracting with ether, drying (Na_2SO_4), filtering and removing the ether under reduced pressure. The material was purified both by chromatography over basic aluminum oxide (Merck) and eluted with benzene-chloroform (1:1) and recrystallizing it from carbon tetrachloride-ethanol (1:1) by which method an analytical sample was obtained: mp 208 (dec) (orange-red needles); uv max (methanol) 483 (ϵ 9700), 420 (ϵ 5310), 325 (ϵ 7490), 281 (ϵ 11200), 242 (ϵ 16100), 226 nm (ϵ 20000); ir ($CHCl_3$) 1661 m, 1582 w, 1486 m, 1453 m, 1443 str, 1422 m, 1370 w, 1348 str, 1316 str, 1300 w, 1267 str, 1124 m, 1020 cm^{-1} w, nmr (dmso- d_6) δ 7.43-8.87 (m); mass spectrum (30 eV) m/e (M^+) 236.

Anal. Calcd for $C_{14}H_8N_2S$: C, 71.14; H, 3.41; N, 11.86; mol wt 236.30. Found: C, 70.94; H, 3.54; N, 11.84.

The aqueous solution (pH 5) gave upon basifying with sodium hydroxide, extracting with ether, drying (Na_2SO_4), filtering and evaporating the ether, 25 mg (13.1%) of 10-aminocyclohept[b]indole 12, verified by comparison of an ir spectrum ($CHCl_3$) and tlc plate with the data of 12 obtained in experiment B.

CYCLIC THIOUREA OF 6-AMINOCYCLOHEPT [b] INDOLE (25).

To a solution of 50.0 mg (0.258 mmole) of 18 in 10 ml of methylene chloride (dried ($CaCl_2$) and distilled) and 1 ml of triethylamine (distilled from phenyl isothiocyanate) were added three drops of thiophosgene. The mixture was heated to reflux and kept at this temperature for half an hour, then cooled in an ice-bath, diluted with 50 ml of diethylether and extracted with a 2N hydrochloric acid solution after basifying with 2N sodium hydroxide and extracting with ether, drying (Na_2SO_4) and removing the solvent under reduced pressure, 16 mg of crude material was obtained. Both an ir spectrum ($CHCl_3$) and a tlc plate indicated the presence of 18 and 25 by comparing with "authentic"³ data. The components were separated by preparative thin layer chromatography (Chromar Sheet 1000, Mallinckrodt) and eluted with chloroform-ethanol (4:1). The thiourea 25, moving fast with the solvent, could be isolated in a yield of 9 mg (14.7%). Its identity was established by comparing an ir spectrum and tlc plate with the authentic data.

α -OXYMETHYLENCYCLOHEPTANONE (14)²¹.

To an ice cold mixture of 1.10 mole powdered sodium methoxide (freshly prepared) and 1.10 mole of ethyl formate (dried over anhydrous K_2CO_3) in 1 liter of anhydrous ether (Fisher Scientific Co.) was added 61.0 g (0.545 mole) of cycloheptanone, $n_D^{24.5}$ 1.4593 (lit. $n_D^{21.9}$ 1.4607). The mixture stood for 12 hrs at room-temperature and was then treated with water. The aqueous layer was extracted with ether and the ether layer was extracted with water. From the combined etheric extractions, 3.2 g (5.0%) of cycloheptanone was recovered. The ice cooled aqueous alkaline solution gave upon acidifying with 20% aqueous hydrochloric acid, extraction with ether, drying (Na_2SO_4) and evaporating of the ether 67.4 g (90.8%) of crude 14. Distillation under reduced pressure yielded 55.2 g (72.5%) of colorless 14; bp 58-60°/0.2 mm (lit. bp 55°/0.05 mm).

CYCLOHEPTADIONE-1,2-MONOPHENYLHYDRAZONE (15)²².

A phenyl diazonium salt solution from 18 ml of concentrated sulphuric acid, 90 ml of water, 18 g (21.6 mmole) of aniline (distilled from Zn-dust), 125 g of crushed ice and 13 g of sodium nitrite in 50 ml of water was treated with a concentrated sodium acetate solution (50g/ 50 ml of water). At a temperature of 0°C 20 g (14.3 mmole) of 14 was added dropwise with stirring. During the slow addition care was taken to disperse an orange semi-solid mass as it formed. Stirring was continued for another 15 min. The solvent was decanted and the residue dissolved in hot alcohol, which gave upon concentration 15 g (48.2%) of 15; 53-54° (lit. 54-55°)

6-KETO-5,7,8,9,10-PENTAHYDROCYCLOHEPT[b]INDOLE (16)²².

A solution of 10 g (4.6 mmole) of 15 in a mixture of 40 ml of acetic acid and 4 ml of concentrated hydrochloric acid was heated for 25 min on a boiling waterbath under an atmosphere of nitrogen. The dark colored crystalline material was separated by filtration in a sintered-glass funnel. It was washed with an ice cooled water-alcohol mixture and then with a large excess of water. Yellow plates were "eluted" by benzene from a column of silicagel packed in n-hexane. The yield was 5 g (54.3%), 16, mp 149-151° (lit. ^{22a} mp 148°); uv max (methanol) 311 nm (20200); ir ($CHCl_3$) 3436 str (N-H) 3300 w , 1626 cm^{-1} str (C=O); nmr ($CDCl_3$) δ 9.46 (diffuse, 1, N-H), 7.72-6.87 (m, 4, aromatic), 3.07 (m, 2, CH_2 -C=O), 2.82 (m, 2, =C- CH_2); 1.96 (m, 4, $(CH_2)_2$).

6-KETOXIME-5,7,8,9,10-PENTAHYDROCYCLOHEPT[b]INDOLE (20).

A mixture of 500 mg (2.5 mmole) of 2,3-indolycycloheptadone 16, 500 mg (7.2 mmole) of hydroxylamine hydrochloride, 5 ml of ethanol and 0.5 ml of pyridine was refluxed on a waterbath for 90 min. The ethanol was removed under reduced pressure and 5 ml of water were added. After cooling in an ice-bath the solvent was decanted from sticky organic material. No starting material could be detected by tlc. The residue was dissolved in benzene, dried (Na_2SO_4) and concentrated. Upon adding n-hexane, cooling and scratching 150 mg (28%) of 20 was obtained as colorless crystals: mp 118-124° (n-hexane-benzene 1:2). Concentration of the mother liquid afforded

another crop of 124 mg, mp 116-124°C, a combined yield of 274 mg (51.2%). An analytically pure sample was obtained after recrystallizing twice from benzene-n-hexane (2:1) and twice from CCl₄; mp 125.5-128.5° (colorless prisms and needles; uv max (methanol) 304 nm (ϵ 20400); ir (CHCl₃) 3570 str (O-H), 3448 str (N-H), 3279 m (bonded N-H), 939 cm⁻¹ str (vN-O); nmr CDCl₃) δ 1.90 (m, 4, CH₂-CH₂), 2.97 (m, 4 allylic CH₂), 7.26 (m, 4, aromatic), 8.07 (s, 1, sharp), 8.84 (diffuse, 1,) the latter two vanish after addition of D₂O.

Anal. Calcd for C₁₃H₁₄N₂O: C, 72.87; H, 6.59; N, 13.08; O, 7.47; mol wt. 214.27. Found: C, 73.13; H, 6.64; N, 13.28.

6-AMINO-5,7,8,9,10-PENTAHYDROCYCLOHEPT[b]INDOLE (21).

A solution of 200 mg (0.935 mmole) of 20 in 100 ml of dry diethylether was refluxed for 3 hrs with 100 mg of lithiumaluminum hydride. Following a procedure⁵³ for precipitating inorganic hydroxides, 3 drops of water, 9 drops of 2N sodium hydroxide and again 3 drops of water were added. After filtration the colorless ether solution was dried (Na₂SO₄) and the ether removed. Both a tlc plate and an ir spectrum indicated some unreacted 20. The colorless sticky residue gave upon treatment with carbon tetrachloride 16 mg of colorless crystals 21; mp 106-108°. From the mother liquor another 30 mg was obtained upon concentration, a combined yield of 46 mg (25.7%). An analytical sample was obtained upon recrystallization from carbon tetrachloride: mp 111-112°; uv max (methanol) 284 nm (ϵ 7500); ir (CHCl₃) 3448 cm⁻¹ (N-H); nmr (CDCl₃) δ 1.79 (m, 8, -(CH₂)₂), 1.6 (s, 2, NH₂), 2.90 (m, 2, allylic CH₂) δ 8.9 (broad, 1, α H), δ 7.3 (m, 4, aromatic), δ 8.9 (broad, 1, N-H indole) (Assignment of N-H protons is based upon integration and change in spectrum after addition of D₂O); mass spectrum (70 eV) m/e (rel intensity) 200 (50), 183 (100), 182 (80), 171 (22), 168 (36), 167 (22), 156 (16), 155 (20), 154 (20), 143 (12), 130 (20)

Anal. Calcd for C₁₃H₁₆N₂: C, 77.94; H, 8.06; N, 13.99; mol wt 200.29. Found: C, 77.77; H, 8.02; N, 13.92

CYCLOHEPT[b]INDOLE-6(5H)-ONE (17)²⁵.

A. A mixture of 195 mg (1.0 mmole) of 1-oxo-2,3,4,5-tetrahydroheptindole 16 and 64 mg (2.0 mmole) of sulfur in a small tube (3 ml) provided by a condenser with gas outlet on top was immersed in a Wood's metal bath kept at a temperature of 235°. The evolved gas was trapped in a gas buret. Within 7 min, 48.5 ml gas was trapped (calc 48 ml). The reaction mixture was immediately removed from the heating source and allowed to cool. The black solid mass triturated with 6N hydrochloric acid and the insoluble part was washed several times with acid. The combined acidic solution was filtered, cooled in ice and neutralized with aqueous 6N sodium hydroxide. A yellow precipitate was collected and dried by air, 75 mg (38.0%). The material was purified by sublimation (220-230°, 15 mm) giving 55 mg (28.0%) of bright yellow needles 17: mp 249.5-250.5°; uv max (methanol) 402 (ϵ 8824), 384 (ϵ 6580), 336 (ϵ 11780), 320 (ϵ 15760), 308 (ϵ 16470), 275 (ϵ 21700), 225 nm (ϵ 24000); ir (CHCl₃) 3413 m, (N-H), 3175 m, (intramolecular H-bonding), 1618 str (C=O), 1558 str, 1488 str, 1449 w, 1418 m, 1404 m, 1376 w, 1326 cm⁻¹ w; nmr (dmso-d₆) δ 12.7 (s, 1, N-H), 8.38 (m, 2), 7.87-6.87 (m, 6); mass spectrum (70 eV) m/e (rel intensity) 195 (86), 194 (<1), 168 (17), 167 (100), 166 (19), 140 (16), 139 (22), 97.5 (10), 83.5 (17), 70.5 (10), 69.5 (6).

Anal. Calcd for $C_{13}H_9NO$: C, 79.97; H, 4.65; N, 7.18; mol wt 195.22. Found: C, 79.93; H, 4.49; N, 7.28. Neither starting material 16 nor carbazole could be detected in the black residue.

B. A solution of 60 mg (0.31 mmole) of 6-aminocyclohept[b]indole 18 and 170 mg of sodiumhydroxide in 4 ml ethanol-water (1:1) was heated under reflux for 15 hrs. The solution was cooled and diluted to 25 ml with water and extracted with methylene chloride. The organic layer was dried (Na_2SO_4) and treated with 1 g of silicagel. The residue, obtained upon evaporating the solvent, was put on top of a small column of silicagel packed in n-hexane and fractionated with benzene-chloroform mixtures. Chloroform eluted 45 mg (74.5%) of 17. The identity was established by comparison of an ir- and uv-spectrum and a tlc plate with the authentic data. No starting material was recovered by eluting with ether-ethanol mixtures.

6-AMINOCYCLOHEPT[b]INDOLE (18)²⁶.

A mixture of 100 mg (0.5 mmole) of 17, 5 g of ammonium acetate and 3 ml of acetic acid was refluxed for 10 hrs (155-130°). The mixture was poured into water and 75 mg (75%) of 17 fell out. The filtrate was basified, extracted with ether, dried (Na_2SO_4) and filtered. Evaporation of the solvent afforded about 5 mg of a red solid material, ir ($CHCl_3$) 1694 (C=O), 1666 cm^{-1} (C=O or C=N). The material was dissolved in aqueous 2N hydrochloride acid, heated for 90 min at 85-90° and gave after the usual work-up procedure a trace of 18, established after comparing an ir spectrum ($CHCl_3$) and a tlc plate with the authentic data.

CYCLOHEPT[b]INDOLE FROM 6-AMINO-5,7,8,9,10-PENTAHYDROCYCLOHEPT[b]INDOLE (21).

A solution of 175 mg (0.87 mmole) of 21 in 50 ml of decalin and 50 mg of 5% palladium on charcoal¹⁴ was kept at reflux temperature for 14 hrs. Ether was added after cooling. The ether solution was extracted with aqueous 2N hydrochloride acid. Cyclohept[b]indole 22 was detected in the aqueous acidic layer, after neutralizing with base, extraction with ether, drying (Na_2SO_4) and evaporating the ether as was shown by an ir spectrum and a tlc plate. The yield was about 3 mg. The ether layer containing decalin was not further investigated.

2,3'-DINITROBIPHENYL (7)¹².

This was prepared according to Case and Idelson by adding with stirring 10 g (0.050 mole) of powdered commercial 3-nitrophenyl¹⁴ (mp 59-60°) to 230 ml of nitric acid¹¹ (69-71%; ACS-Standard). A side product, 3,4'-dinitrophenyl was less soluble in methanol and was removed by filtration. Colorless chalky crystals of 2,3'-dinitrophenyl 7, 4.0 g (32.6%) were obtained from the filtrate: mp 113-115° (lit¹² 113-115°).

2,3'-DIISOCYANOBIPHENYL (10)¹¹.

Following the procedure for the preparation of the N,N'-difonyl derivative of 2,2'-

diaminobiphenyl, the N,N'-diformyl derivative of 2,3'-diaminobiphenyl was obtained by reduction of dinitrobiphenyl 7 and formylation of the unisolated diaminobiphenyl⁸. The final product in the dehydration of N,N'-diformyl-2,3'-diaminobiphenyl 9 was purified by column chromatography giving a yield of 1.8 g of 2,3'-diisocyanobiphenyl 10; 54.0% based upon 3.99 g (8.8 mmole) of the corresponding dinitrobiphenyl; mp 145-146°; uv max (methanol) 280 sh (ϵ 1540), 250 sh (ϵ 10400); uv max (cyclohexane) 280 sh (ϵ 860), 244 sh (ϵ 10350); ir (CHCl₃) 2127 cm⁻¹ str (N≡C); nmr (CDCl₃) δ 7.53 (narrow multiplet); mass spectrum (70 eV) m/e (rel intensity) 204 (100), 203 (25), 178 (16), 177 (44), 176 (25).
Anal. Calcd for C₁₄H₈N₂: C, 82.37; H, 3.95; N, 13.72; mol wt 204.13. Found: C, 82.32; H, 4.09; N, 13.55.

IRRADIATION OF 2,3'-DIISOCYANOBIPHENYL (10) IN CYCLOHEXANE.

A solution of 200.0 mg (1.0 mmole) of 10 in 400 ml of cyclohexane was irradiated for 1.5 hr under conditions similar to those described in part A for the irradiation of 2,2'-diisocyanobiphenyl. Analysis of the uv absorption for a sample taken after 45 min revealed a conversion into 26 and 27 of 30 ± 5 percent; after 90 min of 45 ± 5 percent. In the usual work-up (see part A) 90 mg (45%) of starting material was eluted with n-hexane-benzene (1:1) and identified by comparison of ir spectra and a tlc plate with those of authentic data. The isomers 26 and 27 were eluted with benzene-chloroform (1:1); of one isomer 18 mg (9.0%), of the other 63 mg (31.5%), was obtained. The product with the lower yield (minor product) was first eluted and gave on recrystallizing from benzene transparent violet plates, mp > 280°. The crystals darken on heating around 210° in a Koffler-microscope, hot stage; uv max (benzene) 514 (ϵ 280), 412 (ϵ 1900), 389 (ϵ 4200), 373 (ϵ 4600), 314 (ϵ 33000), 302 (ϵ 36000); ir (CHCl₃) 2119 str (N≡C), 1618 w, 1608 str, 1595 str, 1439 m, 1404 str, 1337 m, 915 cm⁻¹ m, nmr (CDCl₃) δ 8.65-6.87 (m); mass spectrum (70 eV) m/e (rel intensity) 205 (23), 204 (100), 203 (26), 178 (13), 177 (31), 176 (16), 102 (15), 88.5 (18).

Anal. Calcd for C₁₄H₈N₂: C, 82.37; H, 3.95; N, 13.72; mol wt 204.13. Found C, 82.46; H, 4.06; N, 13.88. The major product gave on recrystallizing from cyclohexane tiny dark brown needles: mp > 280°; uv max (benzene) 518 (ϵ 411), 410 (ϵ 2400), 389 (ϵ 4500), 362 (ϵ 4700), 332 (ϵ 16600), 322 (ϵ 20000); ir (CHCl₃) 2119 str (N≡C), 1609 str, 1484 str, 1433 str, 1410 str, 1381 str, 1368 m, 908 str; nmr (CDCl₃) δ 8.60-6.78 (m); mass spectrum (70 eV) m/e (rel intensity) 205 (18), 204 (100), 203 (24), 178 (13), 177 (27), 176 (9), 102 (9), 88.5 (7).

Anal. Calcd for C₁₄H₈N₂: C, 82.37; H, 3.95; N, 13.72; mol wt 204.13. Found: C, 82.07; H, 4.17; N, 13.58. The isomers 26 and 27 were each hydrolyzed to the corresponding amines by shaking its violet methylenechloride solution with aqueous 2N hydrochloric acid. The organic layer decolorized rapidly, while the aqueous layer turned orange. Basifying with aqueous 2N sodiumhydroxide and shaking decolorized the aqueous layer and gave the methylenechloride layer an intense blue color; uv max (CH₂Cl₂) major product 28, 548 nm (about 1000) and uv max (CH₂Cl₂) minor product probable 29, 575 nm. The amines were isolated from the methylene chloride layer by filtering and removing the solvent by evaporation; ir 28 (CHCl₃) 3497 w, 3401 str (N-H), 3215 w, 1626 str, 1495 str, 1397 m, 1366 m, 909 str. ir 29 (CHCl₃): 3484 w, 3401 str (N-H) 3205 w, 1631 str, 1618 str, 1585 str, 1563 w, 1477 str, 1429 m, 1403

str, 1353 w, 1325 m, 1311 m, 1266 cm^{-1} str. Each amine melted above 220° (Koffler microscope, hot stage). The amines were insoluble in n-hexane, benzene, cyclohexane, slightly soluble in chloroform and soluble in methylenechloride, methanol or ethanol. Purification by recrystallization was unsatisfactory. The amines were not eluted from silicagel with regular organic solvents, but they were eluted with diethyl-ether-methanol mixtures from basic aluminumoxide (Merck). The hydrochloride of 28 crystallized as orange needles from aqueous 2N hydrochloric acid and was recrystallized from methanol-aqueous 2N hydrochloric acid (1:1); mp >280°; mass spectrum (70 eV) m/e (rel intensity) 195 (16), 194 (100), 193 (19), 167 (19), 166 (19), 140 (14), 139 (12), 97 (7), 83.5 (7).

Anal. Calcd for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{Cl}\cdot 1.75 \text{H}_2\text{O}$: C, 59.54; H, 4.23; N, 10.68; mol wt 262.22. Found: C, 59.54; H, 4.81; N, 10.66.

Anal. Calcd for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{Cl}$: C, 67.68; H, 4.81; N, 12.14; mol wt 230.70. Found: C, 66.82; H, 4.72; N, 12.13 after dried to constant weight. (Micro-tech laboratories, Skokie, Illinois determined the elemental content of this compound from a 2 mg sample after it was dried to constant weight on a hot-plate under atmospheric pressure without a desiccant. A difference between two weighings of 0.05 mg was considered evidence for constant weight).

2,4'-DINITROBIPHENYL (47).

This was prepared following a procedure by Gull and Turner¹³ by adding 20.0 g (0.1 mole) of commercial 2-nitrobiphenyl¹⁴ to 280 ml of concentrated nitric acid (d 1.416-1.424).¹¹ The yield of long pale yellow needles 47 was 6.4 g (26.2%) after several recrystallizations from 95 percent ethanol: mp 92.5-93.5° (lit.¹³ mp 92.5-93.5°).

2,4'-DIISOCYANOBIPHENYL (30).

The diamine and its diformyl derivative were isolated in crude form from product mixtures obtained in reactions patterned after the preparation of the 2,2'-isomers. The dehydration of crude amide was carried out according to the dehydration of the 2,2'-isomer. After the usual work-up, 2.1 g (39.3%) of 30 (based upon 6.4 g of 2,4'-dinitrobiphenyl (26.2 mmole)) was eluted slowly from a column of silicagel with n-hexanebenzene (1:1) mp 94.5-95.5°C (lit.¹¹ 97-98°); ir (CHCl_3) 2126 cm^{-1} ($\text{N}\equiv\text{C}$); mass spectrum (70 eV) m/e (rel intensity) 205 (23), 204 (100), 203 (27), 178 (13), 177 (27), 176 (18).

IRRADIATION OF 2,4'-DIISOCYANOBIPHENYL (30) IN CYCLOHEXANE.

A solution of 200.0 mg of 30 (1.0 mmole) in 400 ml of cyclohexane was irradiated for 1.5 hr under conditions described for the 2,2'-isomer. During the irradiation aliquots were taken after 45 and 90 min. The solvent was evaporated from these samples under reduced pressure and the residue dissolved in 5 ml of benzene. Visible spectra, max (benzene) 525 nm (ϵ 326), of these solutions revealed conversions into 31, of 62 and 73 percent respectively. Irradiation was stopped after 90 min. The irradiated solution upon concentration (about 10 ml of the solvent was left) gave 93

mg of 31 as black needles. From this sample no starting material could be detected either by ir or tlc analysis. Tlc showed only a trace of an impurity. Chromatography of the filtrate over silicagel yielded 43 mg (21.5%) of 30 which was eluted with n-hexane-benzene (2:3) and characterized by ir and tlc in an identical comparison with authentic data. An additional fraction of 31, 32 mg, was eluted with benzene chloroform (1:1) bringing the yield of 31 to 125 mg (78%, when corrected for recovered starting material). Prior to elution of 31 a dark band developed and was also eluted with benzene-chloroform (1:1) to give about 3 mg of a semi-solid material; ir (CHCl₃) 2123 cm⁻¹ ($\overset{\oplus}{\text{N}}\equiv\overset{\ominus}{\text{C}}$). This material was not further investigated. An analytical sample of 31 was obtained upon recrystallizing from benzene. The long transparent faintly violet plates turned brown at 170° with no further change on heating to 320° by a Koffler-microscope, hot-stage; uv max (benzene) 523 (ε 324), 404 (ε 3300), 389 (ε 6650), 370 (ε 6100), 322 (ε 33700); ir (CHCl₃) 2114 str ($\overset{\oplus}{\text{N}}\equiv\overset{\ominus}{\text{C}}$), 1613 m, 1477 m, 1408 str, 1366 w, 1330 cm⁻¹m. nmr (CDCl₃) δ 9.13-7.66 (m); mass spectrum (70 eV) m/e (rel intensity) 204 (100), 205 (20), 203 (24), 177 (24), 178 (10), 176 (14).

Anal. Calcd for C₁₄H₉N₂: C, 82.37; H, 3.95; N, 13.72; mol wt 204.13. Found: C, 82.52; H, 4.19; N, 13.88.

8-AMINOCYCLOHEPT [b] INDOLE (32).

A solution of 31.6 mg (0.15 mmole) of 31 in 50 ml of benzene [uv max (benzene) 525 nm (ε 326)] was shaken in a separatory funnel with 50 ml of aqueous 2N hydrochloric acid for 2 minutes. The deep violet color of 31 in benzene disappeared rapidly, whereas the aqueous acid layer turned deep yellow. The layers were separated and the organic layer was again shaken with 20 ml of acid. Aqueous layers were combined and the yield of 32 was determined spectroscopically, 104% [uv max 2N HCl) 392 nm (ε 17100)]. The acid solution was basified and extracted with methylenechloride. The organic layer was dried (Na₂SO₄) and filtered. The quantitative yield of 32 was again checked spectroscopically, uv max (CH₂Cl₂): 396 nm (ε 7700). In addition to these yield determinations 29 mg (96.5%) of tiny yellow needles were obtained upon concentrating the methylenechloride solution. The amine 32 was eluted in a further purification attempt with methanol from basic aluminum oxide (Merck) and than digested several times with methylenechloride and very carefully filtered to remove insoluble particles (apparently material from the aluminum oxide column). Upon concentrating tiny yellow needles were obtained: mp 174° (dec) (Koffler microscope, hot-stage); uv max (CH₂Cl₂) 413 (ε 626), 396 (ε 7700), 341 nm (ε 32600); ir (KBr) 2.93 str (N-H), 1656 m, 1613 str, 1592 str, 1570 str, 1548 m, 1497 w, 1471 m, 1410 str, 1350 m, 1328 m, 1311 m, 1272 w, 1232 str, 1203 str, 1130 w, 889 m, 858 w, 833 m, 782 m, 751 m, 712 w; nmr (dmso-d₆) δ 8.96 (d, 1, J=11Hz), 8.66 (m, 2), 8.2 (d, 1, J=8Hz), 8.01-7.47 (m, 3), 7.27 (d, 1, J=11Hz), each peak a doublet J=2Hz; mass spectrum (70 eV) m/e (rel intensity) 194 (100), 195 (19), 193 (15), 167 (60), 168 (11), 166 (60), 140 (13), 139 (13), 97 (13), 83.5 (11). M⁺ 194. The hydrochloric acid salt 30a of 30 was prepared by shaking a benzene solution of 60 mg (0.29 mmole) of 31 with 50 ml of aqueous 2N hydrochloric acid. The acidic solution was allowed to stand overnight and yielded 42 mg (54.5%) of 30a as tiny bright yellow needles: mp >280°; uv max (benzene) 392 (ε 17100), 332 (21400); mass spectrum (70 eV) m/e (rel intensity) 194 (100), 195 (20), 193 (15), 167 (70), 168 (10), 166 (30), 140 (15), 139 (15), 97 (12), 83.5 (10). M⁺ (12 eV) 194.

Anal. Calcd for C₁₃H₁₁N₂Cl: C, 67.68; H, 4.81; N, 12.14; Cl, 15.37; mol wt 230.70. Found: 67.20 (67.12); H, 4.73 (4.84); N, 11.76 (12.03). 49

QUANTUM YIELDS.

Potassium ferrioxalate was used as the actinometer³¹. The ferrous ions formed upon irradiation at 254 nm of a 5.90×10^{-3} M solution of the actinometer were complexed with 1,10-phenanthroline. The ferrous complex shows a characteristic absorption in the visible region, λ_{max} 510 nm (ϵ 1.11×10^4) (Cary 14, UV spectrophotometer). The spectrophotometer was calibrated with standard ferrous sulfate solutions to which 1,10-phenanthroline and sodiumacetate buffer were added in recommended quantities. The final pH was checked with a pH meter and if necessary adjusted to pH 4.5. For concentrations in ferrous ions of 0.845×10^{-5} , 2.534×10^{-5} , 4.224×10^{-5} and 6.756×10^{-5} M, we found respective extinction coefficients of 1.12×10^4 , 1.14×10^4 , 1.13×10^4 and 1.00×10^4 . The preparation and use of potassium ferrioxalate and the preparation of calibration solutions were done under red light. Samples of 10 ml from the standard actinometer solution were irradiated under vacuum (three freeze-thaw cycles were conducted with liquid nitrogen on a vacuum line at 2×10^{-5} mm Hg). The solutions, in small quartz tubes (I.D. 15 mm, length 17.5 cm), were put in a merry-go-round assembly in a Rayonet reactor equipped with 16 mercury low pressure lamps emitting a narrow band of 254 nm light. After an irradiation time of 30.0 and 60.0 sec we found a conversion of 1.25×10^{-3} respectively 2.50×10^{-3} M into ferrous ions. The quantum yield (1.25) allowed the calculation of the intensity of the absorbed light. This was found to be 2.0×10^{16} quanta $\text{sec}^{-1} \text{cc}^{-1}$. Irradiation of the *ortho* isocyanobiphenyls was carried out under identical conditions as used for the actinometer, except for irradiation time and exclusion of oxygen. Samples of 10 ml (2.5×10^{-3} M) were irradiated for 5.0 minutes under atmospheric conditions without the exclusion of oxygen. After evaporation of the solvent the residue was completely dissolved in 5 ml of benzene (volumetric flask). The yield of insertion products was determined spectrophotometrically. IR spectra in chloroform of these mixtures (starting material and product) did not indicate the presence of an isocyanate, a product that might have been the result of a reaction between isocyanocyclohept [b] indoles with oxygen. No attempts were made to determine the amount of unreacted starting materials other than 2-isocyanobiphenyl. A yield of 14.9 percent of cyclohept [b] indole was calculated from the uv spectrum (λ_{max} 527.5, ϵ 366), whereas a loss 14.5 ± 0.4 percent of *ortho*-isocyanobiphenyl was calculated from integrated areas of several gaschromatograms compared with gaschromatograms from the standard solution. (Barber Colman: Flame Ionization Gas Chromatograph, model 5320; column: stainless steel coil, $8 \times \frac{1}{4}$ ", 5% GE-XE-60 on Chromosorb-G, 60/80 AW DMGS; temperature: 208°).

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CHAPTER IV

SPECTRAL DATA AND pK_a VALUES OF PHOTOCHEMICAL ISOMERIZATION PRODUCTS FROM *ORTHO* ISOCYANOBI-PHENYLS.

4.1. Introduction.

Of the spectral properties of the isocyano group extensive studies have been reported about the ir spectra only. The ir stretching frequency of the isocyano function¹, at 2120-2150 cm^{-1} , has been found to be sensitive to the polarity of the solvent² and its ability to form a hydrogen bond with the isocyano carbon³. A slight frequency decrease has been observed when strongly electron withdrawing p-substituents were introduced in phenylisocyanide⁴. No detailed studies of uv spectra have been made.^{4,5}

Besides these spectral properties, the mass spectra and pK_a values will be discussed for the isocyanocyclohept[b]-indoles. Further a comparison of the pK_a values of the aminocyclohept[b]indoles with the isomeric amino-acridines seemed of interest. A comparison with other model compounds, like the amino-azulenes is lacking, because only the 1-, 2- and 6-substituted amino-azulenes⁶ are known and no spectral data or pK_a values seem to be reported. To our knowledge no examples are known in which an isocyanide group is attached to a seven-membered ring, which is part of an aromatic system.

4.2.1. MASS SPECTRA OF *ORTHO* ISOCYANOBI-PHENYLS AND THEIR PHOTOCHEMICAL ISOMERIZATION PRODUCTS.

The mass spectra of phenyl- and α -naphthyl-isocyanide have been studied by Zeeh⁸. The main feature of fragmentation in these compounds is the loss of HCN. A similar fragmentation is observed for 2-isocyanobiphenyl. The 2,'-diisocyanobiphenyls lose two molecules of HCN. An additional feature in the spectra of *ortho*-isocyanobiphenyls is the abundance of the $(M-1)^{\oplus}$ fragment, which has not been found for either the phenyl- or α -naphthyl-isocyanide.

Because photochemical and electron impact processes are

Table 4.1.

Compounds	Mass Spectrum ^a							IR Spectrum ^b	
	205	204	203	178	177	176	150	cm ⁻¹	solvent
Fragments m/e	Relative Intensity								
2,2'-diisocyanobiphenyl	22	100	39	16	40	16	11	2122	CHCl ₃
10-isocyanocyclohept[b]indole	28	100	41	18	33	18	10	2109	CHCl ₃
2,3'-diisocyanobiphenyl	19	100	25	16	44	25	12	2127	CHCl ₃
7-isocyanocyclohept[b]indole	18	100	24	13	27	9	10	2119 2113	CHCl ₃ CCl ₄
9-isocyanocyclohept[b]indole	23	100	26	13	31	16	13	2119	CHCl ₃
2,4'-diisocyanobiphenyl	23	100	27	13	27	18	12	2126	CHCl ₃
8-isocyanocyclohept[b]indole	20	100	24	10	24	14	10	2114	CHCl ₃

a. Only fragments with a relative intensity >10 are reported.

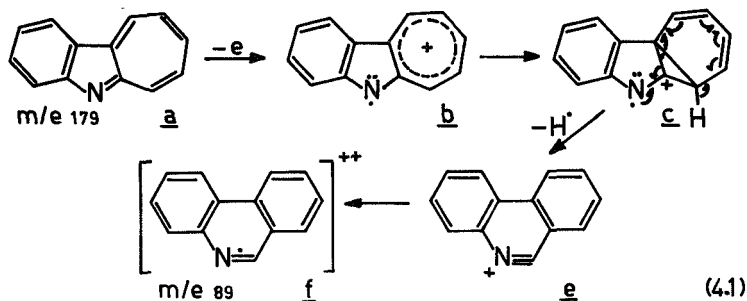
b. Stretching vibration band of the isocyanogroup.

Table 4.2.

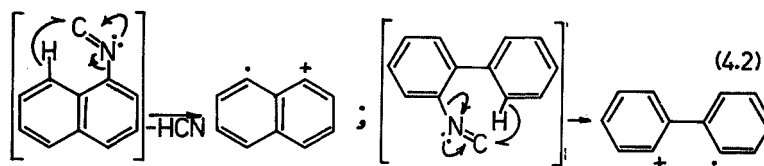
Compounds	Mass Spectrum						
	180	179	178	152	151	89.5	89
Fragments m/e	Relative Intensity						
Cyclohept[b]indole	23	100	29	17	15	15	29
2-Isocyanobiphenyl	16	100	28	28	24	6	8
Phenanthridine	15	100	18	15	10	5	2.5

often parallel, it is of interest to examine the spectra of the isomeric cyclohept[b]indole and phenanthridine. The fragmentation of these compounds is similar to that of isomeric 2-isocyanobiphenyl, i. e., occurrence of $(M-1)^{\oplus}$ and a fragment due to the loss of HCN. The loss of HCN has also been reported for similar molecules like pyridine and quinoline.⁹ Noteworthy is the occurrence of the doubly charged ions at m/e 89.5 and m/e 89 (M^{++} and $(M-1)^{++}$). The relative intensity of $(M-1)^{++}$ for cyclohept[b]indole (29 percent) indicates that upon loss of hydrogen from M^{\oplus} a very stable species has been formed, which subsequently may lose another electron upon electron impact. This process appears to be preferred above double impact of the molecular ion of cyclohept[b]indole (Table 4.2). The feature is reversed for phenanthridine as can be seen from the figures in Table 4.2. Moreover, the loss of a hydrogen atom from phenanthridine is less probable than it is from the isomeric 2-isocyanobiphenyl and cyclohept[b]indole.

In rationalizing these observations the following mechanism may describe the "fragmentation" of cyclohept[b]indole. It is assumed that the proton at the 6 position plays an important role. Its easy loss from *c*, followed by the isomerization into highly stabilized *e*, eventually with the loss of a second electron upon electron impact, *f*, is conceivable.

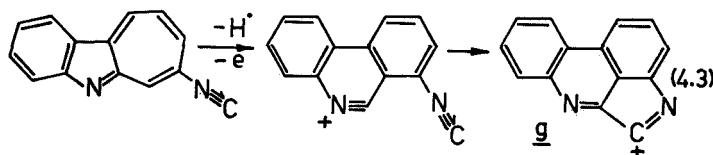


Whereas the $(M-1)^{++}$ fragment from 2-isocyanobiphenyl may be due to an initial isomerization into cyclohept[b]indole from which a proton is lost, this route is certainly not the major one for other fragmentation reactions (like the loss of HCN) as may be deduced from a comparison of the relative intensities of the fragments obtained from each isomer (Table 4.1). A mechanism for the loss of HCN similar to that proposed for α -naphthylisocyanide may apply (4.2).



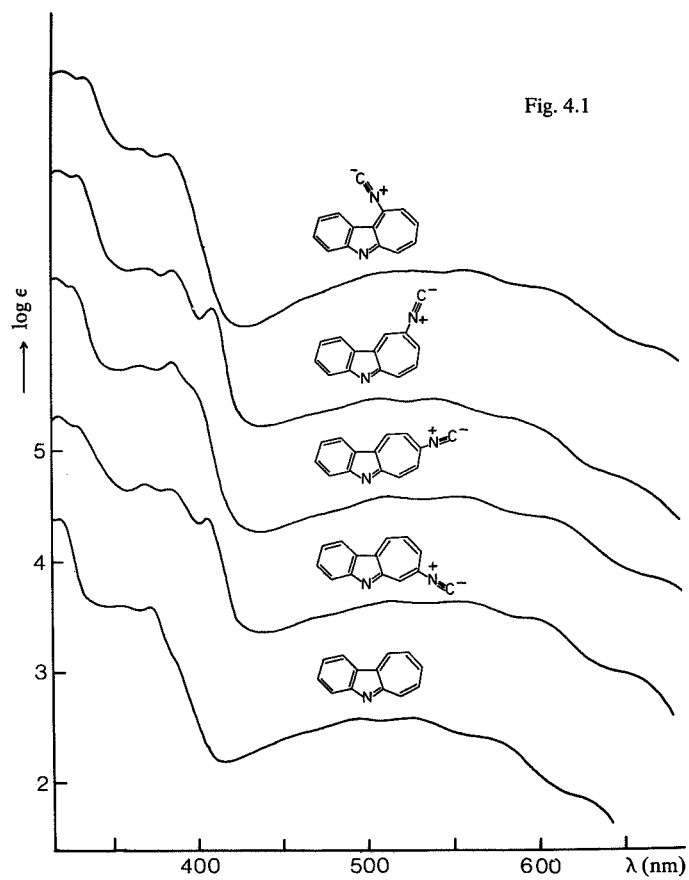
The mass spectra of the isocyanocyclohept[b]indoles show a similar fragmentation pattern. Doubly charged ions are observed for $(M-1)^{++}$ and $(M-HCN)^{++}$, i. e., at m/e 101.5 and m/e 88.5 with intensities of < 5 and < 18 percent respectively. The fragmentation to $(M-1)^+$ also occurs easily (24 percent or more). The occurrence of m/e 176 suggests that upon loss of hydrogen and subsequent isomerization into an isocyanophenanthridine cation e , the elements of HCN are lost.

It should be remembered that upon irradiation of 2,3'-diisocyanobiphenyl two isomeric isocyanocyclohept[b]indoles were obtained. The major product was assigned to be 7-isocyanocyclohept[b]indole, as reported in Table 4.1. Additional evidence for this assignment is found from the mass spectrum, i. e., the low relative intensity for m/e 176 (9 percent). This is rationalized by the fact that HCN is lost in a non-random process⁸ consisting of combination of the CN radical with an *ortho* hydrogen atom. Since in 7-isocyanocyclohept[b]indole only one *ortho* hydrogen is present in the $(M-1)^{\oplus}$ fragment (e), the m/e 176 fragment is expected to have half the intensity of the other isocyanocyclohept[b]indoles, when the statistical factor was product determining. This expectation is surprisingly well borne out by the data in Table 4.1. An alternative explanation for the low intensity is found in the subsequent cyclization of $(M-1)^{\oplus}$ to a highly stabilized molecule g .



4.2.2. OPTICAL SPECTRA OF ORTHO ISOCYANOBIPHENYLS AND THEIR PHOTOCHEMICAL ISOMERIZATION PRODUCTS.

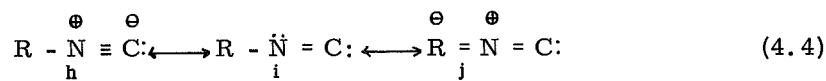
The ir stretching vibration frequencies of the isocyanogroup in chloroform have been recorded for the diisocyan-



The UV spectra of the isocyanocyclohept[b]indoles taken in benzene. For convenience the spectra of the substituted cyclohept[b]indoles have been shifted upward each time over one log unit.

biphenyls and for their photochemical isomerization products (Table 4.1). For the diisocyanobiphenyls this band is consistently found at lower wavenumbers in comparison with phenylisocyanide (2132 cm^{-1}) in the same solvent³ (ortho effect). Similar observations have been made by Ugi.⁴

In the isocyanocyclohept[b]indoles it shows up at even lower wavenumbers. This is ascribed to a relieve of triple bond character due to participation of mesomeric structures of the type j .^{2,3,4}



The importance of a contribution from such a structure is increased when the isocyano group is attached to an aromatic seven-membered ring, which may accommodate negative charge.

For 7-isocyanocyclohept[b]indole this band is found at 2119 cm^{-1} in chloroform and at 2113 cm^{-1} in carbon tetrachloride. The shift to a higher wavenumber in chloroform is likely due to hydrogen bonding of the solvent with the terminal carbon of the isocyano group.³

Charge alternation over the carbon atoms of the seven-membered ring is possibly responsible for the variation in the observed wavenumbers for the isomers.¹¹ An additional interaction with the *peri* hydrogen may account for the lower wavenumber found for 10-isocyanocyclohept[b]indole (2109 cm^{-1}).⁴

The uv spectra in benzene of cyclohept[b]indole and the isocyanocyclohept[b]indoles are given in figure 4.1. Azulenes and substituted azulenes show in the visible region of the spectrum a transition of low intensity. In apolar solvents the transition has a remarkable fine structure. This band has been considered as diagnostic for azulenes.¹² Alkyl substitution may cause a hypsochromic or bathochromic shift of the absorption band in the visible region, depending on the position of the substituent.^{13,15} Similar effects have been observed for otherwise substituted azulenes.¹² Further, uv spectra of phenyl substituted azulenes show fairly small bathochromic shifts only (of the order of a few hundred cm^{-1}), indicating that the mesomeric effect of the phenyl group is small in all positions.¹⁴ An inductive effect of the phenyl group when attached to azulene is not expected. Theoretical evaluations in terms of inductive and mesomeric effects have shown that the color alternation relative to the unsubstituted molecule is mainly due to the inductive effect

of the substituent.¹⁶ These regularities allow the following generalization. Substituents which have mainly an inductive effect upon the azulene system show either hypsochromic or bathochromic displacements of the long wavelength band, whereas substituents with a major mesomeric interaction with the azulene give rise to bathochromic shifts only.

A comparison of the spectra of fig. 4.1 clearly indicates that the isocyano substituted cyclohept[b]indoles absorb at longer wavelength than unsubstituted cyclohept[b]indole. Thus the conclusion must be that the mesomeric effect of the isocyano group predominates over the inductive effect in this transition. From a MO approach¹⁶ it has been shown that the frequency shift $\delta\nu$ with respect to the position of the equivalent absorption of the parent compound and caused by the inductive effect of the substituent obeys in a first order approximation the relation:¹⁵

$$\delta\nu = (C_{R7}^2 - C_{R6}^2) \delta\alpha_R / h \quad (4.5)$$

in which, C_{R6} and C_{R7} are the coefficients of the atomic orbitals of atom R in the highest occupied and lowest unoccupied MO of the unsubstituted molecule; $\delta\alpha_R$ is the change in Coulomb integral on atom R upon substitution of a particular substituent. If the substituent is more electronegative than the aromatic carbon R (i.e. an electron withdrawing substituent) $\delta\alpha_R$ will be < 0 ; for an electron-donating substituent (a less electronegative substituent) $\delta\alpha_R > 0$. A HMO treatment for cyclohept[b]indole gave the terms C_{R7} and C_{R6} . The deduced terms $C_{R7}^2 - C_{R6}^2$ are reported in Table 4.3.

Considering only the inductive effect of the isocyanide function ($\delta\alpha_R < 0$) one predicts upon substitution at the 6-, 8- and 10-position of cyclohept[b]indole ($(C_{R7}^2 - C_{R6}^2) > 0$) a bathochromic shift and at the 7- and 9-position a hypsochromic shift (Table 4.3.). Although not very pronounced, this trend (superimposed on the bathochromic shift, due to the mesomeric effect) is revealed by the absorptions for the isocyanocyclohept[b]indoles (Table 4.3.). The λ_{max} 518 nm observed for 7-isocyanocyclohept[b]indole versus λ_{max} 514 nm for 9-isocyanocyclohept[b]indole furnishes additional evidence for the proper assignment of products obtained upon irradiation of 2,3'-diisocyanobiphenyl (Chapter III).

Table 4.3.
UV maxima of isocyano- and amino substituted cyclohept[b]indoles ^a

	λ_{\max} (ϵ) nm	^b $C_{R7}^2 - C_{R6}^2$	^c $\Delta\nu_{\text{calc}}$ cm^{-1}	λ_{calc} nm	λ_{\max} (ϵ) observed nm	
6-isocyano	-	+ 0.194	+ 2670	440	480 (4000) ^d	6-amino
7-isocyano	518 (410)	- 0.060	- 825	522	548 (\pm 1000) ^e	7-amino
8-isocyano	523 (324)	+ 0.212	+ 2920	436	413 (625) ^e	8-amino
9-isocyano	514 (280)	- 0.038	- 520	514	575 (-) ^e	9-amino
10-isocyano	520 (380)	+ 0.160	+ 2200	450	4208 (700) ^e	10-amino
cyclohept[b]indole	500 (366)				500 (366) ^d	cyclohept[b]indole

a. For numbering see Table 4.4.

b. Coefficients obtained from HMO calculations using $k_N = 0.5$ and $k_{CN} = 1$ (see introduction Chapter III).

c. Equation 4.5.; $\delta\alpha_R/h(\text{NH}_2) = + 13750$ (ref. 16).

d. Solvent benzene.

e. Solvent CH_2Cl_2 .

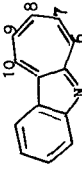
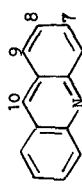
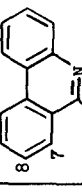
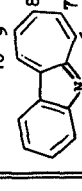
4.2.3. pK_a VALUES OF THE ISOCYANOCYCLOHEPT[B]INDOLES.

For three isocyanocyclohept[b]indoles pK_a values have been determined in methanol-water (1:1) (Table 4.4.). The values are lower than was observed for the parent compound cyclohept[b]indole. Since it is very likely that protonation occurs at the indolo-nitrogen atom, these results reveal an inductive effect of the isocyano group. How far hydrogen bonding of the solvent with the terminal carbon of the isocyano function will additionally enhance the inductive effect and consequently influence the basicity of the indolo-nitrogen atom can be hardly estimated. In this respect it should be kept in mind that hydrogen bonding diminishes mesomeric contributions of the type j (4.2.2.):

4.3.1. SPECTRA OF THE AMINOCYCLOHEPT[b]INDOLES.

The sign of the observed shifts in the uv spectra of the aminocyclohept[b]indoles is in the expected direction as can be deduced from the sign of $(C_{R7}^2 - C_{R6}^2)$ (Table 4.3.) and the sign of the Coloumb term. (Godfrey and Murrell¹⁶ reported for $-\text{NH}_2$, $\delta\alpha_R/h = + 13750$). The calculated shifts by using these figures and equation 4.5 are given in the same table. Although the agreement is rough, the trend of the values is more or less the same in the observed and calculated results. Only the 6-amino isomer seems to be ano-

Table 4.4
pK_a values

Substituent					Substituent
none	6.7	5.60 ^a	3.30 ^b	6.75	none
6-amino	7.8	4.4 ^a	6.88 ^a	-	6-isocyanato
7-amino	9.2	8.04 ^a	-	4.9	7-isocyanato
8-amino	9.7	5.88 ^a	-	4.9	8-isocyanato
9-amino	9.7	6.04 ^a	7.31 ^a	4.5	9-isocyanato
10-amino	9.3	9.99 ^a	-	-	10-isocyanato

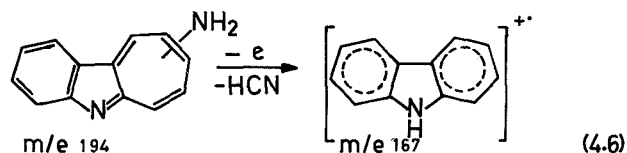
a. ref. 7.

b. ref. V. de Gacuck and R.J.W. Le Fèvre, J. Chem. Soc., 1959, 1792.

malous. It must be kept in mind, that the amino substituent is known to exert a considerable mesomeric effect, which may well invalidate a treatment by the formula 4.5. On the other hand the discussion given earlier on the role of mesomeric substituents (causing a rather small and not very different bathochromic shift) may be the reason for the agreement. A subsequent factor which is responsible for a certain imprecision in the measured values is the loss of fine structure in our compounds. The long wavelength band of 6-aminocyclohept[b]indole is not only found at an unpredicted position, but also the extinction coefficient is higher than expected and also higher than found for the other isomers. The latter are in the right order of magnitude for an azulene type transition. The anomaly of the 6-amino isomer is undoubtedly due to the interaction of the substituent with the indolo-nitrogen atom.

Not much can be said about the ir and the complex nmr spectra. It is noteworthy that 7-aminocyclohept[b]indole is unstable in dimethylsulfoxide, about the only solvent in which it is soluble to an appreciable extent (other solvents tried were deuterio-acetonitrile and deuteropyridine).

The mass spectra show the expected fragmentation into carbazole m/e 167 and so do the hydrochloric acid salts. ^{18, 19}



4.3.2. THE pK_a VALUES OF THE AMINOCYCLOHEPT[b]INDOLES.

The pK_a values for cyclohept[b]indole and aminocyclohept[b]indoles are given in Table 4.4. A comparison of the pK_a value of cyclohept[b]indole with those of phenanthridine and acridine emphasizes again the electron donating character of the seven-membered ring. The basicity of the aminocyclohept[b]indoles is in the same order of magnitude as for 2-amino- and 5-aminoacridine. Since the anti-bacterial properties of the latter have been ascribed, in part, to their high basicity ¹⁷ it would be of interest to study similar properties of the former. The lower basicity of 6-aminocyclohept[b]indole is ascribed to intramolecular hydrogen bonding and is in this respect comparable to the value observed for 1-amino-acridine ⁷ (Table 4.4).

Experimental Part.

The determinations of the pK_a values were carried out by means of a Sargent-Welch (model LS) pH meter, mechanically-stirred solutions of the bases (16-20 mg) in 50% aqueous methanol (25 ml) being titrated with 0.05 N-aqueous hydrochloric acid at 26-27°C under a stream of nitrogen; the pK_a values were read from the titration curves at half-neutralization points.

The ir spectra were obtained on a Perkin-Elmer 237B grating infrared spectrophotometer and were calibrated with polystyrene (1602 cm^{-1}). The reported values for $\nu_{N\equiv C}$ are accurate to within 3 cm^{-1} . Chloroform used as a solvent was of spectrophotometrical quality (Baker Chemical Co.).

The uv spectra were recorded on a Cary 14 spectrophotometer. Benzene or methylenechloride used as a solvent were of spectrophotometrical quality (Fisher Scientific Co.). The mass spectra were obtained on a Perkin-Elmer 270 mass spectrometer at 70 eV and 12 eV.

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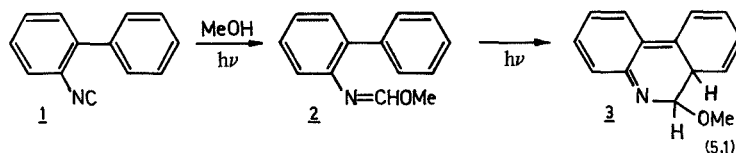
CHAPTER V

THE FORMATION OF PHENANTHRIDINE UPON IRRADIATION OF *ORTHO*-ISOCYANOBIPHENYL AND METHYL-N-(*o*-BIPHENYLYL)FORMIMIDATE

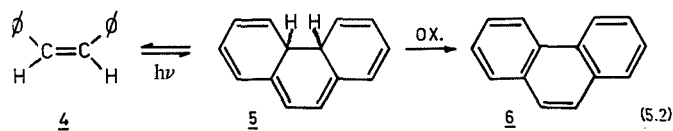
5.1. *Introduction.*

Having shown that the isocyano group on excitation behaves as a carbenoid species by inserting into the aromatic carbon-carbon bond of the adjacent phenyl ring of *o*-isocyanobiphenyls, we extended our search in order to obtain evidence of other carbenoid properties of the terminal isocyano carbon atom on excitation.

The isocyano group can easily undergo α -addition with suitable molecules HX, with or without a copper catalyst.^{1,2} It seemed therefore of interest to irradiate *o*-isocyanobiphenyl in methanol. The anticipated product would be methyl-N-(*o*-biphenyl)formimide 2.²⁴



No examples have been found in the literature in which the photosensitivity of the formimide group had been investigated. However, in analogy with the known cyclization reactions of systems containing a hexatriene skeleton subsequent formation of 3 was considered as a possibility.³ The photochemical cyclization of stilbene 4 to phenanthrene 6 in the presence of an oxidant can be considered as a representative example, in which an intermediate dihydrophenanthrene 5 has been shown to be formed.¹⁸

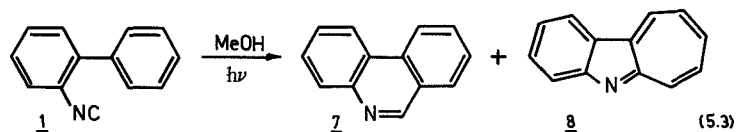


Detailed reviews of the photocyclization of stilbene type compounds have been published.⁴

5.2. Results and discussion.

5.2.1. IRRADIATION OF ORTHO-ISOCYANOBIPHENYL.

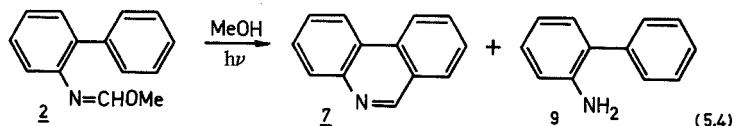
When o-isocyanobiphenyl 1 was irradiated (254 nm) in methanol for about 50 hrs, only two compounds could be isolated from the crude reaction mixture upon chromatography on silica, i. e., starting material 1 and phenanthridine 7. For both the identity was established by comparing ir spectra, gaschromatograms and tlc plates with similar data from authentic samples. The precise yields were determined gaschromatographically from a solution of 8 mmole of o-isocyanobiphenyl 1 in 400 ml of methanol, which was irradiated for 57 hrs at 254 nm. It was found that 51 percent of o-isocyanobiphenyl 1 was left and that 25 percent of the reacted starting material 1 was converted into phenanthridine 7. This conversion was monitored by ir spectroscopy with intervals of 19 hrs. The ir spectra revealed an initial formation of cyclohept[b]indole. All the bands in these ir spectra (region 1700-1300 cm^{-1}) could be assigned to either o-isocyanobiphenyl 1, phenanthridine 7 or cyclohept[b]indole 8. No absorptions were shown indicating the formation of the formimide 2. After 57 hrs of irradiation a characteristic band for cyclohept[b]indole 8 at ν 1404 cm^{-1} (str) had disappeared. (The region around this band is free from bands due to other products). The instability of cyclohept[b]indole 8 in methanol toward prolonged irradiation was confirmed by irradiating cyclohept[b]indole 8 in methanol independently. The formation of phenanthridine or acridine could not be detected.⁹ Evidently cyclohept[b]indole 8 is not an intermediate in the transformation of o-isocyanobiphenyl 1 into phenanthridine 7.



While no formimide 2 was detected as an intermediate during the transformation of 1 into 7, irradiation of the formimi-

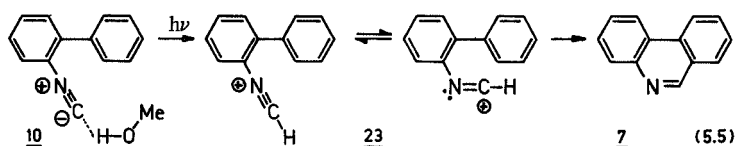
date 2 under similar conditions in methanol gave besides recovered starting material 2, phenanthridine 7 and o-aminobiphenyl 9 as was revealed by comparing ir spectra and gaschromatograms of the crude reaction mixture with similar data of authentic samples.

(The formimidate was prepared according to a general method described by Roberts⁴ in a yield of 55.4 percent, while a side product N,N'-bis-(o-biphenyl)formamidine was obtained in a yield of 19.6 percent; see experimental part)



Since o-aminobiphenyl 9 was not found as a product in the reaction mixture from irradiated o-isocyanobiphenyl 1 these results furnish additional evidence against the formimidate to be an intermediate in the transformation of 1.

In rationalizing these results it was realized that phenanthridine might have been formed by a direct insertion of the isocyano carbon into the C-H bond of the adjacent phenyl ring. This would parallel the C-C insertion of the isocyano group upon irradiation of o-isocyanobiphenyl in cyclohexane. Alternatively a mechanism was considered in which protonated isocyanide 23 is the key compound (5.5). Isocyanides are known to form "strong" hydrogen bonds* with the terminal carbon atom.⁵



The latter mechanism would give rise to the formation of deuterated phenanthridine upon irradiation of o-isocyanobiphenyl in methanol-d. Direct insertion, however, would of course not give any incorporation of deuterium from methanol-d. Alternatively an intermediate 23 may react with the solvent to the formimidate 2.

A ground state intermediate like 23 is very probably operating in the hydrolysis of o-isocyanobiphenyl to o-N-formyl-

*A $\Delta\nu$ of 127 cm^{-1} (ir spectrum) measured from the free peak of methanol at 3635 cm^{-1} and hydrogen bonded methanol to 1 is in agreement with the values reported for other isocyanide-alcohol systems.⁵

minobiphenyl in analogy with the established hydrolysis mechanism of *tert*-butylisocyanide.¹⁷ Upon shaking an ether solution of the isocyanide with 2N-hydrochloric acid, no phenanthridine had been formed, as was shown after basifying and gc analysis of the residue of the ether layer.

A solution of *o*-isocyanobiphenyl (6 mmole) in 400 ml of methanol-d was irradiated for 64 hrs at 254 nm. Column chromatographic separation of the residue on silica gave 53.6 percent of unreacted isocyanide 1. From the reacted amount (46.4 percent), 29.1 percent was found to be converted into phenanthridine and 8.2 percent into cyclohept[b]indole. The ir spectrum of the purified phenanthridine indicated deuterium incorporation (ν_{C-D} 2220 cm^{-1}). This was confirmed by nmr spectroscopy and mass spectroscopy. The nmr spectrum revealed incorporation of deuterium at the 6-position (δ 9.22).⁷ Comparing integrated nmr peak areas for H-6 and H-1,10 in samples of authentic phenanthridine with product partially deuterated at the 6-position gave a ratio $D/H = 1.23 \pm 0.16$. In addition the isotope ratio was determined from mass spectra. A plot of peak heights for " M^{\oplus} " at m/e 180 versus m/e 179 obtained from a solid sample gave a straight line with a slope of 1.23, which after natural abundance isotope correction gave a ratio $D/H = 1.09$. Combining the data, somewhat over 50 percent deuterium incorporation was found.

Under otherwise identical conditions, the isocyanide gave a higher yield of phenanthridine and a lower yield of cyclohept[b]indole when partially converted by irradiation over a short period in methanol rather than in methanol-d. After irradiation for 2.0 and 3.5 hrs in each solvent, the amount of phenanthridine formed in methanol averaged 1.65 ± 0.07 times the amount formed in methanol-d. In the same experiment the amount of cyclohept[b]indole was increased about three fold in methanol-d. Further it was found that the loss of starting material is roughly the same in methanol and methanol-d (Table 5.1).

The results, described in the last paragraphs, indicate at least that another mechanism than a direct insertion is operating. A mechanism consistent with the data is the following:

Table 5.1.1. Irradiation of o-isocyanobiphenyl in methanol and methanol-d.^a

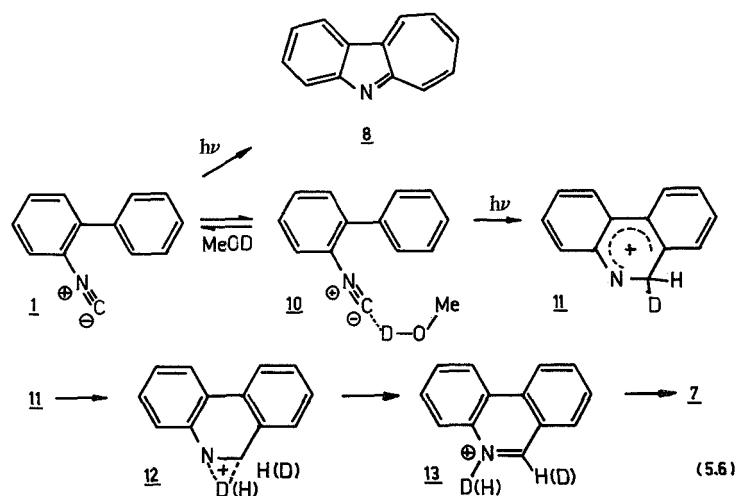
solvent	o-isocyanobiphenyl conc (mM) t = 0	irr. time (hrs)	b phenanthridine yield (dup.) %	c cyclohept[b]indole area OC yield	d o-isocyanobiphenyl unreacted OC area
MeOH	23.85	2	4.9 (5.0)	100	447
MeOH	23.30	3.5	8.9 (9.0)	125	393
MeOD	24.40	2	3.0 (3.0)	270	475
MeOD	23.00	3.5	5.2 (5.2)	500	400

a. The conversion into phenanthridine and cyclohept[b]indole was determined by gaschromatography with disc integration.

b. Based on the initial amount of starting material; determined with absolute calibration method (reproducibility 2 to 3 percent).

c. Triangulation method (mm², reproducibility 7 to 10 percent).

d. Disc integration (reproducibility better than 3 percent) (see experimental part).



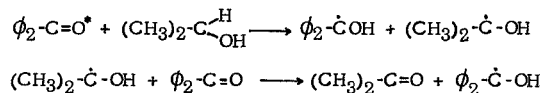
For partial substitution of hydrogen by deuterium in the 6-position of phenanthridine, solvent participation, presumably by hydrogen bonding to the excited isocyanide 1, is required.⁵ Since the predominant isomerization in the absence of hydrogen bonding transforms 1 into 8, it is assumed that cyclization must be concerted with or follow initial hydrogen bonding.* Further, C-H bond formation at carbon with simultaneous bond breaking from oxygen of the methanolic hydrogen (deuterium) apparently controls the faster formation of phenanthridine in methanol. Hydride transfer, concerted with or following cyclization, generates a required intermediate 11 from which hydrogen and deuterium compete for separation from the same ring carbon atom.

Dissociation of hydrogen (deuterium) could lead directly to phenanthridine; however, isomerization into a weaker conjugate acid of phenanthridine by transferring a proton (deuteron) to the adjacent nitrogen would be expected and is supported by the isotope ratio for the product. The low value of 1.09 or 1.23 is in agreement with a non-linear transition state 12 for an intramolecular transfer.¹⁰ Dissociation of the conjugate acid 13 gives phenanthridine 7.

In the foregoing discussion it was assumed tacitly, that the hydrogen found at the 6-position in phenanthridine, when 1 was irradiated in methanol-d, originates from the adjacent phenyl ring and not from the solvent. This raises directly the question whether an ionic- or radical mechanism is operating, since in the latter case hydrogen from the CH₃ group of

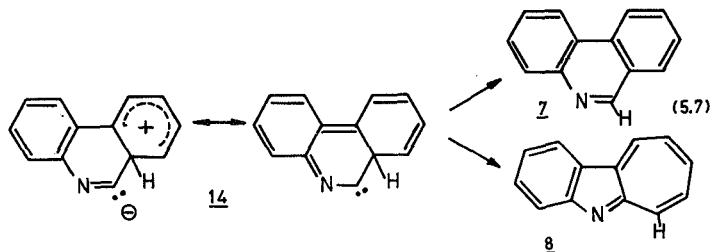
*Indole could not be detected in the unidentified product mixture obtained by the irradiation of o-tolyl isocyanide in methanol. The apparent inability for isocyano carbenoid insertion into a C-H bond of the adjacent methyl group tends to confirm the absence of cyclization from 1 by isocyano carbenoid insertion into the ortho C-H bond.

methanol is expected to be introduced. In an ionic mechanism O-D breakage is favored over C-H breakage, whereas for homolytic bond breakage an energy of 92 kcal/mole¹² is required for H-CH₂OH and 102 kcal/mol for H-OCH₃.¹³ An example illustrating the preferred C-H breakage is found in the photoreduction of, e.g., benzophenone in isopropylalcohol.¹⁹



The preferred ionic mechanism is supported by not finding glycol.¹¹

Alternatively cyclization of o-isocyanobiphenyl prior to solvent participation would lead to an intermediate carbene 14 (5.7). The carbene might stabilize in several ways, either directly to phenanthridine 7 or to cyclohept[b]indole 8. A competitive solvent participation in the formation of phenanthridine from 14 would eventually explain the partial deuterium incorporation; however, less obvious in such a description is that (almost) no phenanthridine was found on irradiation of o-isocyanobiphenyl in cyclohexane (Chapter II).



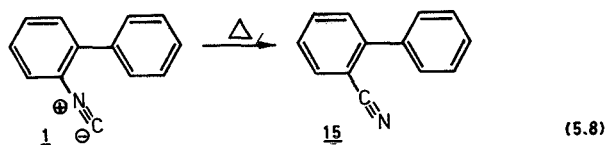
The relative differences in the rate of formation of products are ascribed to interaction of the isocyanide with the solvent, apparently via hydrogen bonding.⁵

5.2.2. THERMAL ISOMERIZATION OF ORTHO-ISOCYANOBIPHENYL.

A hot ground state¹⁶ has been considered to be responsible for either the formation of cyclohept[b]indole or phenanthridine from o-isocyanobiphenyl upon irradiation at 254 nm in either

cyclohexane or methanol. The behavior of *o*-isocyanobiphenyl was therefore investigated at elevated temperatures in a protic and a non-protic solvent.

Using diphenylether as the solvent, *o*-isocyanobiphenyl was rapidly converted quantitatively into *o*-cyanobiphenyl 15 (5.8).



Such a rearrangement is not new and has been extensively studied for similar systems by Rabinowitch¹⁴ and Casanova.¹⁵ When glycol was used as the solvent, the rearrangement is apparently not the only process. Besides *o*-cyanobiphenyl, *o*-aminobiphenyl and *o*-formamidobiphenyl could be detected (See experimental part).

Since no phenanthridine nor cyclohept[b]indole was formed at elevated temperature (in boiling glycol about 200°C, and boiling diphenylether about 260°C) it is believed that a hot ground state is not involved in the isomerization of *o*-isocyanobiphenyl into 8 or 7 on excitation. Of course it is realized that even higher vibrational groundstate levels may be involved. But these are apparently not reached under the applied conditions.

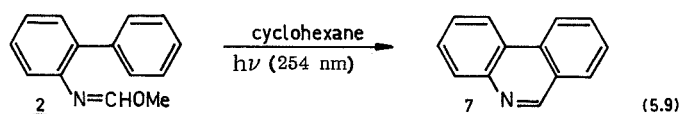
5.2.3. FORMATION OF PHENANTHRIDINE UPON IRRADIATION OF METHYL-N-(*o*-BIPHENYLYL)-FORMIMIDATE.

When methyl-N-(*o*-biphenyl)-formimidate 2 was irradiated in methanol at 254 nm, two products were detected, and identified, i. e., phenanthridine and *o*-aminobiphenyl (5.4). Several lines of evidence were obtained to exclude the formation of phenanthridine through the intermediate formation of *o*-isocyanobiphenyl, i. e., α -elimination of methanol and subsequent isomerization. Irradiation of the formimidate in methanol-d afforded no phenanthridine-6-d. The ir spectrum of the isolated phenanthridine did not show a characteristic C-D band at 2220 cm⁻¹, neither did a mass spectrum indicate any deuterium incorporation. This observation furnished evidence that phenanthridine does not exchange deuterons (protons) with the solvent (methanol-d) and also that the formation of phenanthridine here follows a quite different route.

Support for a different mechanism is also found in the following observations.

a. When irradiation of the formimidate in methanol was stopped, the solution had adopted a red color, which vanished gradually within twenty-five minutes. The red color could be regenerated by exposure to 254 nm light.

b. A solution of the formimidate (8.4 mmole) in cyclohexane (500 ml) was irradiated under a stream of nitrogen for 37.5 hrs at 254 nm. The yield was determined by gaschromatography with disc integration. It appeared that 47.1 percent of the formimidate was lost, which was quantitatively converted into phenanthridine.

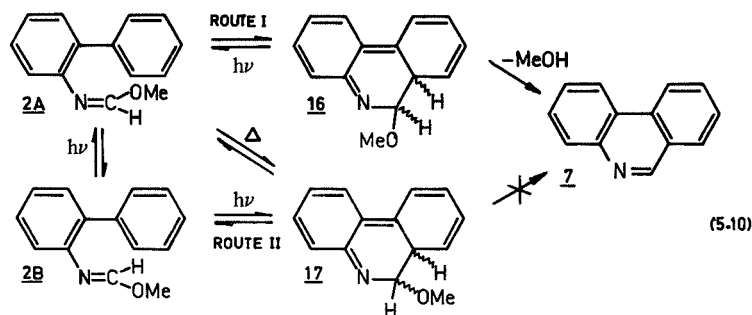


The conversion in cyclohexane was monitored by gaschromatography with disc integration for solutions of equal concentration and identical conditions under nitrogen and oxygen. The results are depicted in fig. 5.1 and fig. 5.2.

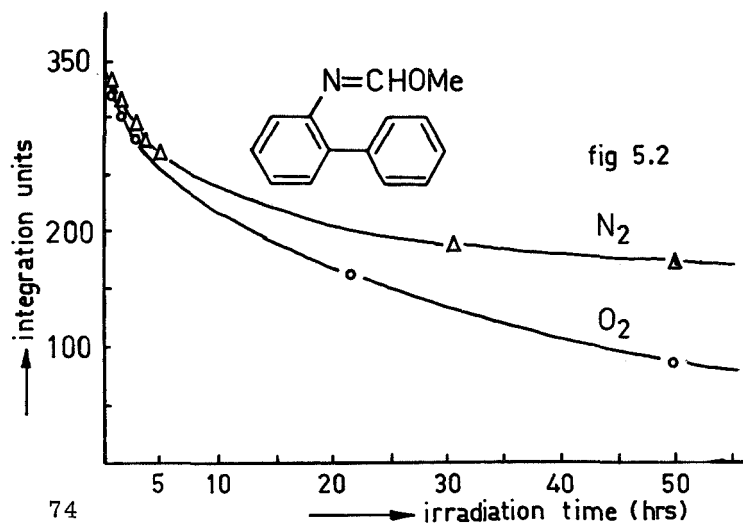
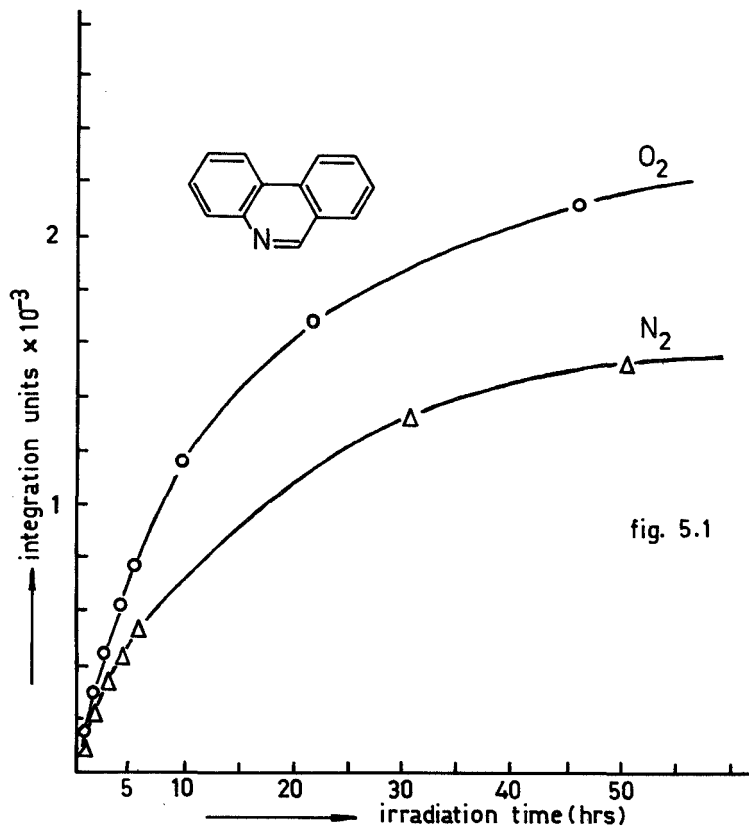
The graphs show clearly the faster reaction under oxygen.*

c. A solution of the formimidate in diphenylether was heated for 17 hrs under reflux (temp. 260-270°). Analysis of the cooled solution by glc with disc integration revealed that no starting material was lost.

A mechanism consistent with these data is the following (5.10),

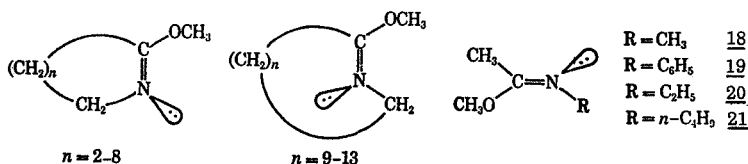


*These graphs are similar to the graphs obtained by irradiation of o-isocyanobiphenyl in cyclohexane under oxygen and nitrogen (Chapter II). There, the difference is ascribed to coating of the glass wall. This was not observed in the irradiation of the formimidate in cyclohexane. Moreover the quantitative conversion tends to eliminate that these differences are due to unknown material, absorbing a high percentage of the light, formed by irradiation under N₂.



Two geometrical isomers of formimidates have to be considered, i.e., the *anti* isomer 2A and the *syn* isomer 2B.

Moriarty et al. have recently published a configurational study on O-methyl imidates.²⁰ NMR data have been reported for members of the series of cyclic O-methyl imidates from ring size five to sixteen as well as for four open chain derivatives 18-21.



From these data, together with the results obtained from a nmr study of their conjugated acids, it has been deduced that the *anti* isomers for 18-21 are configurationally stable. Moreover, nmr spectra of 18 and 19 were found to be invariable with temperature over a range of -100 to 120°C, which could indicate a high barrier (> 23 kcal mole⁻¹). A chemical shift of $\delta = 3.73$ ppm was found for O-CH₃ in 19, whereas 18 showed a shift for O-CH₃ of $\delta = 3.50$ ppm. The difference of 0.23 ppm results from the diamagnetic shielding due to the anisotropy of the phenyl in the configuration drawn in 19.

A nmr spectrum of methyl-N-(o-biphenyl)formimide in chloroform at 40°C showed only one absorption for the protons of the methoxy function at $\delta = 3.73$, indicating that under these conditions only one isomer is present. We have not studied the temperature dependence of the nmr spectrum for this formimide. However, it is conceivable that the formimide possesses the *anti* configuration 2A in analogy with the O-methyl imidates.

Photocyclization of the *anti*-isomer would proceed according to the Woodward Hoffmann rules (assuming that these are valid for hetero-atomic systems) in a conrotatory manner.¹⁸ The expected intermediate in the formation of phenanthridine is the cyclization product 16, in which the leaving groups, H and OMe, are *trans* to each other. Supporting evidence for the formation of such an intermediate is found in the phenomenon described under a. Similar observations have been made upon irradiation of stilbenes²¹ and 1,2-di-(3-thienyl)ethene.^{4c} The color has been ascribed to the quinoid dihydro-cyclization products. The disappearance of the color has been ascribed to thermal or photochemical reversion into starting materials.²²

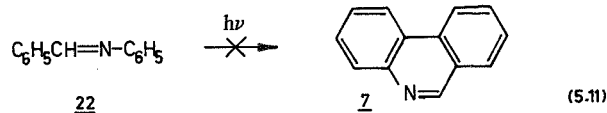
From the results upon irradiation of the formimidate under oxygen and nitrogen under identical conditions it is deduced that photocyclization is not the only process. From the fact that oxygen does not quench the reaction (5.10), the formation of phenanthridine probably does not proceed via a triplet. A competing process gradually suppresses the formation of phenanthridine under nitrogen. This process, in which apparently a triplet is involved, occurs to a lesser extent in the presence of oxygen and is probably a photochemical isomerization of the *anti* isomer into the *syn* isomer in analogy with the well known *trans-cis* (or *cis-trans*) isomerization of stilbene.²³ Upon prolonged irradiation a photostationary state will be reached.

Photocyclization of the *syn*-isomer would give in a conrotatory manner¹⁸ the cyclization product 17, in which the leaving groups are *cis* to each other. Elimination of methanol in forming phenanthridine is at best expected to be less favored in comparison with the isomer 16 in which the leaving groups are *trans* to each other. Moreover, there is evidence that phenanthridine is not formed at all by route II.

Thermal cyclization of the formimidate is expected to proceed in a disrotatory manner¹⁸ according to the Woodward-Hoffmann rules. The expected cyclization product of the *anti* formimidate over a long period of time in boiling diphenylether did not produce any phenanthridine. In fact the formimidate did not give any product (experiment described under c). This in itself is evidence for the correct assumption that the prepared formimidate possesses the *anti*-configuration.

In summarizing these results it is concluded that upon irradiation of the formimidate in cyclohexane two main processes are competing. First there is the cyclization to 16 with subsequent elimination of methanol. The cyclization apparently proceeds via a singlet state. Second, a triplet induces isomerization of the *anti* formimidate into the *syn* isomer from which conceivably no phenanthridine is formed. It is not impossible that phenanthridine built up along route I (5.10) sensitizes the isomerization of the *anti* isomer into the *syn* isomer. By irradiation under oxygen the isomerization of the *anti*-isomer may be less efficient by triplet quenching.

This picture accommodates very well the assumed high inversion barrier of the *anti* isomer into the *syn* isomer. A low barrier would not enhance product formation by oxygen quenching of the *anti-syn* isomerization (it is assumed that the *anti* isomer is thermodynamically favored). An example of a low inversion barrier has been found in anils.²⁵ Irradiation of anil under oxygen did not produce any phenanthridine.



It has been shown that the *cis-trans* isomerization of anil is extraordinarily fast, the half life of the *cis* isomer being about 1 sec at room temperature;^{26,27} thus, although *trans*-(22) is known to undergo photo isomerization to *cis*-(22), the photostationary *cis/trans* concentration ratio has been found to be extremely small except at low temperature.

More data are required to substantiate the proposed mechanism, which is based mainly on well known and established phenomena. The fact that no 6-methoxyphenanthridine was found might indicate the favored methanol elimination from 16 over the loss of two hydrogen atoms by oxidation. However it is alternatively quite well possible that route II (5.10) is not involved at all.

A comparison of the bond strengths of $\text{H}-\text{CH}_2\text{C}_6\text{H}_5$ and $\text{C}_6\text{H}_5\text{CH}_2-\text{OCH}_3$ reveals that homolytic bond cleavage of methoxy is favored over hydrogen cleavage (bond strength $\text{C}_6\text{H}_5\text{CH}_2-\text{H} = 85$ kcal/mole, bond strength $\text{C}_6\text{H}_5\text{CH}_2-\text{OCH}_3 = 66$ kcal/mole).² If these data are applicable to an intermediate like 16, the absence of the formation of 6-methoxyphenanthridine can be understood. The higher yield under oxygen is then explained by oxidation of 16. It is hoped that the proposed mechanism will serve as a valid working-hypothesis for further experiments.

Experimental Part.

IR spectra were obtained on a Perkin-Elmer 237B grating infrared spectrophotometer. NMR spectra were obtained on a Varian A 60, a spectrometer working at 60 Mc/sec, with tetramethylsilane as an internal standard. The chemical shifts are reported in ppm in the δ scale, the tetramethylsilane peak is defined as $\delta=0$. UV spectra were recorded on a Cary 14 spectrophotometer. Hexane or methanol of spectrophotometric quality, supplied by J.T. Baker Chemical Co., was used as solvent. Mass spectra were obtained on a Perkin Elmer 270. Gas chromatographic analysis were carried out on a Barber Coleman Flame Ionization Gas chromatograph model 5320 using a $8 \times \frac{1}{4}$ stainless steel coil packed with 5% Ge-Xe-60 on Chromasorb-G, 60-80 AW DMGS (supplied by Nuclear Chicago), with nitrogen as carrier gas. The column temperature in the experiments was 210-220°C. A flow rate of 60-70 ml min⁻¹ was used. The temperature of the injection port was about 250°C and of the detector about 280°C. The retention time for phenanthridine was about 6-6.5 min. Conditions throughout one experiment were kept constant. For column chromatography silicagel (Baker analyzed, J.T. Baker Chemical Co) was used. The irradiations were carried out in a Rayonet RPR 100 photochemical chamber reactor (Southern New England Ultraviolet Co.) equipped with 16 low-pressure mercury 2537 Å lamps. Cyclohexane (Baker, spectro grade) used as an irradiation medium, was always distilled from lithiumaluminum hydride straight into the quartz irradiation tube. Methanol was treated with magnesium activated by iodine and distilled.²⁸ The deuterated methanol was used without further purification (Diaprep Inc. supplied CH₃OD with a minimum of 99 percent isotope purity) but was checked on its purity by nmr spectroscopy (better than 99 percent). Solutions, when irradiated under nitrogen (Matheson, high purity grade) were degassed with a heavy stream of nitrogen previous to irradiation. The nitrogen was dried over Molecular Sieves and Drierite. Elemental analysis were carried out by Micro-Tech Laboratories Inc., Skokie, Illinois, U.S.A. Melting points and boiling points are uncorrected. Melting points were determined in a silicone oil-bath unless otherwise stated.

PHENANTHRIDINE-6(5H)-THIONE.²⁹

A mixture of 5.6 g (0.034 mole) of phenanthridine-6(5H)-one (Aldrich Chemical Co.), 10 g of phosphorus pentasulfide and 100 ml of pyridine was heated under reflux for two hrs. The reaction mixture was poured into 300 ml of water and the precipitated yellow solid was separated by filtration, washed thoroughly with water and recrystallized from aqueous dimethylformamide. The yield was 5.2 g (72.5 percent), mp. 280-282.5 (lit.²⁹ mp 281-283°; lit.²⁹ yield 94 percent)

PHENANTHRIDINE²⁹.

A mixture of 1.5 g (0.0070 mole) of Phenanthridine-6(5H)-thione, 6 g of Raney-Nickel (weighed wet) (W.R. Grace and Co., So. Pittsburg Tenn., Raney active catalyst no. 28) 15 ml of dimethylformamide and 15 ml of ethanol was heated under reflux for two hours. The slightly yellow solution was filtered and the filtrate acidified with hydrochloric acid and evaporated to dryness under reduced pressure. The residue was recrystallized from acetone-water giving 720 mg (56.6 percent) of phenanthridine mp 99-101°C (lit.²⁹ 106°C). Yield lit. 95 percent. Phenanthridine purified by sublimation gave a mp 103.5-105°.

IRRADIATION OF ORTHO-ISOCYANOBIPHENYL IN METHANOL.

A solution of 1.410 g (8.0 mmole) of o-isocyanobiphenyl was irradiated in methanol for

57 hrs at 254 nm under nitrogen. Aliquots were taken at intervals of 19 hrs. IR-spectra of the residues in chloroform revealed upon comparison with authentic materials the formation of phenanthridine and cyclohept[b]indole. Characteristic absorptions from cyclohept[b]indole had disappeared after 57 hrs of irradiation. The yield of phenanthridine and the amount of remaining starting material were determined by gaschromatography with disc integration. The yield of phenanthridine was determined by using an absolute calibration method, 51.0 percent, whereas the amount of starting material was determined by using phenanthridine as an internal standard, 24.8 percent. Additional to the detection of phenanthridine by ir and glc, its formation was confirmed by tlc.

IRRADIATION OF ORTHO-ISOCYANOBIPHENYL IN METHANOL-D.

A solution of 1.104 g (6.2 mmole) of o-isocyanobiphenyl in 400 ml of methanol-d was irradiated for 64 hrs at 254 nm under a stream of nitrogen. The methanol-d was distilled off and the residue chromatographed on silica. Eluted with n-hexane-benzene (2:3) was 592 mg (53.6 percent) of starting material, identified by ir spectroscopy. With benzene-chloroform (3:1) was eluted impure partly deuterated phenanthridine 149 mg (29.1 percent corrected for recovered starting material). Its ir spectrum was identical to an ir spectrum of authentic material except for an additional band at 2220 cm^{-1} , ascribed to a C-D stretching vibration mode. The deuterium incorporation was confirmed by the nmr and the mass spectrum of the purified material. Phenanthridine (partly deuterated) sublimed ($85\text{-}90^\circ$, 0.1 mm) as a colorless solid mp and mixture mp $103.5\text{-}105^\circ$ (lit.⁷ 104°); ir CHCl_3 : 2220 cm^{-1} (C-D); nmr (CDCl_3): δ 9.22 (s, 0.5, H-6); 8.50 (m, 2, H-1, 10) and 8.28 to 7.45 (m, 6). (lit.⁷ δ 9.06 (s, H-6), 8.43 (m, H-1,10).

From the nmr spectrum of an authentic sample of phenanthridine was found H-6/H-1,10 0.98/2.0. For the product partially deuterated at the 6-position was found H-6/H-1,10 = 0.44/2.0. The ratio $(0.98-0.44)/0.44 = \text{D-6/H-6} = 1.23 (\pm 0.16)$.

Spectra were taken from the partly deuterated sample and from an authentic sample at about equal concentration at similar setting of the instrument (Varian A-60). For each sample H-6 was integrated 8 to 10 times and compared with the integration for H-1,10. In addition the isotope ratio was determined from mass spectra. At the applied low ionization potential (12 eV) no fragmentation was observed. A plot of peak heights for M^+ at m/e 180 versus m/e 179 obtained from the solid sample gave a straight line with a slope of 1.23, which after natural abundance isotope correction gave a ratio D/H = 1.09. The slope was determined from 13 points by a TR 4 computer using the method of least squares. An isotope correction for m/e 180 due to M "179" for thirteen carbon atoms and one nitrogen was made. Only a very small peak was additionally observed in the mass spectrum at m/e 178 (12 eV, relative intensity 5), and is ascribed to the loss of hydrogen from undeuterated, and deuterium from partly deuterated, phenanthridine. No correction was made for the loss of hydrogen from the deuterated molecule. But if m/e 178 is due to a mainly random fragmentation of hydrogen from the undeuterated molecule a correction should be made on m/e 179 for the random loss of hydrogen from phenanthridine-6-D. The correction is than less than five percent.

Finally 42 mg of cyclohept[b]indole (8.2 percent, corrected for recovered starting material) was eluted with chloroform and characterized by ir spectroscopy.

IRRADIATION OF CYCLOHEPT[b]INDOLE IN METHANOL.

A solution of 55 mg (0.30 mmole) of cyclohept[b]indole in 450 ml of methanol was irradiated under nitrogen at 254 nm. The loss of cyclohept[b]indole was monitored by uv spectroscopy by taking aliquots after 1, 2, 5, 8 and 24 hrs. The reacted quantities of cyclohept[b]indole amounted to 2, 4, 7.5, 11.3 and 95 percent respectively. After 24 hrs of

irradiation the solvent was removed and the residue was dissolved in 5 ml of chloroform. Gaschromatographic analysis at high attenuation of a 2 μ l sample (Hamilton syringe) did not indicate the formation of any phenanthridine. A solution of 1.65 mg phenanthridine in 5 ml chloroform was prepared. After injection of 0.1 μ l of this solution phenanthridine could just be detected at the same high attenuation. This means that if any of the cyclohept b indole was converted into phenanthridine, it must be less than 0.08 mg (1.5%).

IRRADIATION OF ORTHO-ISOCYANOBIPHENYL IN METHANOL AND METHANOL-D.

Solutions of o-isocyanobiphenyl in either methanol or methanol-d were prepared by dissolving a known amount in 50 ml of solvent (volumetric flask) (Table 5.1). Samples of 10 ml from these solutions were pipetted into small quartz tubes (I.D. 15 mm) and degassed on a vacuum-line, in freeze-thaw cycles using liquid nitrogen, up to a pressure of 2 microns. A three-way stopcock connected the sample tubes to the vacuum line and also served in keeping the vacuum during the irradiation. The samples in duplicate were put in a merry-go-round assembly and irradiated for 2 and 3.5 hrs.

After the irradiation the samples were analyzed by gaschromatography, injecting undiluted quantities of 3 μ l with a 10 μ l Hamilton syringe. o-Isocyanobiphenyl, phenanthridine and cyclohept b indole were found to have retention times of resp. 2 min 44 sec, 6 min 20 sec, and about 16 minutes. Identification of the peaks was achieved by enriching irradiated samples with authentic materials. No other products could be detected from the solutions upon concentrating, either by ir or by tlc or by glc at low attenuation. For suitably recording of o-isocyanobiphenyl use was made of an attenuation ten times the one used for phenanthridine and cyclohept[b]indole. The yields for phenanthridine were quantitatively determined by comparing the integrated area with the area of samples with known concentration. Each solution was injected two or three times and each time all compounds were recorded. The average of these integrations was taken as being representative for the actual concentrations (reproducibility of 2 to 3 percent). The integrated area for o-isocyanobiphenyl was obtained by measuring the sharp symmetrical peak for o-isocyanobiphenyl and by neglecting the long flat tailing (about 30 percent of the area of the sharp peak, found in the photochemical samples as well as in unirradiated authentic solutions). The tailing was apparently caused by o-cyanobiphenyl because it cuts off sharply after the retention time for o-cyanobiphenyl (4 min). The reported average values found were reproducible within 3 percent. The area for cyclohept[b]indole was determined by using the triangulation method. The reproducibility is within 7 to 10 percent due to the low intensity of the peak and the uncertainty in determining the width (2.5 min).

THERMAL REARRANGEMENT OF o-ISOCYANOBIPHENYL, INTO o-CYANOBIPHENYL IN DIPHENYLETHER.

Two experiments have been done.

I. In a 50 ml round bottomed flask with a reflux condenser a solution of 1.79 g of o-isocyanobiphenyl in 10 ml diphenylether was heated under reflux for 16 hrs. From the cooled crude reaction mixture only $\text{-C}\equiv\text{N}$ (2227 cm^{-1}) could be detected either by ir or glc. Pure o-isocyanobiphenyl in low yield was obtained after distilling off most of the diphenylether under reduced pressure. However some of the product co-distilled. Only 180 mg of material was obtained from the residue (about 1 ml diphenylether was left) after chromatography over silicagel. The remaining diphenylether was removed by eluting it with n-hexane. The product, o-cyanobiphenyl, was eluted with n-hexane-benzene (4:1). This fraction yielded upon concentration a stickily colorless residue, from which upon cooling (dry ice-acetone), adding

some n-hexane-benzene and scratching colorless needles were obtained: 35.5-36.5° [lit. 30,31 mp 36°]; ir (CHCl₃) 2227 cm⁻¹ (C≡N).

II. This time 500 mg of o-isocyanobiphenyl was heated under reflux for 3 hrs in diphenyl-ether. The cooled reaction mixture was diluted with chloroform in a volumetric flask to 50 ml. The yield of o-cyanobiphenyl was calculated from the integrated area's of gaschromatograms. In comparing the area of a known injected amount of the reaction mixture (1 μl; 675 integration-units) with a known amount (1 μl) of a solution with known concentration of o-cyanobiphenyl (40 mg/5 ml; CHCl₃ 540 integration-units) a conversion of 100% was calculated. (Retention time o-cyanobiphenyl: 4 min 12 sec).

THERMAL REARRANGEMENT OF ORTHO-ISOCYANOBIPHENYL IN GLYCOL

A solution of 505 mg (2.8 mmole) of o-isocyanobiphenyl in 10 ml of glycol (purified by distillation bp 194° [lit. 32 197°]) was heated under reflux for 3 hrs. After cooling 30 ml of benzene were added and the solution was shaken with an aqueous solution of 2N NaOH. The combined aqueous solution were washed several times with benzene and the combined benzene solutions dried (Na₂SO₄) and concentrated. An ir spectrum (CHCl₃) of the crude reaction mixture showed by comparing with authentic materials: absorptions, likely due to three products, IR (CHCl₃) 3450 and 3370 (amine N-H), 1690 (C=O), 2220 cm⁻¹ (C≡N), a) o-aminobiphenyl, b) o-formamidobiphenyl, c) o-cyanobiphenyl. This was confirmed by glc product analysis. Retention times resp. a, b, c: 2 min and 48 sec, 9 min and 40 sec, 4 min and 12 sec.

METHYL-N-(o-BIPHENYLYL)-FORMIMIDATE (2).

The formimide 2 was prepared according to a general procedure described by Roberts³ for the preparation of, e.g., ethyl-N-phenyl-formimide from ethyl orthoformate and aniline.

To a solution of 59.2 g (0.35 mole) of o-aminobiphenyl (Pfaltz and Bauer Chemical Company) in 74.2 g (0.70 mole) of methyl orthoformate (Aldrich Chemical Company) was added 2.6 g (0.012 mole) of o-aminobiphenyl hydrochloride. The reaction mixture was heated at reflux temperature for one hour. Initially a heavy precipitate formed, which on heating dissolved. Methanol was then slowly distilled off, bp 64-66° (28 ml in 2 hours). Anhydrous potassium carbonate was added to the cooled reaction mixture and the mixture was shaken and allowed to stand for two hours. A precipitate was collected in a Büchner funnel and washed with n-hexane. The filtrate was concentrated in the rotary evaporator. The residue (54.2 g) was distilled, yielding 41.2 g (55.4 percent) of the formimide 2; bp 110-111°/0.2 mm; n_D²² 1.6055; uv (cyclohexane) 238 nm (ε 16350), 278 nm inflection point (ε 4500); ir (CHCl₃) 1650 cm⁻¹ (-N=CHOCH₃), 1245 and 1186 cm⁻¹ (only the very strong bands are reported); nmr (CDCl₃) δ 7.6-6.6 [m, 10 (aromatic protons and vinylic protons)], 3.72 [s, 3 (CH₃)].

Anal. Calcd for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63; mol wt 211.26. Found: C, 80.75; H, 6.14; N, 6.73.

The precipitate (vide supra) was treated with benzene. The inorganic material was filtered off and the organic solution yielded 12.0 g of N,N'-bis-(o-biphenyl)-formamidine, which was recrystallized several times from benzene. The yield was 19.6 percent, mp 157.5-159°.

Anal. Calcd for C₂₅H₂₀N₂: C, 86.17; H, 5.79; N, 8.04; mol wt 348.45. Found: C, 86.44; H, 5.70; N, 7.90.

IRRADIATION OF THE FORMIMIDATE IN METHANOL.

A solution of 1.60 g (7.6 mmole) of the formimide in 400 ml of methanol was irradiated for 37.5 hrs under a stream of nitrogen at 254 nm. A glc analysis of the crude reaction mixture revealed the formation of phenanthridine and o-aminobiphenyl. Under the conditions employed, some doubt arose as far as the identity of o-aminobiphenyl was concerned since the retention time was about the same as for o-isocyanobiphenyl: 2 min 19 sec; retention time 2-isocyanobiphenyl: 2 min 20 sec.

Ir-analysis and a tlc plate confirmed however the formation of o-aminobiphenyl and excluded o-isocyanobiphenyl for which in the ir spectrum a band around 2125 cm^{-1} was expected. Chromatography of the reaction mixture did not bring about a good separation of o-aminobiphenyl and phenanthridine, eluted with benzene chloroform (1:1).

None of the formimide could be recovered in this way. Apparently it was hydrolyzed on the silica to the corresponding amine. No other product has been isolated or detected by ir or tlc analysis.

IRRADIATION OF THE FORMIMIDATE IN METHANOL-d.

A solution of 1.54 g of the formimide was irradiated at 254 nm for 21 hrs ("degassed" with nitrogen).

Analysis of the crude reaction mixture by ir spectroscopy, tlc, gas chromatography and mass spectroscopy revealed the formation of phenanthridine besides some 2-aminobiphenyl. The mass spectrum did not show additional abundance for m/e 180 but the natural isotope abundance for M 179 (12eV spectrum). The mass spectrum was obtained via a gas chromatograph connected with the Perkin Elmer model 270 mass spectrometer, using a GE-XE-60 10% nitrile gum column (stainless steel coil). The ir spectrum of a concentrated solution of the crude reaction mixture in CHCl_3 did not show absorption at 2220 cm^{-1} .

IRRADIATION OF THE FORMIMIDATE 2 IN CYCLOHEXANE.

A. A solution of 1.770 g (8.4 mmole) of the formimide 2 in 500 ml of cyclohexane was irradiated for 37.5 hrs under a stream of nitrogen at 254 nm. Gas chromatographic analysis (absolute calibration method) revealed a loss of 835 mg (47.1 percent) of starting material. By using the same method a yield of 685 mg of phenanthridine was determined (97 percent; corrected for unreacted starting material).

B. Of two solutions of 2.10 g (10.0 mmole) formimide 2 in 400 ml of cyclohexane one was irradiated under a stream of oxygen and the other one under nitrogen at 254 nm. Samples were taken at certain time intervals. The conversion into phenanthridine as well as the remaining formimide was determined by gas chromatography with disc integration for each sample. The results are depicted in figure 5.1 and 5.2 in which the integration units (proportional to the amount of material) for the compounds are plotted against the irradiation time.

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SUMMARY .

Isonitriles (isocyanides) are known to reveal more or less nucleophilic properties in the electronic ground state. So far very little attention has been paid to the chemical properties of the excited state.

This thesis describes the formation of cyclohept[b]indoles by irradiation of o-isocyanobiphenyl in cyclohexane. It is a new reaction which reveals electrophilic properties of the isocyanide group in the excited state. It appears to be the first example of an aromatic ring expansion by insertion of an isocyano carbon. Cyclohept[b]indole is also formed upon irradiation of o-isothiocyantobiphenyl. This reaction proceeds via the initial formation of o-isocyanobiphenyl and sulfur (Chapter II).

The subject has been extended (Chapter III) to the irradiation of 2,X'-diisocyanobiphenyls (X = 2, 3, or 4) in cyclohexane. The produced isomeric 7-, 8-, 9- and 10-isocyanocyclohept[b]indoles are stable compounds. The 6-isocyanocyclohept[b]indole, anticipated to be formed upon irradiation of 2,2'-diisocyanobiphenyl, could not be isolated. However, derivatives were found which indicate its initial formation. It is assumed, that a rapid intramolecular cyclization of 6-isocyanocyclohept[b]indole gives an intermediate which behaves like a nucleophilic amino carbene. This intermediate allows a straightforward explanation of the actual derivatives found.

In Chapter IV a spectroscopic study is made of the isocyanocyclohept[b]indoles. Evidence is obtained for a fairly strong mesomeric interaction between the isocyano function and the heterocyclic system. The basicities of the isocyanocyclohept[b]indoles are appreciably lower (ca 2 pK_a units) than that of the unsubstituted compound.

The isocyanocyclohept[b]indoles are easily hydrolyzed to the corresponding aminocyclohept[b]indoles. The pK_a values of the latter compounds are compared with those of the isomeric aminoacridines and aminophenanthridines. The aminocyclohept[b]indoles turn out to be much more basic than most of the isomers (pK_a ca 9.5).

Irradiation of o-isocyanobiphenyl in methanol (Chapter V) produced phenanthridine as the main product besides a small amount of cyclohept[b]indole. Evidence has been found that the formation of the phenanthridine does not result from a direct insertion reaction of the isocyano-carbon into the *ortho* C-H bond of the adjacent phenyl ring. A theory has been developed, which explains the different course of the photochemical reaction in cyclohexane and methanol.

SAMENVATTING

Het is bekend dat isonitrillen (isocyaniden) min of meer nucleofiele eigenschappen tonen in de elektronische grondtoestand. Tot dusver is echter zeer weinig aandacht geschonken aan de chemische eigenschappen van aangeslagen toestanden.

Dit proefschrift beschrijft de vorming van cyclohept[b]indool na bestraling van o-isocyanobifenyl in cyclohexaan. Het mag het eerste voorbeeld genoemd worden van een aromatische ring expansie door inschuiving van een isocyano-koolstofatoom. Cyclohept[b]indool wordt ook gevormd bij de bestraling van o-isothiocyanaatobifenyl. Deze laatste reactie verloopt via de vorming van o-isocyanobifenyl en zwavel (Hoofdstuk II).

Het onderzoek werd uitgebreid tot de bestraling van 2, X'-diisocyanobifenylen in cyclohexaan (X=2, 3 of 4). De gevormde isomere 7-, 8-, 9- en 10- isocyanocyclohept[b]indolen zijn stabiele verbindingen. Niet geïsoleerd kon worden het 6-isocyanocyclohept[b]indole, dat uit 2, 2'-diisocyanobifenyl gevormd zou kunnen worden. Derivaten konden echter geïsoleerd worden, die een sterke aanwijzing vormden voor de aanvankelijke vorming van dit isomeer. Verondersteld wordt, dat een snelle intramoleculaire cyclizatie van het 6-isocyanocyclohept[b]indool leidt tot een tussenproduct dat zich gedraagt als een nucleofiel aminocarbeen. De aanname van dit tussenproduct geeft een zeer sluitende verklaring voor de werkelijk gevonden verbindingen.

In hoofdstuk IV worden spectroscopische gegevens van de isocyanocyclohept[b]indolen vergeleken. Er zijn aanwijzingen voor een vrij sterke mesomere interactie tussen de isocyano-functie en het heterocyclische systeem. De basiciteiten van de isocyanocyclohept[b]indolen zijn aanmerkelijk lager dan voor de ongesubstitueerde verbinding (ca 2 pK_a eenheden).

De isocyanocyclohept[b]indolen zijn gemakkelijk te hydrolyseren tot de overeenkomstige aminocyclohept[b]indolen. De pK_a waarden van deze laatste verbindingen worden vergeleken met die van de isomere aminoacridines en aminofenanthridines. Het blijkt dat de aminocyclohept[b]indolen basischer zijn dan de meeste genoemde isomeren (pK_a ca 9.5).

Bij de bestraling van o-isocyanobifenyl in methanol (Hoofdstuk V) wordt fenanthridine als hoofdproduct gevormd naast een kleine hoeveelheid cyclohept[b]indool. Er zijn aanwijzingen gevonden dat de vorming van het fenanthridine niet het resultaat is van een directe insertie reactie van het isocyano-koolstofatoom in de *ortho* C-H binding van de naburige fenylring. Een mechanisme wordt voorgesteld, dat het verschillend fotochemisch reactieverloop in cyclohexaan en methanol verklaart.