



THE ACTION OF METAL CATALYSTS
ON ORGANIC NITROGEN COMPOUNDS.

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By

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CONTENTS

Introduction	1
Chapter I.	
The effects of the phenyl derivatives of the typical elements of Groups V, VI, and VII on Raney nickel.....	24
Experimental.....	46
Chapter II.	
The action of degassed Raney nickel on some derivatives of aniline	
A. The formation of carbazole from aniline.....	61
B. The formation of indoles from <u>o</u> -alkylanilines and <u>N</u> -alkyl- <u>o</u> -alkylanilines.....	78
Experimental.....	109
Chapter III.	
The formation of biaryls from quinoline under the influence of catalysts derived from the metals of Group VIII.....	144
Experimental.....	152
References.....	156

SUMMARY

The poisoning coefficients of the phenyl derivatives of the typical elements of Groups V, VI, and VII have been measured in the hydrogenation of trans-crotonic acid with W-7 Raney nickel. The coefficients obtained have been correlated with the degree to which these phenyl derivatives undergo hydrogenolysis in the presence of W-7 Raney nickel. It is suggested that those phenyl derivatives which are hydrogenolysed are adsorbed preferentially through their hetero-atoms. It is further postulated that the amines which are hydrogenolysed to only a small extent, are chemisorbed preferentially via their aromatic electrons.

The formation of 2,2'-diaminobiphenyl, 2-aminobiphenyl, diphenylamine, cyclohexylaniline, and carbazole in the reaction of aniline with degassed Raney nickel is described. A pathway is proposed for the formation of carbazole in the reaction of quinoline with W7-J Raney nickel.

The reactions between degassed Raney nickel and a series of o-alkylanilines and N-alkyl-o-alkylanilines have been studied. On the basis of the results obtained, pathways are proposed for the formation of indole and 3-methylindole in the reaction of quinoline with W7-J Raney nickel. Also, mechanisms have been postulated for the formation of some of the basic products occurring in this reaction.

Finally, the abilities of some supported noble metal catalysts to form 2,2'-biquinolyl from quinoline have been compared. It has been found that a rhodium-on-charcoal catalyst gives the highest yield of 2,2'-biquinolyl yet reported.

The work described in this thesis is part of a more extensive investigation being conducted by a number of other workers in this Department, but incorporates no material previously submitted for a degree in any University except where due reference has been made.

G.D.F. JACKSON

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INTRODUCTION



INTRODUCTION

Since the introduction of activated metal catalysts to the field of organic chemistry, many catalytic reactions have been discovered. Although Sir Humphrey Davy¹ is acknowledged as being the first to notice the catalytic effect of a metal in a chemical reaction, much of the early work was carried out by Sabatier and his colleagues.² The most important reaction is that of catalytic hydrogenation, to which Sabatier contributed greatly, and today there are a number of catalysts available for the various reducible systems. For simple systems such as carbon-carbon double bonds, nitro-groups, keto-groups, etc., it is relatively easy to choose a catalyst to give the desired result. However for systems complicated by either their structure or requirements of selective reduction, it is even today by no means easy to obtain suitable catalysts. Most of the catalysts in use today are derived from the transition metals of Groups VIII and I (Table I), which exhibit catalytic activities in a wide variety of reactions.

Table I

Iron	Cobalt	Nickel	Copper
Fe	Co	Ni	Cu
Ruthenium	Rhodium	Palladium	(Silver)
Ru	Rh	Pd	Ag
Osmium	Iridium	Platinum	(Gold)
Os	Ir	Pt	Au

and for this catalyst a number of preparations differing in activity have been described.⁹

Since the present work is concerned with some reactions in the presence of Raney nickel catalysts, it is appropriate that current views regarding the nature of these catalysts should be briefly summarised.

The various nickel catalysts differ primarily in their hydrogen content, and it has been shown that the most active catalysts in hydrogenation reactions are those which contain the most hydrogen.^{10,11} In other reactions, such as the dimerisation of pyridine mentioned above, best yields of 2,2'-bipyridyl are obtained from catalysts which contain the least amount of hydrogen.

Hydrogen can be easily removed from a nickel catalyst by heating. This process is exothermic,^{11,12} but no change in the surface structure is noticed until high temperatures (300-400°) are reached, where the surface area is decreased substantially (50-75% of original area).^{13,14} At these high temperatures 85-95% of the hydrogen is removed,^{13,14} and this is accompanied by a decrease in activity in hydrogenation.^{11,14,15}

In the last decade there has been much controversy concerning the nature of Raney nickel catalysts. Early workers held the view that the hydrogen on the catalyst was present in the form of a hydride¹⁶ or in solution.^{11,15} The more recent work of Kokes and

Emmett^{13,14} has suggested that the nickel is promoted by aluminium, and that the hydrogen is held in the nickel in the form of substitutional replacement of nickel atoms in the lattice. The process of degassing removes hydrogen from the nickel-aluminium alloy, creating a large number of lattice vacancies which are available for occupation by hydrogen, and other reacting species. These authors also assume that the d-band of nickel is capable of accepting one electron from each hydrogen atom and three electrons from each aluminium atom. On this basis they have calculated that for the hydrogen-rich neutral W-6 Raney nickel catalyst containing 3% aluminium, 1.85 electrons per unit cell have been added, this value being decreased to 0.76 when the catalyst is degassed.

In a catalytic reaction there must be some form of interaction between the substrate and the catalyst. Where a catalyst is used repeatedly in a reaction, it may be noticed that its efficiency gradually decreases, due to the presence of foreign material, which can either react with the catalyst, destroying its activity permanently, or cover the surface preventing interaction of the substrate. The presence of a poison may either reduce the rate, or suppress a reaction completely. This phenomenon of poisoning can either act as a help or a hindrance in catalytic reactions.

Marted and his colleagues¹⁷ have been among the principal workers in the field of catalytic toxicity, and much of the present

knowledge is due to their efforts. They have been concerned in the main with platinum catalysts. Maxted¹⁷ defines poisons as being "strongly adsorbed species which even if they are present in traces only, tend by virtue of their strong bonding to a catalyst and of their consequently long adsorbed lives to accumulate in the adsorbed phase in the course of the adsorption-desorption equilibrium at the catalyst surface, which by reason of this obstructive occupation by the poison, is rendered free for its normal participation in the adsorption and catalysis of less strongly held potential reacting species." This definition complies with the arguments of Taylor¹⁸ and findings of Armstrong and Hilditch¹⁹ concerning the "active point" theory of catalysis which states that, of the total area of the catalyst only a small part consists of patches of maximum activity, the greater part of the surface being much less active. More recent experimental evidence was found when a Raney nickel catalyst was poisoned with hydrogen chloride.²⁰

Maxted and Morrish²¹ proposed that poisoning is due to the availability by the compounds of one or more "lone-pairs" of electrons which are capable of forming strong bonds with the metal catalysts. Also, if these "lone-pairs" are bonded within the molecule, the compounds are said to be shielded and do not exhibit any toxicity. Thus it was found²¹ that an organic sulphide (III) was toxic due to the available "lone-pairs" on the sulphur atom, but when the

The typical elements of Groups V, VI and VII (Table II) are known to exhibit poisoning effects in the presence of the metal catalysts in Table I. Maximum toxicity is generally assumed to be associated with the elements of Group VI, and the toxicities of some sulphur compounds have been compared.^{23,24} Until recently^{25,26,27} reactions with selenium and tellurium compounds have received little attention, although it is known that they undergo hydrogenolysis similar to sulphur compounds. Using a platinum.

Table II

Group V	Group VI	Group VII
N	O	F
P	S	Cl
As	Se	Br
Sb	Te	I
Bi		

catalyst in a hydrogenation reaction, Maxted and Marsden²⁸ determined the extent of poisoning by the elements of Group V. Pattison and Degering²⁰ have compared the toxicities of some compounds of the elements of Group VII in a hydrogenation reaction using W-4 Raney nickel. For both series of results it was found that the poisoning ability increased with atomic weight in each Group. The determining factor was thought to be the relative sizes of the poisoning atoms.

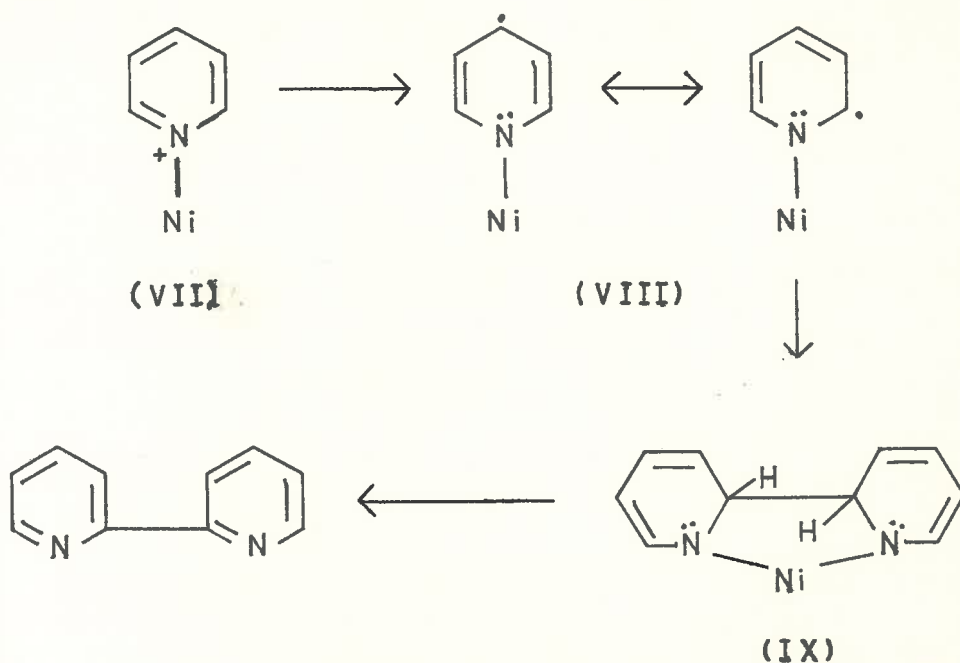
Simple nitrogen compounds, although poisonous to a small extent, are less toxic than the analogous compounds of the other elements of Group V.²⁸ Ammonia is weakly toxic towards a platinum catalyst,^{22,29} and pyridine was shown to be poisonous as it decreased the rate of its own hydrogenation.^{22,30} For pyridine it is assumed that the poisoning is due to adsorption by the catalyst via the "lone-pair" electrons of the nitrogen atom. The probability that adsorption can also occur by means of the aromatic electrons will be discussed in Chapter I.

The first step in a catalytic reaction is generally assumed to be the adsorption of the reactant by the catalyst surface.^{31,32,33,34} Hence every compound which is catalytically reactive may be regarded as a potential poison. In a heterogeneous reaction at least three stages can be distinguished. Firstly, the reactants must be adsorbed by the catalyst. Then the required reaction must occur, and finally the product(s) should be desorbed easily. If the first two steps take place readily but the third does not, the reaction may continue at a slower rate or stop completely, thus poisoning the catalyst.

Since this thesis is concerned with a number of reactions involving Raney nickel and nitrogen compounds, a study of the catalytic toxicities of the phenyl derivatives of the typical elements of Groups V, VI, and VII in hydrogenation reactions using the hydrogen-rich W-7 Raney nickel was carried out. Also the poisoning properties of some heterocyclic nitrogen compounds on

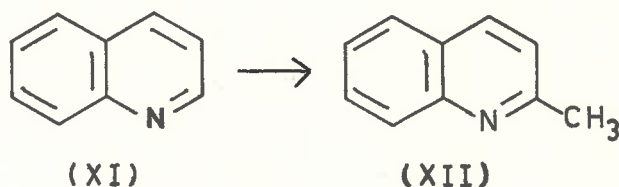
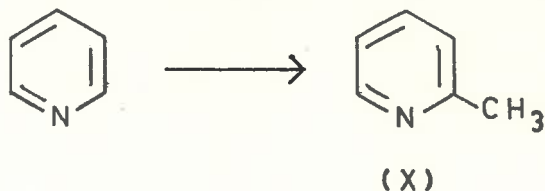
several Raney nickel catalysts were studied.

It has been noticed by several workers that the hydrogenations of pyridines and quinolines, using nickel catalysts, are accompanied by four side reactions. Dimerisation to 2,2'-bipyridyl and 2,2'-biquinolyl has received some attention since these compounds are difficult to prepare by other means. Wibaut and van de Lande³⁵ found that trace amounts of 2,2'-bipyridyl were formed in a reaction between pyridine and ammonia, using a variety of catalysts. Wibaut and Willink further developed this preparation by reacting pyridine³⁶ and 2-methylpyridine³⁷ with a nickel-aluminium catalyst. 2,2'-Biquinolyl has also been prepared by this method. 38,39,40 Badger and Sasse⁷ obtained 2,2'-bipyridyl in preparative yield by reacting pyridine with a degassed Raney nickel catalyst. Subsequent studies with alkyl substituted pyridines were also shown to give good yields of substituted 2,2'-bipyridyls.⁴¹ The mechanism most recently proposed for this reaction⁴² involves as the first step the bonding of the nitrogen atom of the pyridine to the nickel (VII). This is followed by a transfer of an electron, resulting in the localisation of a free electron in the 2-(or 4-) position (VIII), which can interact with a similarly bonded pyridine molecule attached to the same nickel atom. The hydrogenated bipyridyl (IX) so formed would be expected to dehydrogenate readily and the 2,2'-bipyridyl could then be desorbed from the catalyst.

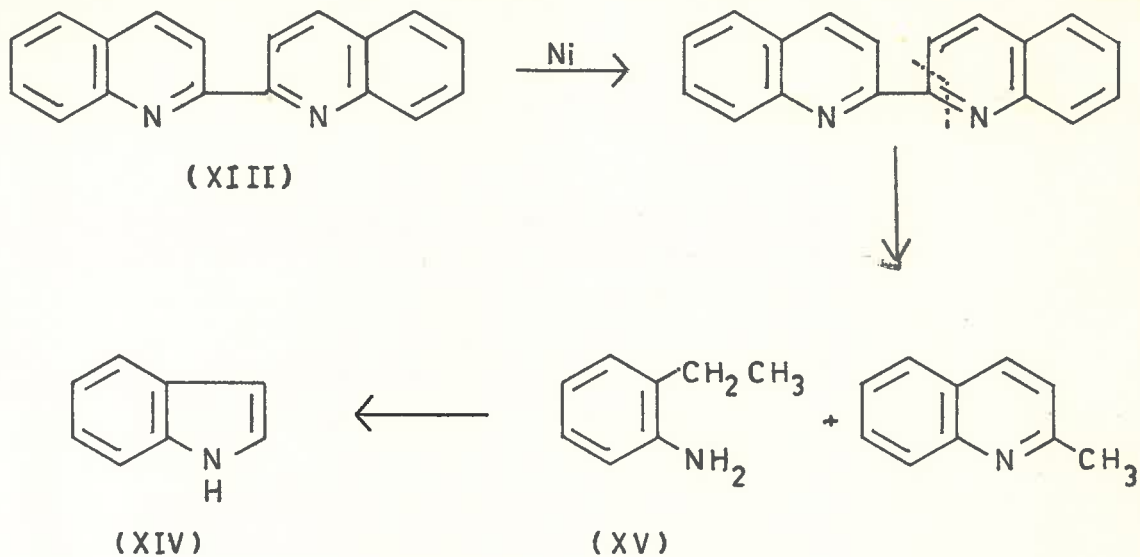


2,2'-Biquinolyl can be prepared by the same method,⁴³ but in lower yield than 2,2'-bipyridyl, its formation being hindered by the benzene ring which has a similar effect as a 2-substituent in the pyridine ring.

Also found in the hydrogenation reactions of pyridines and quinolines are dealkylated products. Dealkylation has been noticed with both 2-alkylpyridines^{41,44} and 2-alkyl quinolines⁴³ in the presence of nickel catalysts. The fate of the alkyl group is uncertain. Equally interesting is the reverse process of methylation, where pyridine yields a trace of 2-methylpyridine (X) and quinoline (XI) yields 2-methylquinoline (XII).^{43,44}



As will be seen later, the origin of the "extra" carbon atom may be connected with the formation of anilines. It has been demonstrated repeatedly that methylation of pyridine and quinoline occurs solely at the 2-position,^{7,41,43,44} although Jones⁴⁴ has suggested that alkylation also takes place at the other positions. Other products arising out of the alkylation have not been identified. Sasse⁴³ suggests that free radical methylation is unlikely due to the absence of other methylated products. Rather than alkylation by this reaction he suggests that the 2-methyl compounds are derived from the dimerised product by further reaction with the catalyst. 2,2'-Biquinolyl was shown to react further with the nickel to give quinoline, 3-methylindole, indole, and although not definitely characterised, 2-methylquinoline. The formation of quinoline suggests a reversible reaction. A sequence of steps leading from 2,2'-biquinolyl (XIII) to 2-methylquinoline were envisaged, the other product formed could be indole (XIV), arising from the dehydrocyclisation of o-ethylaniline (XV) (see later).

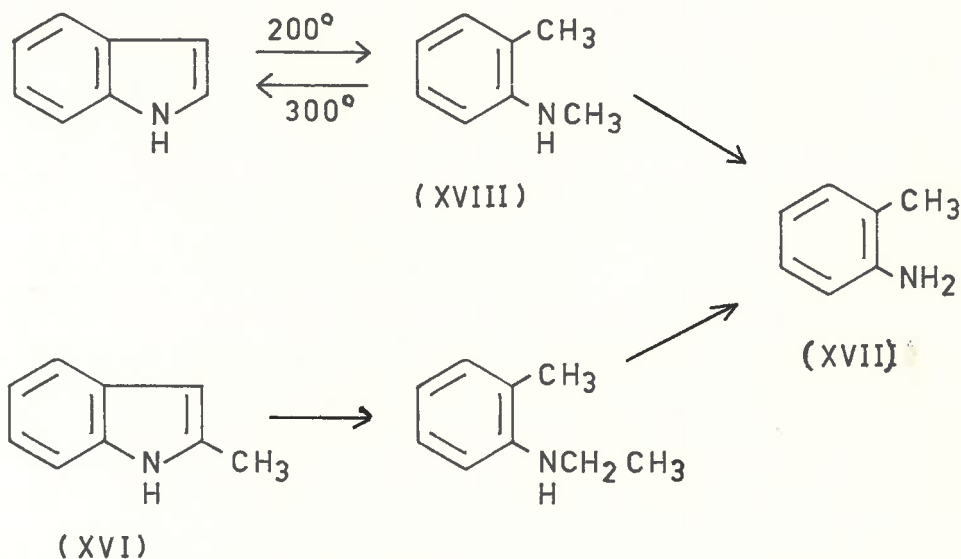


Another important side reaction in the action of nickel catalysts on pyridines and quinolines is that of ring opening. Rupture of pyridine in hydrogenation reactions with the formation of amines has been noted several times. Jones⁴⁴ studied systematically the products of the hydrogenation of pyridine under conditions similar to those used by Adkins.³⁰ Besides traces of 2,2'-bipyridyl, cleavage occurred to give a number of amines. N-n-amyl, N-n-butyl and N-cyclopentylpiperidine and 1,5-dipiperidino-pentane were obtained; greater yields occurring when the temperature of reaction was raised. Similar products were obtained from the hydrogenation of 2-methylpyridine,⁴⁵ and Sabatier and Maihle⁴⁶ obtained n-amylamine from a vapour-phase hydrogenation of pyridine at 180°.

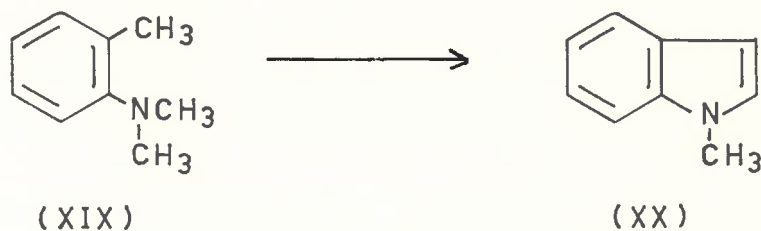
The earlier work of Padoa with quinoline (p. 16) leaves some doubt as to the mechanism of the ring opening. In particular it is uncertain whether the hydrogenation of the heterocyclic ring precedes ring fission. Quinoline was thought to undergo fission at the 1,2- and 3,4- bonds in preference to the 2,3-bond.⁴⁷ For 1,2,3,4-tetrahydroquinoline it was concluded that the 2,3-bond was more likely to break.⁴⁸

Where ring fission has occurred under catalytic conditions, no unsaturated amines have been detected. In this respect the ring fission differs markedly from the desulphurisation reaction where ring cleavage can occur without first reducing the ring, resulting in the isolation of unsaturated products.⁴⁹ Thate⁵⁰ proposed that in the hydrogenation of pyridine in an iron autoclave, ring reduction preceded its rupture, and Yamaguchi⁵¹ inferred from his results (p. 19) that hydrogenation of quinoline preceded ring fission.

The aniline derivative resulting from the ring cleavage of quinoline can undergo dehydrocyclisation to form indoles. This important side reaction has been noticed in the pyridine and the quinoline series. Padoa and Carrasco⁵² showed that in the hydrogenation of indole and 2-methylindole (XVI) at 200°, o-toluidine (XVII) was the major product. They concluded that the

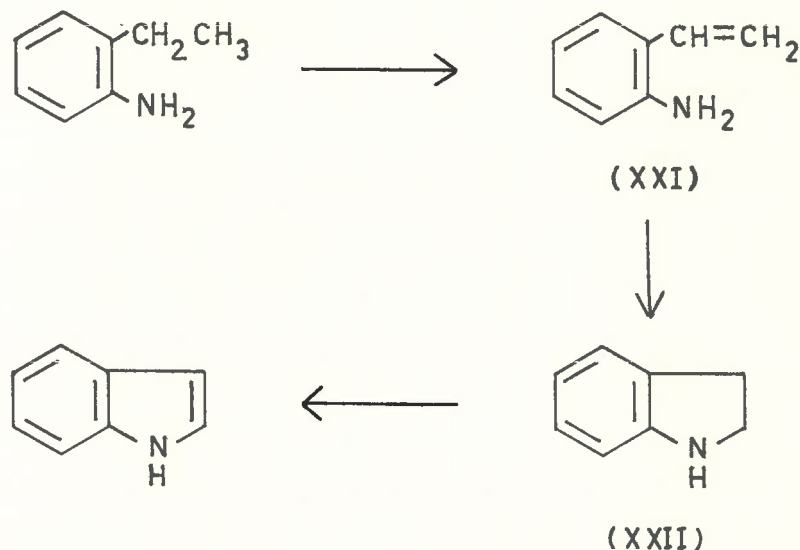


2,3-bond had been broken, this being followed by dealkylation at the nitrogen atom. They showed that the reverse reaction occurred with *N*-methyl-*o*-toluidine (XVIII) at 300° to form indole. *N,N*-dimethyl-*o*-toluidine (XIX) gave *N*-methylindole (XX) under similar conditions.⁵³



The dehydrocyclisation of *o*-alkylanilines^{54,55,56,57,58} and *N*-alkyl-*o*-alkylanilines^{52,53} has been known for many years. Baeyer and Caro⁵⁴ passed *o*-ethylaniline through a red-hot tube at 400° to obtain indole. Recently, a number of dehydrocyclisation reactions with *o*-ethylaniline have been carried out with a variety of metal catalysts.^{55,56,57,58} Hansch and Helmkamp⁵⁵ reacted *o*-ethylaniline with a chromium copper-on-charcoal catalyst at 670° to obtain indole.

Similar conditions using o-isopropylaniline yielded 3-methylindole. In the first reaction, o-aminostyrene (XXI) was isolated as an intermediate. Hence it was concluded that the dehydrogenation of the side chain occurred before cyclisation. These authors then proposed that the resultant indoline (XXII) was dehydrogenated to indole. This mechanism was supported by Lesiak.⁵⁶

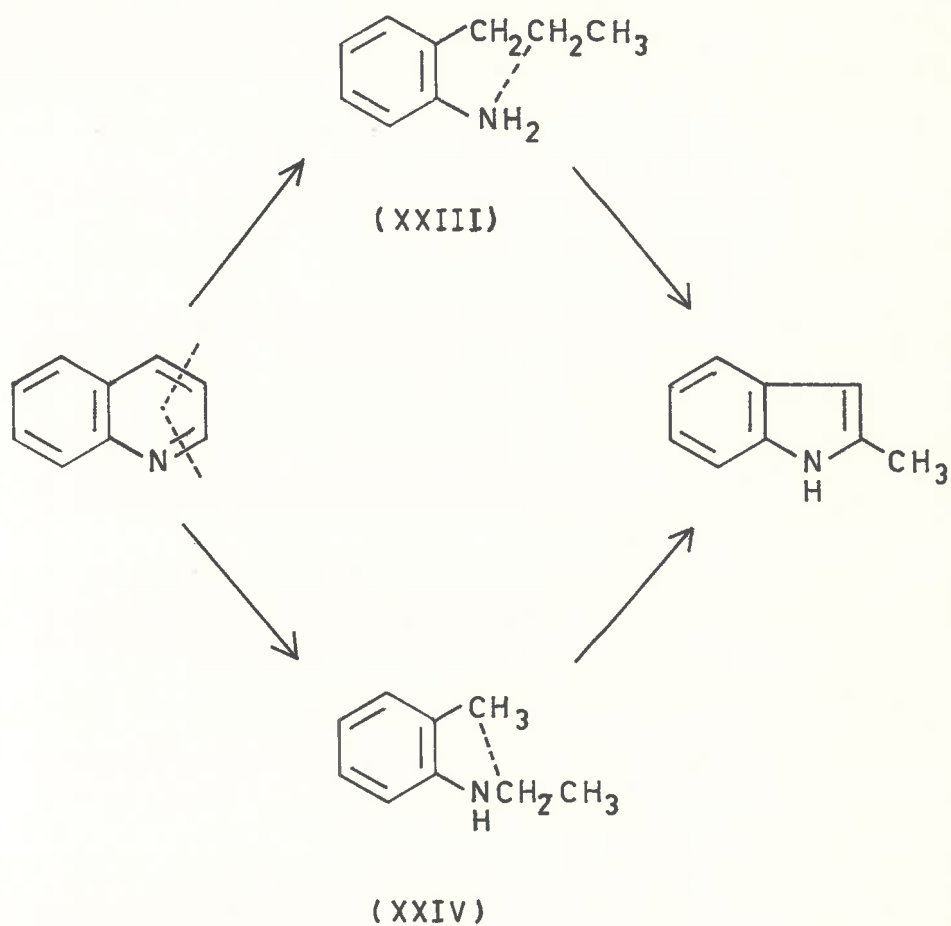


The fission of pyridine rings under the influence of metal catalysts appears to be related to the occurrence of pyrroles and indoles in these reactions. Padoa⁵⁹ was the first to notice the formation of non-basic nitrogenous materials during the action of a reduced nickel catalyst on pyridine. On the basis of colour tests, he suggested that these compounds were pyrroles, but he could not obtain any pure pyrroles. Granelli⁶⁰ also observed this reaction and he too was unable to obtain sufficient pyrrolic material

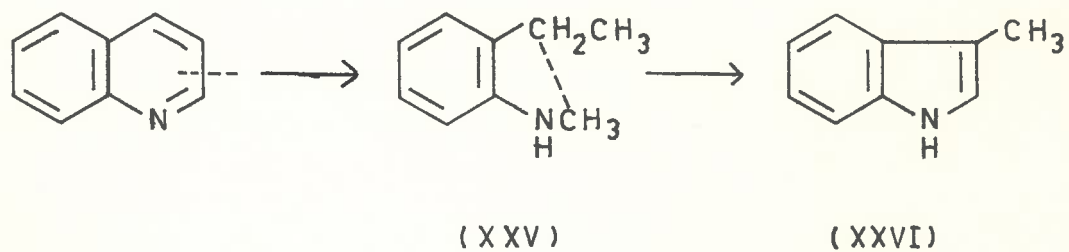
to effect isolation and characterisation. In the reaction of pyridine and degassed Raney nickel, evidence for the existence of pyrrole was obtained.⁶¹ Using physical methods, 3-methylpyrrole has been identified among the products of the hydrogenation of pyridine.⁶²

Indoles, which are more stable than pyrroles, have been isolated as products from the reaction of quinoline with nickel catalysts. Padoa and Carughi⁴⁷ reported that quinoline, when reacted with hydrogen over a reduced nickel catalyst at 260-280°, gave 2-methylindole. However Sasse⁴³ has pointed out that the properties of this product are those of a mixture of indole and 3-methylindole. When Padoa and Carughi reacted quinoline with the nickel catalyst in the absence of hydrogen, no indoles were formed. In the presence of hydrogen and the reduced nickel catalyst, 1,2,3,4-tetrahydroquinoline was shown to give 3-methylindole as the only indole derivative.⁴⁸ Besides 3-methylindole formed in this reaction, aniline and o-toluidine were also isolated. Their presence was ascribed to the rupture of the pyridine ring.

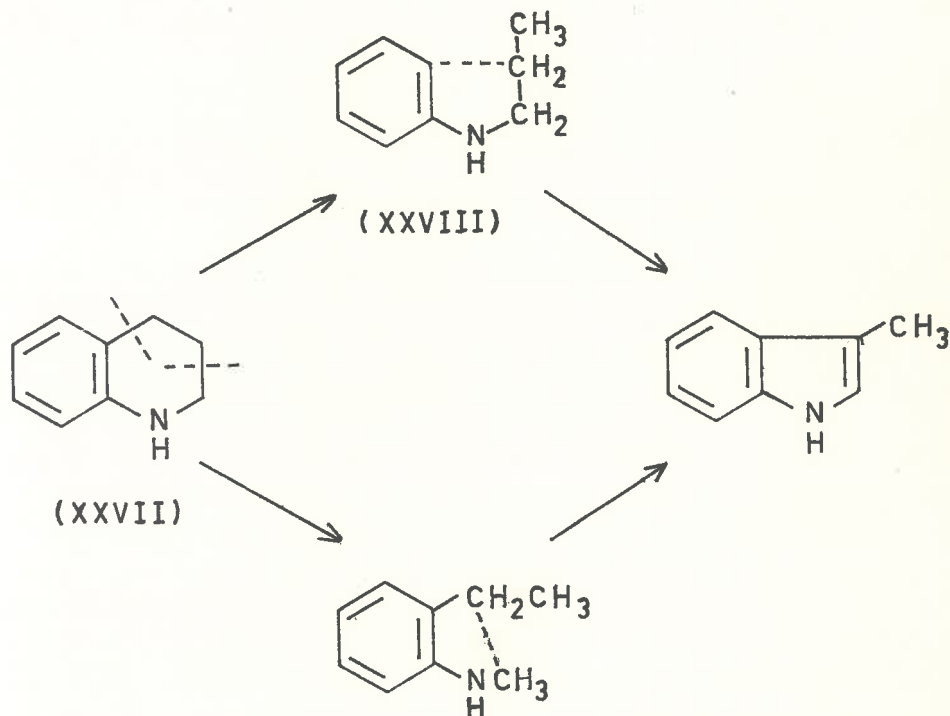
In order to explain the formation of 2-methylindole from quinoline, Padoa and Carughi,⁴⁷ (as mentioned above) suggested that either the 1,2-bond was ruptured to give o-propylaniline (XXIII) which underwent dehydrocyclisation forming 2-methylindole, or that the 3,4-bond was broken to give N-ethyl-o-toluidine (XXIV), also yielding 2-methylindole on dehydrocyclisation. It was also



intimated that the 2,3-bond could not have broken since this would yield N-methyl-o-ethylaniline (XXV) which on dehydrocyclisation would give 3-methylindole (XXVI), none of which was detected in the reaction mixture.



1,2,3,4-Tetrahydroquinoline (XXVII), which gave 3-methylindole when reacted with nickel,⁴⁸ was assumed to have undergone ring cleavage either at the 2,3- or 4,9-bonds. The products of these cleavages, *N*-propylaniline (XXVIII) and *N*-methyl-*o*-ethylaniline, were both expected to yield 3-methylindole on dehydrocyclisation.



N-propylaniline was shown to be an unlikely intermediate, since only a trace of indolic material was obtained on reaction with the reduced nickel catalyst.⁴⁸

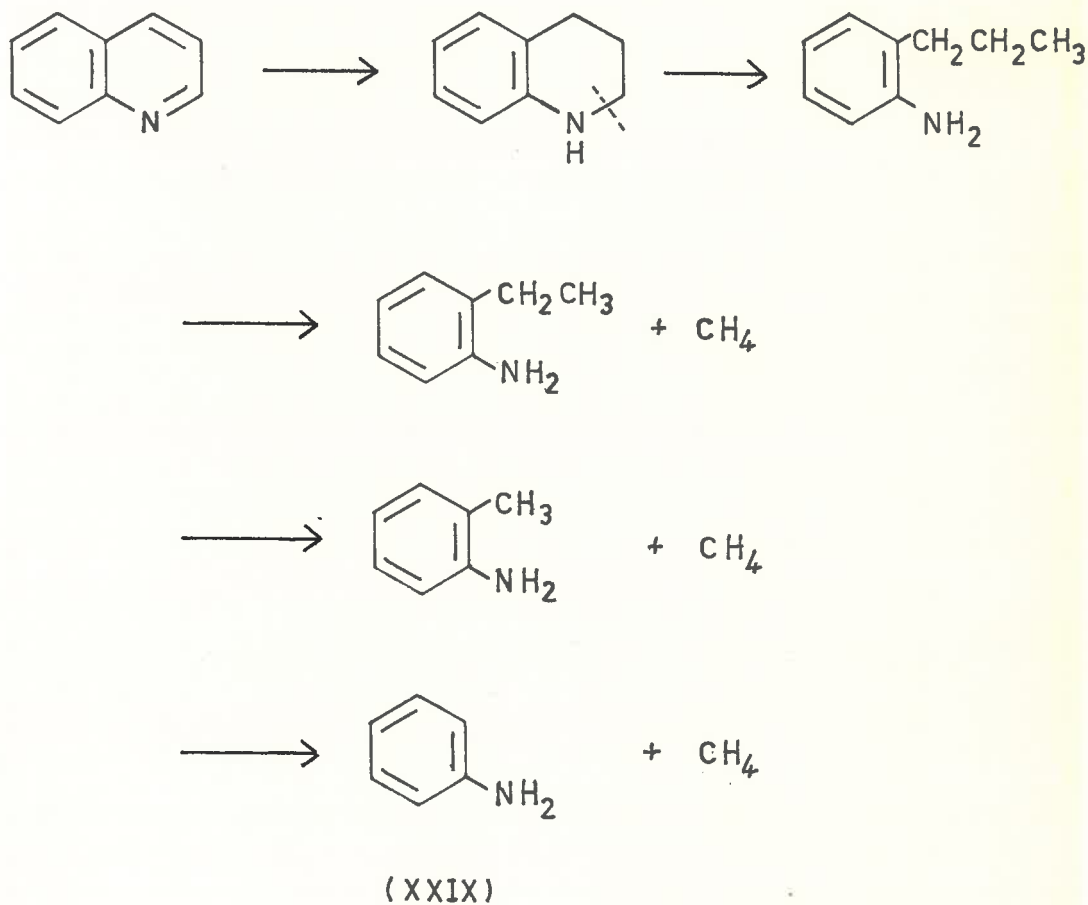
Earlier, Hoffmann and Königs⁶³ had reacted 1,2,3,4-tetrahydroquinoline with nickel and isolated indole. Granelli⁶⁰ agreed with Padoa's suggestion that indoles arose from the dehydrocyclisation

of either o-alkylanilines or N-alkyl-o-alkylanilines which were the products from the ring fission of quinoline. He also reported that N-ethyl-o-toluidine was isolated from a reaction of quinoline and a reduced nickel catalyst.

The hypotheses of Padoa did not rely on reliable analytical methods to isolate products from the reaction. More recent experiments involving the use of better analytical methods have given results which have led to some confusion as to the exact pathway leading from six-membered to five-membered heterocyclic rings. Many of the hydrogenation reactions of pyridine and quinoline carried out since Padoa's time have been of a destructive nature, and the cracking procedures have yielded products which would appear to differ from observations and ideas to be discussed later. It is difficult to conveniently differentiate between pure catalytic reactions and cracking procedures, but where temperatures greater than 400° and pressures exceeding 50 atmospheres are used, the rupture of bonds would be expected to be more random, yielding products which are not obtained in pure catalytic reactions.

Yamaguchi⁵¹ reacted quinoline with calcium chloride under the destructive conditions of 450° and 200 atmospheres. Ring rupture was only apparent in the pyridine ring, and he isolated o-propylaniline, o-ethylaniline, o-toluidine, and aniline as basic products. An unspecified methylindole was also isolated. He concluded that cleavage of the 1,2-bond had occurred. The isolation

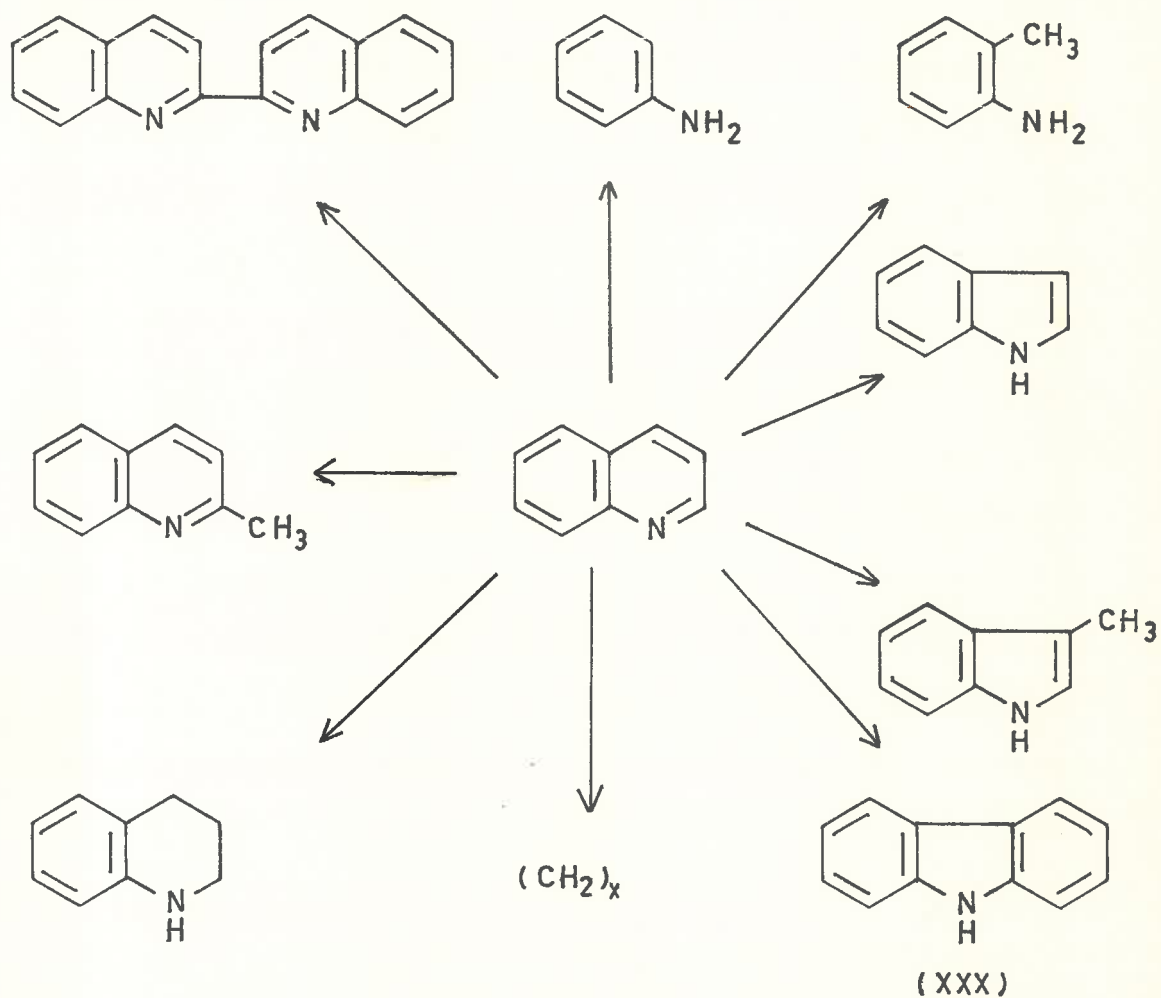
of similar products by Rapoport⁶⁴ and Eru, Sakhnovskaya, and Pychco,⁶⁵ in their destructive hydrogenations of quinoline led them to conclude also that the 1,2-bond was broken. Rapoport further suggested that a stepwise degradation of the side-chain occurred. The quinoline was thought to be first hydrogenated, and then after rupture of the 1,2-bond, o-propylaniline was formed which lost methane to give o-ethylaniline. Successive losses of methane were then proposed, leading to o-toluidine and aniline (XXIX).



Yeh and Kalechits⁶⁶ hydrogenated quinoline and reacted 1,2,3,4-tetrahydroquinoline at 460° under a pressure of 85 atmospheres (at 0°) in an autoclave with an iron catalyst. Cleavage occurred giving products similar to those obtained under the destructive conditions mentioned above. Deamination was also noted, yielding a mixture of alkylbenzenes. Indole and some unspecified homologues were isolated. 1,2-Bond fission leading to the observed products, was again postulated.

A recent study of the hydrogenation of pyridine and 2-methylpyridine over a Raney nickel catalyst yielded results that are difficult to reconcile with the fission of the 1,2-bond.⁶² 3-Methylpyrrole was isolated from the hydrogenation of both compounds. On the basis of the hypotheses discussed above, the only way in which the formation of this pyrrole could be explained is by the fission of the 2,3-bond of the hydrogenated pyridine, this being followed by dehydrocyclisation.

A more recent study of the reaction of quinoline (and substituted quinolines) with a Raney nickel catalyst has been carried out by Sasse.⁴³ After refluxing quinoline over a degassed Raney nickel catalyst for 50 hours the following products were isolated from the reaction mixture; 2,2'-biquinolyl, 2-methylquinoline, 1,2,3,4-tetrahydroquinoline, o-toluidine, aniline, indole, 3-methylindole, carbazole (XXX) and an aliphatic hydrocarbon of unknown structure, but which on the basis of its infrared spectrum and analysis was thought to be a polymethylene (CH₂)_x.



Although these compounds are not unexpected on the basis of the results of previous workers, two discrepancies exist. Firstly, there is an absence of o-alkylanilines other than o-toluidine, and secondly, no 2-methylindole was detected. The neutral reaction products formed from 2-, 3-, and 4-methylquinolines were the same as obtained from quinoline, only the yields differing slightly. From the quinolines substituted in the benzene ring, analogous products were isolated. On the basis of gas-liquid chromatography

only, N-ethylaniline was detected from the reaction with 2-methylquinoline. Care was taken to show that no 2-methylindole was formed in any of the reactions. This result does not agree with the mechanism proposed by Padoa and later authors which involves the rupture of the 1,2- or the 3,4-bonds of quinoline.

One of the aims of this project has been to understand more fully, the mode of formation of some of the products, particularly the indoles and carbazoles, from the reaction between quinoline and a degassed Raney nickel catalyst.

As was mentioned earlier, many authors have noted the formation of 2,2'-bipyridyl and 2,2'-biquinolyl from the parent bases, when they were reacted with metal catalysts, and there were a number of early attempts to use this as a method of preparation of these useful compounds. Recently⁶⁷ it was shown that these biaryls can be prepared in small yield by heating pyridine and quinoline with a palladium-on-charcoal catalyst. With this in mind, a comparative study of the dimerising ability of some noble metal catalysts (supported on charcoal) using quinoline has been carried out.

CHAPTER I

The effects of the phenyl derivatives of the typical elements of Groups V, VI, and VII on Raney nickel.

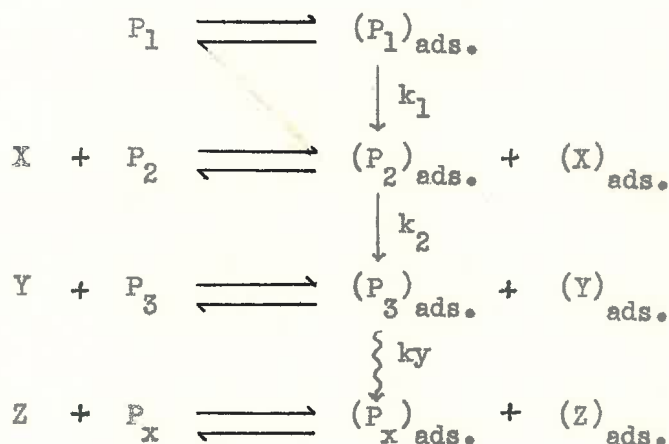
CHAPTER I

The adverse effect of sulphur compounds on catalytic hydrogenations has been known for many years. There is a decrease in the rate of hydrogenation which is due to the preferential adsorption of the sulphur compounds, thus reducing the number of sites available for hydrogenation. Although sulphur compounds are among the most powerful catalyst poisons, compounds of certain other elements are also capable of poisoning metal catalysts.

All compounds which undergo reactions in the presence of a metal catalyst must, in the first instance, be chemisorbed by the catalyst; and in a sense, each compound, under certain circumstances, can act as a catalyst poison. From Maxted's definition of toxicity (see p. 5), it appears that the essential property of a poison is its ability to form a strong bond with the catalyst. It is the strength of this bond which determines the length of time which an individual molecule of poison spends bonded to the catalyst, and the stronger the bond, the larger is the percentage of the surface area, which at any given time, is covered by the poison. Furthermore one poison is more toxic than another because of a stronger poison-catalyst bond. This process can be described in terms of an adsorption-desorption equilibrium.

As will be discussed below, many toxic compounds react in the presence of a catalyst to produce other compounds which may also be poisonous. In such cases toxicity is a measure of the combined effect of all the poisonous components of the system.

Unless the stability of a poison is known with certainty it is difficult to compare, for example, the poisoning ability of two compounds one of which is stable on the catalyst, the other undergoing reaction. Where a series of reactions is possible, giving products which may also contribute to the poisoning, the following scheme indicates the state of affairs.



In the general case, P_1 is the poison which, in solution, is in equilibrium with a chemisorbed species $(P_1)_{\text{ads.}}$. As mentioned above, this is the equilibrium which determines the toxicity of the compound P_1 . A reaction $(P_1)_{\text{ads.}} \longrightarrow (P_2)_{\text{ads.}} + (X)_{\text{ads.}}$ may occur, producing another poison P_2 which is also capable of being desorbed and adsorbed by the catalyst. The fragment X from the reaction may also be toxic. $(P_2)_{\text{ads.}}$ may also undergo reaction to $(P_3)_{\text{ads.}} + (Y)_{\text{ads.}}$, $(P_3)_{\text{ads.}}$ reacting further until some end product P_x is obtained, which may or may not be poisonous. Therefore the toxicity measured is the total effect of all the poisons. In the hydrogenation and

dehydrogenation of aromatic compounds, where adsorption occurs via the aromatic electrons, the reactions $(P_1)_{\text{ads.}} \longrightarrow (P_2)_{\text{ads.}}$ may be reversible. However in the hydrogenolysis reactions to be discussed below, these steps are assumed to be irreversible. On general grounds it may be expected that in this reaction sequence, as for those to be discussed below, the rates ($k_1, k_2,$ etc.) increase as $(P_x)_{\text{ads.}}$ becomes smaller. This implies that $(P_2)_{\text{ads.}}$ reacts faster than $(P_1)_{\text{ads.}}$, but more slowly than $(P_3)_{\text{ads.}}$

For reactions involving Raney nickel catalysts it is generally accepted that the initial step is the chemisorption of the reactant to the catalyst surface.^{31,32,33,34} Later chapters describe some reactions of nitrogen containing compounds with Raney nickel catalysts. To help in the understanding of these reactions, the poisoning properties of some related compounds were investigated. This study was extended to the phenyl derivatives of the other typical (stable) elements of Group V. To facilitate comparison, the toxicities towards W-7 Raney nickel of the phenyl derivatives of the Group VI and VII elements were also measured.

The toxicities of compounds in the hydrogenation of trans-crotonic acid using some Raney nickel catalysts are expressed as their poisoning coefficients, a , obtained from the equation $k_c = k_o (1 - ac)$, where k_o is the original activity of the catalyst, and k_c is the activity in the presence of a concentration, c , of the poison, a , representing the specific effect of each unit of

poison.⁶⁸ In determining the poisoning coefficients of various compounds, Maxted and his colleagues kept constant the weights of catalysts and substrates, while the amounts of poisons added to the hydrogenations were varied. Linear relationships between the rates of hydrogenation and the quantities of poisons added were obtained, from which the poisoning coefficients were determined. In the present work, dealing with the pyrophoric Raney nickel catalysts, it was not practicable to carry out the hydrogenations in this fashion. Therefore the weights of substrate and poisons were kept constant and the weights of the catalysts were varied. The fact that linear relationships between the rates of hydrogenation and the weights of catalysts were obtained, show this to be a valid method for comparison. Furthermore, it was found that in the presence of constant weights of poisons, and while the weights of catalysts were varied, other linear relationships of lower slope than for the unpoisoned hydrogenations were obtained.

The activity of a particular weight of catalyst was measured at the start of an hydrogenation, i.e., the slope of the tangent at zero time was taken as the activity (Fig. 1). When four unpoisoned hydrogenations were completed and the activities of the catalyst plotted against their weights, the activity of

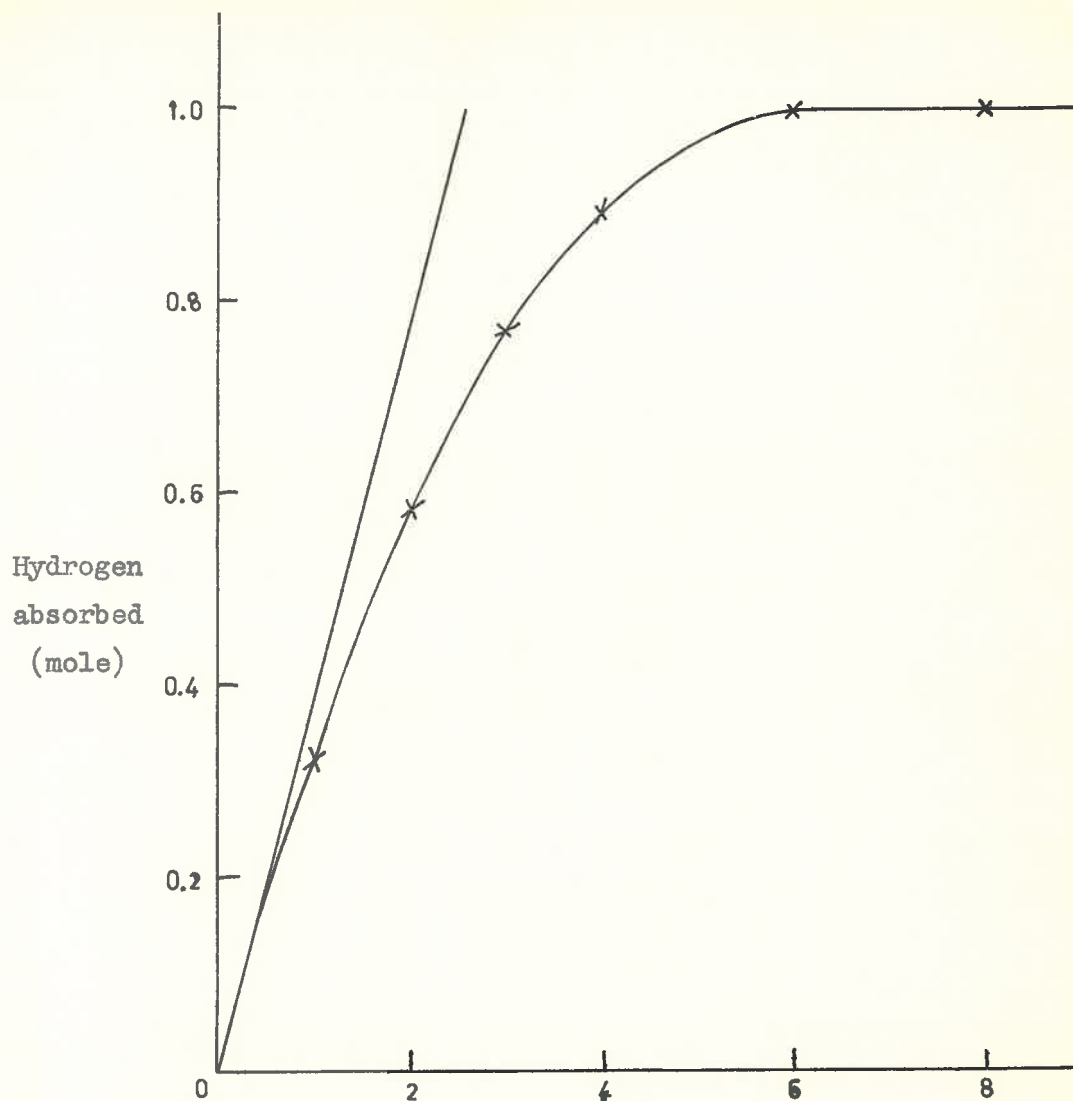


Fig. 1. Time (min.)

0.05 g. of catalyst was read off, and taken as the standard activity for that particular catalyst. The activity of 0.05 g. of catalyst in four poisoned hydrogenations was obtained in the same manner. From the concentration of poison used, the value of the poisoning coefficient was calculated. A typical case showing the points obtained for hydrogenations in the presence and absence of catalyst poisons is shown in Fig. 2.

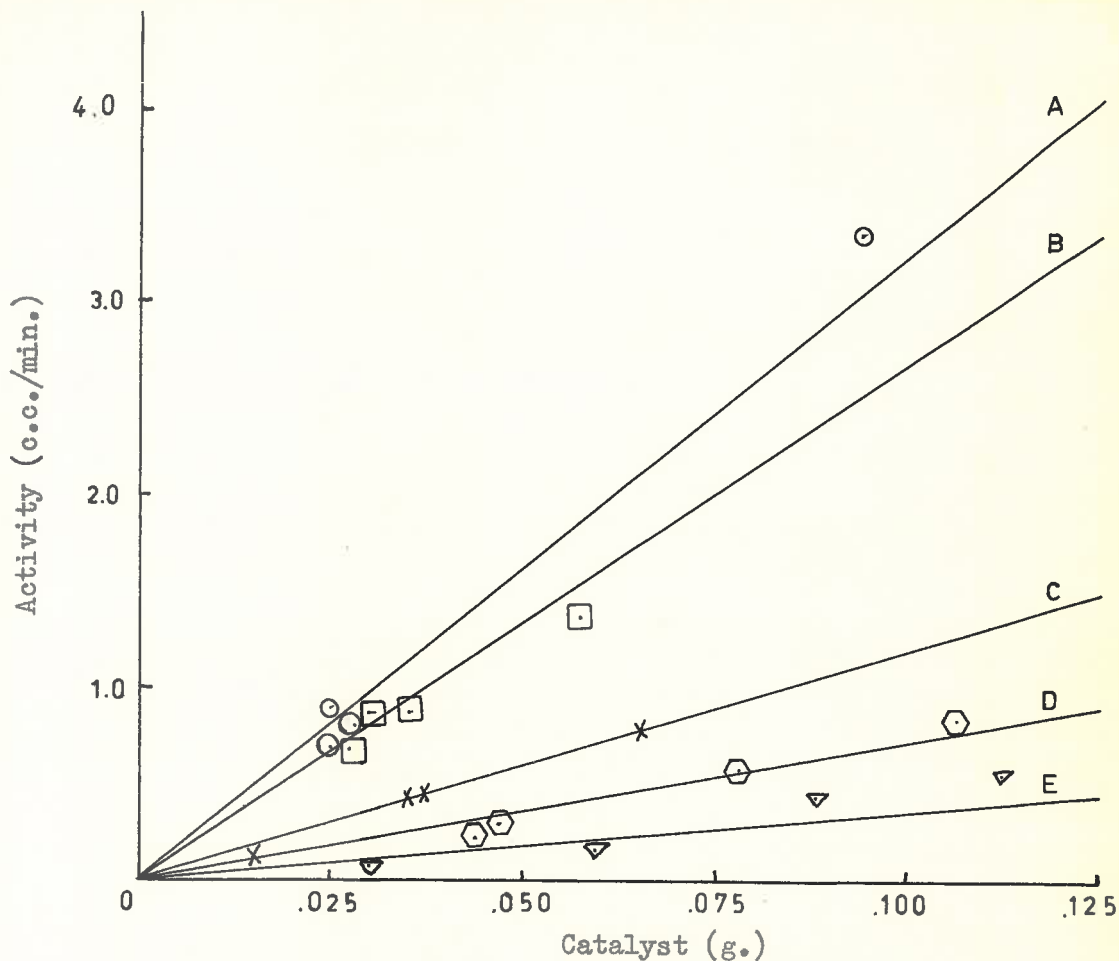


Fig. 2. The relation between the rate of hydrogenation of crotonic acid and the weight of W-7 Raney nickel catalyst; (A) in the absence of poison; (B) in the presence of fluorobenzene; (C) in the presence of chlorobenzene; (D) in the presence of bromobenzene; (E) in the presence of iodobenzene.

The values of the activities of 0.05 g. of catalyst in the presence of poisons, and the poisoning coefficients of the phenyl derivatives of the elements of Group V when poisoning W-7 Raney nickel are listed in Table I.

Table I

Compounds of Group V	Activity of 0.05 g. ^a (c.c.)	Poisoning coefficient (X 10 ⁻²)
Aniline ^b	1.13	2.5
Diphenylamine	1.41	2.2
Triphenylamine	1.41	2.2
Triphenylphosphine	1.31	3.5
Triphenylarsine	1.10	5.6
Triphenylstibine	0.91	7.6
Triphenylbismuthine	0.73	9.2

^a The unpoisoned activity of 0.05 g. of W-7 Raney nickel in this and succeeding tables is 1.64 c.c. (avge.).

^b Ratio of substrate to poison was 10:1. For other compounds ratio was 20:1.

A study of the triphenyl compounds indicates an increase in the values of the poisoning coefficients with the size of the hetero-atoms. It is well known that after triphenylamine, which shows no basic properties due to the nitrogen "lone-pair" electrons being conjugated with the benzene rings, the basicity decreases in the order $\text{Ph}_3\text{P} \longrightarrow \text{Ph}_3\text{Bi}$. In fact triphenylbismuthine is regarded as being non-basic.⁶⁹ From a consideration of basicity alone it would be expected that the poisoning coefficients would be larger with the more basic compounds. As this is not the case other

factors must be contributing to the final results.

For purely steric reasons it might be expected that an increase in size of the hetero-atom would raise the value of the poisoning coefficient, due to the greater area covered by the larger molecule. Inspection of models suggests that the nickel atoms could bond to the central atom more easily as the hetero-atoms increase in size. From Fig. 3 it is clear that a linear relationship exists between the poisoning coefficients of the triphenyl derivatives of phosphorus, arsenic antimony and bismuth, and the covalent radii⁷⁰ of these elements.

There is some controversy in the literature concerning some of the electronic properties of these triaryl compounds. All workers agree that for triphenylamine, conjugation of the nitrogen "lone-pair" with the benzene rings occurs with the resultant loss of basicity. However, from the interpretation of ultraviolet absorption spectra, dipole moments, and other physical data, two opposing ideas have arisen relating to the triphenyl derivatives of the other elements in this Group.

It has been postulated that the decrease in dipole moment when proceeding from triphenylphosphine to triphenylbismuthine⁷¹ indicates a gradual increase in the carbon-metal-carbon bond angle; and for triphenylbismuthine (which has a zero dipole moment) it has been suggested that the molecule is planar.⁶⁹ Jaffé has interpreted ultraviolet spectra in this light and concluded that the "lone-pair" electrons of the central atom are conjugated with the

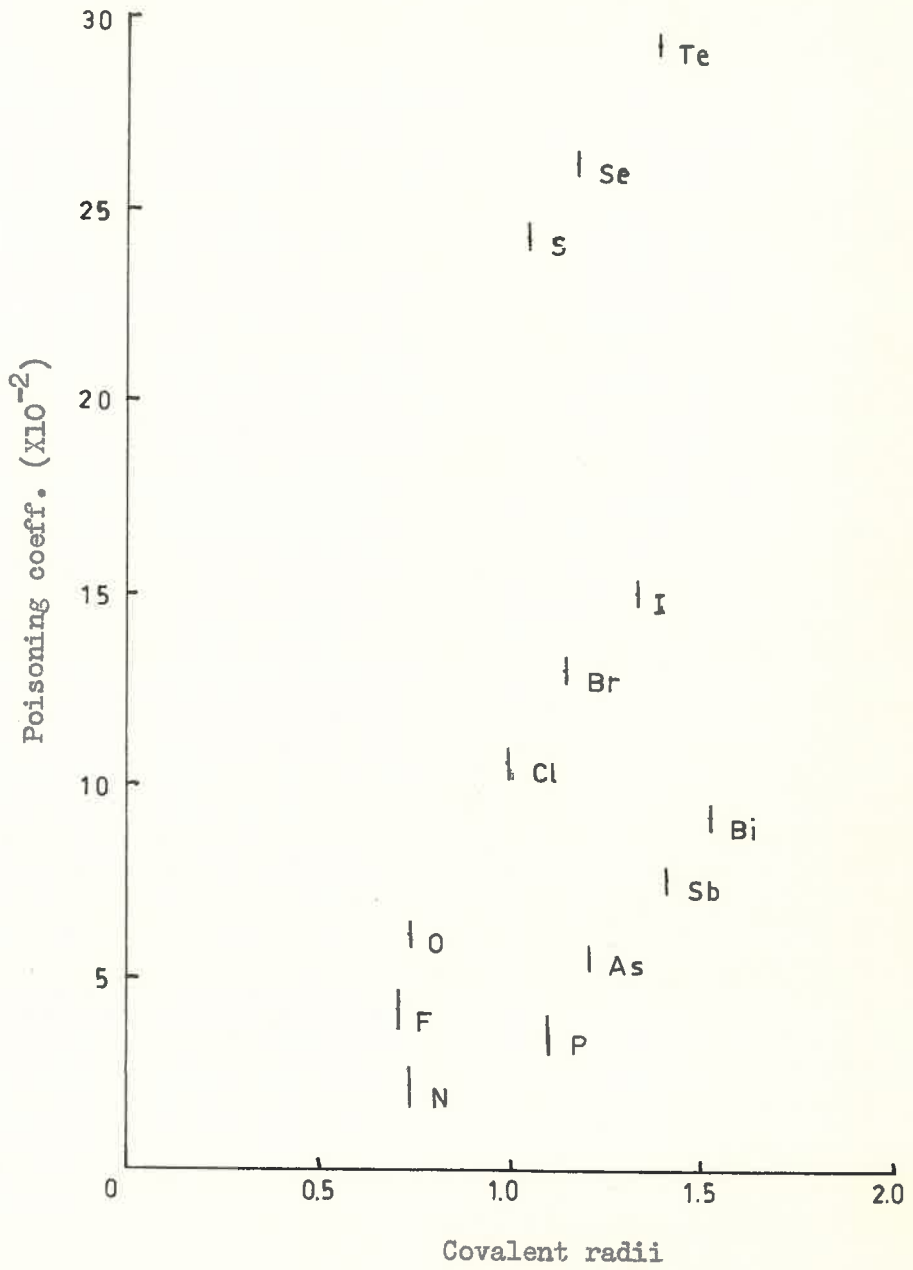


Fig. 3. Relation of covalent radii and Periodic Group to poisoning coefficient for W-7 Raney nickel in hydrogenation of crotonic acid.

phenyl rings.⁷² On the other hand, the more detailed study by Cullen and Hochstrasser⁷³ of the ultraviolet spectra of triphenylarsine and related compounds has indicated that there is little or no conjugation between the arsenic atom and the benzene rings or between the benzene rings, and that this is likely to be the case for the triphenyl derivatives of phosphorus, antimony, and bismuth. Recently, data which were originally thought to support conjugation have been reinterpreted to suggest non-conjugation.⁷⁴

Until the electronic structures of these compounds are known with certainty it is not possible to discuss their catalytic toxicities in terms of their electronic properties; but it would appear that these properties do not affect the poisoning coefficients greatly, and that the size of the poisoning molecule is of prime importance.

Maxted and Marsden²⁸ studied the relative toxicities of simple phosphorus, arsenic, antimony, and bismuth compounds towards a platinum catalyst in hydrogenations. It was found that for phosphorus and arsenic the poisoning coefficients were identical; antimony was slightly higher, and with bismuth a definite increase occurred. These results were explained on the basis of the effective area covered by the poisons. Hence if the atomic radii of the poisoning elements were less than the atomic radius of platinum, their coefficients would be similar, and not until the radius of the toxic atom exceeds that of platinum would an increase in toxicity occur. In the present work it was noticed that there

is an increase in the poisoning coefficients from phosphorus to arsenic. Firstly, the sizes of all triaryl compounds are in excess of the atomic radius of nickel so that any differences in size of the hetero-atom would be noticed in the value of the poisoning coefficient. Also, as will be discussed below, these results indicate that at least a percentage of the original poison "survives" the equilibration with the catalyst and thus poisons the catalyst. It has been shown by Sasse²⁷ that W-7 Raney nickel in refluxing methanol hydrogenolyses the triphenyl derivatives of Group V elements, (except for triphenylamine) to give benzene in yields exceeding 80%, and with no hydrogenation of the starting material. The triphenylamine was largely recovered, and most of the remainder was converted to tricyclohexylamine. As the electronic and steric effects of the phenyl groups in triphenylamine should reduce the availability of the nitrogen "lone-pair" for adsorption by the catalyst, aniline and diphenylamine were also examined. These bases underwent hydrogenation more readily than hydrogenolysis. Furthermore, under the conditions used for the hydrogenolysis, benzene gave cyclohexane in 10% yield.

As benzene poisons W-7 Raney nickel (Table II), via its aromatic electrons it must be concluded that the triphenyl compounds interact with the catalyst surface not only through their hetero-atoms but also through their π -electrons. The values of the

Table II.

Compound	Activity of 0.05 g. (c.c.)	Poisoning coefficient ($\times 10^{-2}$)
benzene ^a	1.32	3.1

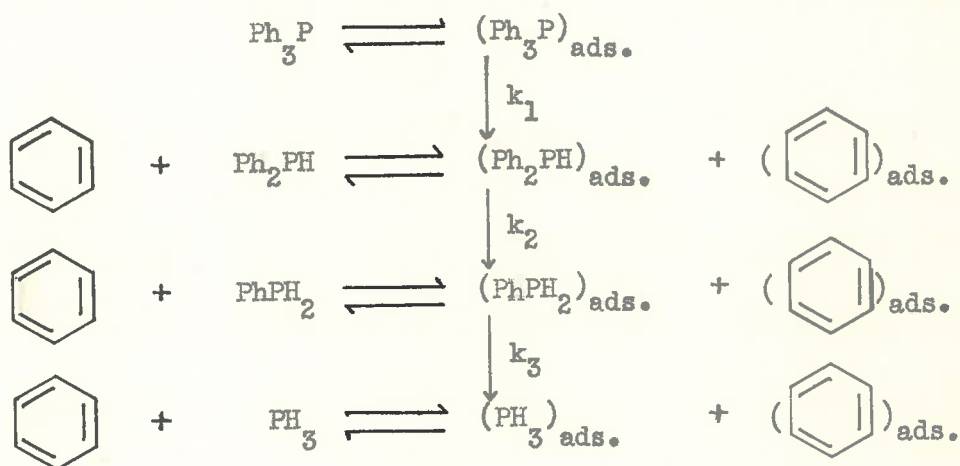
^a Ratio of substrate to poison was 20:1.

poisoning coefficients of the phenyl derivatives of the Group V elements show that the compounds whose coefficients exceed that of benzene are hydrogenolysed, while the amines which are less poisonous than benzene are mainly hydrogenated. It is therefore probable that the amines - like benzene - interact with W-7 nickel preferentially through their aromatic electrons, and that adsorption of these compounds via the nitrogen atom is of minor importance. Further evidence is found by comparing the poisoning coefficients of aniline and diphenylamine, which are almost identical with that of triphenylamine. It is suggested that the phenyl derivatives of the lower elements of Group V are chemisorbed by W-7 Raney nickel predominantly through their hetero-atoms, and that this is a prerequisite for the occurrence of hydrogenolysis.

Earlier, mention was made of the possibility that the poisoning coefficients measured in the present work are actually composite values of all the possible reaction products which are poisonous. The time used for equilibration of the poison with

the catalyst before hydrogenation was one hour. It is known that under comparable conditions triphenylphosphine is hydrogenolysed to a measurable extent.⁷⁵ Due to the increased accessibility of the hetero-atom it is expected that the rate of hydrogenolysis would increase in the order, triphenylphosphine, triphenylarsine, triphenylstibine, and triphenylbismuthine.

It is improbable that in the hydrogenolysis of triphenylphosphine all the phenyl rings are removed in one step, and a stepwise mechanism is envisaged. The rate of removal would be expected to increase with each successive loss of benzene, i.e. $k_3 > k_2 > k_1$, since the phosphorus atom should become more accessible on removal of the phenyl groups. Similarly the basicity of the phosphorus atom should increase in the order, Ph_3P , Ph_2PH , PhPH_2 , PH_3 . Also each hydrogenolysed phenyl group would become benzene and hence add to the poisoning effect. Schematically this may be represented as follows.



The results obtained with the derivatives of Group VI elements (Table III) demonstrate the highly toxic nature of these elements, and with sulphur compounds this property forms the basis of the desulphurisation reaction. Hauptmann and Wladislaw³¹ suggested that the first requirement for hydrogenolysis of sulphur compounds must be their adsorption by the catalyst via the sulphur atom. Although this hypothesis has not been proved, it has been widely accepted^{33,34} and is compatible⁷⁶ with current views concerning the mechanism of the poisoning by sulphur compounds of metal catalysts in hydrogenations.¹⁷ The values of the poisoning coefficients for the phenyl derivatives of the typical elements of Group VI, apart from oxygen, again increase linearly with the increase in covalent radii of the hetero-atoms (Fig. 3). As with the elements of Group V, the increase in poisoning coefficients appears to be dependent on the sizes of the hetero-atoms rather than on any electronic factors. The

Table III.

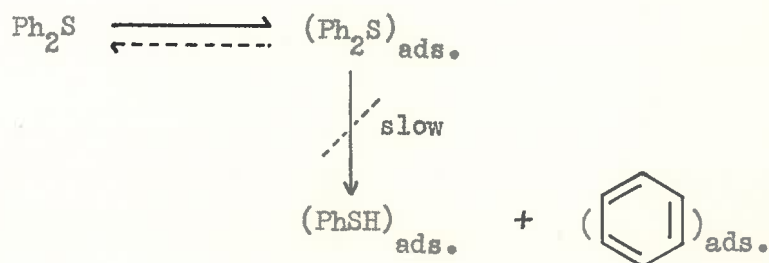
Compounds of Group VI	Activity of 0.05 g. (c.c.)	Poisoning coefficient ($\times 10^{-2}$)
Diphenyl ether ^a	1.05	6.1
Tetrahydrofuran ^a	1.5-1.6	1.5
Diphenyl sulphide ^b	0.45	24.3
Thiophen ^a	0.82	8.0
Tetrahydrothiophen ^a	0.51	11.5
Diphenyl selenide ^b	0.36	26.3
Diphenyl telluride ^b	0.20	29.3

^a Ratio of substrate to poison was 20:1

^b Ratio of substrate to poison was 40:1

actual magnitude of the toxicity values is important and agrees with present ideas that the elements of this Group are among the most toxic towards metal catalysts.

Diphenyl sulphide is known not to undergo hydrogenolysis under the conditions of hydrogenation used in the present work.⁷⁵ If it is assumed that the diphenyl derivatives of selenium and tellurium are also stable under the conditions used for the hydrogenations, then the poisoning coefficients measured must be regarded as those of the diphenyl derivatives. This implies that once adsorption has occurred, the adsorption-desorption equilibrium lies largely to the right, i.e. in the case of diphenyl sulphide,



and that no further reaction takes place (unless heat is applied). Assuming that this is also true for diphenyl selenide and diphenyl telluride, it is suggested that while these compounds are more toxic than the elements of the other Groups under consideration, they are also more stable on a Raney nickel catalyst at low temperatures than the triphenyl derivatives of Group V, and the halogenated benzenes (see later). It is also noteworthy that the toxicity values for thiophen and tetrahydrothiophen are approximately one third to one

half that of diphenyl sulphide, yet even so they are quite large compared to either benzene or pyrrole (see later) which are similar in molecular size.

Oxygen does not fit into the pattern of the lower members of the Group. As other workers^{77,78} have found diphenyl ether to be quite stable towards Raney nickel it was surprising to find it relatively toxic towards W-7 nickel. Moreover, diphenyl ether was shown to undergo hydrogenolysis to a large extent.²⁷ Fig. 3 shows that the poisoning coefficient of diphenyl ether lies in the range of the halogenated benzenes. It has been suggested that the species responsible for the poisoning is the phenoxide ion.⁷⁹

With regard to the chemisorption of oxygen it may be added that Kokes and Emmett¹³ have detected traces of methane gas from nickel catalysts which have been stored under alcohol for any length of time. Moreover, Bonner³² observed that the desulphurisation of optically active sulphones resulted in retention (with inversion) of the optical activity, and suggested that chemisorption to the nickel had occurred via the oxygen atoms.

The value of the poisoning coefficient of tetrahydrofuran was just measurable, but the accuracy of the method at such a low value does not justify any conclusion, except that it is adsorbed by the catalyst to a small extent.

The dehalogenation of chloro-, bromo-, and iodo-organic compounds using Raney nickel has been employed for a number of years.^{80,81,82,83} Only recently an example of the hydrogenolysis

of an organic fluorine derivative has been observed.⁸⁴ Pattison and Degering²⁰ found that the activity of W-4 Raney nickel was lowered in the hydrogenation of styrene in the presence of organic derivatives of chlorine, bromine and iodine. In the present work the poisoning coefficients of the halogenated benzenes have been measured (Table IV). Again there is noticed a linear increase in toxicity with increasing covalent radii of the elements (Fig. 3).

Table IV.

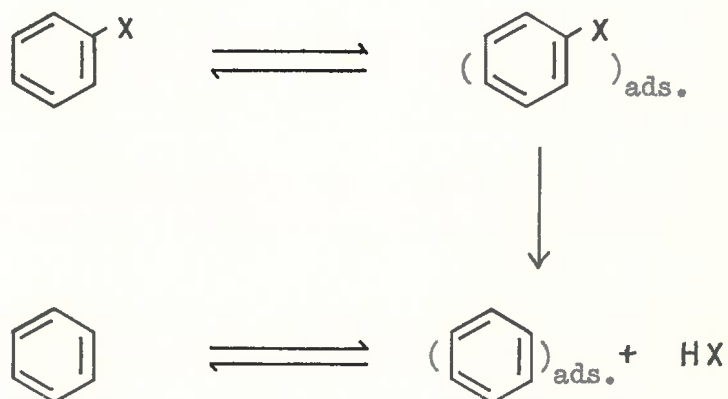
Compounds of Group VII	Activity of 0.05 g. (c.c.)	Poisoning coefficient ($\times 10^{-2}$)
Fluorobenzene ^a	1.40	4.3
Chlorobenzene ^a	0.67	10.6
Bromobenzene ^a	0.36	13.0
Iodobenzene ^a	0.18	14.9

^a Ratio of substrate to poison was 20:1

The values of the poisoning coefficients are again larger than that of benzene, and it is suggested that the halogenated benzenes are adsorbed via their halogen atoms, and that this is a prerequisite for their hydrogenolysis.

With the halobenzenes it has been shown that, under the mild conditions used for hydrogenation, a slow reaction commences almost immediately.⁷⁵ Thus the poisoning coefficient measured is not solely due to halobenzene, but is also due to some benzene

formed during the equilibration of the poison with the catalyst. Also formed in the hydrogenolysis is a halogen hydride which reacts with nickel. This explains the presence of nickel (II) halides in the reaction mixture.



From a comparison of the poisoning coefficients of the phenyl derivatives of Groups V, VI and VII it is seen that the greatest toxicity is associated with the elements of Group VI and the least with those of Group V. It is suggested that this trend is associated with the stability of these compounds on the catalyst surface. This implies that for a given period, the stability at room temperature of the phenyl compounds decreases in the order Group VI, Group VII, Group V. This order has been observed with triphenylphosphine, which is hydrogenolysed faster than chlorobenzene which in turn reacts faster than diphenyl sulphide.

As part of the present work is concerned with the reactions of some heterocyclic nitrogen compounds on Raney nickel, the

poisoning coefficients of pyridine, 2,2'-bipyridyl, and pyrrole towards several Raney nickel catalysts were determined (Table V).

Table V.

Poisoning coefficients ($\times 10^{-2}$)

Catalyst	Pyridine	2,2'-Bipyridyl	Pyrrole
W-1	6.3	6.0	-
W-2	6.8	5.3	-
W-6	2.2	3.6	-
W-7	1.7	4.9	4.2
W7-J	5.4	5.5	2.7

Table VI.

Catalyst (temp)	Activity of unpoisoned catalyst (0.05 g.)	Activity in presence of pyridine	Activity in presence of 2,2'-bipyridyl	Activity in presence of pyrrole
W-1 (22°)	0.56	0.14	0.16	-
W-2 (18°)	1.08	0.20	0.40	-
W-6 (20°)	1.64	1.20	0.94	-
W-7 (19°)	1.64	1.30	0.68	0.78
W7-J (20°)	0.60	0.21	0.21	0.33

It is noticed that the activities of the unpoisoned catalysts (Table VI) in the hydrogenation of trans-crotonic acid are in the expected order, as the activity of Raney nickel catalysts is dependent on the amount of hydrogen on the nickel.¹⁰ Although these

hydrogenations were carried out at slightly different temperatures, poisoning coefficients are known to be unaltered by small temperature changes.⁶⁸

When refluxed over degassed Raney nickel (W7-J), pyridine is known to yield 2,2'-bipyridyl in good yield,⁷ along with traces of pyrrole⁶¹ and piperidine.⁸⁵ The formation of 2,2'-bipyridyl is assumed to involve the interaction of two adjacent pyridine molecules adsorbed by the nickel via their nitrogen atoms. When W-7 Raney nickel is used, the yield of 2,2'-bipyridyl is only one twentieth of that with degassed nickel.^{12,61} As piperidine is formed in the hydrogenation of pyridine over Raney nickel, it would be expected that more piperidine would be found in the reaction with the more active catalyst. W-7 Raney nickel brings about the hydrogenation of pyridine to a much greater extent than its dimerisation, and it is suggested that on this catalyst, adsorption takes place mainly through the aromatic electrons. Similar observations would be expected with W-6 Raney nickel. For the W-1, W-2, and W7-J catalysts, from which some hydrogen has been removed, the poisoning coefficients of pyridine suggest that dimerisation should be preferred rather than hydrogenation; that is, adsorption takes place mainly through the nitrogen atom. In agreement with this hypothesis pyridine, when refluxed over W-1 Raney nickel, gave a substantially increased yield of 2,2'-bipyridyl compared with that obtained over W-7 nickel.

The lowering of the activities of all nickel catalysts by pyridine and 2,2'-bipyridyl corroborates Maxted and Walker's findings,²² and in agreement with other observations,¹⁷ the most active preparations are least affected by these bases. Pyrrole poisons the hydrogen-rich W-7 nickel to a greater extent than the W7-J nickel; but it is likely that the poisoning coefficient measured with W-7 nickel is actually that of a more basic hydrogenation product of pyrrole, namely pyrrolidine.⁸⁶

The less active nickel catalysts are more susceptible to poisoning by pyridine than by 2,2'-bipyridyl, while the opposite holds for W-6 and W-7 nickel. This reversal of the toxicities might well suggest that adsorption of 2,2'-bipyridyl on the more active catalysts is followed by further changes leading to compounds which are more toxic than pyridine. It has been shown that 2,2'-bipyridyl reacts with W-7 nickel to give pyrrole derivatives,⁸⁷ and such a change could account for the increase in catalytic toxicity of 2,2'-bipyridyl observed with the W-6 and W-7 catalysts.

Summarising the main ideas of this section, it is apparent that within the Groups V, VI, and VII the poisoning coefficients of the phenyl derivatives increase with the sizes of the hetero-atoms. As benzene itself can interact with the catalyst via its π -electrons, it may be expected that the phenyl derivatives also interact with the catalyst through their aromatic

electrons. However it has been shown that the phenyl derivatives whose poisoning coefficients exceed that of benzene are hydrogenolysed, while the amines, which are less toxic than benzene, are mainly hydrogenated. It is suggested that the amines interact with W-7 Raney nickel preferentially through their π -electrons, and that chemisorption via their nitrogen atoms is of minor importance. Toxicities of the phenyl derivatives of a given Period towards W-7 Raney nickel were found to increase in the order, Group V, Group VII, Group VI.

For aromatic nitrogen compounds the small poisoning coefficients measured with the more hydrogen-rich catalysts suggest that hydrogenation is the main reaction. With the less active catalysts, dimerisation is preferred, due to adsorption via the nitrogen atoms.

EXPERIMENTAL.

Materials.- Methanol was distilled from sodium hydroxide through a fractionating column⁸⁸ (reflux ratio 1:5), and the fraction of b.p. 64.5° (n_D^{21} 1.32859) was used. trans-Crotonic acid (m.p. 72°) was obtained by recrystallisation from light petroleum (b.p. 60-80°). W-1,⁸⁹ W-2,⁹⁰ W-6,⁹¹ W-7,⁹¹ W7-J¹² nickel catalysts were prepared from 50:50 aluminium-nickel alloy (B.D.H.). Pyridine was fractionated from potassium hydroxide (reflux ratio 1:10) and the fraction of b.p. 115-115.5° (n_D^{21} 1.5020) was used. 2,2'-Bipyridyl (m.p. 71.5-72°) was purified by chromatography on alumina and crystallised from light petroleum (b.p. 40-60°). Synthetic pyrrole was distilled under nitrogen and in the absence of light. A fraction, b.p. 131°, was used immediately. The following compounds were commercial samples which were purified by repeated crystallisation or fractional distillation under nitrogen; benzene, b.p. 80° (n_D^{25} 1.4980); fluorobenzene, b.p. 85° (n_D^{25} 1.4620); chlorobenzene, b.p. 131-132° (n_D^{25} 1.5214); bromobenzene, b.p. 155-156° (n_D^{21} 1.5592); iodobenzene, b.p. 188° (n_D^{21} 1.6190); aniline, b.p. 184.5° (n_D^{20} 1.5863); tetrahydrofuran, b.p. 65° (n_D^{25} 1.4039); thiophen, b.p. 84.1° (n_D^{25} 1.5286); tetrahydrothiophen, b.p. 119° (n_D^{18} 1.4871); diphenyl sulphide, b.p. 155°/13 mm.; diphenyl ether, b.p. 252°; triphenylphosphine, m.p. 80.5-81°; diphenylamine, m.p. 52.5-53°.

I am grateful to Dr. W.H.F. Sasse for gifts of pure triphenylamine, triphenylarsine, triphenylstibine, triphenylbismuthine

diphenyl selenide, and diphenyl telluride.

Hydrogenations.- The hydrogenations were carried out in two Towers microhydrogenators at atmospheric pressure in methanol (volume of mixture made up to 10 c.c.) the flasks being shaken at 290 ± 20 vibrations per min. A constant temperature of $30 \pm 0.2^\circ$ (except where otherwise stated) was used for the hydrogenations. When new preparations of the catalysts were required, re-standardising was carried out. Poisons (0.000003 - 0.000012 mole.) were added and equilibrated for 50-60 min. with the catalyst⁹² before the crotonic acid (0.0104 g.) was introduced. After completion of a run, the catalyst was filtered off, dried and weighed. The results of hydrogenations in the presence and absence of poisons are listed in Tables VII-XVIII under the catalyst used.

Method of comparison.- The rate of hydrogenation of crotonic acid was measured in each run by the slope of the hydrogenation curve at its origin. As the weight of catalyst cannot be determined accurately until the completion of a run, a series of experiments was carried out in which the weight of catalyst was varied (0.01 - 0.2 g.) while the other variables were kept constant. In this way a linear relationship between the weight of catalyst and the rate of hydrogenation was obtained. Repetition of these experiments in the presence of each poison gave linear relationships of lower slope. From these graphs the activity of 0.05 g. of each catalyst (poisoned and unpoisoned) was read off; these values being expressed as poisoning coefficients⁶⁸ calculated

from the expression $k_c = k_o(1 - ac)$. The accuracy of the value is regarded as being $\pm 0.5 \times 10^2$ for values less than 5×10^2 and $\pm 0.3 \times 10^2$ for values greater than 5×10^2 .

Hydrogenolyses.- All hydrogenolysis reactions were carried out by Dr. W.H.F. Sasse.²⁷

Reaction between Pyridine and W-1 Nickel.- Pyridine (150 c.c.) was refluxed over W-1 nickel⁸⁹ (prepared from 125 g. of alloy) for 50 hr. The mixture was worked up as described,⁷ to give 2,2'-bipyridyl (19.5 g.) and complex (2.5 g.).

Hydrogenations of trans-crotonic acid with W-7 Raney nickel.

Table VII.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0412	1.26	-
0.0648	2.09	-
0.0300	1.13	-
0.0112	0.22	-
0.0238	0.57	Triphenylphosphine
0.0089	0.20	"
0.0186	0.50	"
0.0152	0.38	"
0.1003	2.26	Triphenylarsine
0.0458	1.07	"
0.0084	0.11	"
0.0192	0.47	"
0.0250	0.50	Triphenylstibine
0.0510	0.87	"
0.0082	0.11	"
0.0186	0.35	"
0.0622	0.90	Triphenylbismuthine
0.0729	0.97	"
0.0998	2.69	"
0.0180	0.24	"

Table VIII.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0150	0.49	-
0.0134	0.36	-
0.0424	1.23	-
0.0482	1.69	-
0.0850	2.46	Triphenylamine
0.0298	0.78	"
0.0100	0.27	"
0.0238	0.65	"
0.0350	1.04	Diphenylamine
0.0372	1.51	"
0.0216	0.51	"
0.0304	0.88	"

Table IX.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0638	2.10	-
0.0463	1.52	-
0.0300	0.91	-
0.0250	0.76	-
0.2357	6.02	Aniline
0.0185	0.72	"
0.0543	0.32	"
0.0305	0.54	"
0.0269	0.55	Benzene
0.0637	1.62	"
0.0570	1.61	"
0.1305	3.42	"

Table X.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0186	0.42	-
0.0202	0.68	-
0.0590	1.93	-
0.0698	2.08	-
0.0216	0.49	Diphenyl ether
0.0484	0.90	"
0.1292	2.70	"
0.0704	1.50	"
0.1940	1.93	Diphenyl sulphide
0.2090	1.81	"
0.0494	0.39	"
0.0414	0.27	"
0.0206	0.71	-
0.0136	0.45	-
0.1348	3.88	-
0.0480	1.51	-
0.1000	0.78	Diphenyl selenide
0.1170	0.75	"
0.1070	0.82	"
0.1760	1.26	"

Table X (cont'd).

0.1852	0.85	Diphenyl telluride
0.1496	0.66	"
0.0800	0.16	"
0.1912	0.71	"
0.0684	2.09	Tetrahydrofuran
0.0840	2.71	"
0.0344	1.08	"
0.0876	2.26	"

Table XI.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0544	1.69	-
0.0324	0.97	-
0.0464	1.35	-
0.0186	0.71	-
0.0460	0.85	Thiophen
0.0776	1.13	"
0.1078	1.69	"
0.0956	1.59	"

Table XII.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0554	1.94	-
0.0382	1.13	-
0.0464	1.36	-
0.0154	0.59	-
0.0820	0.90	Tetrahydrothiophen
0.0754	0.85	"
0.0606	0.58	"
0.0436	0.36	"

Table XIII.

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison
0.0916	3.39	-
0.0250	0.68	-
0.0250	0.90	-
0.0272	0.78	-
0.0356	0.85	Fluorobenzene
0.0274	0.68	"
0.0306	0.86	"
0.0574	1.36	"
0.0658	0.80	Chlorobenzene
0.0368	0.42	"
0.0162	0.09	"
0.0350	0.43	"
0.1068	0.84	Bromobenzene
0.0776	0.58	"
0.0470	0.31	"
0.0438	0.18	"
0.1128	0.54	Iodobenzene
0.0882	0.43	"
0.0300	0.09	"
0.0592	0.16	"

Hydrogenations of trans-crotonic acid with other Raney nickel catalysts.

Table XIV.

W-1 Nickel, 22°

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison	Ratio of substrate to poison
0.0960	1.09	-	-
0.0368	0.45	-	-
0.0865	0.94	-	-
0.0121	0.13	-	-
0.0147	0.04	Pyridine	10:1
0.0422	0.13	"	"
0.0420	0.11	"	"
0.0530	0.15	"	"
0.0669	0.22	2,2'-Bipyridyl	10:1
0.0570	0.20	"	"
0.0640	0.20	"	"
0.0239	0.07	"	"

Table XV.

W-2 Nickel, 18°

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison	Ratio of substrate to poison
0.0437	0.91	-	-
0.0164	0.42	-	-
0.0298	0.65	-	-
0.0818	1.70	-	-
0.0732	0.32	Pyridine	10:1
0.0339	0.13	"	"
0.0843	0.42	"	"
0.0510	0.15	"	"
0.0739	0.57	2,2'-Bipyridyl	10:1
0.0397	0.33	"	"
0.0203	0.17	"	"
0.0423	0.33	"	"

Table XVI.

W-6 Nickel, 20°

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison	Ratio of substrate to poison
0.0359	1.14	-	-
0.0281	1.00	-	-
0.0324	0.99	-	-
0.0150	0.48	-	-
0.0290	0.60	Pyridine	10:1
0.0382	2.20	"	"
0.0318	0.66	"	"
0.0190	0.45	"	"
0.0710	1.37	2,2'-Bipyridyl	10:1
0.0188	0.35	"	"
0.0602	1.08	"	"
0.0340	0.62	"	"

Table XVII.

W-7 Nickel, 19°

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison	Ratio of substrate to poison
0.0252	0.83	-	-
0.0062	0.12	-	-
0.0604	1.85	-	-
0.0501	1.80	-	-
0.0527	1.34	Pyridine	10:1
0.0344	0.88	"	"
0.0160	0.30	"	"
0.0584	1.63	"	"
0.0409	0.43	2,2'-Bipyridyl	10:1
0.0350	0.45	"	"
0.0187	0.28	"	"
0.0787	1.22	"	"
0.1143	1.79	Pyrrrole	10:1
0.0268	0.45	"	"
0.0240	0.39	"	"
0.0364	0.55	"	"

Table XVIII.

W7-J Nickel, 20°

Weight of catalyst (g.)	Initial rate (c.c./min.)	Poison	Ratio of substrate to poison
0.0346	0.44	-	-
0.0276	0.34	-	-
0.1170	1.36	-	-
0.0780	0.86	-	-
0.0809	0.38	Pyridine	10:1
0.0414	0.17	"	"
0.0613	0.25	"	"
0.0700	0.27	"	"
0.0900	0.37	2,2'-Bipyridyl	10:1
0.0396	0.16	"	"
0.0789	0.37	"	"
0.0770	0.34	"	"
0.0302	0.21	Pyrrole	10:1
0.0630	0.42	"	"
0.1115	0.66	"	"
0.0272	0.22	"	"

CHAPTER II

The action of degassed Raney nickel on
some derivatives of aniline.

- A. The formation of carbazole from aniline.
- B. The formation of indoles from o-alkylanilines
and N-alkyl-o-alkylanilines.

CHAPTER II

PART A: The Formation of Carbazole from Aniline

In the reaction of quinoline with degassed Raney nickel,⁴³ trace amounts of carbazole are formed. Sasse⁴³ has suggested that the first step is the fission of the hetero-ring, and that the 1,2- and 4,9-bonds are ruptured to produce an intermediate (I) which could either react with hydrogen to form aniline, or combine with an adjacent intermediate to give a 2,2'-diaminobiphenyl derivative (II), which loses ammonia to form carbazole (III). As phenazine was not detected in the reaction, it was suggested that the intermediates (I) remains attached to the catalyst during these transformations. This mechanism is supported by the observation that aniline is formed from all methylquinolines which produce carbazole. The present study was undertaken in order to examine the mode of formation of carbazole from quinoline under the influence of degassed Raney nickel.

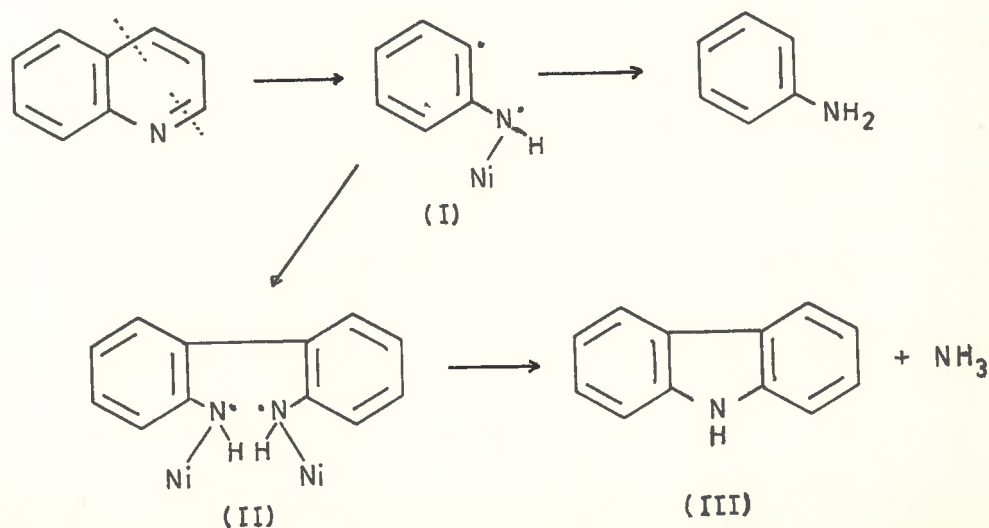


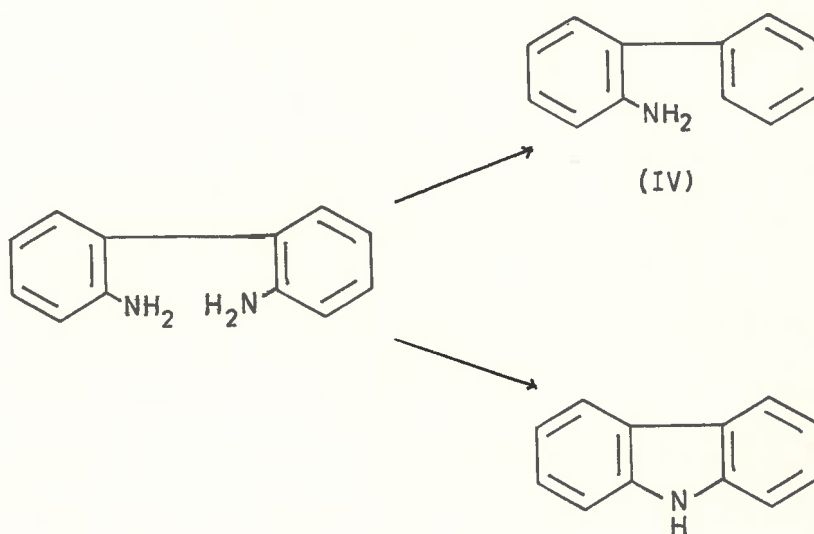
TABLE I

Reactant	Wt. of reactant (g.)	Wt. of Ni:Al alloy (g.)	Products isolated (g.)				
			Carbazole	Diphenylamine	2-Aminobiphenyl	2,2'-Diaminobiphenyl	Cyclohexylaniline
2,2'-Diaminobiphenyl	125	104	6.6 (5.8%)	-	11.0 (9.6%)	-	-
Carbazole	68.2	62.5	-	-	-	-	-
2-Aminobiphenyl	135	122	4.34 (3.3%)	-	-	-	-
Diphenylamine	140	125	1.84 (1.3%)	-	-	-	-
Aniline	149	250	0.24 (0.2%)	0.23 (0.2%)	0.02 (0.01%)	0.54 (0.4%)	5.14 (3.7%)
Aniline + Cyclohexyl- amine	Aniline (75) Cyclohexylamine (16)	125	-	-	-	-	25.6 (89%)
Azobenzene ^{a, b}	75	125	-	0.6 (0.9%)	-	-	-

^a Reaction was not worked up to isolate all products.

^b Aniline (10 g.) was also isolated.

In an attempt to test the validity of this hypothesis, 2,2'-diaminobiphenyl was treated with W7-J Raney nickel at 220-240°/120 mm. for 50 hr. Under these conditions carbazole and 2-aminobiphenyl (IV) were formed (see Table I). This finding not only supports the proposed pathway, but represents a new route to carbazole which has previously not been prepared from 2,2'-diaminobiphenyl with the aid of metal catalysts.⁹³ Under similar conditions, carbazole was not detectably affected by the catalyst, and this suggested that 2-aminobiphenyl was formed from 2,2'-diaminobiphenyl and not from carbazole.

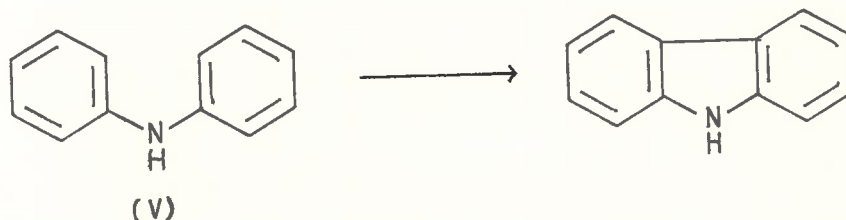


As several authors have described the conversion of 2-aminobiphenyl to carbazole under the influence of various metal catalysts,^{94,95,96,97} the action of W7-J Raney nickel on 2-aminobiphenyl was also examined. This experiment showed that degassed Raney nickel is also capable of converting 2-aminobiphenyl to carbazole. However, the table shows that 2,2'-diaminobiphenyl

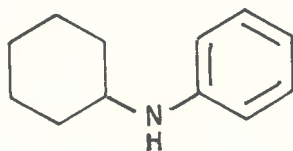
is converted to carbazole more efficiently than 2-aminobiphenyl.



Another route to carbazole involves the dehydrocyclisation of diphenylamine (V) under the influence of a platinum catalyst,⁹⁸ and this prompted inclusion of diphenylamine in the present work. Again carbazole was obtained, but in lower yield than from 2-aminobiphenyl.

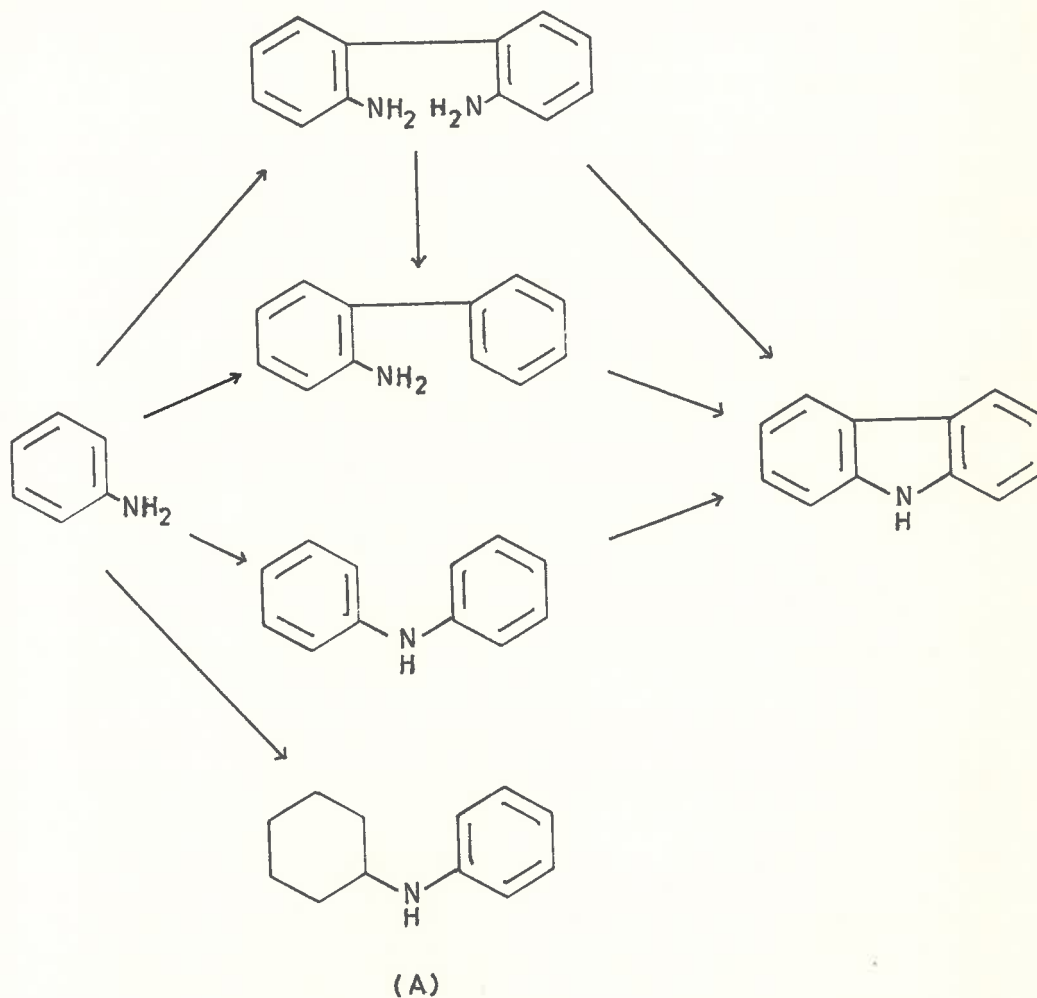


In connection with this work the action of W7-J Raney nickel on aniline was also investigated. This showed the formation of traces of carbazole, 2,2'-diaminobiphenyl, 2-aminobiphenyl and diphenylamine, but the main product was cyclohexylaniline (VI). While the formation of 2-aminobiphenyl and 2,2'-diaminobiphenyl in reactions with aniline and metal catalysts have not been observed previously, the formation of secondary amines during the catalytic hydrogenation of aniline is well authenticated. Thus,



(VI)

Magisima⁹⁹ obtained dicyclohexylamine, diphenylamine, cyclohexylaniline and cyclohexylamine as well as ammonia, benzene and cyclohexane (products of hydrogenolysis), from the hydrogenation of aniline over nickel at 260-300°. He suggested that cyclohexylamine reacted with itself to give dicyclohexylamine which on dehydrogenation gives firstly cyclohexylaniline and then diphenylamine. Debus and Jungers¹⁰⁰ studied the role of various intermediates in the reduction of aniline over nickel. These authors envisaged a sequence of reactions leading firstly to cyclohexylamine which then reacted with aniline to yield cyclohexylaniline. This was assumed to undergo further reduction to give dicyclohexylamine which was observed as the only product besides cyclohexylamine. Other workers^{101,102,103} have also noticed the formation of dicyclohexylamine in the reduction of aniline and Winans¹⁰⁴ showed that the hydrogenation of aniline gave better yields in the presence of dicyclohexylamine. The results described in this section so far may be summarised as in the following scheme (A).



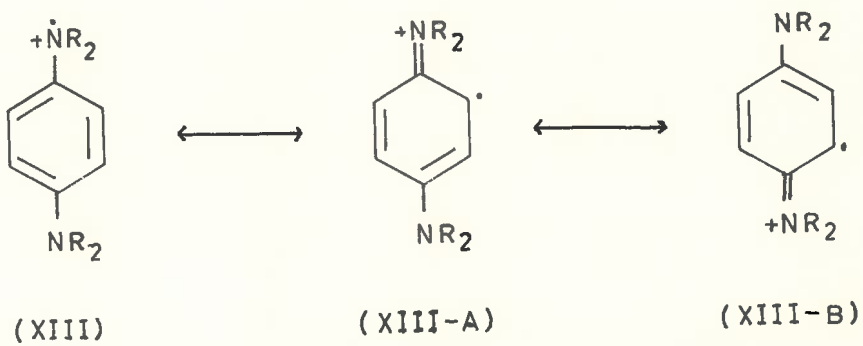
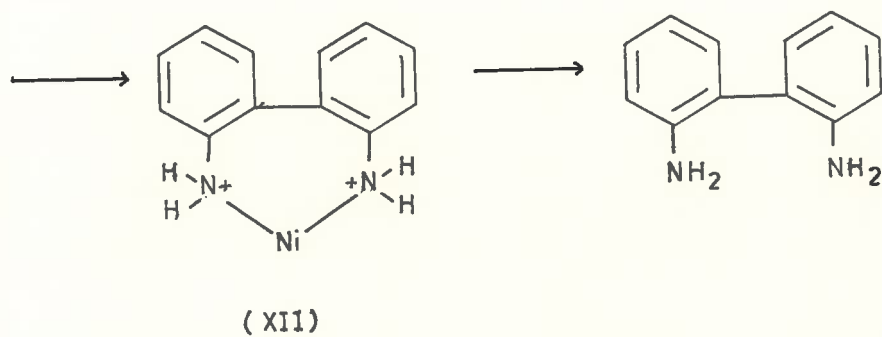
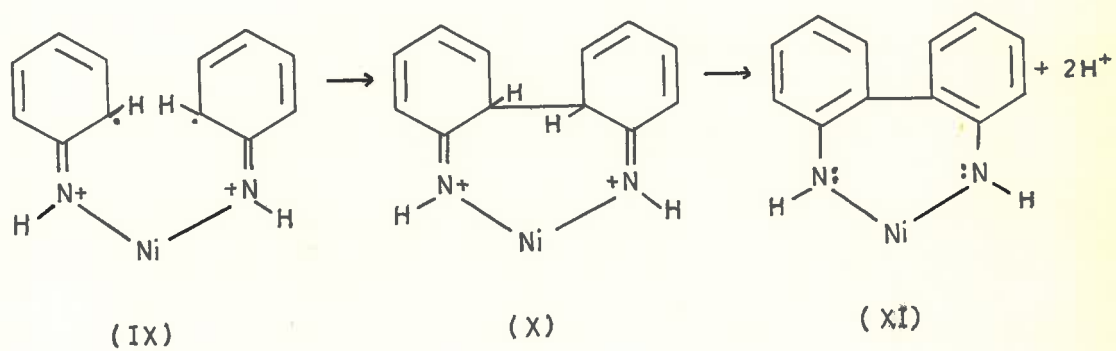
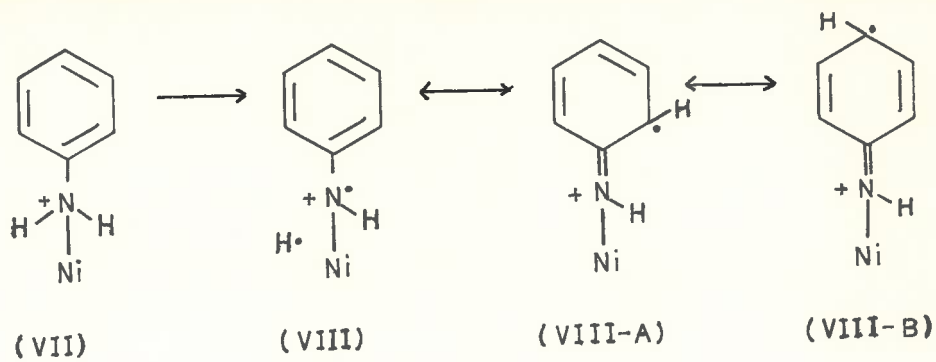
The formation of carbon-carbon bonds and secondary amines either inter- or intramolecularly, constitutes the two main types of reactions involved in the formation of carbazole from aniline on a degassed Raney nickel catalyst.

Earlier in this thesis it was shown that aniline retards only slightly the hydrogenation of trans-crotonic acid with W-7 Raney nickel. In view of the results obtained with pyridine, it

is probable that aniline interacts more strongly with the degassed Raney nickel which is employed in the reactions described in the present chapter.

In the first chapter it was suggested that pyridine is chemisorbed by the hydrogen-rich W-7 catalyst mainly by means of its aromatic sextet, and that chemisorption of pyridine on the degassed catalyst involves mainly the lone electron pair of the nitrogen atom. This hypothesis is now extended to the chemisorption of aniline on degassed Raney nickel.

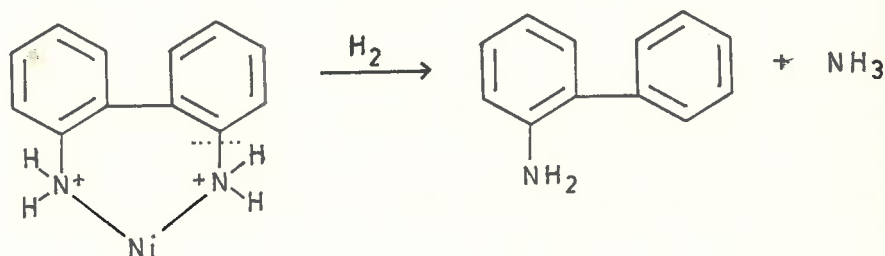
Accordingly, it is now proposed that the first step in the formation of 2,2'-diaminobiphenyl from aniline is the chemisorption of aniline by the catalyst via the lone electron pair of the nitrogen atom to yield (VII). The next step is assumed to involve the homolytic fission of one of the N-H bonds to yield the adsorbed radical (VIII). An analogous dehydrogenation has been postulated by Kindler,^{105,106} and it is now suggested that the hydrogen atom that is removed is transferred to a vacant position in the lattice of the catalyst. The intermediate (VIII) may be regarded as a resonance hybrid, and several of its contributing structures (e.g. VIII-A and VIII-B) are reminiscent of some of the canonical structures of the so called "Wurster's salts" (XIII, XIII-A and XIII-B).^{107a}



Provided the intermediates (VIII) are formed sufficiently close to one another, bond formation to give (X) may be expected to occur. Inspection of Catalin models shows that the required orientation of two molecules of aniline is achieved when they are bonded to the same nickel atom (IX), but the possibility of adsorption on two adjacent nickel atoms cannot be excluded at present.

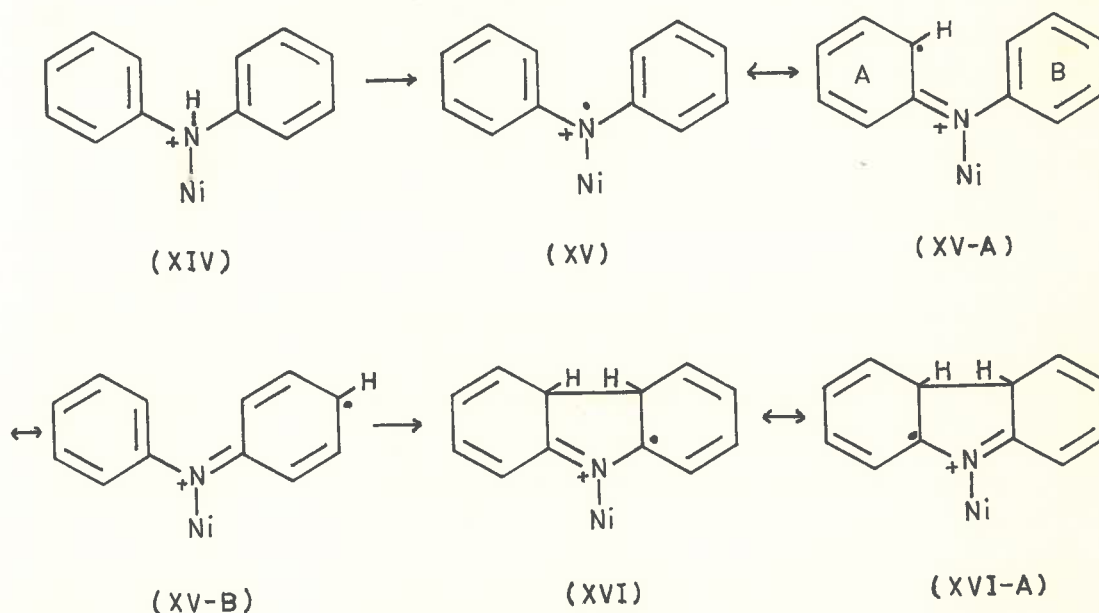
The final stages of the reaction may conceivably proceed by the 1,3-shift of two protons from the inter-annular bond with concomitant aromatisation of the two benzene rings; but the process need not be a concerted change. Finally, desorption could give rise to 2,2'-diaminobiphenyl.

On the other hand, deamination, as has been observed with aniline,²⁷ will produce 2-aminobiphenyl. The mechanism of this hydrogenolysis is not known, but it is presumably analogous to similar reactions discussed in Chapter I for a variety of heteroatoms.

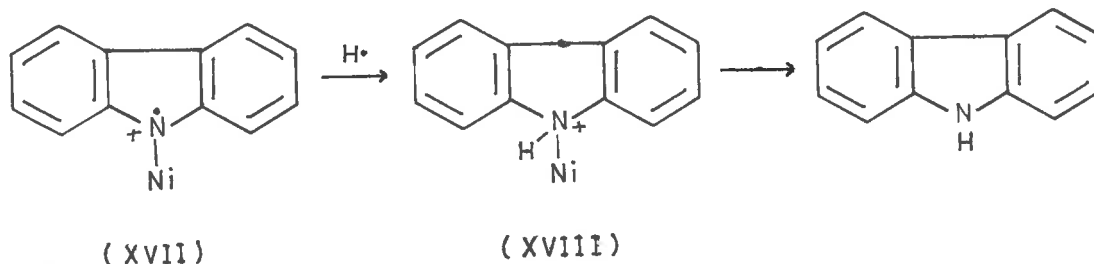


The relatively low yields of both 2-aminobiphenyl and 2,2'-diaminobiphenyl are probably caused by several factors. Thus, the small poisoning coefficient of aniline suggests that interaction of this base with the catalyst will be relatively small. Also, the dehydrogenation (VII \longrightarrow VIII) postulated, requires a high energy of activation. Finally, the geometric requirements for the formation of (X) may be realised only rarely.

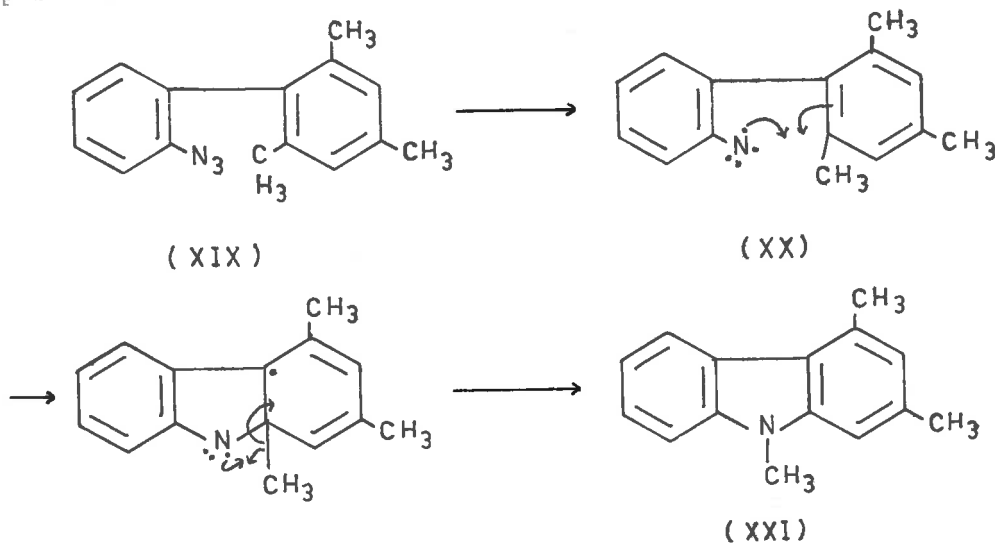
The formation of carbazole from diphenylamine is thought to be initiated by the bonding of a molecule of diphenylamine to one atom of nickel (XIV). Homolytic fission of the N-H bond, of the type postulated with aniline, yields the chemisorbed radical (XV), the structure of which is analogous to the diphenylamino radicals which are met with in the dissociation of tetraphenylhydrazine.^{107b} Addition of the uncoupled electron of ring A to



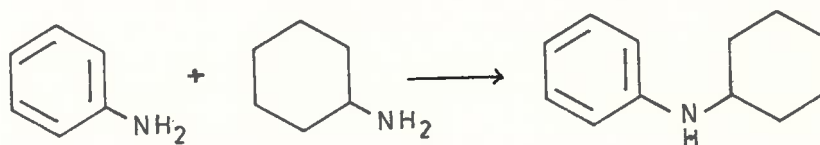
ring B leads to (XVI) which is also stabilised by resonance (e.g. XVI-A). Dehydrogenation leads to (XVII), and after hydrogen addition at the nitrogen atom to give (XVIII), desorption occurs to give carbazole.



In connection with this work it is noteworthy that "nitrenes", prepared by the pyrolysis of organic azides, possess great reactivity enabling an intramolecular reaction forming heterocyclic compounds.^{108,109,110} For example, 2-azido-2',4',6'-trimethylbiphenyl (XIX) has been shown to yield 2,4,9-trimethylcarbazole (XXI), and a reactive "nitrene" intermediate (XX) has been postulated.¹⁰⁸

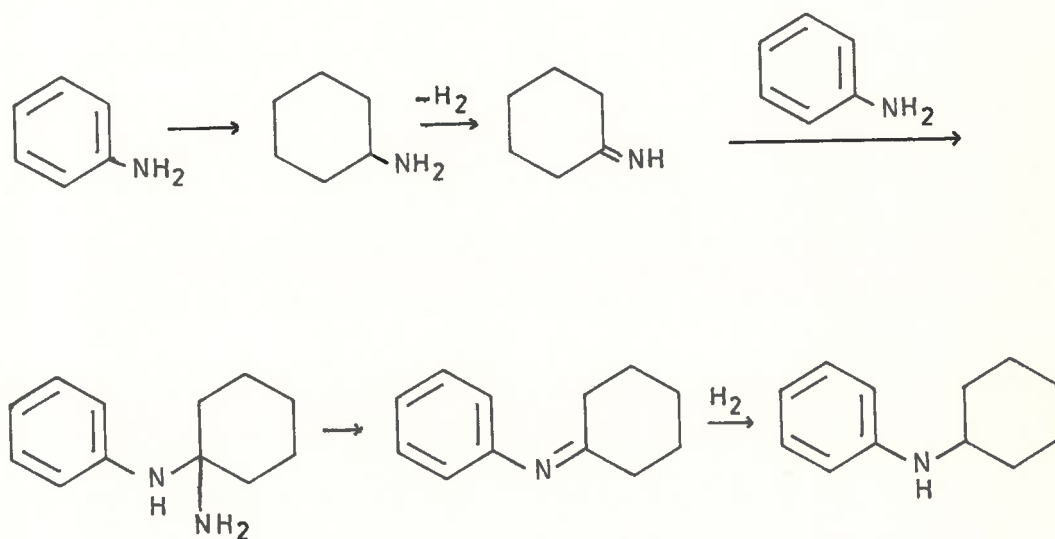


The scheme (A) (p. 66) shows that in two cases, secondary amines are formed from primary amines. Cyclohexylaniline, the major product, cannot have arisen from the partial reduction of diphenylamine, as neither cyclohexylaniline or dicyclohexylamine were formed in the reaction of diphenylamine with degassed Raney nickel. It is now known that cyclohexylaniline arises from the reaction of aniline with cyclohexylamine over W7-J Raney nickel. Such a reaction produces an almost 90% yield of cyclohexylaniline. In the reaction of aniline it is assumed that at least some aniline

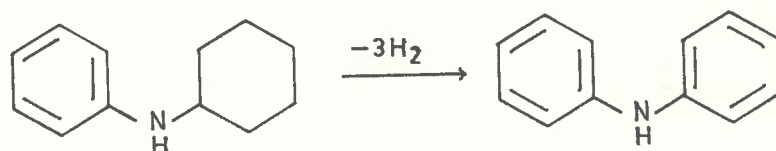


is hydrogenated to give cyclohexylamine. Reaction of this compound with aniline would then give cyclohexylaniline. It is surprising that no dicyclohexylamine could be detected in these reactions. The alkylation of amines using alcohols in the presence of Raney nickel is a common preparative method,¹¹¹ and some authors have noticed the formation of secondary and tertiary amines in reactions of primary amines with catalysts.^{105,106,111,112,113,114}

formation of cyclohexylaniline can at present not be excluded. The following scheme of reactions indicates the formation of cyclohexylaniline according to Kindler's mechanism.

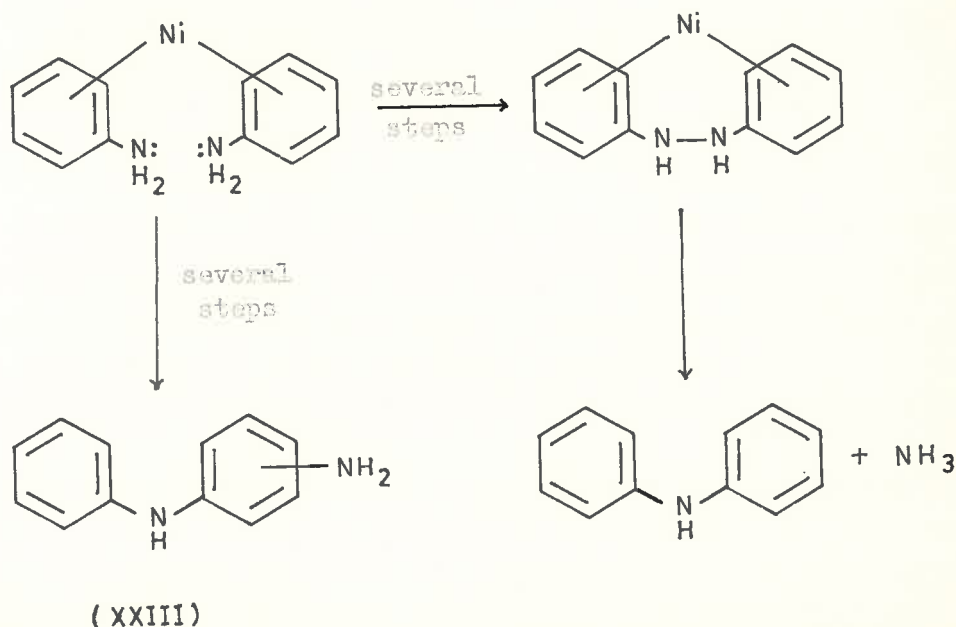


Kindler further stated that aniline could not react in this fashion to give diphenylamine, as it is impossible to dehydrogenate aniline to give the required intermediate. As mentioned earlier, Mugisima⁹⁹ proposed that diphenylamine arose from the dehydrogenation of dicyclohexylamine. It is possible that in the present work, diphenylamine results from the dehydrogenation of cyclohexylaniline.

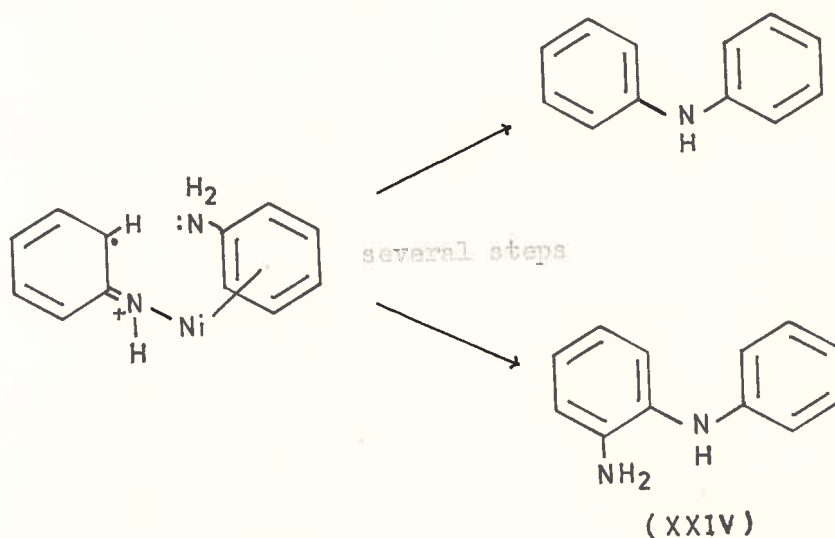


Alternatively, consideration of reactions occurring on the catalyst surface suggest other pathways by which diphenylamine can be formed. Inspection of Catalin models shows that it is sterically possible for two molecules of aniline to be chemisorbed on a single atom of nickel either through their π -electrons or the electron lone pair of the nitrogen atoms. As both methods of adsorption are likely, three alternative pathways are possible.

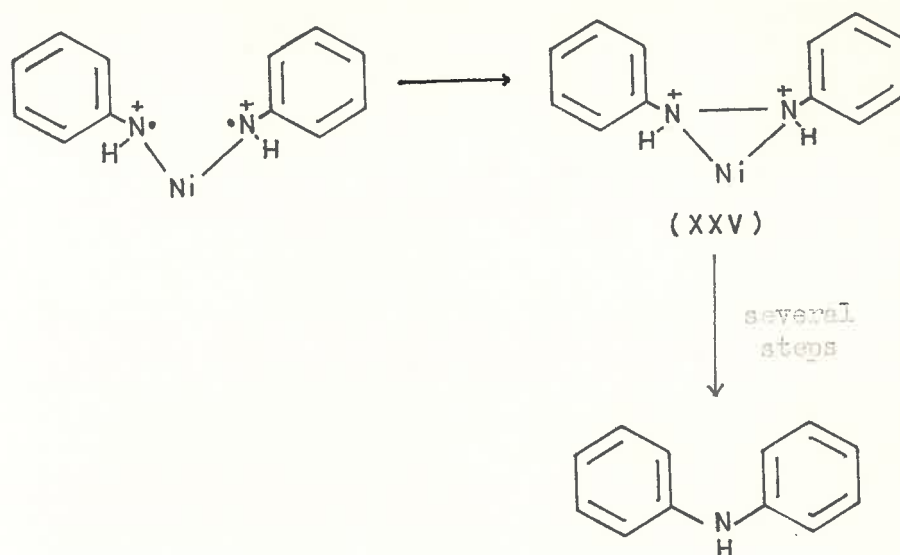
Firstly, if both aniline molecules are chemisorbed via their aromatic electrons, the interaction of the amino groups with the subsequent elimination of ammonia would produce diphenylamine. However, it should also be possible for one of the amino groups to react with any of the positions of the phenyl ring of the other molecule. If this were the case, then a mixture of aminodiphenylamines (XXIII) would be formed. This is in contrast to the results obtained.



The second possibility involves chemisorption of one molecule of aniline through its aromatic electrons and of a second molecule via its nitrogen atom. Reaction between the free amino group with the 2-position of the other molecule, followed by the hydrogenolysis of the amino group attached to the catalyst would produce diphenylamine. However, one may expect that some 2-aminodiphenylamine (XXIV) should be formed. This compound has not been detected.



Thirdly, chemisorption of two molecules of aniline through their nitrogen atoms to a single nickel atom could occur. After the removal of hydrogen from the aniline molecules in the manner described previously (p. 67), reaction between the nitrogen atoms would lead to a hydrazobenzene derivative (XXV) which would have to eliminate ammonia to yield diphenylamine.



To test this hypothesis, azobenzene was reacted with degassed Raney nickel. Aniline and diphenylamine were isolated (Table I), and the relative amount of diphenylamine formed was more than expected on the basis of the quantity of aniline present. This finding supports a path through azobenzene (or hydrazobenzene).

The results obtained in the present work furnish evidence that carbazole is formed from aniline and 2,2'-diaminobiphenyl in the presence of degassed Raney nickel. As aniline is formed in the reaction of quinoline with this catalyst, this represents one method of formation of carbazole. Statistically however, as can be seen from Table I, carbazole is formed from aniline in trace only, and the amount of aniline present in the quinoline reaction is hardly sufficient to account for the quantity of carbazole isolated. However, more carbazole is formed from 2,2'-diaminobiphenyl than from aniline, supporting the hypothesis of Sasse.⁴³

PART B: The Formation of Indoles from o-Alkylanilines and
N-Alkyl-o-Alkylanilines

As discussed in the introduction to this thesis, numerous authors have isolated pyrroles and indoles from the reactions of pyridine and quinoline with a variety of metal catalysts. The present study is primarily concerned with the mode of formation of indole and 3-methylindole from the reaction of quinoline with degassed Raney nickel.⁴³

It was Padoa⁴⁷ who first proposed that the formation of indoles from the reaction of quinoline with a reduced nickel catalyst involved as intermediates either o-alkylanilines or N-alkyl-o-alkylanilines, which underwent cyclisation to give indoles. Other authors assumed that hydrogenation of the hetero-ring preceded its cleavage.^{50,51,64} Also, the fission of the ring was suggested to occur primarily at the 1,2-bond.

The working hypothesis for the present work was based on Padoa's suggestion. Accordingly, a series of o-alkyl- and N-alkyl-o-alkylanilines were reacted with degassed Raney nickel, the results of which are summarised in Table II.

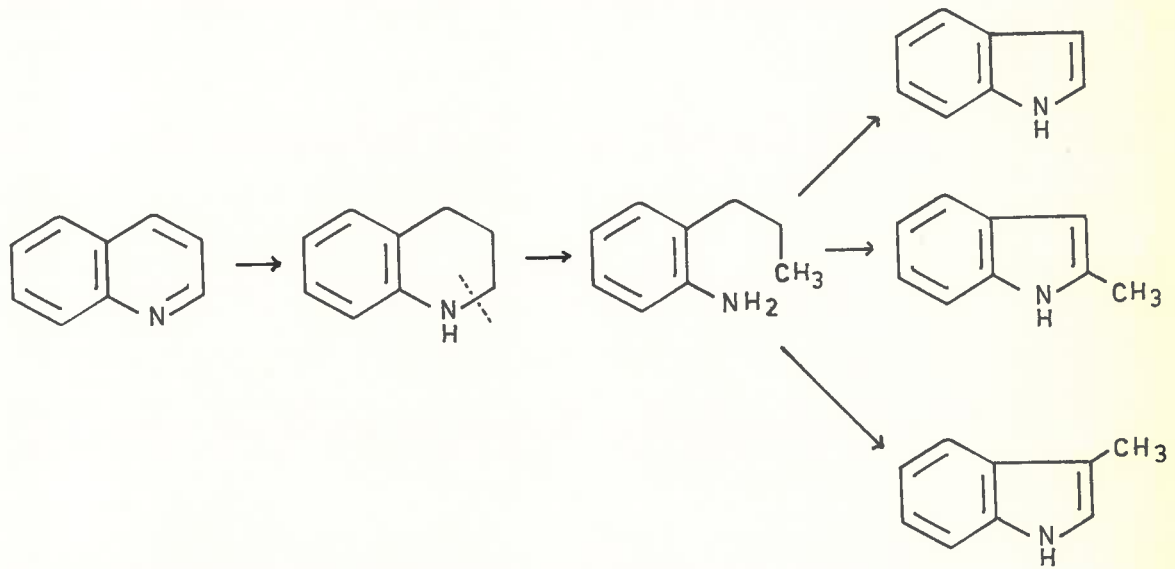
Several possibilities may be distinguished, depending on the bond which is broken. Firstly, hydrogenation and cleavage of the 1,2-bond should lead eventually to o-propylaniline. Refluxing this compound over the nickel catalyst for fifty hours yielded small amounts of indole, 2-methylindole and 3-methylindole.

TABLE II

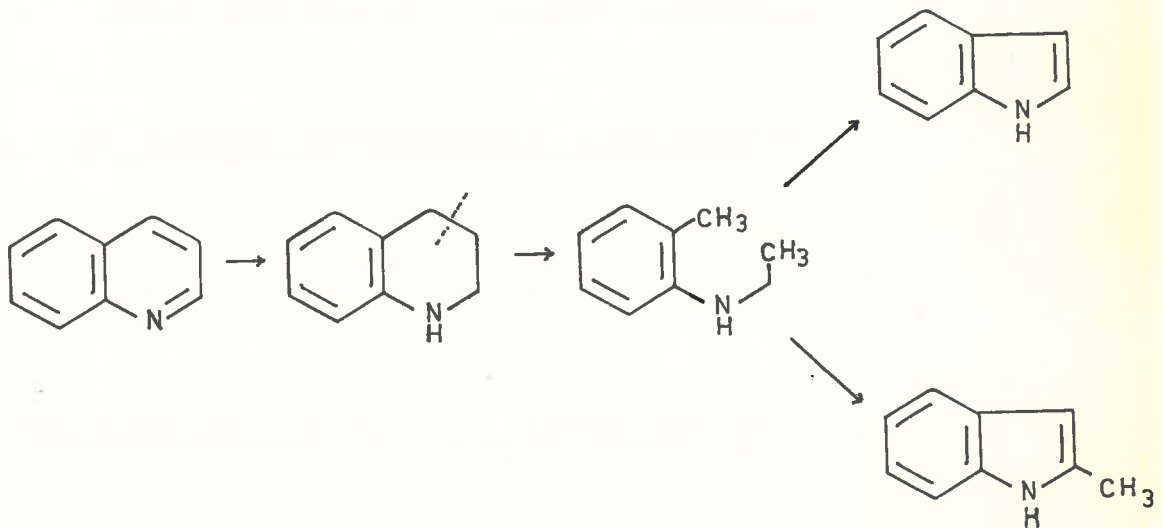
Reactant	Products isolated (g.)%							Other Products
	Indole	2-Methyl-indole	3-Methyl-indole	Aniline	<i>o</i> -Toluidine	<i>o</i> -Ethyl-aniline	(CH ₂) _x	
<i>o</i> -Propylaniline (56 g.)	0.37 (0.8%)	1.48 (2.7%)	a	1.1 (2.9%)	1.8 (4.1%)	0.2 (0.4%)	0.25	2-propylcyclohexanone
<i>N</i> -Ethyl- <i>o</i> -toluidine (56 g.)	a	a	-	4.15 (10.7%)	12.5 (28%)	-	0.25	
<i>N</i> -Allylaniline (56 g.)	-	-	a	9.2 (24%)	-	-	-	<i>N</i> -propylaniline, brown neutral gum (9 g.)
<i>N</i> -Methyl- <i>o</i> -ethylaniline (56 g.)	1.8 (3.7%)	-	5.5 (10.1%)	2.2 (5.7%)	3.3 (7.4%)	16.4 (33%)	0.76	carbazole, 2-ethylcyclohexanone
1,2,3,4-Tetrahydroquinoline (110 g.)	1.5 (1.6%)	-	7.5 (7.5%)	1.2 (1.6%)	5.6 (6.3%)	0.7 (0.7%)	6.0	5,6,7,8-tetrahydroquinoline, 2-methyl-1,2,3,4-tetrahydroquinoline, quinoline, 2,2'-biquinolyl, 2-methylquinoline, 5,6,7,8-tetrahydro-2,2'-biquinolyl, 5,5',6,6',7,7',8,8'-octahydro-2,2'-biquinolyl.
Quinoline (100 g.)	a,b	-	a,b	0.8 (1%)	2.5 (2.7%)	-	b	carbazole, ^a 2,2'-biquinolyl, 2-methylquinoline
Indoline (50 g.)	16.0 (33%)	-	-	1.0 (2.0%)	5.6 (12.5%)	0.2 (0.4%)	0.2	quinoline, 2,3'-biindole (9.2 g.)
<i>o</i> -Ethylaniline (100 g.)	3.6 (3.7%)	-	-	2.6 (3.4%)	7.5 (8.3%)	-	0.75	2-ethylcyclohexanone
Xylene (87 g.)	-	-	-	-	-	-	-	toluene, benzene
<i>p</i> -Toluidine (89 g.)	-	-	-	-	-	-	-	toluene, benzene

^a Detected by paper chromatography only

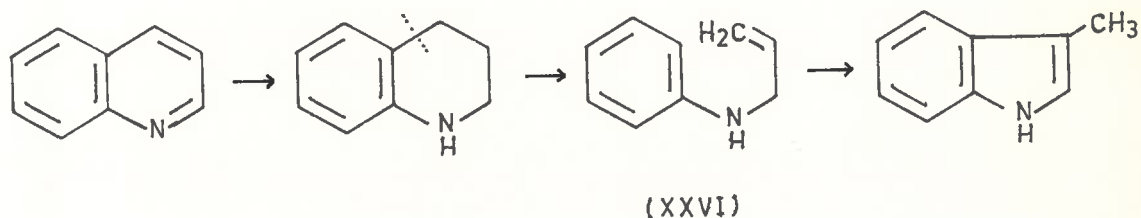
^b Mixture of indoles (1.37 g.) not separated.



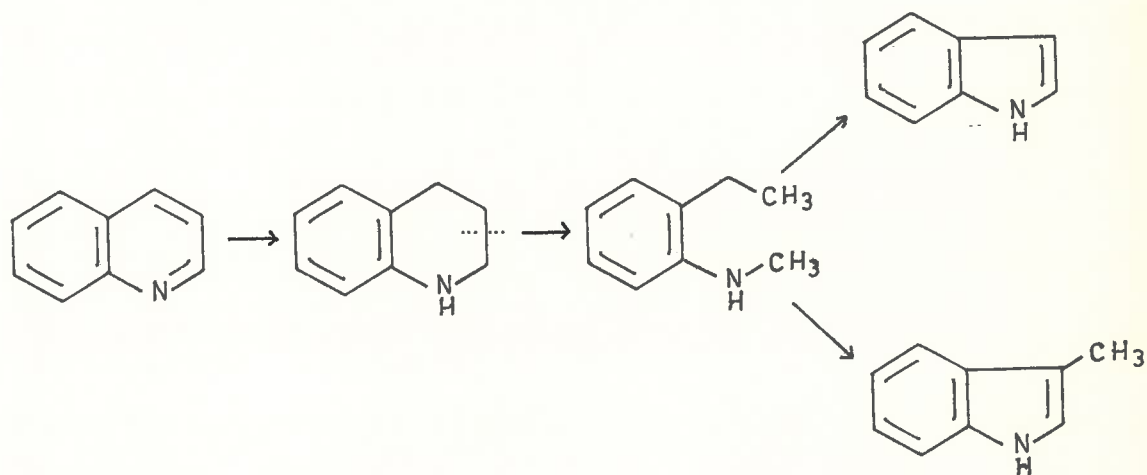
N-Ethyl-o-toluidine would be expected to be the product from the fission of the 3,4-bond. When this compound was reacted with the catalyst, paper chromatography showed the presence of indole and 2-methylindole in the neutral reaction products.



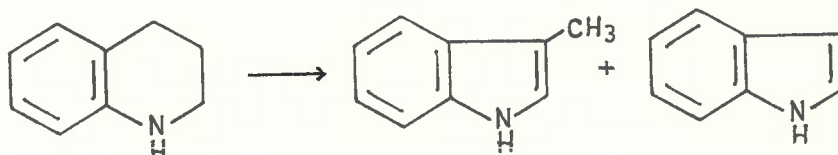
Cleavage of the 4,9-bond should lead to N-propylaniline. It was thought that N-allylaniline (XXVI) would be a more likely intermediate, and be more reactive, than N-propylaniline. For this reason, N-allylaniline was also reacted with the catalyst. Among the products of this reaction, 3-methylindole was detected by paper chromatography.



The reaction of N-methyl-o-ethyl-aniline (resulting from the rupture of the 2,3-bond) with W7-J Raney nickel was studied, and a mixture of indole and 3-methylindole was obtained.



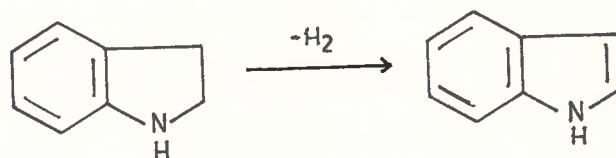
As 1,2,3,4-tetrahydroquinoline was isolated from the reaction of quinoline with degassed Raney nickel,⁴³ the reaction of this base with the catalyst was examined. From this experiment, indole and 3-methylindole were isolated in relatively larger yield than from the reaction with quinoline.



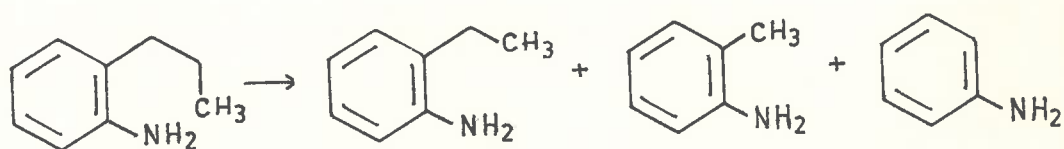
W7-J Raney nickel, although degassed at 100°, still has a large amount of hydrogen associated with it. To decrease the hydrogen content, thereby lowering the quantity of quinoline hydrogenated, a catalyst was prepared in which the degassing process was carried out at 360°. At this temperature it is known that 85-95% of the hydrogen is evolved.^{13,14} A reaction of quinoline with this nickel catalyst yielded much less neutral material than the reaction using W7-J Raney nickel.

Cyclisation of the aniline derivatives may be expected to give indoline derivatives in the first instance, and this could be followed by dehydrogenation to form indoles. In fact, no indolines were detected in any of the reaction mixtures examined in the present experiments. There are two possibilities; either indolines are not formed, or, their dehydrogenation is a

rapid process. To decide this, indoline was treated with degassed Raney nickel, and it was found that dehydrogenation to indole occurred readily, and indoline was not recovered.

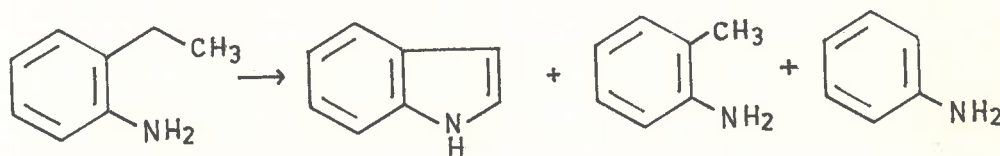


From each of the reactions with o-alkyl- and N-alkyl-o-alkylanilines described in this section, a mixture of aniline and some o-alkylanilines was obtained. The loss of the o-alkyl side chains was observed in all cases. For example, aniline, o-toluidine, and o-ethylaniline were isolated from the reaction with o-propylaniline. It can be seen from Table II, that in



these reactions less aniline than o-toluidine is formed. This finding suggests that this "dealkylation" is a stepwise process which involves the elimination of single carbon atoms. In

apparent contradiction to this view, the yield of o-ethylaniline was lower than that of o-toluidine in the reaction of o-propylaniline. However, this is probably the result of the conversion of part of the o-ethylaniline to indole, as it is known that this base under the influence of degassed Raney nickel yields indole. This is in agreement with the numerous observations that o-ethylaniline gives indole when reacted with a variety of metal catalysts. Most of the remainder of the o-ethylaniline was dealkylated, and as a result, o-toluidine and aniline were isolated as the major products. A stepwise sequence was suggested

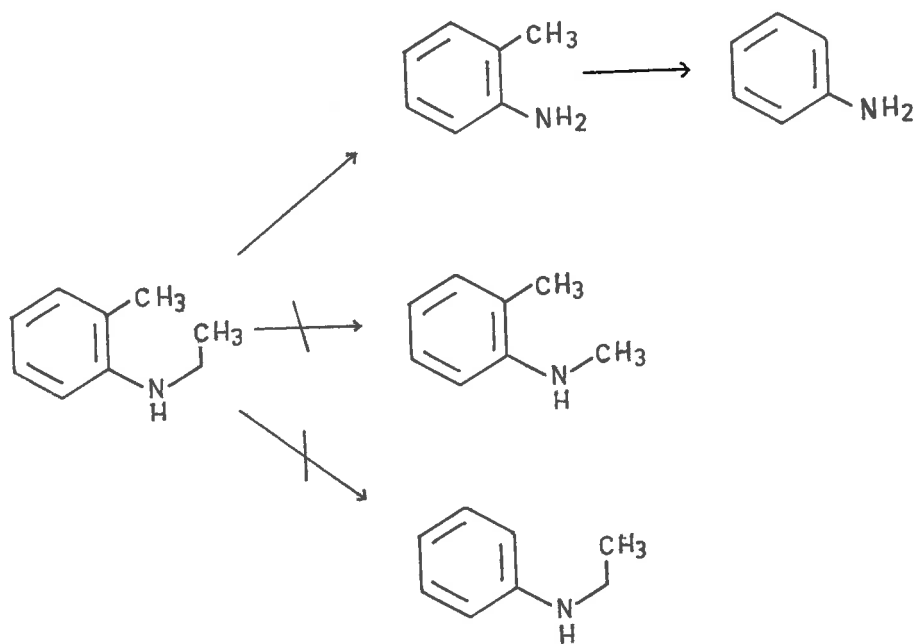


by Rapaport⁶⁴ when he isolated dealkylated products from the destructive hydrogenation of quinoline (p. 20). Furthermore, he suggested the shed methyl groups were eliminated as methane.

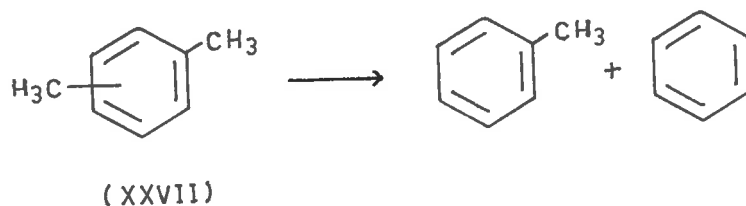
Apart from this o-dealkylation, another type of dealkylation has now been observed involving the elimination of alkyl groups from a secondary nitrogen atom under the influence of W7-J Raney nickel. For example, N-allylaniline yielded aniline when reacted with the catalyst. The results



obtained in the present work suggest that in contrast to the C-dealkylation, the N-dealkylation proceeds in one step. For example, in the reaction of N-ethyl-o-toluidine, no N-methyl-o-toluidine was detected. Furthermore, no N-ethylaniline was found, which indicates that N-dealkylation precedes C-dealkylation.



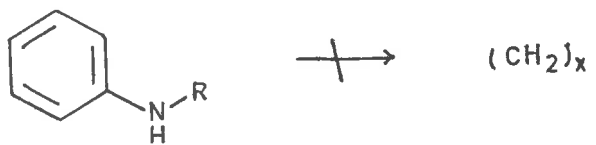
The process of C-dealkylation is apparently not confined to aniline derivatives, for it has now been found that a mixture of the isomeric xylenes (XXVII) when treated with degassed Raney nickel gives traces of toluene and benzene.



The fate of the alkyl groups eliminated from the nitrogen atom has not yet been examined in detail. However, in the reaction of W7-J Raney nickel with N-methyl-o-ethylaniline, evidence for the formation of methane was obtained, and it is thought that this alkane is derived from the N-methyl group. This view is consistent with the observation that detectable quantities of "polymethylene" were not formed in the reaction with N-allylaniline. This aliphatic hydrocarbon, which was isolated from all experiments in which C-dealkylation occurred, was first described by Sasse.⁴³ He found that irrespective of the origin of the polymethylene $(\text{CH}_2)_x$, it always has the melting point 59-60°, and a constant infrared spectrum. It has now been found that the n.m.r. spectrum clarifies to a small extent the unknown structure of this compound. A strong, narrow peak ($\tau=8.8$) indicates the presence of many CH_2 units, with little or no branch-chaining. However, the possibility

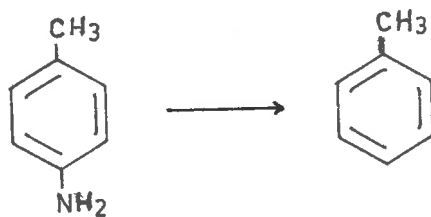
of a ring structure cannot be excluded. Evidence for aromaticity and unsaturation was not obtained. It is suggested that the carbon atoms eliminated from the side-chain link together to form a long-chain polymer having little or no branch-chaining.

The compound $(\text{CH}_2)_x$ must arise from the side-chain of the o-alkylaniline and not from the phenyl ring. This is shown by the fact that no polymethylene was formed in the reaction of aniline with degassed Raney nickel (Part A).



By far the greatest yield was obtained from the reaction with 1,2,3,4-tetrahydroquinoline. It is unlikely that any free radicals exist in solution, as anilines substituted in either m- or p-positions were not detected. Therefore, it is further suggested that polymethylene is formed on the surface of the catalyst.

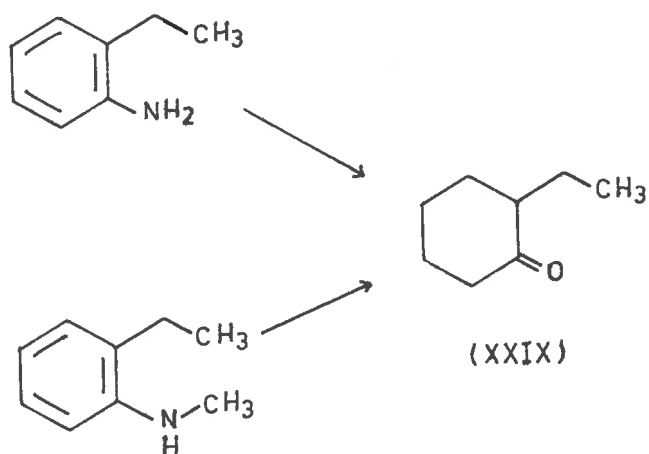
In the reactions with the o-alkyl- and N-alkyl-o-alkylanilines, the smell of ammonia was detected, and in the case of N-methyl-o-ethylaniline, ammonia was detected by means of its infrared spectrum. However, alkylbenzenes could not be isolated. This suggests that hydrogenolyses of the amino groups are a minor occurrence. However, when p-toluidine (XXVIII) was reacted with the catalyst, toluene was isolated as the major product. Apparently, the effect of increasing the basicity of the aniline derivative by placing a methyl group in the p-position, results in hydrogenolysis of the amino group. Furthermore, no aniline was detected. In Chapter I it was



(XXVIII)

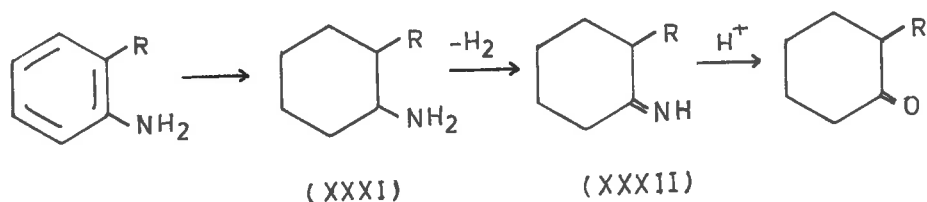
proposed that the prerequisite for the hydrogenolysis of an atom or group from a phenyl ring is its chemisorption by the catalyst via the hetero-atom. For p-toluidine it is suggested that adsorption through the nitrogen atom is preferred, thus enabling hydrogenolysis to occur. The other alternative, chemisorption through the π -electrons, should promote hydrogenation of the phenyl ring. In the series of reactions described now, hydrogenated amines were not detected.

The only products not containing nitrogen apart from $(CH_2)_x$ were isolated from experiments with o-ethylaniline, o-propylaniline, and N-methyl-o-ethylaniline. o-Ethylaniline and N-methyl-o-ethylaniline gave traces of 2-ethylcyclohexanone (XXIX), and o-propylaniline gave a trace of 2-propylcyclohexanone (XXX). Also, a trace of a ketone was detected in the reaction with N-ethyl-o-toluidine. However, its structure was not determined. The formation of these compounds is consistent with the results

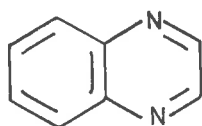




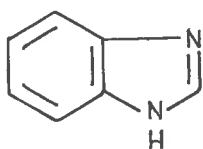
obtained by Debus and Jungers¹⁰⁰ who isolated cyclohexanone from the hydrogenation of aniline at 200° using a nickel catalyst. Imines have been postulated as intermediates in the reactions of amines with Raney nickel. Kindler and his colleagues^{105,106} proposed that the formation of secondary amines involved imine intermediates. However, imines were not detected in Kindler's experiments or in the present series of reactions. Indirect evidence for their formation was based on the observation that carbonyl compounds were not detected (spectroscopically) in the reaction mixtures until they had been treated with dilute hydrochloric acid, and imines are known to be converted to ketones under such conditions. It is suggested that the first step in the formation of a ketone is the hydrogenation of the phenyl ring (chemisorption by the catalyst via the aromatic electrons) to give an o-alkylcyclohexylamine (XXXI). Dehydrogenation leads to an imine derivative (XXXII) which may be expected to be hydrolysed in the presence of mineral acid.



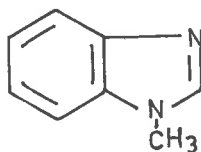
As quinoxaline (XXXIII) was readily available, it was of interest to examine the effect of a second nitrogen atom in the hetero-ring. Reaction of this compound with W7-J Raney nickel gave benzimidazoles as the major products. From the reaction mixture, the following compounds were isolated (Table III); benzimidazole (XXXIV), N-methylbenzimidazole (XXXV), 2-methylbenzimidazole (XXXVI), biquinoxalyl (XXXVII), and 2,2'-benzimidazolylquinoxaline (XXXVIII). However, o-phenylenediamine derivatives were not detected.



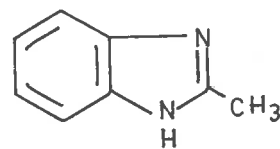
(XXXIII)



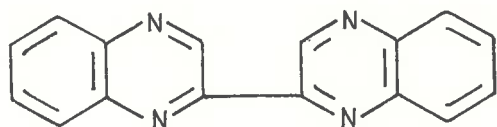
(XXXIV)



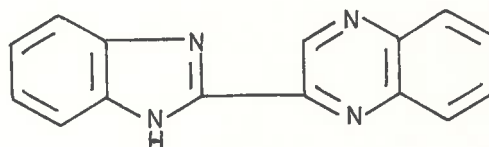
(XXXV)



(XXXVI)



(XXXVII)



(XXXVIII)

Table III

Yields (g.) in reaction between quinoxaline (55 g.) and W7-J

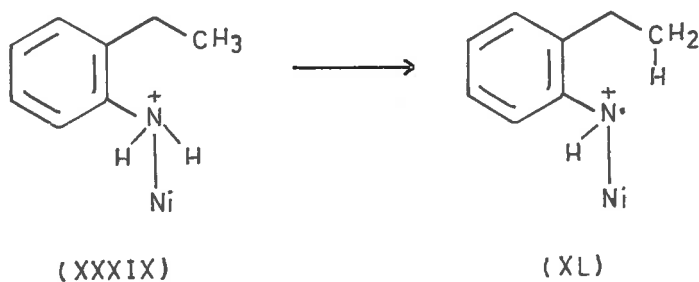
Raney nickel at 223°

Benzimidazole	6.5 (13%)	2,2'-Biquinoxalyl	0.25 (0.5%)
<u>N</u> -Methylbenzimidazole	0.7 (1.3%)	2,2'-Benzimidazolylquinoxaline	0.65 (1.2%)
2-Methylbenzimidazole	1.73 (3.1%)		

The dehydrocyclisation of o-alkylanilines to form indoles with metal catalysts has been widely applied for synthetic purposes. Hansch and Helmkamp⁵⁵ proposed that for the cyclisation of o-ethylaniline, dehydrogenation to o-aminostyrene was the first step. This was to be followed by cyclisation involving the double bond (p. 15). Evidence supporting this hypothesis was obtained by Lesiak.⁵⁶ This mechanism is unsatisfactory in the sense that it does not specify the role of the catalyst.

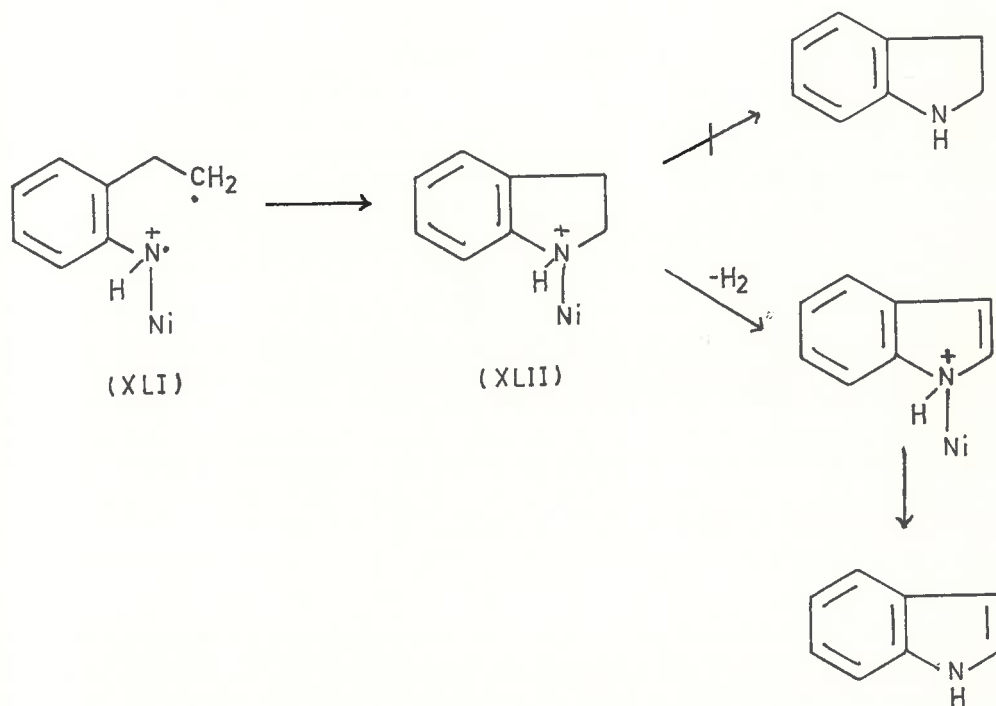
As Hansch and Helmkamp's reactions were carried out at temperatures far in excess of those used in the present work, dehydrogenation might be expected to predominate. In the present work, amines with olefinic side-chains were not detected. This of course does not conclusively discount the probability of their formation.

For reasons discussed in the previous section, it is proposed that the first step in the formation of indole from o-ethylaniline is the chemisorption of the amine by the degassed nickel catalyst via the lone electron pair of the nitrogen atom to give the intermediate (XXXIX). Homolytic fission of one of the N-H bonds, as postulated previously, leads to the radical (XL). Inspection of Catalin models indicates that the β -carbon atom of the ethyl side-chain is situated close to the catalyst and to the nitrogen atom. It is assumed at this stage that one



of C-H bonds (of the β -carbon atom) is homolytically ruptured to give a radical (XLI) which subsequently cyclises as shown to

give (XLII). The intermediate (XLII) could undergo either desorption to give indoline, or dehydrogenation followed by desorption to yield indole. The second possibility is preferred



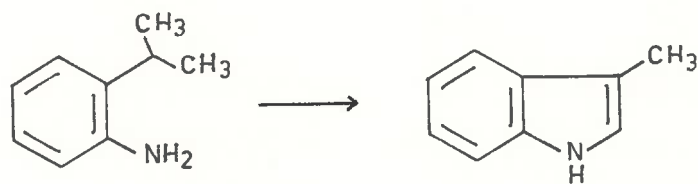
as it has been shown that indoline is readily dehydrogenated by degassed Raney nickel.

The basis of this mechanism is the assumption that homolytic fission of one of the N-H bonds and one of the C-H bonds occurs. The energies of activation required for these cleavages are high, and thus, these reactions would not be expected to occur readily. This is in keeping with the low yield of indole obtained. The eliminated hydrogen is assumed to enter the vacancies of the

lattice of the catalyst. It is well known that aliphatic hydrocarbons can be cyclised at high temperatures under the influence of metal catalysts, but the generally accepted mechanism¹¹⁵ gives no indication as to the actual bond formation step. The only driving force behind these reactions seems to be the presence of the catalyst.

When this tentative mechanism is applied to the reactions of the other alkylnilines with W7-J Raney nickel, the yields of indoles formed in these experiments may be explained. For example in the reaction with o-propylaniline, more 2-methylindole than indole or 3-methylindole was produced. Again by inspection of Catalin models, the proximity of the β -carbon atom to the nitrogen atom and the catalyst becomes apparent. Hence the formation of 2-methylindole would be expected to predominate. The indole formed in this reaction is most likely to have arisen from the o-ethylaniline produced by the C-demethylation of the starting material. It is unlikely that the indole results from the demethylation of 2-methylindole as it is known that under the influence of degassed Raney nickel, 2-methylindole is stable.⁸⁷ The formation of the trace of 3-methylindole is difficult to understand. Although definite evidence is not available, it may be that isomerisation of the n-propyl side-chain to an isopropyl side-chain occurs. This type of isomerisation is very well known in the Friedel-Crafts reaction and in the catalytic cracking of

aromatic hydrocarbons. If o-isopropylaniline (XLIII) can be formed, then cyclisation to 3-methylindole could occur, for it is known that when o-isopropylaniline is reacted with either a platinum or palladium catalyst,⁵⁸ 3-methylindole is obtained.

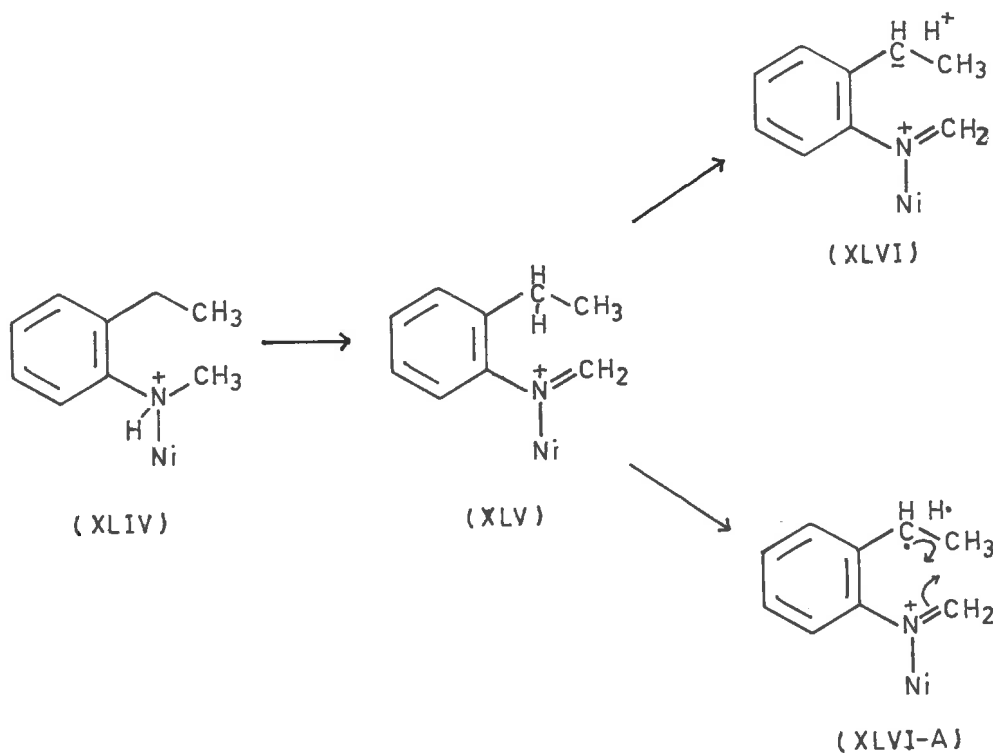


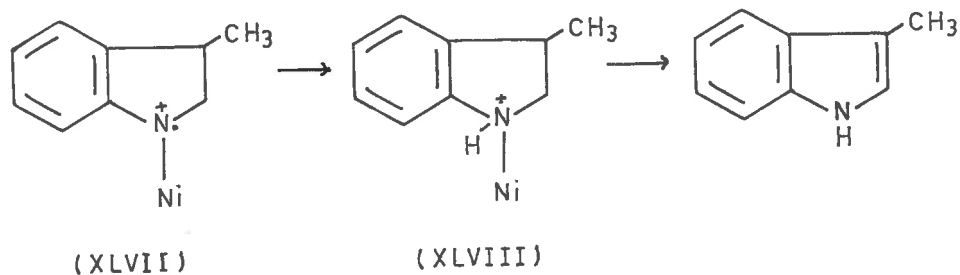
(XLIII)

It is noteworthy that o-propylaniline did not undergo cyclisation to form a six-membered ring. In fact, none of the alkyylanilines with the required number of carbon atoms in the side-chains cyclised to six-membered rings.

N-Methyl-o-ethylaniline, which gave the greatest yields of indole and 3-methylindole in the present series of reactions, can cyclise in two ways to yield either N-methylindole or 3-methylindole. N-Methylindole was not detected. However, its formation cannot be excluded as its N-demethylation may be expected to occur. N-Demethylation of the starting material to give o-ethylaniline was the major reaction, and it is suggested that indole is formed from this compound. Alternatively, cyclisation could occur between the α -carbon atom of the ethyl side-chain and the carbon atom attached to the nitrogen atom.

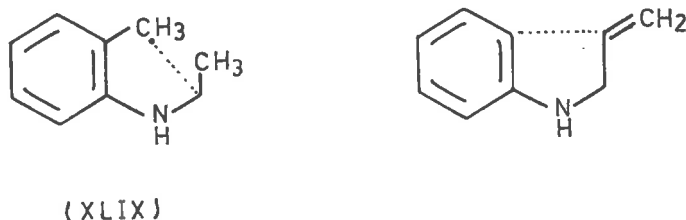
Inspection of Catalin models shows that these two atoms are close enough, and provided "activation" of the molecule occurs, bond formation between them would be possible. This mode of cyclisation has in fact been observed by Padoa and Carrasco⁵² who cyclised N-methyl-o-toluidine to give indole. It is now suggested that N-methyl-o-ethylaniline is chemisorbed by the catalyst via the nitrogen atom (XLIV). Loss of hydrogen as proposed by Kindler^{105,106} would yield the intermediate (XLV). Ionic or homolytic fission of one of the C-H bonds of the α -carbon atom leads to (XLVI) or (XLVI-A). Cyclisation in the way shown gives (XLVII). The hydrogen eliminated from the





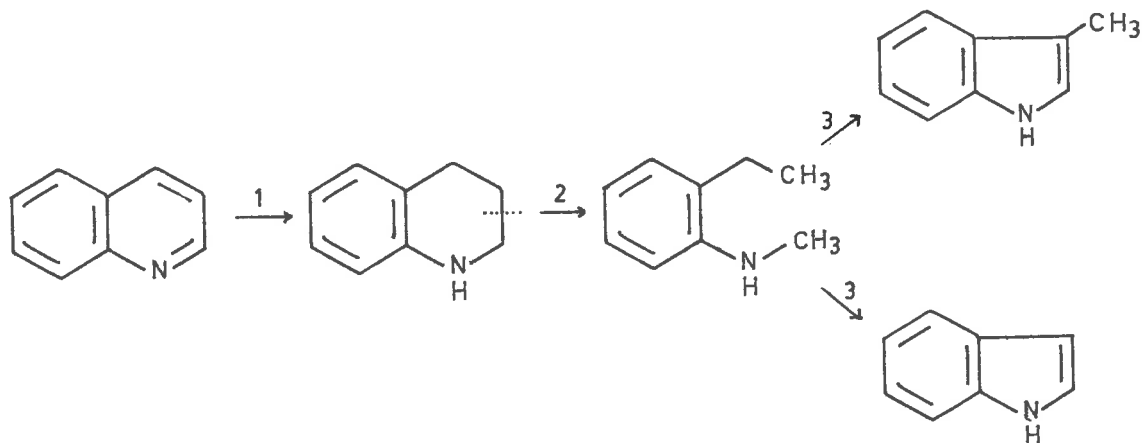
α -carbon atom may add to the nitrogen atom, but this could be a concerted 1,3-shift. The resulting indoline derivative (XLVIII), on the basis of the reaction with indoline, would be expected to dehydrogenate rapidly to give 3-methylindole on desorption.

N-Allylaniline and N-ethyl-o-toluidine were shown to give only traces of indoles. The formation of 2-methylindole from N-ethyl-o-toluidine may have occurred by cyclisation between the carbon atoms shown (XLIX) according to the mechanism for the formation of 3-methylindole from N-methyl-o-ethylaniline. The low yield of 3-methylindole obtained from the reaction of N-allylaniline with the catalyst is consistent with the results of Padoa.⁴⁸ He showed that only a trace of "indole-like" material was obtained from N-propylaniline.



The results discussed in this section have a bearing on the problem of the mode of formation of indole and 3-methylindole in the reaction of quinoline with degassed Raney nickel. As o-propylaniline and N-ethyl-o-toluidine yield not only indole and 3-methylindole, but also 2-methylindole, these two bases cannot be intermediates in the formation of indole and 3-methylindole in the reaction with quinoline. Moreover, the present results suggest that N-methyl-o-ethylaniline rather than N-allylaniline is the required intermediate. It is of interest that N-methyl-o-ethylaniline gave more carbazole than any of the other anilines examined. This provides further evidence for the occurrence of this amine in the reaction of quinoline with W7-J Raney nickel.

On the basis of these results, it is proposed that three main steps are involved in the formation of indole and 3-methylindole from quinoline. Firstly, hydrogenation to 1,2,3,4-tetrahydroquinoline occurs, followed by the rupture of the 2,3-bond to give N-methyl-o-ethylaniline. The third step then involves the dehydrocyclisation to either yield indole or 3-methylindole.

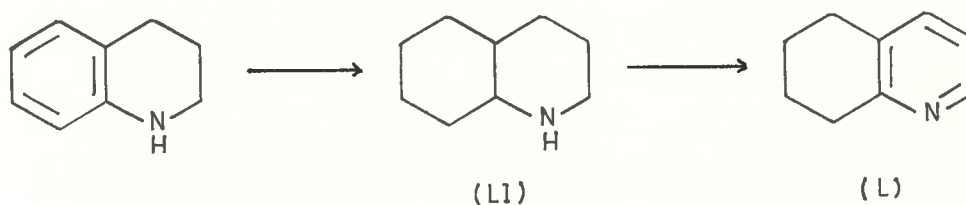


In agreement with this hypothesis, the yields of indole and 3-methylindole in the present series of experiments from 1,2,3,4-tetrahydroquinoline exceeded those isolated from the reaction with quinoline. The finding that the yield of non-basic nitrogenous products from the reaction of quinoline with a Raney nickel catalyst degassed at 360° was much lower, also supports the view that indoles result from 1,2,3,4-tetrahydroquinoline.

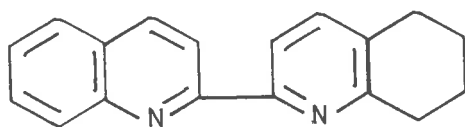
Besides indole and 3-methylindole, a number of other compounds were isolated from the reaction with 1,2,3,4-tetrahydroquinoline (Table II). As expected, ring fission occurred, and aniline, *o*-toluidine and *o*-ethylaniline were separated from the basic fraction. The fact that *o*-ethylaniline was isolated lends further support to the hypothesis that it is the 2,3-bond which is broken. A relatively large amount of the paraffin (CH₂)_x was isolated, indicating that extensive C-dealkylation of the amines had occurred.



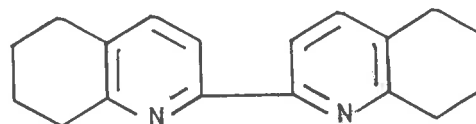
A number of quinoline derivatives were separated from the basic fraction. Quinoline itself was isolated, resulting presumably from the dehydrogenation of the starting material. Consequently, the presence of 2,2'-biquinolyl was not unexpected. 5,6,7,8-Tetrahydroquinoline (L) was a major product. It could be formed from 1,2,3,4-tetrahydroquinoline by hydrogenation to decahydroquinoline (LI) which could then be dehydrogenated to 5,6,7,8-tetrahydroquinoline. It is known that when a palladium-on-asbestos catalyst is employed, decahydroquinoline is first dehydrogenated to 5,6,7,8-tetrahydroquinoline before complete dehydrogenation.¹¹⁶



Two new partially hydrogenated 2,2'-biquinolyls were isolated, and they are assumed to have been formed by the mechanism discussed earlier for the formation of biaryls (p. 9). 5,6,7,8-Tetrahydro-2,2'-biquinolyl (LII) was formed by the reaction of quinoline with 5,6,7,8-tetrahydroquinoline. Combination of two molecules of 5,6,7,8-tetrahydroquinoline produced 5,5',6,6',7,7',8,8'-octahydro-2,2'-biquinolyl (LIII).



(LII)



(LIII)

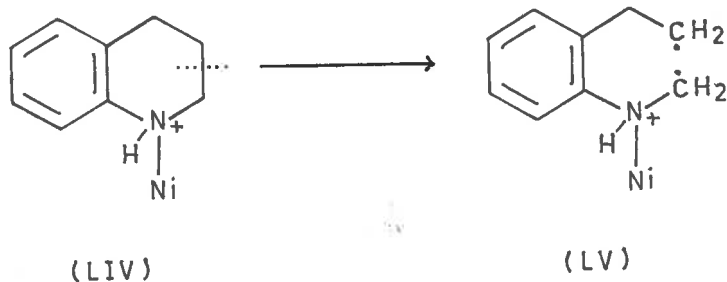
The carbon skeleton of these compounds was shown to be that of 2,2'-biquinolyl from their dehydrogenation over 20% palladium-on-charcoal. The ability of each compound to form a chelate with cuprous ions suggests the presence of the typical $-N=C-C=N-$ system. The positions of the extra hydrogen atoms were shown by the n.m.r. spectrum to be located in the benzene rings of the compounds.

It is interesting to note that no biaryls were isolated in which the heterocyclic rings were saturated. This is due to the inability of 1,2,3,4-tetrahydroquinoline to form an intermediate radical of the type required for reaction with an adjacent intermediate.

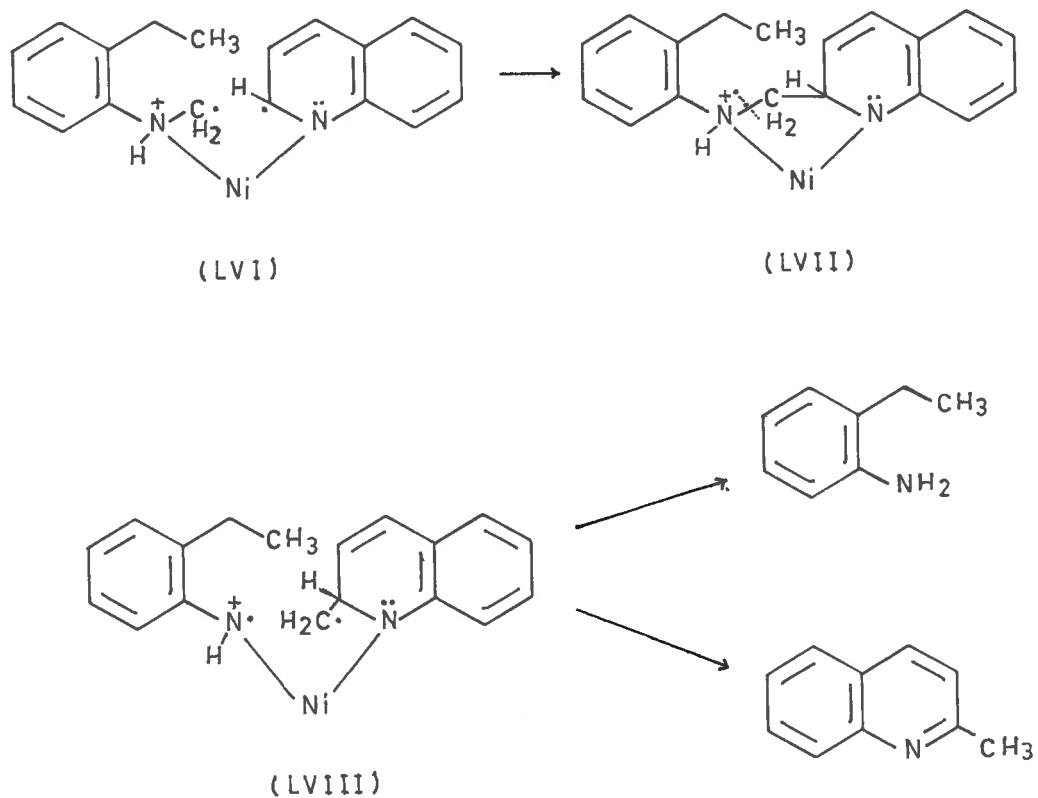
2-Methylquinoline is the major product in this experiment, and its formation, although not unexpected on the basis of its occurrence in the reaction with quinoline,⁴³ is none the less puzzling as it is present in such large quantities. Sesse⁴³ concluded that it was not the result of methyl radical substitution of quinoline, as no other methylquinolines were detected in the

reaction mixture. Furthermore, it is improbable that such an amount of 2-methylquinoline could have arisen from the breakdown of 2,2'-biquinolyl (p.11). It seems probable at this stage that the 2-methylquinoline isolated in the reaction of quinoline with the nickel catalyst results from 1,2,3,4-tetrahydroquinoline.

The following scheme is proposed as a tentative mechanism for the formation of 2-methylquinoline in these reactions. It is assumed that 1,2,3,4-tetrahydroquinoline is chemisorbed by the catalyst to give the intermediate (LIV). Inspection of Catalin models shows that the 3-carbon atom lies very close to the catalyst, and can interact with the nickel atom far more easily than the 2-carbon atom. It is then assumed that a homolytic cleavage of the 2,3-bond occurs to give the radical (LV) which can accept hydrogen from the catalyst to give N-methyl-o-ethylaniline. This base is known to yield aniline, o-toluidine, o-ethylaniline, indole, 3-methylindole and carbazole.



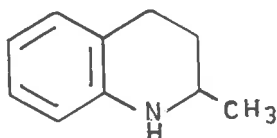
An alternative pathway of the radical (LV) can be envisaged in which it interacts with a molecule of quinoline bonded to the same nickel atom as shown (LVI). The resulting intermediate (LVII) has a 5-membered ring which is assumed to undergo fission across the carbon-nitrogen bond shown, to give the adsorbed species (LVIII). Desorption would lead to 2-methylquinoline and



o-ethylaniline which in turn can be converted into indole.

2-Methylquinoline could undergo hydrogenation to give 2-methyl-

1,2,3,4-tetrahydroquinoline (LIX) which is also isolated from the reaction mixture.



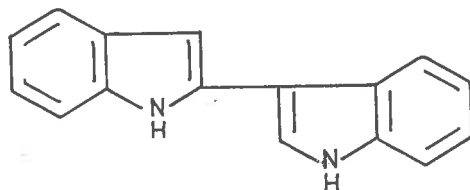
(LIX)

This sequence of steps explains the formation of indole, 3-methylindole, o-ethylaniline (o-toluidine and aniline), and 2-methylquinoline (and 2-methyl-1,2,3,4-tetrahydroquinoline). It is further suggested that this mechanism is responsible for the same products isolated from the reaction of quinoline with degassed Raney nickel.

It is obvious that ring fission, followed by C-dealkylation, are important reactions because of the relatively large amount of $(\text{CH}_2)_x$ formed. As was shown earlier, the polymethylene comes from the o-alkyl side-chains of the aniline derivatives.

It was mentioned previously that when aniline derivatives (with the required number of carbon atoms on the side-chains) were reacted with W7-J Raney nickel, cyclisation to a six-membered ring did not occur. However, in the reaction of indoline with the catalyst, a trace of quinoline was isolated along with aniline, o-toluidine, and o-ethylaniline. It is known that 2-methylindole can undergo ring expansion to form quinoline,¹¹⁷ but as none was

detected in the present reaction, another pathway must be operating. The major product from the reaction was 2,3'-biindole (LX). The formation of this compound is hard to



(LX)

understand in the light of the observations that biaryl formation under the influence of Raney nickel usually occurs across the 2,2'-positions. However, it is known that 2,2'-biindole is converted into 2,3'-biindole under acid conditions.¹¹⁸

The position of ring cleavage in this reaction is of interest as a trace of o-ethylaniline was isolated. Hence it would appear that a small amount of 1,2-bond fission had occurred. Willstätter, Seitz, and v. Braun¹¹⁹ reported that indole gave o-ethylcyclohexylamine when treated with a nickel catalyst at 225°. On the other hand, Padoa and Carrasco⁵² stated that indole and methylindole underwent cleavage at the 2,3-bond. In the present reaction, o-toluidine was isolated as the major basic product. Hence it would appear that both the 1,2-bond and the 2,3-bond are broken, with the second possibility predominating.

The effect of two nitrogen atoms in the one heterocyclic ring was determined by reacting quinoxaline with degassed Raney nickel. As can be seen from Table III (p.92), the formation of

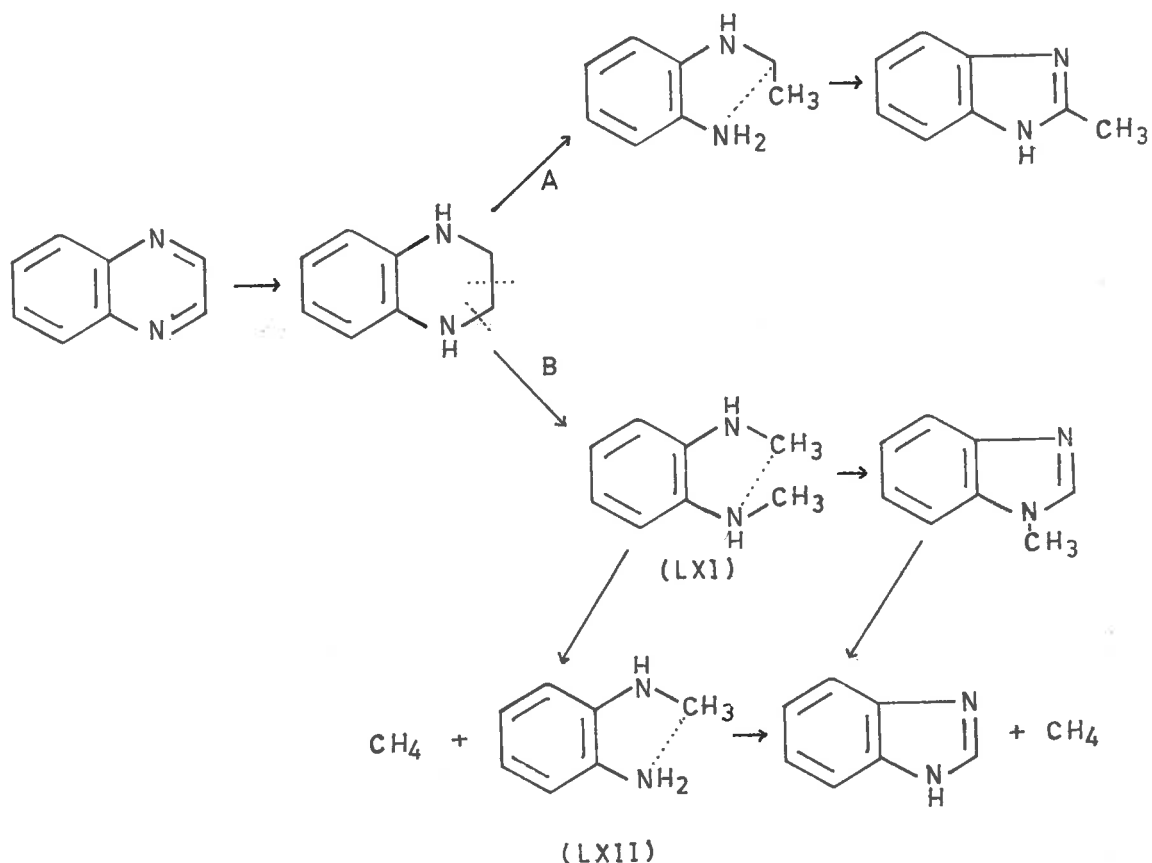
benzimidazoles is the major reaction. The presence of a second nitrogen atom reduces the yield of the expected biaryls, for 2,2'-biquinoxalyl and 2,2'-benzimidazolylquinoxaline were obtained in low yield. The structures of these compounds have not been proved by unambiguous syntheses.

The compound regarded as 2,2'-biquinoxalyl did not give a good analysis for carbon and hydrogen, but the nitrogen determination was correct. A chelate with cuprous ions was obtained, suggesting a $-N=C-C=N-$ system in the molecule. The n.m.r. spectrum is also compatible with that expected for 2,2'-biquinoxalyl.

As far as the structure of 2,2'-benzimidazolyl quinoxaline is concerned, a good analysis was obtained. Also, the compound gave a chelate with cuprous ions which suggests the $-N=C-C=N-$ system. The n.m.r. spectrum showed the presence of an N-H group, and the protons present can be assigned to the positions of 2,2'-benzimidazolylquinoxaline.

o-Phenylenediamine derivatives and $(CH_2)_x$ were not detected in the reaction. It is known that when quinoxaline is reacted with Raney nickel, 1,2,3,4-tetrahydroquinoxaline is formed.⁸⁷ Therefore, if ring rupture occurs, it is suggested that its hydrogenation precedes cleavage. Also, if fission occurs, then cyclisation must occur extremely rapidly. As both N-methylbenzimidazole and 2-methylbenzimidazole were detected, it is possible that fission occurs at both the 1,2-bond (path A) and the 2,3-bond

(path B), with the second predominating. As there is no C-dealkylation occurring no $(CH_2)_x$ can be formed. The benzimidazole



is suggested to arise from either the demethylation of *N*-methylbenzimidazole or from the amine (LXII) which results from the *N*-demethylation of *N,N'*-dimethyl-*o*-phenylenediamine (LXI).

Alternatively, a mechanism not involving ring fission may be occurring, in which there is bond formation between the nitrogen atom and the 3-carbon atom. However, this possibility has not been examined.

EXPERIMENTAL

General:

All melting points and boiling points are uncorrected. Analyses were performed by the Australian Microanalytical Service, Melbourne. The infrared spectra were determined with a Perkin-Elmer Infracord 137 spectrophotometer. Ultraviolet absorption spectra were determined with an Optica CF-4 recording spectrophotometer. W7-J Raney nickel⁷ was prepared from 1:1 aluminium-nickel alloy (B.D.H.) and, except where otherwise stated, the amount of alloy used (125 g.) was constant throughout.

Detection of Ammonia.- In the reactions with aniline, 2-aminobiphenyl, 2,2'-diaminobiphenyl, azobenzene, aniline and cyclohexylamine, quinoline, 1,2,3,4-tetrahydroquinoline, o-ethylaniline, o-propylaniline, N-methyl-o-ethylaniline, N-ethyl-o-toluidine, N-allylaniline, p-toluidine, and indoline, an ammonia like odour was given off in varying amounts soon after the commencement of refluxing. In one case (N-methyl-o-ethylaniline) ammonia was identified by means of its infrared spectrum.

PART A.

Starting materials.- The following compounds were commercial samples which were purified by recrystallisation and distillation: aniline,

b.p. 184-185°, n_D^{21} 1.5857; diphenylamine, m.p. 52.5-53°; azobenzene, m.p. 68°; cyclohexylamine, b.p. 133.5-134°, n_D^{20} 1.4372; carbazole, m.p. 241°. 2-Aminobiphenyl (m.p. 49°) was prepared from 2-nitrobiphenyl by hydrogenation with Raney nickel, and 2,2'-diaminobiphenyl (m.p. 80°) was prepared according to the method of Stephenson.¹²⁰

Addition of Reactants.- Liquid reactants were added directly to the catalyst through the separating funnel. Solid reactants were added after the catalyst had been wetted with sulphur free xylene. After addition of the reactant, the xylene was removed by distillation.

2,2'-Diaminobiphenyl.- 2,2'-Diaminobiphenyl (125 g.) was refluxed over the catalyst (prepared from 104 g. of alloy) for 50 hr. at 220-240°/120 mm. The reaction mixture was filtered and the nickel washed with hot benzene (600 c.c.) and hot ethanol (800 c.c.). The solvents were removed by distillation. The first filtrate and the benzene washings were combined and crystallised from ethanol to give starting material (92.5 g.). The residue from the crystallisation was combined with the ethanol washings of the catalyst and the whole separated into basic (14.6 g.) and neutral (7.3 g.) fractions. Chromatography of the neutral fraction on alumina (25 x 3 cm.) yielded carbazole (6.6 g.),

m.p. 241° , on elution with benzene, and a tarry residue (0.4 g.) on elution with ethanol. Chromatography on alumina (25 x 3 cm.) of the basic fraction gave (i) 2-aminobiphenyl (11.0 g.), m.p. 49° alone and mixed with an authentic sample, on elution with light petroleum (b.p. $60-80^{\circ}$), and (ii) starting material (2.6 g.) on elution with benzene. Elution with ethanol gave a black tar (0.8 g.) which was not further investigated.

Carbazole.- A solution of carbazole (68 g.) in 1-methylnaphthalene (100 c.c.; b.p. 245°) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at $242-245^{\circ}$. The reaction mixture was cooled to 180° and filtered, the nickel being washed with hot ethanol (2 l.) which was then removed by distillation. The reaction mixture was distilled and one fraction, (95 g.), b.p. $210-250^{\circ}$ collected. Gas-liquid partition chromatography (conditions as described on page 120) of this fraction showed the presence of a small amount of naphthalene (based on retention time only (at 220° :3.8 min.)). Carbazole (5.0 g.) codistilled with the solvent and was removed by chromatography through a column of alumina.

The residue from the distillation was crystallised from ethanol and gave carbazole (59.7 g.). The mother liquor was evaporated to dryness and chromatographed on alumina (25 x 3 cm.). Elution with light petroleum (b.p. $60-80^{\circ}$) and benzene gave carbazole (2.1 g.). A tarry residue (0.45 g.) was eluted with ethanol. Paper chromatography (using acetylated paper and the

solvent system described for it on page 117) showed traces of at least six compounds in the tar. These compounds were not identified.

2-Aminobiphenyl.- 2-Aminobiphenyl (135 g.) was refluxed over the catalyst for 50 hr. at 290°. The reaction mixture was filtered and the catalyst washed with hot benzene (500 c.c.) and hot ethanol (700 c.c.). The solvents were removed by distillation. The first filtrate was combined with the benzene washings and distilled under reduced pressure. One fraction (93 g.), b.p. 158-164°/12 mm. was collected and crystallised from ethanol to give unchanged starting material (79.1 g.); the residue (12.5 g.) being chromatographed on alumina (30 x 3 cm.). Elution with light petroleum (b.p. 60-80°) yielded 2-aminobiphenyl (11.1 g.), and elution with benzene gave carbazole (0.69 g.), m.p. 241°. A tarry fraction (0.7 g.) which was obtained on elution with ethanol was not further examined.

The residue from the above distillation was combined with the ethanol washings of the catalyst and separated into a neutral fraction (10.8 g.) and a basic fraction (19.2 g.). Chromatography on alumina (25 x 3 cm.) of the basic fraction gave 2-aminobiphenyl (17.5 g.) on elution with light petroleum (b.p. 60-80°), and a black tar (1 g.) which was not further investigated. The "neutral" fraction when chromatographed on alumina (25 x 3 cm.) yielded starting

material (1.6 g.) on elution with light petroleum (b.p. 60-80°), carbazole (3.65 g.), m.p. 241°, on elution with benzene, and a tarry residue (4 g.) on elution with ether and ethanol.

Diphenylamine.— Diphenylamine (140 g.) was refluxed over the catalyst for 50 hr. at 235°. The mixture was filtered and the nickel washed as described for aniline. After removal of the solvents, the benzene washings were combined with the first filtrate and distilled, two fractions being collected. (i) Xylene (2 c.c.), b.p. 30-40°/12 mm., (ii) diphenylamine (109 g.), b.p. 158-164°/12 mm. The diphenylamine was crystallised from light petroleum (b.p. 60-80°), and the residue (12.5 g.) chromatographed on alumina (25 x 3 cm.). Elution with light petroleum (b.p. 60-80°) gave diphenylamine (11.8 g.), and elution with benzene yielded carbazole (0.06 g.), m.p. 241°.

The residue from the distillation was separated into basic (0.08 g.) and neutral (4.97 g.) fractions in the usual manner. The alcohol washings of the catalyst were similarly separated into basic (0.28 g.) and neutral (0.94 g.) fractions which were combined with the above basic and neutral fractions. Chromatography of the basic fraction on alumina gave traces of many coloured compounds, none of which were characterised. The neutral fraction was chromatographed on alumina and yielded (i) diphenylamine (3.6 g.) on elution with light petroleum (b.p. 60-80°), and (ii) carbazole (1.76 g.), m.p. 241°, on elution with benzene. Elution with ethanol gave black tar which was not further examined.

Aniline.- Aniline (150 c.c.) was refluxed over the catalyst (prepared from 250 g. of alloy) for 50 hr. at 182°. The nickel was filtered off and washed with hot benzene (400 c.c.) and hot ethanol (400 c.c.). The solvents were removed by distillation. Distillation of the first filtrate gave aniline (75 g.), b.p. 78°/11 mm., and a second fraction (3 g.), b.p. 146-148°/11 mm. The benzene washings were distilled to give aniline (30 g.), b.p. 78°/11 mm., and a higher boiling fraction (1.74 g.), b.p. 146-148°/11 mm. The high boiling fractions were combined and redistilled to give a compound, m.p. 8°, which was characterised as cyclohexylaniline (lit.,¹²¹ m.p. 8°) by preparation of the *p*-toluenesulphonyl derivative m.p. 141° (lit.,¹²¹ m.p. 141-142°) (Found: C, 69.6; H, 6.8; N, 4.4; O, 10.2; S, 9.6. Calc. for C₁₉H₂₃O₂NS: C, 69.3; H, 7.0; N, 4.3; O, 9.7; S, 9.7%).

The residues from the distillations were combined (2.8 g.), and separated into neutral (1.68 g.) and basic (1.0 g.) fractions. When eluted with light petroleum (b.p. 40-60°) on a column of alumina (25 x 3 cm.), the "neutral" fraction gave cyclohexylaniline (0.4 g.). Further elution with light petroleum (b.p. 60-80°) yielded diphenylamine (0.23 g.), m.p. 53°, alone and mixed with an authentic sample. Carbazole (0.24 g.), m.p. and mixed m.p. 238°, was eluted with benzene. Elution with ethanol gave a black tar (0.4 g.) which was not further examined.

The basic fraction was chromatographed on alumina (25 x 3 cm.) and eluted firstly with light petroleum (b.p. 60-80°) to give 2-aminobiphenyl (0.02 g.), m.p. and mixed m.p. 49°. Elution with benzene yielded 2,2'-diaminobiphenyl (0.54 g.), m.p. 80° alone and mixed with an authentic sample. Elution of the column with ethanol gave a black tar (0.32 g.) which was not further investigated. Carbazole, diphenylamine, 2-aminobiphenyl, and 2,2'-diaminobiphenyl were further characterised by their infrared spectra.

Aniline and Cyclohexylamine.- A mixture of aniline (75 g.) and cyclohexylamine (16 g.) was refluxed over the catalyst for 50 hr. During this time the temperature of the reaction gradually fell from 184° to 160°. The reaction mixture was filtered and the nickel washed with hot ethanol (1 l.). The ethanol was removed by distillation. The first filtrate (58.5 g.) was distilled to give fractions (i), aniline (28.7 g.), b.p. 88-90°/24 mm., (ii) a liquid (12.1 g.), b.p. 92-160°/24 mm., and (iii) cyclohexylaniline (13.8 g.), b.p. 162-164°/24 mm., characterised as its *p*-toluenesulphonyl derivative, m.p. and mixed m.p. 141°. Gas-liquid partition chromatography showed that fraction (ii) contained aniline (83%) and cyclohexylaniline (conditions as described on page 120, retention times (min.) at 196°: aniline 1.65; cyclohexylaniline 6.5). Using gas

chromatography no evidence was found for the presence of dicyclohexylamine. Aniline and cyclohexylaniline were found in the ethanol washings of the catalyst. Based on the amount of cyclohexylamine used, the yield of cyclohexylaniline was 89%. The highly fluorescent residue from the distillation of the reaction mixture was not examined.

Azobenzene.- Azobenzene (75 g.) was refluxed over the catalyst (prepared from 60 g. of alloy) for 50 hr. at 220-230°. It was observed that the reaction mixture darkened; it was black after 30 hr. of refluxing. The catalyst was removed and washed with hot benzene (500 c.c.) and hot ethanol (500 c.c.). The solvents were removed by distillation. The first filtrate and the benzene washings were combined and distilled at atmospheric pressure. Aniline (15 g.), b.p. 183-185°, was collected and the pale red liquid characterised as its *p*-toluenesulphonyl derivative, m.p. 103° alone and mixed with an authentic specimen. A part (3 g.) of the residue (56 g.) was separated into basic (0.3 g.) and neutral (2.2 g.) fractions. A black tar (0.45 g.) was also obtained which was insoluble in acid, base or ether.

Chromatography of the basic fraction on a short column of alumina yielded traces of a number of highly coloured compounds, none of which were characterised. The neutral fraction on alumina

(25 x 3 cm.) gave azobenzene (1.9 g.) and diphenylamine (0.04 g.). The remainder was recovered as a black tar which was not further investigated.

PART B.

Detection and Determination of Indoles.- (a) A solution of p-dimethylaminobenzaldehyde (5 g.) in 6N hydrochloric acid (100 c.c.) was used to detect the presence of indoles¹²² and carbazole in a mixture containing large quantities of anilines and quinolines. A characteristic red-colour was obtained when these compounds were present.

(b) Chromatography on acetylated paper was used to detect and characterise indoles. The papers were prepared according to Spotswood¹²³ but more sulphuric acid (0.8 g. of 92% acid per l. of acetic anhydride) was used. Development by descent using the solvent system acetone-water-ether (50;20:6 v/v)¹²⁴ was used and the spots were made visible by exposure to iodine vapour. Different batches of papers gave different R_F values and standards were run simultaneously with unknown samples; typical values are: indole 0.13; 2-methylindole 0.30; 3-methylindole 0.36; carbazole 0.40.

(c) Gas-liquid partition chromatography (see below) was used to approximate the composition of mixtures of indole and 3-methylindole.

Paper Chromatography of the Basic Reaction Products.-

(a) Development by descent on Whatman paper No. 1 using the solvent system butan-1-ol-concentrated hydrochloric acid-water (80:20:60 v/v) was used for the hydrochlorides of the basic compounds.⁴³ Spots were made visible by exposure to iodine vapour. Some typical R_F values are: quinoline 0.66; 2-methylquinoline 0.73; 1,2,3,4-tetrahydroquinoline 0.78; 5,6,7,8-tetrahydroquinoline 0.71; 2,2'-biquinolyl 0.74; aniline 0.72; o-toluidine 0.77.

(b) For the detection of aniline, o-toluidine, and o-ethylaniline, their hydrochlorides were developed by descent on Whatman No. 1 paper using the solvent system benzene-acetic acid-butanol-water (60:8:4:1 v/v). Spots were made visible by exposure to iodine vapour. Typical R_F values are: aniline 0.06; o-toluidine 0.10; o-ethylaniline 0.12; 1,2,3,4-tetrahydroquinoline 0.12.

Starting materials.- The following compounds were commercial samples which were purified by fractional distillation: quinoline, b.p. 238°, n_D^{25} 1.6246; 1,2,3,4-tetrahydroquinoline, b.p. 251°, n_D^{23} 1.5930; o-ethylaniline, b.p. 215-216°; indoline, b.p. 70-72°/2 mm., n_D^{20} 1.5923; p-toluidine, b.p. 200°; quinoxaline, b.p. 115-118°/19 mm. The following compounds were prepared and purified by standard procedures: o-propylaniline,¹²⁵ b.p. 222-223°; N-methyl-o-ethylaniline,¹²⁶ b.p. 96-97°/12 mm.

N-allylaniline (b.p. 106-107°/12 mm.) and N-ethyl-o-toluidine (b.p. 214-215°) were prepared from p-toluenesulphonyl aniline by using Morgan and Micklethwait's method¹²⁷ for preparation of N-methyl-m-nitroaniline.

Nuclear Magnetic Resonance Spectra.- The n.m.r. spectra were determined with a Varian Associates high-resolution nuclear magnetic resonance spectrometer, model D.P.60. Tetramethylsilane was used as an internal standard ($\tau = 10$) to determine the chemical shifts.

(CH₂)_x.- The physical properties of the unknown aliphatic hydrocarbon (CH₂)_x as described by Sasse⁴³ were identical with those obtained for the material from the reactions in the present series of experiments. The n.m.r. spectrum (CDCl₃) showed a single narrow peak at $\tau = 8.8$ corresponding to a series of CH₂ units, with the probability of little or no chain-branching.

Countercurrent Distribution.- A Quickfit countercurrent distribution apparatus (50 tubes, of 50 c.c. each) was used. The moving phase was ether which was added to the tubes in 25 c.c. lots. Tubes 1 and 2 contained 25 c.c. lots of 5% hydrochloric acid which equilibrated the moving ether. Except for tubes nos. 12, 22, 32 and 42 which were kept empty to allow for overlap of excess added to the other tubes, the tubes were filled with 25 c.c.

lots of hydrochloric acid of increasing concentration (3-11, 1%; 13-21, 2%; 23-31, 5%; 33-41, 7%; 43-50, 8%). To the third tube of the apparatus was added 25 c.c. lots of the reaction mixture (dissolved in ether). Ether was then transferred through the system (mixing period, 1.5 min.; settling period, 1.5 min.; decanting period, 6 sec.; transfer period, 6 sec.) and collected until no positive Ehrlich test was obtained. The ether was washed with water, dried over magnesium sulphate and evaporated to dryness to give the neutral fraction. The acid solutions in the apparatus were divided into groups and combined. These solutions were basified with ammonium hydroxide and extracted with ether. The ether solutions were dried over magnesium sulphate and evaporated to dryness to give the basic fractions.

Gas-Liquid Partition Chromatography.- (a) A Griffin V.P.C. apparatus Mk. II was used with 4 ft. column packed with "Celite" (40-80 mesh, coated with 20% (wt.) of Apiezon L). With a flow rate of one l. per hr. of nitrogen, an inlet pressure of 450 mm., and an outlet pressure of 80 mm., the following retention times (min.) were observed; at 100^o: benzene 2.52; toluene 3.15; at 196^o: aniline 1.65; o-toluidine 2.36; o-ethylaniline 3.10; o-propylaniline 5.70; N-methyl-o-ethylaniline 4.40; quinoline 5.20; 1,2,3,4-tetrahydroquinoline 7.71; 5,6,7,8-tetrahydroquinoline 4.38; 2-methylquinoline 6.56; 2-methyl-

1,2,3,4-tetrahydroquinoline 5.70; at 188°: N-ethyl-o-toluidine 5.0; at 198°: N-allylaniline 2.80; at 202°: indole 4.29; 2-methylindole 7.15; 3-methylindole 6.30. By comparison of the areas under the peaks, the approximate composition of a number of mixtures were obtained. Standard mixtures were run wherever possible.

(b) A Beckman Megachrom instrument was used with the column packed with C-22 Firebrick/Apiezon-J. With the carrier gas nitrogen, an inlet pressure of 8 lb., and an outlet pressure of 2 lb., the following retention times (min.) were observed; at 240°: aniline 4.0; o-toluidine 6.0; o-ethylaniline 8.0; o-propylaniline 11.5; N-ethyl-o-toluidine 20.0; quinoline 13.3; 2-methylquinoline 17.0; 5,6,7,8-tetrahydroquinoline 6.3; 2-methyl-1,2,3,4-tetrahydroquinoline 22.0; at 210°: N-methyl-o-ethylaniline 20.0; N-allylaniline 26.5; at 290°: indole 8.0; 3-methylindole 10.5.

o-Propylaniline.- o-Propylaniline (56 g.) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at 218-220°. The cooled reaction mixture was filtered and the nickel washed with hot benzene (500 c.c.) and hot ethanol (500 c.c.). The solvents were removed by distillation. A portion of the first filtrate (36.5 g.) was separated by countercurrent distribution. The neutral fraction (5.0 g.) was distilled and two fractions

collected: (i) b.p. 40-60°/3 mm. (0.48 g.), and (ii) b.p. 60-130°/3 mm. (2.42 g.). Fraction (i) contained 2-propylcyclohexanone, characterised as its 2,4-dinitrophenylhydrazone, m.p. 153-153.5° (lit.,¹²⁸ m.p. 153-154°), golden plates from ethanol (Found: C, 56.2; H, 6.3; N, 17.7; O, 20.1. Calc. for C₁₅H₂₀O₄N₄: C, 56.2; H, 6.3; N, 17.4; O, 20.0%).

Fraction (ii) was investigated by paper chromatography (evidence for indole, 2-methylindole, 3-methylindole (trace), and an unknown compound) and gas-liquid partition chromatography. A part (2.0 g.) was dissolved in benzene (2 c.c.) and injected into the Beckman Megachrom. In this way were collected (i) indole, m.p. 52°, (ii) 2-methylindole, m.p. 61°; picrate, m.p. 136° (lit., m.p. 136°); trinitrobenzene complex, m.p. 166° (lit., m.p. 166°) (all three compounds were identified by comparison with authentic specimens), and (iii) a viscous liquid which decomposed rapidly in air, and was not identified. It did however, give a red colour with p-dimethylaminobenzaldehyde. The composition of the distilled indoles, based on the areas under the peaks were; indole (10%) and 2-methylindole (40%). The residue from the distillation (1.8 g.) was chromatographed on alumina and yielded (CH₂)_x (0.15 g.), m.p. 59-60° on elution with light petroleum (b.p. 60-80°). No further separation was effected.

From the countercurrent distribution, tubes 23-43 were shown to contain only o-propylaniline (24.3 g.). Tubes 44-50 (1.9 g.) contained o-propylaniline and an unidentified base (5%) (retention time at 198°:8.3 min.). The basic mixture from tubes 3-22 (2.53 g. of distillate) was separated with the Beckman Megachrom to give (i) aniline (28%), (ii) o-toluidine (46%), (iii) o-ethylaniline (5%), and (iv) o-propylaniline. These compounds were characterised by their p-toluenesulphonates. No pure compounds were isolated from the residue of the distillations of the basic fractions (2.2 g.) by chromatography on alumina.

N-ethyl-o-toluidine.- N-ethyl-o-toluidine (56 g.) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at 209°. The reaction mixture was filtered (33.4 g.) and the catalyst washed with hot benzene (600 c.c.) and hot ethanol (800 c.c.). The solvents were removed by distillation. The first filtrate was separated manually into basic (26.49 g.) and neutral (5.14 g.) fractions. The basic fraction was distilled to give a liquid (24.75 g.), b.p. 90-115°/18 mm., and a residue (1.8 g.) which gave no pure compounds when chromatographed on alumina. Gas-liquid partition chromatography of the liquid revealed the presence of aniline (10%), o-toluidine (30%), and starting material. The components were separated with the Beckman Megachrom and identified by their infrared spectra and p-toluenesulphonyl derivatives.

Distillation of the neutral fraction gave a liquid (3.0 g.), b.p. 115-130°/1 mm., and a residue (1.8 g.). Chromatography on alumina (25 x 3 cm.) of the residue yielded (CH₂)_x (0.15 g.), m.p. 59-60°, on elution with light petroleum (b.p. 60-80°). Elution with benzene and ether gave brown oils which were not identified.

The distillate was investigated by paper chromatography and gas chromatography. Separation with the Beckman Megachrom gave five fractions: (i) a trace of a ketonic compound; insufficient quantities did not allow its characterisation, (ii)-(v) were unstable liquids which gave red colours with p-dimethylaminobenzaldehyde. Fractions (ii) and (iii) did not give picrates but (iv) and (v) gave red picrates which decomposed readily. Paper chromatography showed the presence of at least six compounds, one of which corresponded to indole and another to 2-methylindole. However their separation and identification was not effected.

N-allylaniline.- N-allylaniline (55 g.) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at 190°. The reaction mixture was filtered and the catalyst washed with hot benzene (500 c.c.) and hot ethanol (600 c.c.). The solvents were removed by distillation. A part of the reaction product (30 g.) was separated into basic (19.1 g.) and neutral (7.9 g.) fractions. Distillation of the neutral

material gave a brown gum (4.9 g.), b.p. 80-215°/0.2 mm., and a tarry residue (2.5 g.) from which no pure compounds were isolated by chromatography on alumina. Gas-liquid partition chromatography of the distillate showed the presence of a trace of 3-methylindole and one unidentified compound (retention time at 236°: 9.8 min.). Paper chromatography also indicated the presence of 3-methylindole.

Distillation of the basic fraction gave a liquid (16.8 g.), b.p. 80-115°/15 mm., and a residue (2.12 g.) which yielded no pure compounds when chromatographed on alumina. Examination of the distillate by gas chromatography showed the presence of aniline (5 g.), starting material, and a trace of a third compound which had the same retention time (at 205°: 2.10 min.) as N-propylaniline.

o-Ethylaniline.- o-Ethylaniline (100 g.) was refluxed over the catalyst for 50 hr. at 210-215°. The reaction mixture gave a positive Ehrlich test after 5 min. refluxing. The catalyst was removed by filtration and washed with hot benzene (400 c.c.) and hot ethanol (600 c.c.), the solvents being removed by distillation.

A part of the first filtrate (40 g.) was dissolved in ether (35 c.c.) and added in 25 c.c. lots to the third tube of the countercurrent distribution apparatus. Ether was transferred through the system until no positive Ehrlich test was obtained

(2 l.). The ethereal phase gave the neutral fraction (4.2 g.) which was distilled to give a liquid (2.0 g.), b.p. 60-160°/0.5 mm. The residue (2.0 g.) was chromatographed on alumina, and elution with light petroleum (b.p. 40-60°) yielded (CH₂)_x (0.3 g.), m.p. 59-60°. Trace amounts of several compounds were eluted with light petroleum (b.p. 60-80°) and benzene, but none were characterised. Paper chromatography of these fractions showed spots corresponding to carbazole and diphenylamine as well as a number of unidentified compounds. On elution with ethanol a black tar (0.88 g.) was collected which was not further examined.

The neutral fraction, b.p. 60-160°/0.5 mm., was dissolved in benzene (2 c.c.) and injected into the Beckman Megachrom. Trap 1 contained a trace of 2-ethylcyclohexanone which was characterised as its 2,4-dinitrophenylhydrazone, m.p. 162-163° (lit.,¹²⁹ m.p. 162.5-163.5°), golden needles from ethanol (Found: C, 54.8; H, 5.6; N, 18.5; O, 20.8. Calc. for C₁₄H₁₈O₄N₄: C, 55.0; H, 5.9; N, 18.3; O, 20.9%). Trap 3 contained indole, m.p. 52°, alone and mixed with an authentic sample. Traps 5 and 7 contained trace amounts of compounds which gave positive Ehrlich tests, but the picrates were unstable. The compound in trap 5 had infrared absorption bands (in carbon tetrachloride) at 3470 (strong), 3070, 2998, 1450, 1340 and 1280 cm⁻¹. The compound in trap 7 had infrared

absorption bands (as liquid film) at 3450 (strong), 3050, 2950, 1448, 1338, and 1282 cm^{-1} . These compounds were not identified. The overall yield of indole (3.6 g.) was based on its peak area.

Tubes 3-22, 23-32, 33-45, and 46-50 from the countercurrent distribution apparatus were combined and worked up to give (i) 5.3 g., (ii) 13.5 g., (iii) 16.8 g. and (iv) 0.2 g. respectively of basic material. No pure compounds were isolated from tubes 46-50. Distillation of the basic fractions gave liquids (i) b.p. 83-102°/18 mm., (4.35 g.), (ii) b.p. 106-110°/26 mm. (12.77 g.), and (iii) b.p. 98-102°/18 mm. (15.92 g.). Gas-liquid partition chromatography and paper chromatography showed that (i) contained aniline, o-toluidine, and o-ethylaniline, (ii) consisted of o-toluidine and o-ethylaniline, and (iii) contained o-ethylaniline and a trace of one other compound which was not identified. The components of fractions (i) and (ii) were separated with the Beckman Megachrom and characterised by their infrared spectra and p-toluenesulphonates. The total yields of aniline (2.6 g.) and o-toluidine (7.5 g.) were based on peak areas. From the residues of the distillations of the basic fractions, no pure compounds were isolated.

N-methyl-o-ethylaniline.- N-methyl-o-ethylaniline (56 g.) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at 210°. The gases evolved in the early stages were

identified as ammonia and methane by their infrared spectra. An infrared spectrum of the reaction mixture showed that carbonyl compounds were not present. The reaction mixture was worked up as described for o-ethylaniline and part of the first filtrate (33 g.) was separated by countercurrent distribution. From the neutral fraction (7.9 g.) were isolated (i) $(\text{CH}_2)_x$ (0.25 g.), m.p. 59-60°, (ii) 2-ethylcyclohexanone (0.2 g.) (2,4-dinitrophenylhydrazone, m.p. 162-163°, identical with that obtained from o-ethylaniline), (iii) carbazole (0.35 g.), m.p. and mixed m.p. 241°, and (iv) a mixture (5.4 g.) of indole (20%), 3-methylindole (60%), and an unidentified compound (retention time at 234°: 4.9 min.) which did not give either a p-toluenesulphonate or a stable picrate, but gave a red colour with p-dimethylaminobenzaldehyde.

Tubes 3-12, 13-22, 23-36, 37-44 were combined and from the distillates were isolated (i) aniline (1.3 g.), (ii) o-toluidine (1.97 g.), (iii) o-ethylaniline (9.65 g.), (iv) N-methyl-o-ethylaniline (8.1 g.), and (v) a trace of an unidentified base (retention time at 196°: 4.9 min.). The residues from the distillations were combined (1.8 g.) and added to the material obtained from tubes 44-50 (0.17 g.). Chromatography on alumina yielded no pure compounds. Paper chromatography showed the presence of at least six bases in the mixture.

1,2,3,4-Tetrahydroquinoline.- 1,2,3,4-Tetrahydroquinoline (110 g.) was heated under reflux over the catalyst for 50 hr. at 225°. A positive Ehrlich test and the formation of a chelate with cuprous ions were evident within 10 min. of the commencement of the reaction. A large volume of gas was given off in the early stages. One drop of the reaction mixture was removed each hr. for the first 7 hr. and again at 21 and 22 hr. These were examined by paper chromatography and this provided evidence for the presence of quinoline, 2,2'-biquinoly, aniline, and o-toluidine as well as starting material. Similarly, paper chromatography on acetylated paper revealed the presence of indole and 3-methylindole. It was also observed that the relative concentrations of the products increased with time.

The catalyst was removed by filtration and washed with hot benzene (500 c.c.) and hot ethanol (500 c.c.), the solvents being removed by distillation. Part of the first filtrate (20 g.) was dissolved in ether (55 c.c.) and added in 25 c.c. lots to the third tube of the countercurrent distribution apparatus. Ether was transferred until no positive Ehrlich test was obtained (3 l.). A portion (2 g.) of the neutral fraction (3.3 g.) was chromatographed on alumina (600 g.) and elution with light petroleum (1 l.; b.p. 30-40°) yielded $(CH_2)_x$ (0.4 g.), m.p. 59-60°. On elution with two further light petroleums (b.p. 40-

60°, 20 l.; b.p. 60-80°, 15 l.) no compounds were collected. A 50% solution of benzene and light petroleum (b.p. 60-80°) was used as eluent and a positive Ehrlich test was obtained. 550 x 10 c.c. Fractions were collected on an automatic collector and every tenth submitted to paper chromatography on acetylated paper. The presence of 3-methylindole was observed and on combining the 550 fractions and evaporating to dryness, a yellow material (0.54 g.), m.p. 70-80°, was obtained. This was dissolved in ethanol and a saturated solution of picric acid in ethanol was added until no further precipitate occurred. The yellow picrate of 2,2'-biquinolyl (0.2 g.), m.p. and mixed m.p. 201°, was removed by filtration, and the red solution passed through a short column of alumina. The ethanol was removed and the product crystallised from light petroleum (b.p. 40-60°) to give colourless plates of 3-methylindole (0.41 g.), m.p. 93°, alone and mixed with an authentic sample.

A further 40 x 10 c.c. fractions were collected and paper chromatography revealed the presence of indole and 3-methylindole. These fractions were combined and evaporated to dryness, but the mixture (0.4 g.) was not further investigated. Another 400 x 10 c.c. fractions were collected, and paper chromatography showed the presence of indole. Combination and evaporation of these fractions gave indole (0.018 g.); picrate, m.p. and mixed m.p. 174°. On elution with benzene (10 l.) a

brown oil (0.69 g.) was obtained from which no pure compounds could be isolated. Elution with ethanol gave a black tar (0.24 g.) which was not further examined.

After the first neutral fraction had been collected from the countercurrent distribution apparatus, a yellow ethereal solution (4 l.) was collected and concentrated to a smaller volume (200 c.c.). Dilute ammonium hydroxide was added and the ether separated. A further extraction of the aqueous layer with ether was carried out. The ether solutions were combined, dried, and evaporated to dryness to give a pale yellow waxy substance (1.69 g.). A part (0.5 g.) was chromatographed on a short column of alumina. Elution with light petroleum (b.p. 40-60°) yielded $(\text{CH}_2)_x$ (0.3 g.), m.p. 59-60°, and elution with benzene gave no pure products.

The acid solutions from tubes 3-20 were combined and treated to give a brown liquid (7.18 g.) which when distilled gave a colourless liquid (6.9 g.), b.p. 110-118°/25 mm., and a residue (0.15 g.) which gave no pure products when chromatographed on alumina. Combination of tubes 21-31 gave a brown liquid (6.85 g.) which on distillation gave a colourless liquid (4.8 g.), b.p. 115-135°/25 mm., and a brown residue (1.89 g.) which was not examined at this stage. Tubes 32-50 gave a brown solid (0.5 g.) which on crystallisation from

ethanol gave colourless plates (0.4 g.), m.p. 123.5°. This compound gave a purple chelate with cuprous ions. Dehydrogenation of the compound (0.3 g.) using the method of Prelog and Szpilfogel¹³⁰ gave 2,2'-biquinolyl (0.08 g.), m.p. 194°. The compound is 5,6,7,8-tetrahydro-2,2'-biquinolyl (Found: C, 83.2; H, 6.3; N, 10.9; M (cryoscopic in camphor), 227. $C_{18}H_{16}N_2$ requires: C, 83.1; H, 6.2; N, 10.8%; M, 260), $\lambda_{max.}$ (in ethanol) 249, 259, 303, 322, 337 m μ (log ϵ 4.5, 4.4, 4.2, 4.2, 4.0). The n.m.r. spectrum ($CDCl_3$) showed peaks at $\tau = 8.1$ (quintet) corresponding to four protons as alicyclic CH_2 - groups, $\tau = 7.1$ (quintet) for four protons α to an aromatic ring, and a complex region at $\tau = 2.0$ for eight aromatic ring protons.

Gas chromatography showed that the liquids derived from tubes 3-20 and 21-31 each contained three compounds. Separation of the mixture from tubes 3-20 with the Beckman Megachrom yielded (i) 5,6,7,8-tetrahydroquinoline (Found: C, 81.2; H, 8.3; N, 10.3. Calc. for $C_9H_{11}N$: C, 81.2; H, 8.3; N, 10.5%) picrate, m.p. 157° (lit.,¹³¹ m.p. 156°). Dehydrogenation of 5,6,7,8-tetrahydroquinoline using the above method gave quinoline which was characterised as its picrate, m.p. 201°, alone and mixed with an authentic specimen. (ii) 2-Methyl-1,2,3,4-tetrahydroquinoline was collected and characterised by its infrared spectrum and picrate, m.p. 154°, alone and mixed with an authentic specimen (Found: C, 51.4; H, 4.3; N, 14.9; O, 29.9. Calc. for

$C_{16}H_{16}O_7N_4$: C, 51.1; H, 4.3; N, 14.9; O, 29.9%). Further, (iii) 2-methylquinoline was collected and characterised by comparison of its infrared spectrum and picrate, m.p. and mixed m.p. 194° .

Separation of the compounds from tubes 21-31 with the Beckman Megachrom yielded (i) aniline, (ii) o-toluidine, and (iii) o-ethylaniline, identified by its infrared spectrum and p-toluene-sulphonate, m.p. 133° , needles from ethanol (Found: C, 65.4; H, 6.3; N, 5.0. $C_{15}H_{17}O_2NS$ requires: C, 65.5; H, 6.2; N, 5.1%).

A second separation of the reaction mixture by the countercurrent apparatus was carried out on twice the scale used previously. The neutral fraction (5.5 g.) on distillation gave a solid (3.5 g.), b.p. $80-160^{\circ}/0.5$ mm., of which a part (3 g.) was dissolved in benzene (5 c.c.) and injected into the Beckman Megachrom. Benzene was rejected and three fractions were collected, (i) indole (0.08 g.), m.p. and mixed m.p. 52° , (ii) 3-methylindole (1.4 g.), m.p. and mixed m.p. 93° , and (iii) a trace (0.006 g.) of an unidentified compound. Gas chromatography of the mixture of indoles showed the ratio of 3-methylindole to indole to be 5:1. The residue of the distillation (1.85 g.) was chromatographed on alumina (20 x 3 cm.) and elution with light petroleum (b.p. $60-80^{\circ}$) gave $(CH_2)_x$ (0.47 g.), m.p. $59-60^{\circ}$. Elution with benzene gave 2,2'-biquinolyl (0.45 g.), m.p. 194° , alone and mixed with

an authentic sample. Elution with ethanol gave a black tar (0.44 g.) which was not further investigated.

The aqueous phase of tubes 3-21 was basified, and the mixture obtained was distilled to give a liquid (6.95 g.), b.p. 112-118°/25 mm., and a residue (0.76 g.) which yielded no pure compounds when chromatographed on alumina. The distillate was separated with the Beckman Megachrom into its two components, 5,6,7,8-tetrahydroquinoline, and 2-methyl-1,2,3,4-tetrahydroquinoline.

Tubes 22-31 were worked up in the usual way and on distillation gave a liquid (10.37 g.), b.p. 112-130°/22 mm., and a tarry residue (0.95 g.) which was not further examined. Separation of the distillate was effected with the Beckman Megachrom. In this way were obtained (i) 5,6,7,8-tetrahydroquinoline, (ii) quinoline, and (iii) 2-methylquinoline, all of which were characterised by their infrared spectra and picrates.

Tubes 32-41 yielded a liquid (9.58 g.), b.p. 80-138°/22 mm., and a residue (2.72 g.). Examination of the liquid by paper chromatography and gas chromatography showed the presence of aniline, o-toluidine, o-ethylaniline, quinoline and 2-methylquinoline. Separation of these compounds was effected with the Beckman Megachrom, and they were characterised in the usual way.

The residue was chromatographed on alumina (25 x 5 cm.), and elution with a 50% solution of benzene and light petroleum

(b.p. 60-80°) gave 5,5',6,6',7,7',8,8'-octahydro-2,2'-biquinolyl (1.0 g.), m.p. 156°, λ_{max} . (in ethanol) 247, 280, 317 m μ (log 4.2, 4.4, 3.0) (Found: C, 81.4; H, 7.7; N, 10.8; M (cryoscopic in camphor), 250. C₁₈H₂₀N₂ requires: C, 81.8; H, 7.6; N, 10.6%; M, 264). This compound gave an orange-red colour with cuprous ions. Dehydrogenation according to the method of Prelog and Szpilfogel¹³⁰ (used above) gave 2,2'-biquinolyl. The n.m.r. spectrum (CDCl₃) showed peaks at $\tau = 8.1$ (quintet) corresponding to eight protons as alicyclic CH₂- groups, $\tau = 7.1$ (quintet) corresponding to eight protons next to an aromatic ring, and $\tau = 2.0$ (two doublets) corresponding to four aromatic protons. No further compounds were isolated in pure form when the column was eluted with benzene. Paper chromatography of this material (0.3 g.) showed the presence of at least four bases. Elution with ethanol gave a black tar (0.5 g.) which was not further examined.

Tubes 42-50 gave a brown solid (1.8 g.) which on crystallisation from ethanol gave 5,6,7,8-tetrahydro-2,2'-biquinolyl (0.91 g.), m.p. 123.5°. The residue was chromatographed on alumina (20 x 2 cm.) and 5,6,7,8-tetrahydro-2,2'-biquinolyl (0.2 g.) was eluted with benzene/light petroleum (b.p. 60-80°) (1:1 v/v). No further compounds were obtained on elution with benzene or ether.

The table below lists the products from the reaction and their yield in grams.

1,2,3,4-Tetrahydroquinoline	-	Aniline	1.2
5,6,7,8-Tetrahydroquinoline	14.4	<u>o</u> -Toluidine	5.6
Quinoline	15.0	<u>o</u> -Ethylaniline	0.7
2-Methylquinoline	20.3	Indole	1.5
2-Methyl-1,2,3,4-tetrahydroquinoline	8.0	3-Methylindole	7.5
2,2'-Biquinolyl	1.1	(CH ₂) _x	6.0
5,6,7,8-Tetrahydro-2,2'-biquinolyl	2.5		
5,5',6,6',7,7',8,8'-Octahydro-2,2'-biquinolyl	2.3		

Quinoline.- Quinoline (110 g.) was refluxed over the catalyst, which had been degassed at 360° according to the procedure of Whittle,⁸⁵ for 50 hr. at 236°. The reaction mixture was filtered and the nickel washed with hot benzene (600 c.c.) and hot ethanol (600 c.c.). The solvents were removed by distillation. A part of the first filtrate (38 g.) was separated into basic (37.1 g.) and neutral (0.48 g.; this corresponds to 1.37 g. for the whole reaction mixture) fractions in the usual fashion. The neutral fraction was examined by paper chromatography on acetylated paper and indole, 3-methylindole, carbazole and at least three unidentified compounds were detected.

Distillation of the basic fraction gave a liquid (35.4 g.), b.p. 118-120°/22 mm., and a residue (1.5 g.) which was crystallised from ethanol to yield 2,2'-biquinolyl (0.8 g.), m.p. 193-194°.

Paper chromatography of the distillate showed traces of aniline, o-toluidine and 2-methylquinoline as well as quinoline. A part (10 c.c.) was injected into the Beckman Megachrom and four fractions were collected; (i) aniline (p-toluenesulphonate, m.p. and mixed m.p. 103°), (ii) o-toluidine (p-toluenesulphonate, m.p. and mixed m.p. 110°), (iii) quinoline, (iv) 2-methylquinoline (picrate, m.p. and mixed m.p. 195°). Three other compounds were present in amounts which were insufficient to allow collection.

Yields (g.) of bases:

Aniline	0.8	2-Methylquinoline	2.8
<u>o</u> -Toluidine	2.5	2,2'-Biquinolyl	2.4

Indoline.- Indoline (50 g.) was refluxed over the catalyst (prepared from 62.5 g. of alloy) for 50 hr. at 227°. The dark reaction mixture was filtered, and the nickel washed with hot benzene (800 c.c.) and hot ethanol (800 c.c.). After removal of the solvents, a part of the product (25 g.) was separated into neutral (16.05 g.) and basic fractions in the countercurrent distribution apparatus.

Distillation of the neutral material gave a mixture (8.5 g.), b.p. 85-160°/1 mm., and a residue (6.8 g.). Chromatography of the residue on alumina (30 x 4 cm.) yielded (CH₂)_x (0.1 g.), m.p. 59-

60°, on elution with light petroleum (b.p. 40-60°). Elution with a 50% solution of benzene and light petroleum (b.p. 60-80°) gave a brown gum (0.25 g.) from which no compounds were identified. Elution with benzene yielded 2,3'-biindole (4.0 g.), m.p. 209° (lit.,¹¹⁸ m.p. 207-208°), white needles from benzene (Found: C, 83.1; H, 5.2; N, 11.9; M (cryoscopic in camphor), 210. Calc. for C₁₆H₁₂N₂: C, 82.7; H, 5.2; N, 12.1%; M, 232). The ultraviolet absorption spectra λ_{max} (in ethanol) 236 shoulder, 290 shoulder, 313 m μ (log ϵ 4.4, 4.1, 4.3) was identical with that obtained by Young.¹³² Elution with ether gave a black solid (0.8 g.) from which more 2,3'-biindole (0.6 g.) was obtained by repeated crystallisation from benzene using decolourising charcoal. 2,3'-Biindole gave a red colour with p-dimethylaminobenzaldehyde. Elution of the column with ethanol gave a black intractable (0.48 g.) tar. The ethanol washings of the catalyst (3.7 g.) consisted of 2,3'-biindole.

Gas-liquid partition chromatography of the neutral distillate showed the presence of indole only. Separation using the Beckman Megachrom gave indole, m.p. 52°, and a trace of a second compound (retention time 20 min.) which was not identified.

Tubes 3-22 of the countercurrent separation were combined and treated in the usual fashion to give a brown liquid (2.55 g.) which was distilled to give a colourless liquid (2.1 g.), b.p. 76-130°/11 mm., and a residue (0.4 g.) which was not further

investigated. Examination by gas-chromatography of the distillate revealed the presence of aniline, o-toluidine, and quinoline (trace only). These were collected from the Beckman Megachrom and identified by their infrared spectra, p-toluenesulphonates (aniline and o-toluidine), and picrate (quinoline).

Tubes 23-32 yielded basic material (3.0 g.) which was distilled to give a liquid (2.29 g.), b.p. 84-100°/11 mm., and a residue (0.6 g.) from which no pure compounds were isolated by chromatography on alumina. Investigation of the liquid by gas chromatography revealed the presence of aniline, o-toluidine, o-ethylaniline (trace only), and quinoline (trace only). These bases were separated with the Beckman Megachrom and identified by their infrared spectra, p-toluenesulphonates (aniline, o-toluidine, o-ethylaniline), and picrate (quinoline).

Tubes 33-50 gave a brown tar (0.9 g.) which on chromatography on alumina yielded a trace of o-ethylaniline on elution with light petroleum (b.p. 60-80°). Elution with benzene gave a brown oil (0.35 g.) which was not identified, and elution with ethanol gave a black intractable tar (0.38 g.).

Xylene.- Sulphur free xylene (87 g.) was refluxed over the catalyst for 50 hr. at 140°. The colourless reaction mixture was filtered, and the nickel washed with hot benzene (400 c.c.) and hot ethanol (400 c.c.). The solvents were completely removed

by distillation (absence of benzene and ethanol was established by examination by gas-liquid partition chromatography). After the removal of the solvents, the combined benzene and ethanol washings and the first filtrate gave 67 g. of reaction product. Distillation of the mixture gave (i) b.p. 80-130° (3.5 g.), (ii) b.p. 130-135° (15 g.), (iii) b.p. 135-140° (12.5 g.), (iv) b.p. 140-145° (23.9 g.), and (v) b.p. 145-146° (4.4 g.). These fractions were examined by gas chromatography, and comparison of retention times indicated the presence of benzene, toluene and xylene in fractions (i) and (ii). Fractions (iii), (iv) and (v) contained starting material.

A part (2 c.c.) of fraction (i) was separated with the Beckman Megachrom (conditions as used on page 120, with column temperature 120°) and the following fractions were collected; (a) retention time 4 min. (0.15 g.), (b) retention time 9 min. (0.3 g.), and (c) retention time 12 min. (0.4 g.). Fractions (a) and (b) were shown to be benzene and toluene respectively by comparison with ultraviolet spectra of authentic samples. Fraction (c) was xylene. Fraction (ii) was similarly separated to give benzene, toluene and xylene.

The residue from the distillation (2.5 g.) was chromatographed on alumina, but no separation was achieved on elution with light petroleum (b.p. 30-40°).

p-Toluidine.- p-Toluidine (89 g.) was refluxed over the catalyst for 50 hr. at 198°. The light brown reaction mixture was filtered and the nickel washed as for aniline. After removal of the solvents, the benzene washings were combined with the first filtrate and distilled, two fractions being collected; (i) a liquid, b.p. 80-115° (8 c.c.), (ii) p-toluidine (76 g.). Examination of (i) by gas-liquid partition chromatography showed the presence of benzene (8%) and toluene. The residue from the distillation was separated into neutral (0.6 g.) and basic (1.2 g.) fractions. The basic fraction was starting material. Chromatography of the neutral fraction on alumina yielded (CH₂)_x (0.12 g.), m.p. 59-60°, on elution with light petroleum (b.p. 60-80°). Elution with benzene gave a white compound (0.03 g.), m.p. 218° which gave a red colour with p-dimethylaminobenzaldehyde. Lack of sufficient material did not allow its characterisation. Elution with ethanol gave a black tar (0.25 g.) which was not further examined.

Quinoxaline.- Quinoxaline (55 g.) was refluxed over the catalyst (prepared from 62 g. of alloy) for 50 hr. at 223°. The dark reaction mixture was filtered and the nickel washed with hot benzene (600 c.c.) and hot ethanol (800 c.c.). The solvents were removed by distillation and the benzene washings were combined with the first filtrate. The ethanol washings (2.0 g.) were

crystallised from benzene/ethanol using decolourising charcoal. White plates of benzimidazole (1.7 g.), m.p. and mixed m.p. 172° were obtained.

Distillation of the reaction mixture gave (i) quinoxaline (14 g.), b.p. 119-120°/24 mm., and (ii) a mixture (10.3 g.), b.p. 148-164°/2 mm. Fraction (ii) was extracted with light petroleum (b.p. 60-80°) and the extract chromatographed on alumina (40 x 3 cm.) and eluted with the light petroleum to give quinoxaline (1.3 g.). Elution with a 50% solution of benzene and light petroleum (b.p. 60-80°) yielded a yellow oil (0.23 g.) which was not identified. On elution with benzene, a yellow oil (0.7 g.) was obtained which gave a picrate m.p. 246° alone and mixed with an authentic sample of N-methylbenzimidazole picrate¹³³ (Found: C, 46.5; H, 3.2; N, 19.4. Calc. for C₁₄H₁₁O₇N₅: C, 46.5; H, 3.1; N, 19.4%). Further elution with benzene yielded 2-methylbenzimidazole (1.58 g.), m.p. 177°, alone and mixed with an authentic specimen. The column was eluted with ethanol to give a black intractable tar (0.57 g.). The material not extracted by the light petroleum (4.8 g.) was crystallised from ethanol, and shown to be benzimidazole, m.p. 172°.

The residue from the distillation of the reaction mixture (6.0 g.) was chromatographed on alumina (25 x 3 cm.) and elution with light petroleum (b.p. 60-80°) yielded no compounds. Elution with benzene gave (i) 2-methylbenzimidazole (0.15 g.), and (ii) a yellow oil (0.05 g.) which was not characterised. Further

elution with benzene gave a pale yellow solid (0.65 g.), m.p. 254-255°, which gave a wine red colour with cuprous ions. The n.m.r. spectrum (CDCl₃) showed complex absorption at $\tau = 2.2$ for eight ring protons, complex absorption at $\tau = 4.1$ for N-H, and a singlet at $\tau = 0$ for a proton α to a nitrogen atom in a heterocyclic ring. The compound is suggested to be 2,2'-benzimidazolylquinoxaline, λ_{max} . (in ethanol) 247, 267, 296, 361 m μ (log ϵ 4.3, 3.5, 4.1, 4.3) (Found: C, 72.8; H, 4.0; N, 23.0. C₁₅H₁₀N₄ requires: C, 73.1; H, 4.1; N, 22.8%).

On further elution with benzene a black solid (0.25 g.) was obtained which on repeated crystallisation from ethanol (employing decolourising charcoal) gave colourless plates, m.p. 282-283°, λ_{max} . (in ethanol) 266, 272, 343 m μ (log ϵ 4.4, 4.3, 4.3). This compound gave a purple precipitate with cuprous ions. The n.m.r. spectrum (CDCl₃) showed complex absorption at $\tau = 2.1$ and 1.7 corresponding to eight ring protons, and a singlet at $\tau = 0$ for two aromatic protons α to a nitrogen atom in a heterocyclic ring. The compound is probably 2,2'-biquinoxalyl (lit.,¹³⁴ m.p. 274-276°) (Found: N, 21.7. Calc. for C₁₆H₁₀N₄: N, 21.7%). Elution of the column with ethanol gave a black tar (1.5 g.) which was not further examined.

CHAPTER III

The formation of biaryls from quinoline under the influence
of catalysts derived from the metals of Group VIII.

CHAPTER III

The formation of heterocyclic biaryls from the parent bases has been studied many times in the last eighty years. 2,2'-Bipyridyl, 2,2'-biquinolyl, and their alkyl derivatives have found many uses in coordination and biological chemistry, and an economical preparation for these compounds is essential. By far the greatest number of methods used to prepare these compounds employ metal catalysts. 2,2'-Bipyridyl has received more attention than 2,2'-biquinolyl and most preparative studies have been directed towards this end.

2,2'-Bipyridyl is prepared industrially by the reaction of pyridine with a degassed Raney nickel catalyst.^{6,7} When applied to quinoline, this procedure gives a somewhat lower yield of 2,2'-biquinolyl.⁴³

Other methods for the preparation of 2,2'-biquinolyl have been employed with limited success. The reductive coupling of 2-bromoquinoline using palladium-on-calcium carbonate, hydrazine, and alcoholic potassium hydroxide gave poor yields¹³⁵ which varied widely.¹³⁶ Consistent yields can now be obtained by this method.¹³⁷ Similarly, poor yields are obtained in Ullman-type condensations.^{40,136,138} The pyrolysis of calcium quinaldate¹³⁹ and quinaldinic acid in quinoline¹⁴⁰ gave 2,2'-biquinolyl. For both these reactions, an ionic mechanism has been postulated.¹⁴⁰ Better yields have been obtained by using

the method of catalytic dehydrogenation with a nickel-aluminium oxide catalyst in a sealed tube.^{38,39,40} When some elements other than nickel are used as catalysts, other isomeric biquinolyls are isolated. Using selenium, Ueda¹⁴¹ obtained solely 2,3'-biquinolyl. Sodium¹⁴² and sodamide^{143,144} have also been used in the preparation of biquinolyls, usually with the formation of 2,3'-biquinolyl. Recently, palladium-on-charcoal was used as a catalyst for the formation of 2,2'-biquinolyl.⁶⁷

As both nickel and palladium catalysts have been used to prepare 2,2'-biquinolyl it was thought that other transitional metal catalysts might also be able to bring about this reaction. Hence a comparative study of the dimerising ability of some noble metal catalysts (supported on charcoal) has been carried out. Using the conditions of the palladium-on-charcoal reaction⁶⁷ the yields of 2,2'-biquinolyl are listed in Table I.

Table I

Catalyst	Wt. of catalyst (g.)	Yield of 2,2'-biquinolyl (g.)	Yield expressed in g./g. atom of metal.
5% Ruthenium/charcoal	2	-	-
5% Osmium/charcoal	2	-	-
5% Rhodium/charcoal ^a	5	11 ^b	4.5 x 10 ³
5% Iridium/charcoal	2	-	-

5% Palladium/charcoal	2	0.66	7.0×10^2
5% Palladium/charcoal ^a	1	0.70	1.5×10^3
5% Platinum/charcoal	2	-	-
W7-J Raney nickel ^c	62.5	2.5	2.5

^a Indicates a commercial catalyst.

^b 4.0 g. of 2,3'-biquinolyl also formed.

^c Added for comparison.

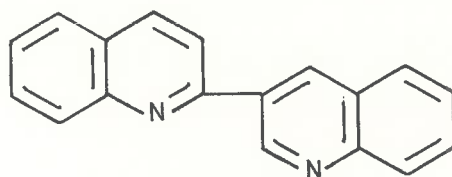
As both the nickel and the palladium reactions yielded 2,2'-biquinolyl it was surprising to find that the platinum catalyst had no effect on quinoline, since these metals belong to the same Group. The difference in the yields of 2,2'-biquinolyl obtained with the commercial and laboratory preparations of palladium-on-charcoal must be related to the methods of preparation of the catalysts. This is not surprising as it is known that even different batches of the "same" palladium-on-charcoal catalyst (prepared according to the same directions) can differ in activity in hydrogenations.¹⁴⁵

Rapoport and his colleagues stated that the reaction of quinoline with palladium-on-charcoal was "clean" in that only 2,2'-biquinolyl and unchanged quinoline were present in the reaction mixture. However, in the present work traces of other products were detected in the experiments carried out with

palladium-on-charcoal catalysts. The quantities formed, however, were too small to allow their identification.

No dimerisation occurred when the ruthenium, osmium, iridium, and platinum catalysts were used although traces of unidentified products were formed.

Besides palladium-on-charcoal, rhodium-on-charcoal was the only other catalyst to yield 2,2'-biquinolyl. In fact the rhodium catalyst gave more 2,2'-biquinolyl than the nickel and palladium catalysts. However, 2,3'-biquinolyl (I) was also formed in appreciable quantities.



(I)

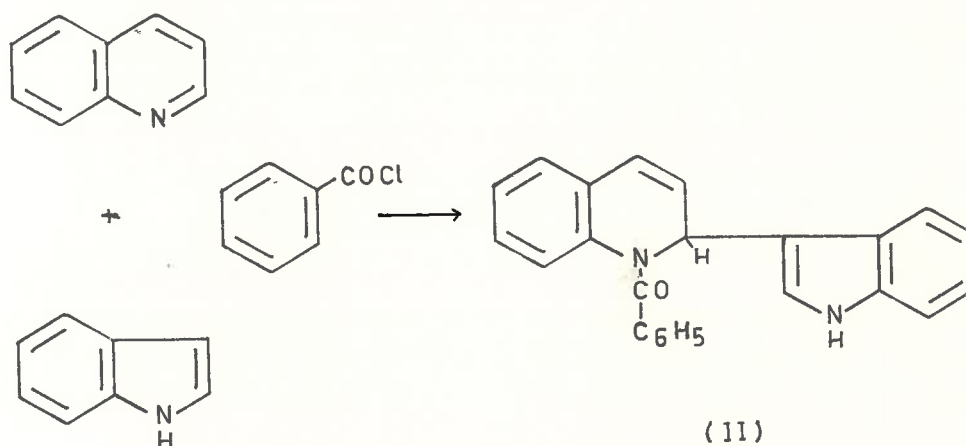
Whittle⁸⁵ studied the formation of 2,2'-bipyridyl from pyridine with all the catalysts used in the present study. He showed that only palladium yielded 2,2'-bipyridyl, and that the other catalysts, including rhodium, formed none. In all known cases of biaryl formation, 2,2'-bipyridyl is formed in greater yields than 2,2'-biquinolyl on the same metallic catalyst. It has been postulated that the inferior yield obtained in the reaction of quinoline with degassed Ramsy nickel is caused by steric interference of the benzene ring with chemisorption via

the nitrogen atom.⁴³ Rapoport suggested that better yields of 2,2'-dipyridyls might be obtained if the temperatures of the reactions were higher. If a similar temperature dependence exists in reactions with the rhodium catalyst, large quantities of 2,2'-bipyridyls should be obtained when pyridines are reacted with this catalyst at higher temperatures.

Whittle pointed out that in the case of the formation of 2,2'-bipyridyl, the yield expressed as grams of 2,2'-bipyridyl per gram-atom of metal was greatest with the palladium catalyst. In the present work the yields of 2,2'-biquinolyl expressed in this fashion (see Table I) show that rhodium is by far the best catalyst, followed by palladium and nickel. The yield with the rhodium-on-charcoal catalyst is such that it warrants consideration as a preparative method. Although 2,3'-biquinolyl is also formed, it can be easily separated from 2,2'-biquinolyl.

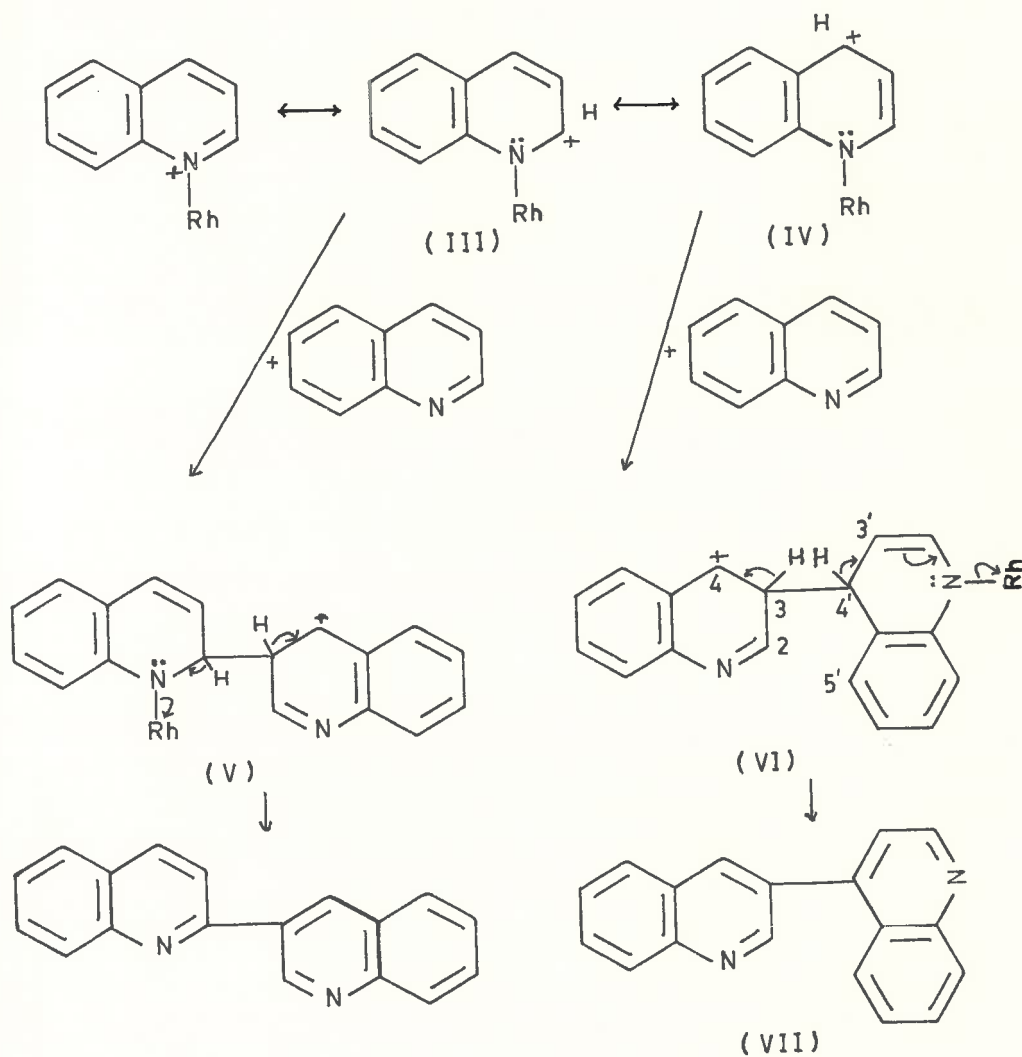
The formation of 2,2'-biquinolyl from quinoline over rhodium-on-charcoal, although not as specific a reaction as that using degassed Raney nickel, it is at least specific to the extent that only two isomers are formed. As far as the mechanism of the formation of these biquinolyls is concerned, it is probable that the 2,2'-isomer is formed by the same mechanism discussed earlier for the formation of 2,2'-biaryls under the influence of Raney nickel (see p. 9).⁴² However, for the occurrence of 2,3'-biquinolyl a different mechanism must be considered.

It has been shown that quinolinium salts in which the 2-position carries a fractional positive charge, may undergo nucleophilic attack by the electron-rich 3-position of indole.¹⁴⁶ For example, the reaction between quinoline, indole and benzoyl chloride yielded 1-benzoyl-2-[indolyl-(3)]-1,2-dihydroquinoline (II). Furthermore, it was observed that in the quinoline series only 2,3'-substituted compounds were isolated. For pyridinium salts, nucleophilic attack by indole was observed at the 4-position.



In the present reaction a quinoline molecule chemisorbed by the catalyst may be regarded as a resonance hybrid (of the possible contributing structures only (III) and (IV) are shown). If it is assumed that these intermediates are favourably situated on the catalyst, nucleophilic attack by the more electron rich 3-position of a quinoline molecule would lead to the intermediates

(V) and (VI) (only shown with a positive charge localised at the 4-position). Elimination of two protons from (V) and (VI) would yield 2,3'-biquinolyl and 3,4'-biquinolyl (VII).



Inspection of Catalin models shows that for the 3,4'-isomer to be formed, steric interference occurs between the 2, 4, 3' and 5' hydrogen atoms; but at this stage the formation of 3,4'-biquinolyl

cannot be excluded. However, as mentioned above, nucleophilic attack of quinolinium salts by indole has only been observed to occur at the 2-position, and in this sense it resembles the reaction of quinoline with rhodium.

The mechanism proposed for the formation of 2,3'-biquinolyl is only tentative, and further studies need to be carried out before a full understanding is gained.

EXPERIMENTAL

Preparation of Catalysts.- One 5% palladium-on-charcoal catalyst and the 5% rhodium-on-charcoal catalyst were commercial preparations. 5% Palladium-on-charcoal was prepared according to the method of Vogel.¹⁴⁷ 5% Platinum-on-charcoal and 5% iridium-on-charcoal were prepared according to the procedure used for the palladium catalyst.¹⁴⁷ 5% Osmium-on-charcoal was prepared according to Zelinskii and Turova-Pollack's method¹⁴⁸ for the preparation of 25% osmium-on-asbestos. 5% Ruthenium-on-charcoal was prepared according to Zelinskii and Turova-Pollack's procedure¹⁴⁹ for the preparation of ruthenium-on-asbestos.

General procedure.- Except where otherwise stated, the reactions of quinoline over 5% noble metals-on-charcoal catalysts were carried out as follows. Quinoline (25.8 g.) was refluxed over the catalyst (2.0 g.) for 24 hr. Hot chloroform (100 c.c.), was added and the mixture filtered through a sintered glass funnel. The catalyst was washed with benzene (100 c.c.), and after removal of the solvents by distillation, the products were combined. The reaction mixture was then distilled under reduced pressure. Analysis of the basic products in the distillate and residue of distillation was carried out using paper and gas-liquid partition chromatography.

Paper chromatography.- As for bases in Chapter II (p. 118).

Palladium-on-charcoal.- (a) The distillate (24.8 g.), b.p. $122^{\circ}/21$ mm., was pure unchanged quinoline. Crystallisation of the residue (0.85 g.) from ethanol gave 2,2'-biquinolyl (0.66 g.), m.p. 192° . Paper chromatography of the residue indicated that at least three other compounds were present in trace amounts.

(b) Using a commercial catalyst (Baker) (1.0 g.), quinoline (10 c.c.) was refluxed with the catalyst for 24 hr. The distillate (9.0 g.) was quinoline and the residue on crystallisation gave 2,2'-biquinolyl (0.70 g.). Again the presence of trace amounts of three other compounds was shown by paper chromatography.

Iridium-on-charcoal.- Reaction yielded unchanged quinoline (25.3 g.) and a residue (0.35 g.) which showed the presence of at least two compounds by paper chromatography. Chromatography on a short column of alumina yielded no pure product. The absence of 2,2'-biquinolyl was shown by the failure to give a chelate with cuprous ions.

Ruthenium-on-charcoal.- Unchanged quinoline (25.4 g.) was recovered, the residue showing the presence of trace amounts of two compounds, neither of which was 2,2'-biquinolyl.

Platinum-on-charcoal.- Other than unchanged quinoline (25.4 g.), only trace amounts of two other compounds were evident. Neither of these were 2,2'-biquinolyl.

Osmium-on-charcoal.- The distillate (25.4 g.) was unchanged quinoline and the residue (0.25 g.) showed the presence of trace amounts of two other compounds. No 2,2'-biquinolyl was formed.

Rhodium-on-charcoal.- Quinoline (64.5 g.) was refluxed over a commercially prepared catalyst (Baker) (5.0 g.) for 24 hr. Within minutes a colouration with cuprous ions was given. The reaction mixture was filtered and the catalyst washed with hot benzene (600 c.c.) and hot ethanol (500 c.c.). The solvents were removed by distillation. The ethanol washings yielded a brown oil (0.1 g.) from which no pure compounds were isolated. After distillation of the benzene from the reaction mixture, ethanol (300 c.c.) was added and the solution cooled in an ice-bath. 2,2'-Biquinolyl (9.0 g.), m.p. 190-191^o, was filtered off. Evaporation of the ethanol gave 54.9 g. of a brown oil which was dissolved in ether (200 c.c.) and extracted four times with 300 c.c. lots of 5% hydrochloric acid. The acid solution was washed once with ether (100 c.c.) and combination of the ether solutions after drying over magnesium sulphate and evaporation to dryness yielded 0.5 g. of neutral material. On chromatography through a short column of alumina this brown oil yielded no pure compounds. The acid solution was basified with ammonium hydroxide solution, extracted with ether (3 x 300 c.c.), the ether solution then being dried over magnesium sulphate and evaporated to dryness. This yielded 54.2 g. of basic material

which was distilled, yielding fractions (i) b.p. $117^{\circ}/25$ mm. (5.1 g.), and (ii) b.p. $118^{\circ}/25$ mm. (41.6 g.). On examination by paper and gas-liquid chromatography unchanged quinoline was detected. A trace amount of another base was detected in fraction (ii) by paper chromatography but this was not identified.

The residue from the distillation (7.0 g.) was chromatographed on a column of alumina (3 x 20 cm.). Elution with light petroleum (b.p. $60-80^{\circ}$) yielded quinoline (0.3 g.) (picrate, m.p. 201° alone and mixed with an authentic sample).

Further elution with a 50% solution of light petroleum (b.p. $60-80^{\circ}$) and benzene, gave (ii) 2,2'-biquinolyl (1.2 g.) and a fraction (iii), colourless plates (1.2 g.), m.p. $170-190^{\circ}$. Elution with benzene gave fraction (iv), colourless needles (3.4 g.), m.p. $175-176^{\circ}$, which was 2,3'-biquinolyl (lit.,¹⁵⁰ m.p. $175-176^{\circ}$) (Found: C, 84.5; H, 4.8; N, 10.5. Calc. for $C_{18}H_{12}N_2$: C, 84.4; H, 4.7; N, 10.9%). Fraction (iii) by paper chromatography was found to be a mixture of 2,2'-biquinolyl and 2,3'-biquinolyl. The ultraviolet spectrum in 95% ethanol of 2,3'-biquinolyl showed maxima (log ϵ values) at 257 (4.8) and 325 m μ (4.2).

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