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RUTHENIUM-CATALYSED REARRANGEMENTS OF AZOBENZENES

IV *. REARRANGEMENT OF DEUTERATED AZOBENZENES TO 1-PHENYLBENZIMIDAZOLE AND *N*-PHENYL-1,2-PHENYLENEDIAMINE DERIVATIVES

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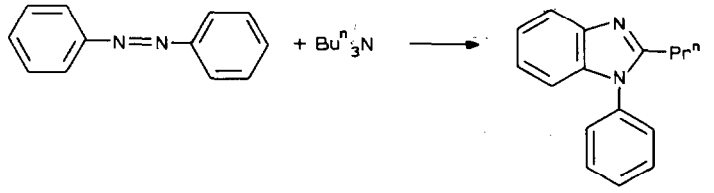
Summary

The ruthenium-catalysed reactions of azobenzene-d_{10} and 4,4′-disubstituted azobenzene-d_8 compounds with non-deuterated tri-n-butylamine, n-butanol or 2-propanol give 1-phenylbenzimidazole or *N*-phenyl-1,2-phenylenediamine derivatives. The distribution of ^1H in the aromatic rings of these products and in the recovered azobenzenes indicates that in all cases *ortho*-metallation of the azobenzene derivative has occurred. The significance of these and other observations for the mechanism of these reactions is discussed.

Introduction

We have already reported the ruthenium-catalysed reactions of azobenzenes with tertiary amines [1,2], primary alcohols [1,3] and secondary alcohols [4,5] giving respectively 1-phenylbenzimidazole (eq. 1, 2) and *N*-phenyl-1,2-phenylenediamine (eq. 3) derivatives.



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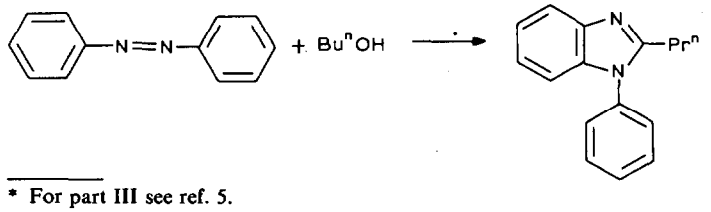

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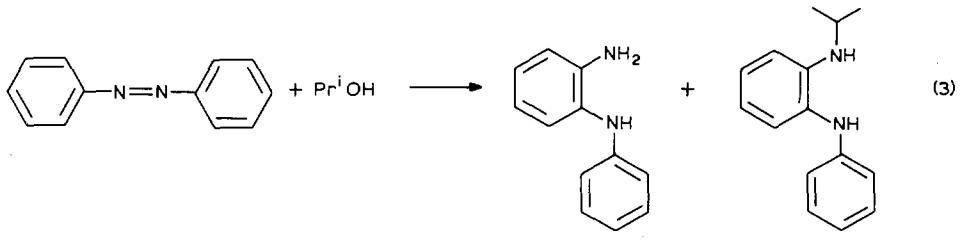
* For part III see ref. 5.



(3)

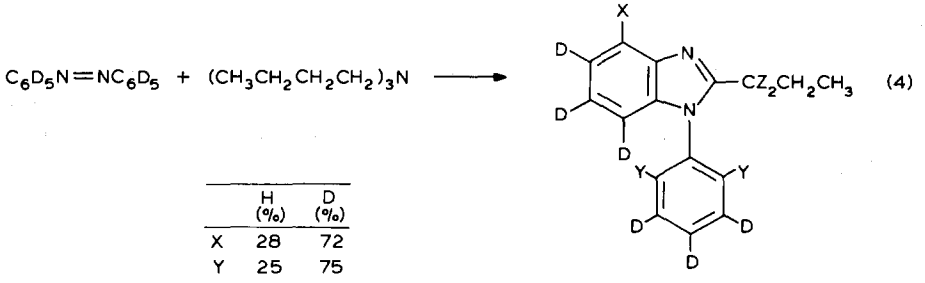
In order better to understand the mechanism of these reactions, the compounds azobenzene-d_{10}, 4,4'-dinitroazobenzene-d_8 and 4,4'-dimethoxyazobenzene-d_8 have been prepared from benzene-d_6, and their behaviour in the above reactions studied. The reactions were normally not permitted to run to completion, so that in addition to the products, some of the azobenzene derivative could be recovered. The distribution of ^{1}H and D over the molecule was then studied by ^{1}H (250 MHz) and ^{13}C NMR spectroscopy.

Results

The aromatic region of the 250 MHz ^{1}H NMR spectra of the products of these reactions when non-deuterated azobenzene derivatives are employed is complex and H/D exchange is therefore far more readily studied using a deuterated azobenzene derivative with non-deuterated tertiary amines, or primary or secondary alcohols as reaction partners.

1-Phenylbenzimidazole derivatives

The reaction of azobenzene-d_{10} with tri-n-butylamine was carried out as previously described [2] but with the reaction time reduced to 7 h (eq. 4).



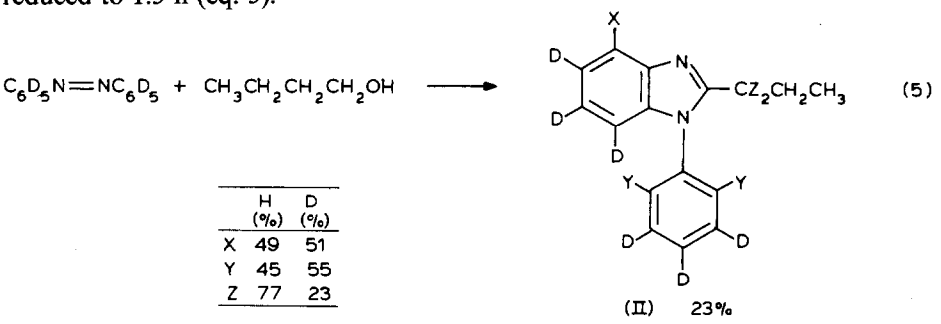
(4)

	H (%)	D (%)
X	28	72
Y	25	75
Z	86	14

(I) 33%

Compound I shows singlets at δ 7.37 and 7.80 ppm, ratio 2/1, in the ^{1}H NMR spectrum, corresponding to the positions X and Y as shown (see below). These are the three *ortho*-positions of the azobenzene-d_{10} which still carry hydrogen, the fourth being occupied by the 1-nitrogen atom of I. No other positions in the aromatic rings underwent exchange. The source of the ^{1}H incorporated into I may be the alkyl groups of the tertiary amine, most probably the α-position, as a result of attack by ruthenium, or possibly the di-n-butylamine formed. Theoretically this should contain a deuterium atom. Whether the by-product is $(C_4H_9)_2ND$ or $(C_4H_8D)(C_4H_9)NH$ is not known and would depend on the relative rates of the ruthenium-catalysed reactions occurring.

For the reaction of azobenzene-d_{10} with n-butanol [3], the reaction time was reduced to 1.5 h (eq. 5).



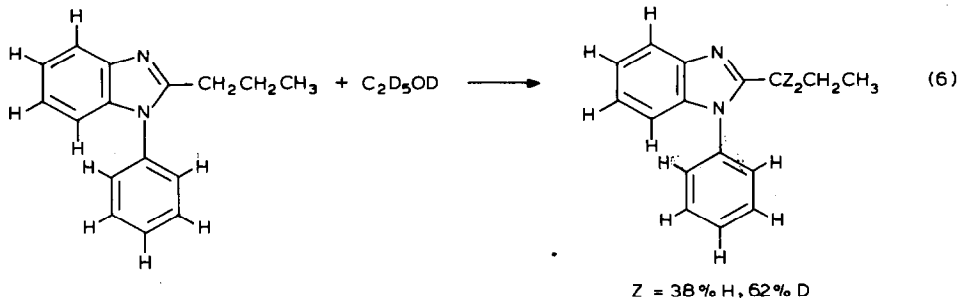
(5)

	H (%)	D (%)
X	49	51
Y	45	55
Z	77	23

For II the ^{13}C NMR spectrum was recorded to confirm that the H/D exchange in the aromatic groups had occurred in the positions shown. The two ^1H singlets in the aromatic region of the spectrum of II were again at δ 7.37 and 7.80 ppm. In reaction 5 the residual azobenzene was isolated and reduced to hydrazobenzene, so as to have an internal standard for NMR integration. In all cases where N–H bonds served as standards for integration, the compound concerned was dissolved in a suitable solvent and shaken several times with H_2O to remove any N–D present before the spectrum was recorded. So as to obviate any possibility of further H/D exchange during the reduction, this was carried out using ammonia and hydrogen sulphide. The hydrazobenzene showed, in addition to the N–H resonance at δ 5.62 ppm, a singlet at δ 6.86 ppm, indicating that exchange in the *ortho*-position of the azobenzene had occurred, these now being 38%H, 62%D.

In both compounds I and II, integration of the ^1H NMR spectra shows that the α-methylene group of the n-propyl residue has undergone exchange in the opposite sense to the aromatic rings, i.e. D for H. The ^1H spectra provide no definate evidence for exchange in the β-methylene or the methyl groups. However, the proton-decoupled ^{13}C NMR spectrum shows the α-carbon of the n-propyl group as a singlet for the $^{13}CH_2$ groups, and marginally to higher field, a 1/1/1 triplet arising from ^{13}CHD. The $^{13}CD_2$ signal, if present, was too weak to be seen. Further, the β-carbon shows a strong singlet and a weak triplet, indicating that limited exchange has occurred at this position. No deuterium could be detected in the methyl group.

In order to investigate whether under reaction conditions any H/D exchange occurred in the product, non-deuterated 1-phenyl-2-(n-propyl)benzimidazole was caused to react with ethanol-d_6 under the conditions of the reaction of eq. 5 above. The ^1H NMR spectrum of the recovered benzimidazole derivative showed extensive deuteration of the α-methylene group, but no deuteration of any other position (eq. 6).

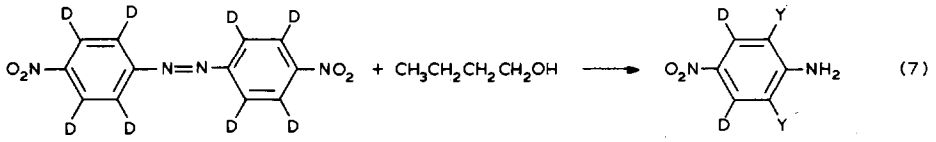


(6)

This was confirmed by the proton-decoupled ^{13}C NMR spectrum, which showed a triplet (roughly 1/1/1) for the α-methylene group, indicating that this is present principally as ^{13}CHD, but that no other carbon atom was deuterated.

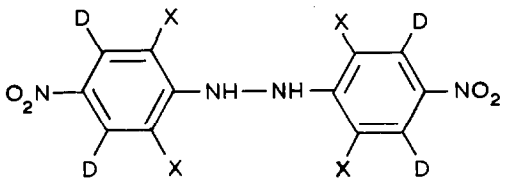
We have previously noted that electron-withdrawing substituents in the azobenzene derivative accelerate the rate of its reduction to the corresponding aniline analogue relative to the benzimidazole synthesis, whilst the latter reaction is simply retarded if strongly electron-releasing groups are present [2]. In order to ascertain whether this was due to substituent effects on the *ortho*-metallation, both 4,4′-dinitroazobenzene-d_8 (III) and 4,4′-dimethoxyazobenzene-d_8 (IV) were prepared from benzene-d_6 (see Experimental) and caused to react with non-deuterated n-butanol. III was obtained isotopically pure but during the preparation of IV, some H/D exchange *ortho* to the oxygen atoms occurred. Since it is the positions *ortho* to the nitrogen atoms of IV which are important, this did not invalidate the results. The exchange occurred during the conversion of the diazonium compound to the phenol by boiling.

The reaction of III with n-butanol (eq. 7) was terminated after only 3 h, so that some of III could be recovered. In this time, no significant amount of the benzimidazole product was formed.



(III) (V) Y = 40% H, 60% D

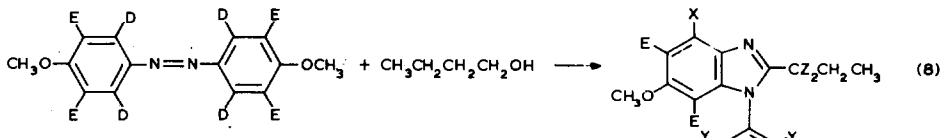
The recovered III was again reduced with ammonia and hydrogen sulphide to give VI.



(VI) X = 39% H, 61% D

Clearly, *ortho*-metallation of the azobenzene derivative has again occurred.

The reaction of compound IV with n-butanol was permitted to proceed for 8 h (eq. 8).



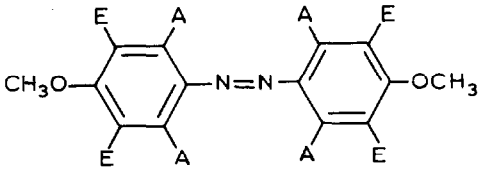
(IV) E = 50% H, 50% D

	H (%)	D (%)
X	57	43
Y	68	32
Z	78	22
E	50	50

(VII) 35%

The difference in the apparent extent of incorporation of ^1H in the X and Y signals here is largely due to the Y multiplet coinciding with the singlet of the residual $CHCl_3$ in the deuterochloroform solvent used, leading to a higher integral

in the ^1H NMR spectrum. No deuterium was present in the β-methylene group of VII according to the ^1H and ^{13}C NMR spectra. The recovered dimethoxyazobenzene (VIII) was also investigated and showed the following distribution of deuterium.



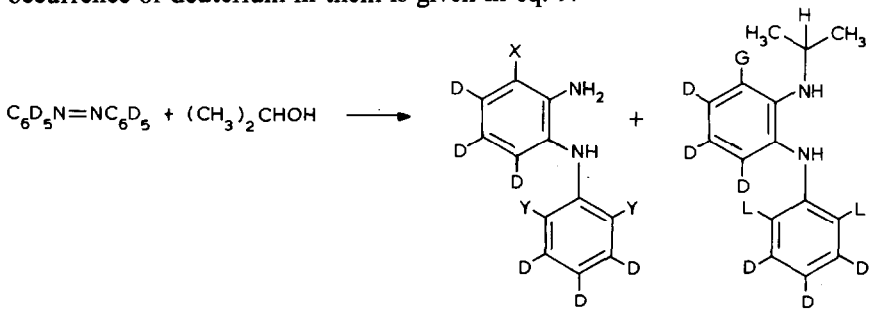
(VIII)

	H (%)	D (%)
A	66	34
E	50	50

The results again indicate that *ortho*-metallation of the azobenzene derivative occurs and that there is then no further significant exchange in the corresponding positions of the benzimidazole product. The effect of substituents in the azobenzene on the benzimidazole product [2,3] would therefore appear not to arise from the *ortho*-metallation step, since this occurs in both the dinitro and dimethoxyazobenzenes.

N-Phenyl-1,2-phenylenediamine derivatives

The reaction of azobenzene-d_{10} with non-deuterated 2-propanol was carried out under conditions where both products of eq. 3 were formed (see Experimental). The occurrence of deuterium in them is given in eq. 9.



(9)

(IX) 35%	H (%)	D (%)
X	62	38
Y	62	38

(X) 8%	H (%)	D (%)
G	55	45
L	55	45

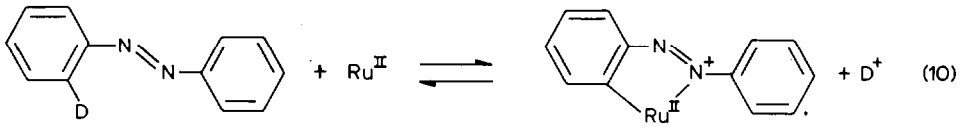
Once again, exchange was observed only in those positions in the aromatic rings which were *ortho* in the azobenzene-d_{10}. However, in X the proton-decoupled ^{13}C NMR spectrum showed that limited incorporation of deuterium in the methyl groups of the 2-propyl residue had occurred, but no deuterium could be detected on the 2-carbon atom itself (see below).

Discussion

We have already provided evidence that the rearrangement of the azobenzene derivative is the first step in these reactions [2]. Although complexes of ruthenium in the oxidation states (0), (II) and (III) have been used as catalyst precursors in these reactions, best results have been obtained with the last two oxidation states ($RuCl_2(DMSO)_4$; $RuCl_3 \cdot 3H_2O$) [2]. A considerable number of ruthenium com-

plexes of azobenzene are now known in which the metal is present as ruthenium(II) [6–9]. In view of the presence of ligands such as carbon monoxide and, for the alcohol reactions, triphenylphosphine, the tertiary amine or the alcohol used may be expected to be able to reduce ruthenium(III), and the complex which attacks the azobenzene derivative is likely to be ruthenium(II). This would lead to the *ortho*-metallation occurring by electrophilic attack on an *ortho* C–H bond. The reaction of $Ru_3(CO)_{12}$ with azobenzene has also been studied and was found to give a number of bi- and tri-nuclear carbonyl complexes which contained *ortho*-metallated azobenzene or deprotonated *o*-semidine (*N*-phenyl-1,2-phenylenediamine) ligands [10]. The formal oxidation states of these complexes varied from (0) to (II) and it is therefore possible that when $Ru_3(CO)_{12}$ is used as catalyst precursor, in the 1-phenylbenzimidazole synthesis [2] ruthenium(II) species are again formed.

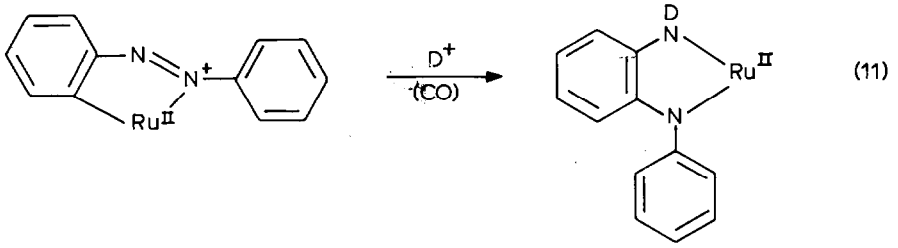
The H/D exchange described above demonstrates clearly that *ortho*-metallation occurs in both the tertiary amine and primary alcohol versions of the 1-phenylbenzimidazole synthesis and in *N*-phenyl-1,2-phenylenediamine formation. This would be expected to occur as shown in eq. 10 in which the ruthenium(II) species is presumed to be a carbonyl complex, probably mononuclear. The coordination sphere would be completed by the available ligands (Cl^-, AcO^-, PPh_3, CO).



(10)

(XI)

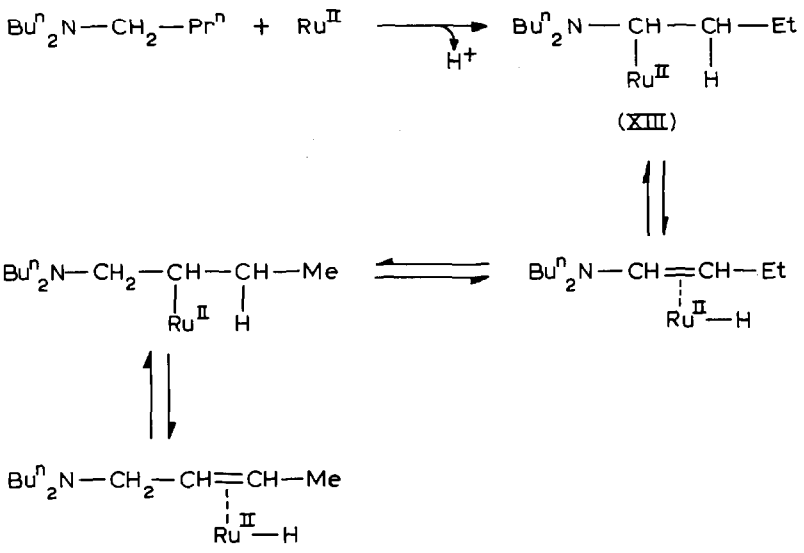
The observation of H/D exchange in the *ortho*-positions of the recovered azobenzene indicates that the *ortho*-metallation is reversible. The occurrence of this reaction does not necessarily prove that the rearrangement to a deprotonated *o*-semidine complex XII occurs via complex XI, but since in this complex the carbon and nitrogen atoms which must form a bond to one another in XII are both coordinated to the ruthenium centre, this seems most probable. The next step of the reaction is therefore believed to be eq. 11.



(11)

(XII)

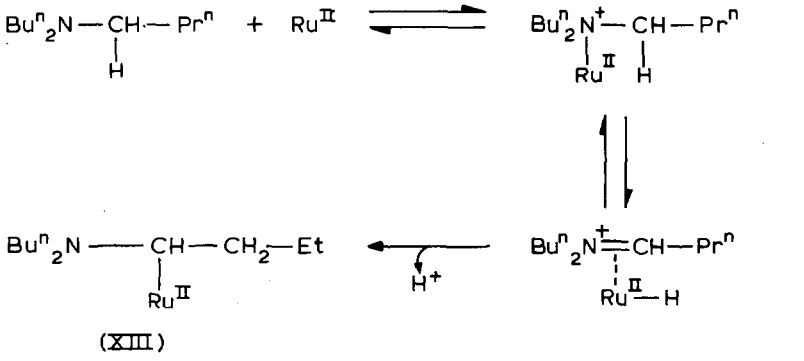
If XII does indeed contain ruthenium in oxidation state (II), then XII as shown leaves two electrons unaccounted for and multiple bonding of nitrogen to ruthenium, as is known in other *o*-semidine complexes [8,10–14], may occur. XII may also be polynuclear. The rearrangement shown in eq. 11 is known for complexes of molybdenum [8], iron [11,12], ruthenium [10], osmium [13], and rhodium [14], and in all cases carbonyl ligands are present. The need to carry out the catalytic reactions described here [1–5] under carbon monoxide is thus readily explained.



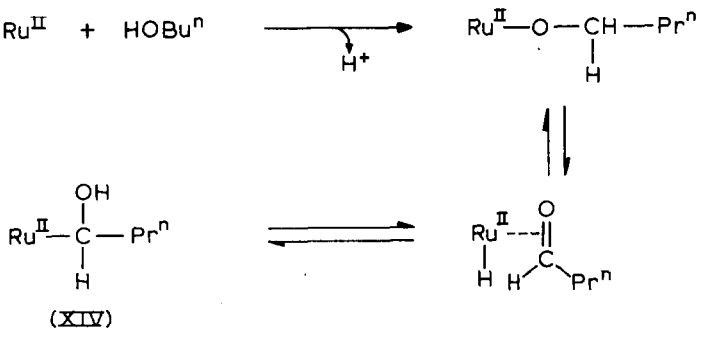
Scheme 1

The next step must involve the amine or alcohol component. In the 1-phenylbenzimidazole synthesis (eq. 4, 5) the occurrence of deuterium on the β-carbon of the n-propyl group is most significant. The reaction of eq. 6, in which deuterium is introduced only at the α-carbon, shows that in the formation of I and II the β-carbon atom is activated. We attribute this to the formation of an Ru–C bond with the alcohol or amine, followed by migration of the ruthenium via alkene elimination and re-insertion (Scheme 1). Exchange of the hydride with D^+, releasing a proton, then accounts for the H/D exchange. A similar process is expected in the primary alcohol reaction (eq. 5). The initial attack on the amine or alcohol may be a direct electrophilic attack on the α C–H bond. An alternative possibility would be the β-elimination shown in Scheme 2. For the n-butanol reaction an alkoxide would presumably be first formed (Scheme 3).

Since alkylation of the nitrogen in XII always involves the α-carbon atom of the



Scheme 2

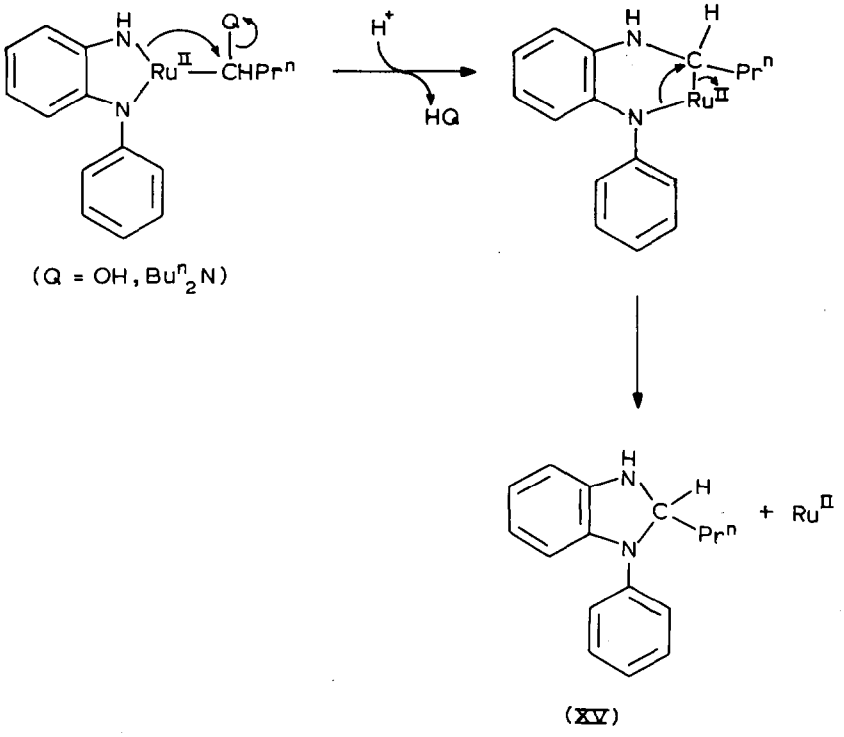


Scheme 3

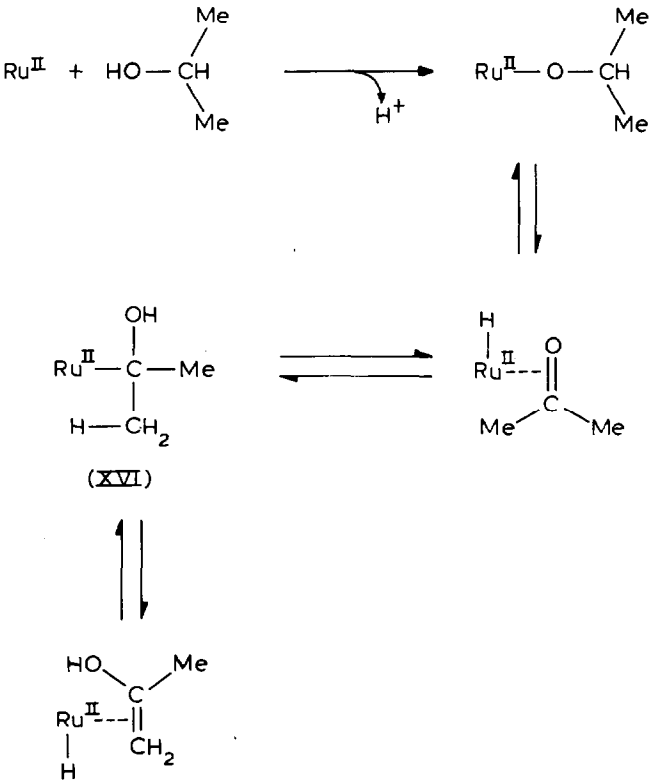
tertiary amine or primary alcohol, XIII or XIV must be involved in this step. Assuming the intermediates are mononuclear, the ring-closure may be envisaged to be as shown in Scheme 4.

The aromatisation of XV may well be a purely thermal process at the temperatures involved, but coordination of ruthenium(II) to the N(3) atom followed by liberation of its proton and then β-elimination of the C(2) hydrogen atom to give the final product and a mole of hydrogen provides a route for catalysis of this step.

In the synthesis of N^1-phenyl-N^2-(2-propyl)-1,2-phenylenediamine (eq. 8), the occurrence of deuterium in the methyl groups of the 2-propyl residue again indicates



Scheme 4



Scheme 5

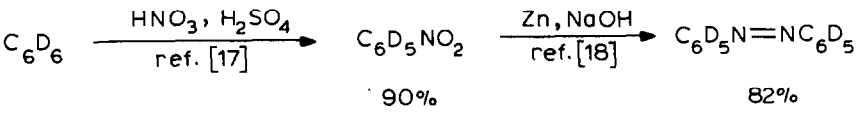
a process such as that of Scheme 5. Here XVI is required for the *N*-alkylation. That no deuterium was observed on the C(2) atom of the propyl group of X is attributed to the statistical distribution of the two types of hydrogen (6/1) which compared with the extent of deuteration of the methyl groups would put any deuteration at the 2-position below the level of detection in the ^{13}C NMR spectrum.

We have no direct evidence for the involvement of ruthenium in the hydrogenolysis of an intermediate such as XII to give *o*-semidine IX, but in view of the well-known ruthenium-catalysed transfer hydrogenations involving 2-propanol [15,16], this may be safely assumed.

The above conclusions regarding the mechanism are based on the probable involvement of ruthenium in oxidation state (II), the demonstration of the occurrence of *ortho*-metallation of the azobenzene derivative in all cases, and the appearence of deuterium on certain carbon atoms which permit conclusions regarding how it got there. The question of whether the complexes occurring in the catalytic cycle are indeed mononuclear remains open, though the involvement of more than one ruthenium centre does not preclude the above mechanistic steps.

Experimental

Chemicals, instruments and techniques were as previously reported [2,3,5]. ^1H NMR spectra at 250 MHz were recorded on a Bruker WM 250 instrument and ^{13}C



Scheme 6

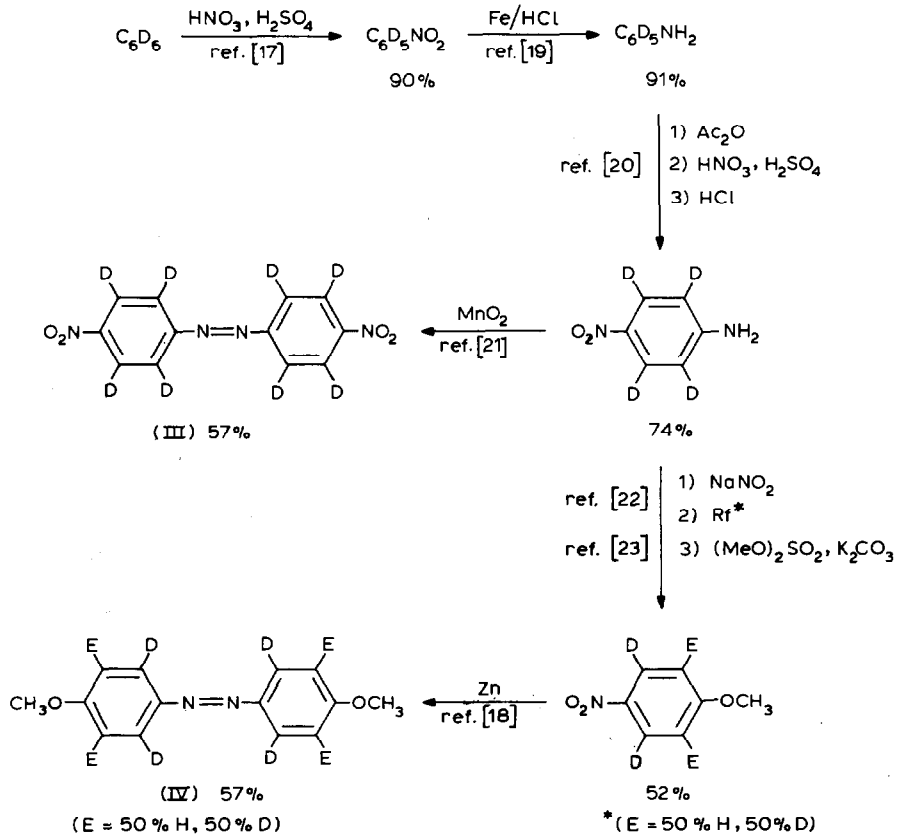
NMR spectra at 25 MHz on a Varian XL-100. Chemical shifts, quoted in ppm, are downfield from TMS in both cases. C_2D_5OD (99 atom% D) was from Fluka.

Deuterated azobenzenes

All deuteroazobenzene derivatives were prepared from benzene-d_6 (Fluka, 99.5 atom% D).

Azobenzene-d_{10} was obtained as shown in Scheme 6 in an overall yield of 74%. Scheme 7 gives details of the preparation of 4,4′-dinitro- and 4,4′-dimethoxy-azobenzene-d_8, which were obtained in overall yields of 35 and 18%, respectively. The yields obtained in the individual stages and the references for the experimental methods are given in these two schemes.

Some of the literature methods for Schemes 6 and 7 are for derivatives other than those used here. In such cases the analogous method was used. In the Béchamp



Scheme 7

reduction [19] water was used instead of methyl alcohol as solvent, with three times the given amount of concentrated HCl and twice the reaction time. Pentadeuteroaniline was acetylated by refluxing with an equimolar amount of acetic anhydride in acetic acid. After nitration, the acetyl group was removed by refluxing with 5 *M* HCl.

Reaction of azobenzene-d_{10} with $(n\text{-}C_4H_9)_3N$

In a reflux apparatus [2] were placed tetramethylurea (12 ml), azobenzene-d_{10} (4.53 g, 23.6 mmol) and tri-n-butylamine (5.62 ml, 23.6 mmol). The mixture was stirred magnetically and carbon monoxide was passed for 5 min. Ruthenium trichloride hydrate (0.0617 g, 0.236 mmol) was added and the mixture was refluxed for 7 h. After removal of the solvents, the residue was distilled in vacuo over a Vigreux column to give I. 1.91 g (33%). Pale yellow liquid. b.p. 149–151°C/0.3 mmHg.

Reaction of azobenzene-d_{10} with $n\text{-}C_4H_9OH$

In a 110 ml glass pressure tube [3] were placed azobenzene-d_{10} (4.80 g, 25 mmol), tetramethylurea (12.5 ml) and n-butanol (6.86 ml, 75 mmol). Carbon monoxide was passed with magnetic stirring for 5 min, and then ruthenium trichloride hydrate (0.0654 g, 0.25 mmol), triphenylphosphine (0.262 g, 1 mmol) and anhydrous sodium acetate (0.615 g, 0.75 mmol) were added. The tube was capped under normal pressure of carbon monoxide and then stirred in an oil-bath at 180°C for 1.5 h. After removal of the solvents, the residue was chromatographed on Kieselgel (100 g) eluting first with dichloromethane and then with diethyl ether. Concentration of the dichloromethane solution gave the recovered deuteroazobenzene (2.78 g) as red crystals. The ether eluate was evaporated and the residue distilled in a Kugelrohr apparatus set at 130°C/0.1 mmHg to give II. Yield 1.38 g (23%). Pale yellow liquid.

The recovered deuteroazobenzene was reduced in methanolic solution with ammonia and hydrogen sulphide [24] to the corresponding hydrazo compound.

Reaction of 1-phenyl-2-(n-propyl)benzimidazole with ethanol-d_6

This reaction was carried out as for the preparation of II above using the benzimidazole derivative and ethanol-d_6 in place of azobenzene-d_{10} and n-butanol.

Reactions of 4,4'-dinitro- and 4,4'-dimethoxy-azobenzene-d_8 with $n\text{-}C_4H_9OH$

These reactions were carried out as for the preparation of II above, the products being seperated by distillation and chromatography on Kieselgel. The recovered dinitrodeuteroazobenzene was reduced to the hydrazo derivative as above [24]. The 4-nitrodeuteroaniline formed was dissolved in dichloromethane and shaken five times with water to remove deuterium from the amino group.

Reaction of azobenzene-d_{10} with $(CH_3)_2CHOH$

In a 110 ml glass pressure tube [3] were placed azobenzene-d_{10} (4.80 g, 25 mmol), anhydrous lithium acetate (1.65 g, 25 mmol), 2-propanol (3.84 ml, 50 mmol) and tetramethylurea (12.5 ml). The mixture was stirred magnetically and carbon monoxide was passed for 5 min. Ruthenium trichloride hydrate (0.065 g, 0.25 mmol) and triphenylphosphine (0.262 g, 1 mmol) were added and the tube was capped under carbon monoxide at normal pressure and stirred in an oil-bath at 180°C for 8 h.

After removal of the solvents the crude product mixture was distilled in vacuo collecting from 120–145°C/0.1 mmHg. The distillate was chromatographed on Kieselgel (100 g) in dichloromethane, X was eluted first and was redistilled in a Kugelrohr apparatus set at 140°C/0.1 mmHg. Yield 0.48 g (8%). Yellow viscous liquid.

IX was eluted second and was recrystallised from a mixture of n-hexane (20 ml) and cyclohexane (20 ml). Yield 1.6 g (35%). White crystals.

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