Metal-assisted Reactions: Part 19.[1] Burst Kinetics in Heterogeneous Catalytic Transfer Hydrogenolysis

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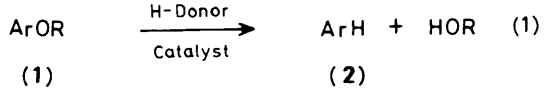
Arene formation by catalytic transfer hydrogenolysis of aryloxytetrazolyl ethers in the liquid-phase shows biphasic concentration-time curves which indicate rate-limiting dissociation of heterogeneous complexes between catalyst and one of the reaction products, a tetrazolone. A dependence of catalytic reaction rate on pH and following modifications made to the catalyst are reported also.

Kinetic studies of heterogeneous, liquid-phase catalytic hydrogen transfer reduction, in which a suitable hydrogen donor (other than molecular hydrogen) transfers its hydrogen to a substrate have been very limited. Kinetic studies of heterogeneous catalytic gas-phase reactions[2] and homogeneous catalytic liquid-phase reactions[3] have been studied extensively and mechanisms are broadly understood. There has been a tendency to regard catalytic transfer hydrogenation as simply a slight extension of catalytic hydrogenation with molecular hydrogen whereby the hydrogen donor serves only to provide an alternative (*in situ*) source of hydrogen for the catalyst. This simplistic approach ignores the complex chemistry associated with binding of donor and substrate to the catalyst surface. Early workers such as Wieland[4] pointed out the remarkable similarities of the donor–catalyst–acceptor model for catalytic transfer reduction to those of an enzyme system, in that adsorption of both the donor and acceptor onto the catalyst are necessary for reduction and may lead to competitive inhibition of the catalyst. This concept has been discussed in a review.[5] Here, we present evidence that the kinetics of heterogeneous catalytic transfer hydrogenolysis, in at least one reaction, show remarkable similarities to the kinetics of complex-mediated reactions[6] or to certain enzyme-catalysed reactions.[7]

Hydrogenolysis of phenolic C–O bonds has been shown to be an effective, rapid means for converting phenols into arenes, a reaction of value in organic synthesis [Equation (1)]. In all these



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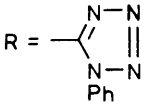

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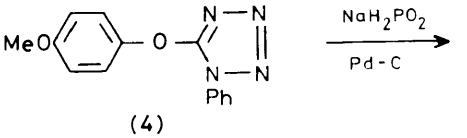

(4) (5) (6) (2)

reactions, the phenol is converted first into an ether in which the group R [Equation (1)] is strongly electron-withdrawing and, for convenience, is often 1-phenyltetrazolyl.[8] With 5-aryloxy-1-phenyltetrazole ethers, it has been shown[8] that phenolic C–O bond hydrogenolysis occurs in *ca.* 10—15 min when using a Pd–C catalyst and a benzene–ethanol–water–sodium phosphinate biphasic system (80 °C). Because of the simplicity of this reaction (very few or no side reactions), the ease of preparation of a wide variety of substituted 5-aryloxy-1-phenyltetrazole ethers (**1**) and the easy detection of the arenes (**2**), formed by hydrogenolysis it was decided to investigate the mechanism of this hydrogenolysis through kinetic studies, especially from the point of view of electronic and steric effects on the rate. The hydrogenolysis of the 1-phenyltetrazolyl ether of 4-methoxyphenol (**4**) [Equation (2)] is typical of a standard reduction; the high regiospecificity of incorporation of hydrogen into the 4-position of the arene product (**5**) has been reported already.[9]

Results and Discussion

Figure 1 shows typical curves relating the variation in yield of anisole and cyanobenzene with time for the competitive hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole and 5-(4-cyanophenoxy)-1-phenyltetrazole. It can be seen that, for each curve, there is an initial rapid formation (burst) of arene followed by an approximately linear formation, the slope of which is the steady-state reaction rate. Extrapolation of this linear portion back to intercept the ordinate axis gives a measure of the initial amount of adsorption of the starting 5-aryloxy-1-phenyltetrazole ether onto the Pd–C catalyst. For various pairs of 5-aryloxy-1-phenyltetrazole ethers, Table 1 gives both observed relative steady-state reaction rates and ratios of extrapolated intercepts. For each experiment the burst in formation of the arene product is readily inferred, because the standard deviation in slope for the subsequent steady-state rate is far greater than the value for its extrapolated intercept. For the 5-aryloxy-1-phenyltetrazole ethers, there is a similar ordering of relative steady-stage reaction rates and extrapolated intercepts. The differences in steady-state rates of hydrogenolysis for a wide range of substituted 5-aryloxy-1-phenyltetrazole ethers are not very great, suggesting that substituents on the aryl ring do not affect the rate-determining step of the reaction electronically to a significant amount. No correlation was observed between the logarithm of the relative rates and Hammett σ, σ^+, or σ^- values. The implications of these observations on the mechanism of the hydrogenolysis of 5-aryloxy-1-phenyltetrazole ethers are two-fold. Firstly, the electron demand at the reaction centre may be very small for the cleavage of the aryloxy

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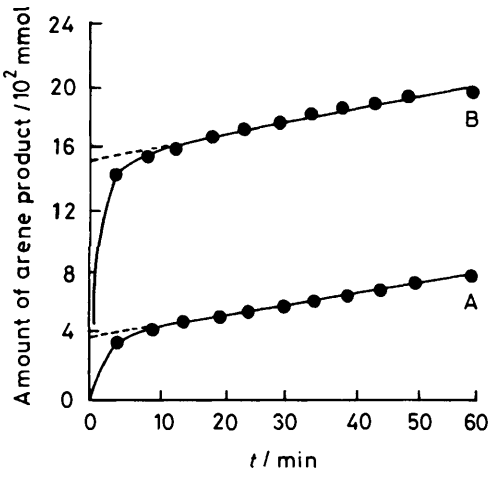


Figure 1. A graph showing respectively the amount of anisole and cyanobenzene formed as a function of time for the competitive reduction of 5-(4-methoxyphenoxy)-1-phenyltetrazole (A) and 5-(4-cyanophenoxy)-1-phenyltetrazole (B). Typical reaction conditions are as described in the Experimental section.

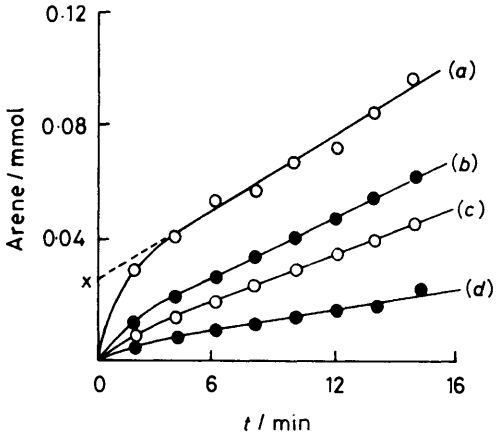


Figure 2. Plots showing the amount of anisole formed with time for increasing initial amounts of 5-(4-methoxyphenoxy)-1-phenyltetrazole. Experiments were carried out at 80 °C using ethanol (3 ml), benzene (11 ml), water (3.0 ml), sodium phosphinate (150 mg), and 10% Pd–C catalyst (30 mg) with initially (*a*) 1.12, (*b*) 0.523, (*c*) 0.224, and (*d*) 0.075 mmol of 5-(4-methoxyphenoxy)-1-phenyltetrazole. Point X represents one of the extrapolated intercepts, its value being 3.5 times the standard deviation of the points on the graph.

Table 1. Relative steady-state rates of cleavage and extrapolated intercepts for the hydrogenolysis of pairs of substituted (XC_6H_4) aryl ethers (**1**) [Equation (1)] at 80 °C

X	Relative steady-state rate[a]	Relative extrapolated intercepts
4-CF_3	0.1	0.2
3-CF_3	0.0(1)	0.1
2-Me	1.2	1.5
3-Me	0.7	1.7
4-Me	0.8	0.9
4-CN	1.2	4.3
3-CN	1.4	5.4
4-NH_2	2.0	10.2
3-NH_2	5.0	9.7
4-COMe	1.4	10.3
4-Bu^t	0.1	0.3
4-Ph	2.4	5.2
4-CO_2Ph	2.7	6.2
3,5-di-Me[b]	0.2	0.2
4-SO_2Me	1.4	14.7
4-OMe	1.0	1.0
3-OMe	0.8	1.5
2,6-di-Me[b]	0.1	0.2
2-Pr^i	0.4	1.0
2,6-di-Pr^i[b]	(c)	(c)

[a] All reactions were carried out under the following typical conditions: the ethers (150 mg) in ethanol (3 ml) and benzene (11 ml) were mixed with sodium phosphinate (200 mg) in water (3.5 ml). To the mixture was added 10% Pd–charcoal catalyst (30 mg; Koch Light; samples were drawn from only one batch for all experiments) and the whole was refluxed. Samples of the reaction mixture were quenched by cooling to room temperature and analysed for arenes by g.c. on an OV 351 capillary column (25 m). Results of separate experiments show that these rate measurements are reproducible to *ca.* ±6%. [b] These are disubstituted aryls, $X_2C_6H_3$. [c] This reaction is so slow that significant rate measurements within 36 h were not obtainable.

Table 2. Estimated (h.p.l.c.) relative adsorptions onto Pd–C catalyst (10% m/m) for pairs of aryl (XC_6H_4) substituted tetrazolyl ethers (**1**) [Equation (1)] at room temperature in benzene

X	Relative adsorption[a]
4-NH_2	2.8
4-CN	2.8
4-COMe	2.0
4-Ph	1.4
3-CN	1.1
4-OMe	1.0
4-Bu^t	0.6
3-CF_3	0.6
3,5-di-Me[b]	0.9
2,6-di-isopropyl[b]	0.2

[a] Experimental conditions are described in the Experimental section. Values for the relative adsorption onto catalyst are an average from experiments with varying quantities of catalyst. [b] These are disubstituted aryls, $X_2C_6H_3$.

C–O bond. If the rate determining step for this reaction were to involve the oxidative addition of the aryloxy C–O bond across a palladium atom, this process would require homolytic cleavage of the aryloxy C–O bond and changing the electronic substituents in the 5-aryloxy ring would not greatly affect the rate determining step. Secondly, changing the electronic substituents in the 5-aryloxy ring may not affect the rate of the reaction simply because they do not have a direct bearing on the rate determining step of the reaction. Other work, carried out in this laboratory,[10] has revealed that catalytic transfer hydrogenolysis of the C–Cl bond in aryl chlorides also exhibits both burst kinetics and a lack of electronic effect of substituents on the rate-controlling step. These results are similar to those observed in the catalytic hydrogenolysis of 2,4,6-tris(aryloxy)-*s*-triazines with molecular hydrogen where the rate was not influenced by the electronic character of substituents in the aryl rings.[11]

Table 2 gives estimated relative adsorptions (from h.p.l.c.) of pairs of 5-aryloxy-1-phenyltetrazole ethers onto the Pd–C catalyst. A comparison of Table 2 with Table 1 indicates a similar trend in measured relative adsorption to relative extrapolated intercept for pairs of ethers. There is not a great difference in relative adsorption onto the catalyst for a wide range of substituted 5-aryloxy-1-phenyltetrazole ethers. This correlation supports the argument that the ratios of extrapolated intercepts represent a measure of the relative initial adsorption of the ethers onto the catalyst.

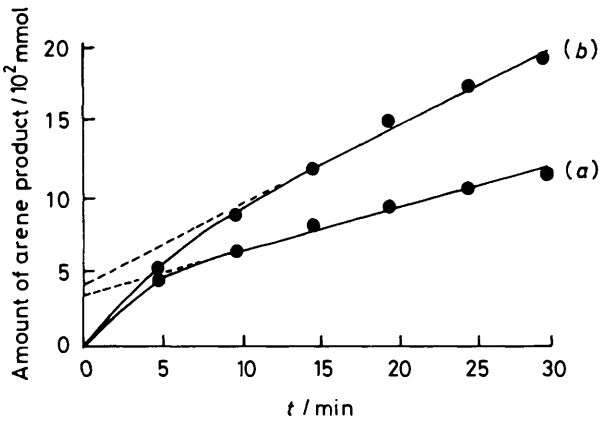


Figure 3. Graph of formation of anisole versus time for the hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole (*a*) with an equimolar amount of 5-hydroxy-1-phenyltetrazole added, and (*b*) without 5-hydroxy-1-phenyltetrazole added.

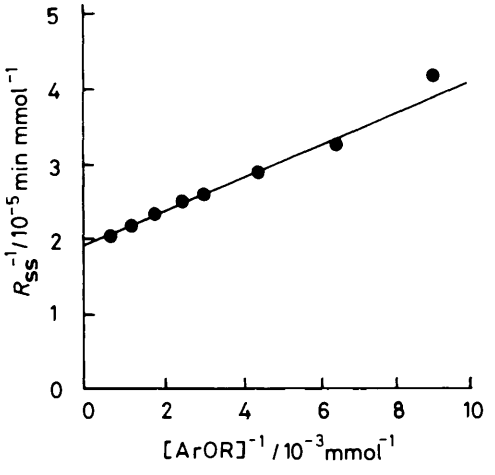
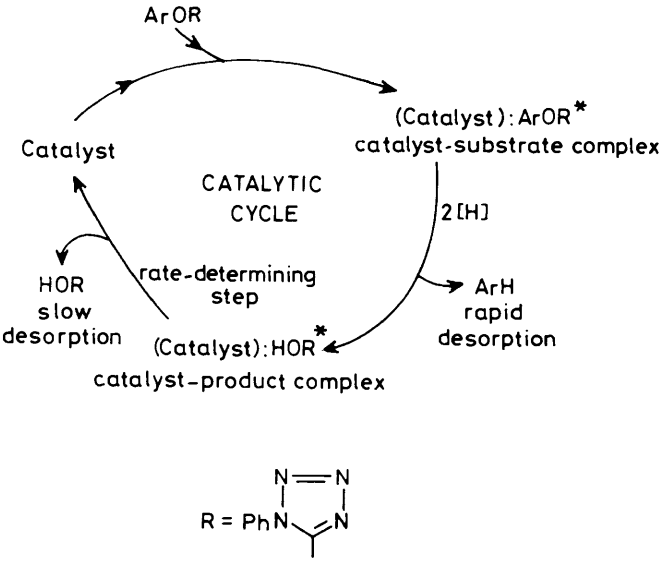


Figure 4. Graph of reciprocal steady-state reaction rate (R_{ss}^{-1}) of formation of anisole versus the reciprocal of the initial concentration of aryl ether ([ArOR]$^{-1}$) for the reduction of 5-(4-methoxyphenoxy)-1-phenyltetrazole.

Figure 2 shows typical arene concentration *versus* time curves for the hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole for a series of experiments in which all reaction conditions are identical except for the initial amount of tetrazolyl ether; the initial burst of arene is due to its rapid formation on and desorption from the catalyst. The first, rapid formation of arene is not maintained because the other product of hydrogenolysis 5-hydroxy-1-phenyltetrazole [1-phenyltetrazolone; (**6**); Equation (2)] does not desorb so readily as the arene itself. The subsequent steady-state formation of arene is largely governed by the rate of desorption of 5-hydroxy-1-phenyltetrazole. Consequently, electronic changes resulting from changes in the substituents in the aryloxy ring of the ether (**1**), [Equation (1)] would not be expected to produce a marked variation in the overall rate of hydrogenolysis. Figure 3 shows the arene concentration *versus* time curves for the hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole with and without the addition of an equimolar amount of 5-hydroxy-1-phenyltetrazole at the start of the reaction. The graphs show a decrease in the steady-state reaction rate (by a factor of *ca.* 0.5) on addition of 5-hydroxy-1-phenyltetrazole without significant decrease in the initial burst of arene product (measured from the extrapolated intercepts on the ordinate axis), in keeping with the suggested self-inhibition of reaction rate by one of the products of reaction, 5-hydroxy-1-phenyltetrazole. The small decrease in the initial burst of arene on addition of 5-hydroxy-1-phenyltetrazole again indicates some competitive binding of this reaction product compared with the starting ethers. Estimation (h.p.l.c.) of the adsorption of 5-hydroxy-1-phenyltetrazole onto the Pd–C catalyst from benzene (at room temperature) showed that it competed effectively with the reactant 5-aryloxy-1-phenyltetrazole ethers for sites on the catalyst surface. For example, in the absence of 5-hydroxy-1-phenyltetrazole, 5-(4-methoxyphenoxy)-1-phenyltetrazole was adsorbed onto Pd–C to the extent of 7.4 μmol/100 mg catalyst; in the presence of an equimolar quantity of 5-hydroxy-1-phenyltetrazole the adsorption fell to 4.0 μmol/100 mg catalyst. Figure 4 shows a plot of the reciprocal of the steady-state reaction rate for the formation of anisole with the reciprocal of the initial amount of 5-(4-methoxyphenoxy)-1-phenyltetrazole used. The linear correlation observed is analogous to 'Lineweaver–Burk' plots for enzyme-catalysed reactions in which the initial substrate concentraton is varied.[6,12,13] For enzymes, this pattern of kinetic behaviour is explained by extending the simple Michaelis–Menten theory[14] of enzyme kinetics to include, as well as an enzyme–substrate complex, an enzyme–product complex, the slow decomposition of which governs the overall rate of reaction. By analogy, the presence of a similar catalyst–product complex in the hydrogenolysis [Equation (1)] would explain the observed small difference in reaction rates for a wide range of substituted 5-aryloxy-1-phenyltetrazole ethers. The rate-determining step in the steady-state phase of the reaction would be the dissociation of an intermediate complex [(Cat):HOR; Scheme 1][9] formed between the catalyst and one of the products of hydrogenolysis (HOR), after decomposition of the initially-formed complex [(cat):ArOR*]; the catalytic cycle is maintained as shown in Scheme 1.



Scheme 1.

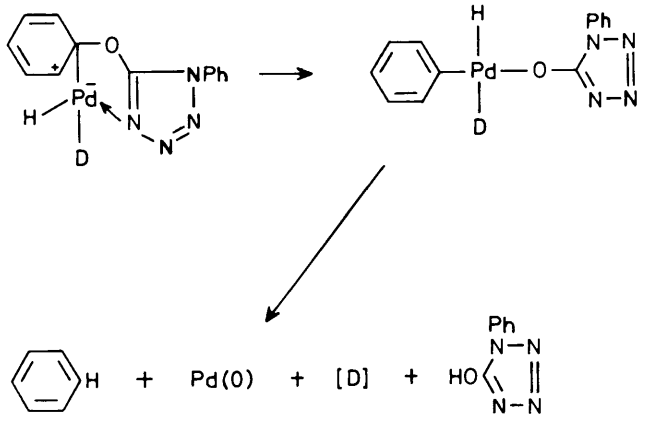
Table 3 gives both relative steady-state reaction rates and ratios of extrapolated intercepts for 5-(4-methoxyphenoxy)-1-aryltetrazolyl ethers in which either, substituents are varied in the aryl ring attached to the tetrazole nucleus or, the nature of the actual heteroaromatic ring itself is changed. It is clear from Table 3 that, of all the groups R, there is not a great difference in steady-state reaction rate or relative initial adsorption onto the

Table 3. Relative steady-state rates of cleavage and relative extrapolated intercepts for substituted aryl ethers 4-$MeOC_6H_4O$-C=N-N=N-NR, and in the last column 4-$MeOC_6H_4O$C=N-C(Ph)=C(Ph)-N=N

R	Ph	Me	$C_6H_4CF_3$-*m*	$C_6H_4NH_2$-*p*	$C_6H_4NO_2$-*p*	3-(4-methoxyphenoxy)-5,6-diphenyl-1,2,4-triazine
Relative steady-state rate of cleavage	1.0	0.8	0.9	0.5	0.3	0.4
Relative extrapolated intercept	1.0	0.6	0.9	0.7	0.4	0.1

[a] All reactions were carried out under the following typical conditions: the aryl ethers (0.42 mmol) in a mixture of ethanol (3 ml) and benzene (11 ml) were treated with sodium phosphinate (150 mg) in water (3 ml). To the mixture was added Pd–C catalyst (10% m/m; 30 mg) and the whole was refluxed (80 °C). Samples of the reaction mixture were quenched by cooling them rapidly to room temperature and were analysed for anisole by g.c. on an OV 351 capillary column (25 m).

catalyst, although, of those heteroaromatic groups investigated, 1-phenyltetrazolyl group effects the most rapid hydrogenolysis. It should be noted that other similar heteroaromatic groups have been investigated[8] for this hydrogenolysis and have been shown to be ineffective. These observations suggest that substituents with different electronic properties in the aryl ring on the tetrazolyl nucleus do not affect the rate determining step of the reaction significantly but the nature of the heteroaromatic ring system does have a significant effect. A possible explanation for all of these observations has been reported already[8] and is outlined in Scheme 2 in which reaction proceeds after com-



Scheme 2.

plexation to a Pd^{II} species. The complex is promoted through coordination to a nitrogen atom in the tetrazolyl nucleus. Support for Scheme 2 has been adduced from hydrogen isotope studies.[9] Here, it is suggested that initial adsorption of the aryl ether and hydrogen donor (HD) onto the catalyst is followed by rapid oxidative addition of the aryloxy C–O bond onto a palladium atom. Such oxidative addition would involve homolytic cleavage of the aryloxy C–O bond and hence there would be little electron demand at the reaction centre. Changes of substituents would have a minimal effect on this homolytic cleavage, and therefore on the rate of reduction. Rapid reductive elimination gives the arene product and a catalyst–5-hydroxy-1-phenyltetrazole complex, the slow dissociation of which is the rate-controlling step of the cycle.

Figure 5 shows that a plot of reciprocal steady-state reaction rate for hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole correlates linearly with the reciprocal of the initial concentration of sodium phosphinate hydrogen donor. This observation implies complex formation of the catalyst with the donor for the transfer reduction. Figure 6 shows arene concentration *versus* time curves for the hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole with different initial amounts of Pd–C catalyst. The steady-state reaction rate appears to corre-

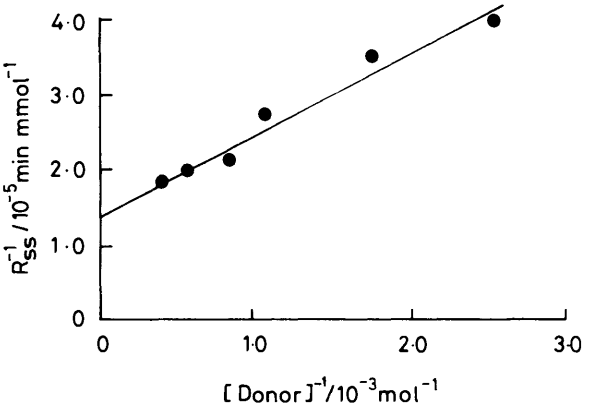


Figure 5. Graph of reciprocal steady-state reaction rate (R_{ss}^{-1}) of formation of anisole *versus* the reciprocal of the initial concentration of sodium phosphinate hydrogen donor ([Donor]$^{-1}$) for reduction of 5-(4-methoxyphenoxy)-1-phenyltetrazole.

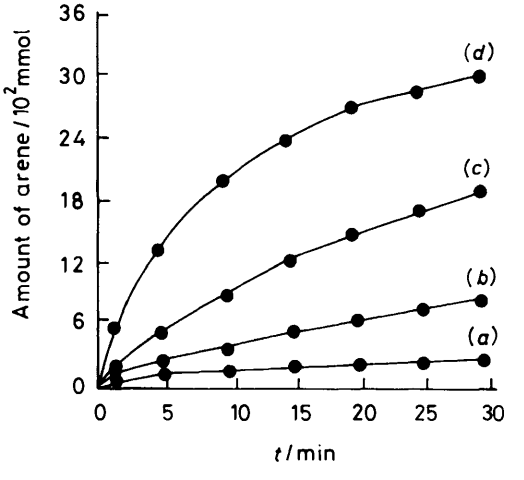


Figure 6. Graph of amount of anisole formed *versus* time, for the reduction of 5-(4-methoxyphenoxy)-1-phenyltetrazole with (*a*) 10 mg, (*b*) 25 mg, (*c*) 50 mg, and (*d*) 100 mg of Pd–C catalyst (10% m/m).

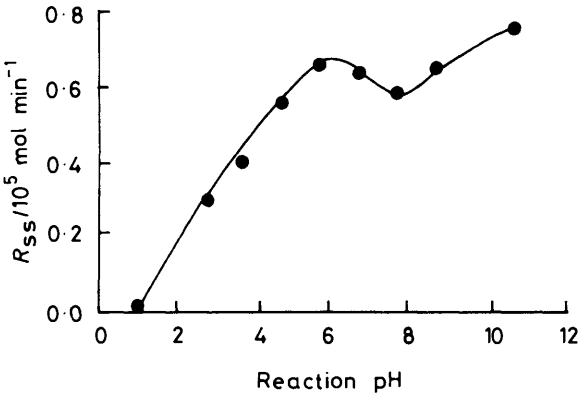


Figure 7. Plot of steady-state reaction rate (R_{ss}) for formation of anisole *versus* pH of the aqueous reaction mixture for the hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole. The pH is based on the value for standard sodium phosphinate solution with a calculated amount of sodium hydroxide or sulphuric acid added.

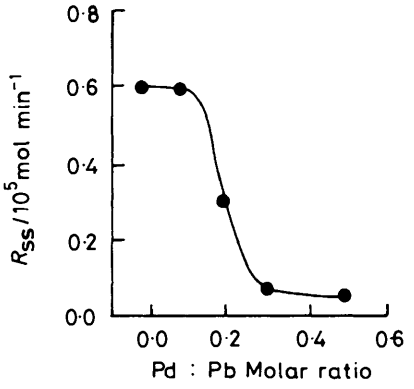


Figure 8. Plot of steady-state reaction rate (R_{ss}) for the formation of anisole *versus* molar ratio of palladium:lead 1:X, X = 0.05, 0.1, 0.2, 0.3, and 0.5, for 10% m/m supported Pd catalyst for the reduction of 5-(4-methoxyphenoxy)-1-phenyltetrazole.

late linearly with the amount of catalyst for small catalyst:aryl ether ratios, but this relationship appears to break down at large catalyst:aryl ether ratios.

The heterogeneous catalytic transfer hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole exhibited a pH dependence.[6,15] Figure 7 shows a plot of steady-state reaction rate of formation of anisole from 5-(4-methoxyphenoxy)-1-phenyltetrazole versus pH of the reaction mixture (pH here is taken to be that of a standard solution of aqueous hydrogen donor, adjusted with calculated amounts of either sodium hydroxide solution or sulphuric acid). Figure 7 indicates that, at low pH, the reaction rate is severely inhibited. The steady-state rate of hydrogenolysis increases with increasing pH up to a first maximum (*ca.* pH 6), and then the rate of reduction begins to fall. However, at a pH value of *ca.* 8, the reaction rate increases again, until at pH 11 the steady-state reaction rate has surpassed the first maximum. This sort of kinetic behaviour must be a result of competing processes, some of which cause the reaction rate to increase with increase in pH and others causing it to decrease with increasing pH; the intersection of such trends gives maximum and minimum reaction rates. Protonation of tetrazole ring nitrogens[16] as well as their co-ordination to transition metal atoms[16] is well documented. Indeed, previous mechanisms for this heterogeneous catalytic transfer hydrogenolysis reaction[8] have indicated the probability of co-ordination of the tetrazole ring nitrogens to a palladium species during the catalytic cycle. The severe inhibition of reaction rate at low pH values can be ascribed to the prevention of adsorption and/or co-ordination of the aryl ether to the palladium catalyst by protonation of nitrogen lone-pair electrons in the tetrazole ring. The effect on reaction rate at high pH values can be two-fold. Firstly, a basic reaction medium can cause the 5-hydroxy-1-phenyltetrazole product of reaction (this compound has a pK_a value similar to that of benzoic acid[17]) to be withheld from the catalyst by virtue of its being an anion, and so causing a higher turnover of free catalytic sites. Secondly, the effect of withholding 5-hydroxy-1-phenyltetrazole from the catalyst could be counteracted by the occupation of catalyst sites by the base itself; a similar effect has been observed for the hydrogenolysis of 2,4,6-tris(aryloxy)-*s*-triazines using Pd–C catalyst and gaseous molecular hydrogen.[11] A third effect of the pH on the rate of hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole may be on the reduction potential of the sodium phosphinate donor. The redox equation for phosphinate in aqueous medium is shown in Equation 3. This equilibrium,

$$H_2PO_2^- + H_2O \rightleftharpoons H_2PO_3^- + 2H^+ + 2e^- \quad (3)$$

which has a calculated redox potential[18] of +0.504 V, will be shifted to the left in an acidic medium (reducing the overall potential) and to the right on addition of hydroxide ion (increasing the overall potential). On this basis, it would be expected that the rate of reduction might correlate with the reducing power of the hydrogen donor at different pH values.

That complexation of substrate to catalyst is directly rate controlling was shown by the effect of changing the substituent at the 2-position in the aryl ring (*ortho* to the C–O bond being hydrogenolysed). As shown in Table 1, for 5-(2-, 3-, and 4-methylphenoxy)-1-phenyltetrazoles, the relative steady-state rates of hydrogenolysis were very similar, as were the extrapolated intercepts. However, with an isopropyl group in the 2-position, the steady-state rate fell but the intercept remained similar to that for the other compounds. With methyl groups occupying the 2,6-positions (both *ortho* positions occupied), both the steady-state rate and the extrapolated intercept fell markedly. With isopropyl groups occupying the 2,6-positions, reaction became so slow that almost no C–O bond hydrogenolysis occurred over a 36 h period. This steric inhibition of reaction rate is shown also by methyl substituents in the 3,5-positions; although not adjacent to the reaction site and not expected to greatly influence reaction rate (methyls *meta* to the reaction site), the two methyl groups caused a marked drop in both steady-state rate and in the extrapolated intercept. Thus, for one methyl group in the 2-, 3-, or 4-position there is little variation in the reaction rate but, with two methyl groups in the 2,6- or 3,5-positions, there is a marked drop in rate. This effect suggests that complexation to the catalyst is still satisfactory with only one substituent on one side of the aryl ring but, with both sides of the ring occupied, complexation is inhibited and, therefore, that the complex is one in which the aryl ring is held at an angle to the catalyst surface rather than being planar with it.

Finally, the effect on the rate of hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole over modified Pd–C catalyst was studied. The modified catalysts were prepared by precipitating a known quantity of lead onto commercially available Pd–C catalyst by use of sodium borohydride.[19] Figure 8 shows the variation of steady-state reaction rate for the heterogeneous catalytic transfer hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole using modified Pd–C catalyst (10% m/m) with X, the molar ratio of Pb:Pd. It is clear from Figure 8 that doping the catalyst with lead to a Pd:Pb molar ratio of 1:0.1 has little effect on the steady-state rate of hydrogenolysis but, with a Pd:Pb molar ratio of 1:0.2, the rate

of hydrogenolysis falls by a factor of 0.5, and by a factor of *ca.* 0.08 for a Pd:Pb molar ratio of 1:0.3 or greater. The doping of the Pd–C catalyst with lead statistically reduces the number of contiguous surface Pd atoms and so, may reduce the number of active sites below a minimum level required for catalytic activity. However, addition of lead may change the electronic band structure of the palladium catalyst.[19]

The dramatic change in catalytic activity at a well-defined level of incorporation of lead indicates that the number of active sites has been affected directly and that the reaction is structure-sensitive,[20,21] requiring multi-atom sites for catalysis. This sensitivity to catalyst structure may be a consequence of a requirement for more than one atom in the catalyst binding site for the phenolic tetrazole ether and/or the necessity for contiguous sites for hydrogen transfer from hydrogen donor to hydrogen acceptor.

Conclusions

In summary, kinetic evidence for the hydrogenolysis of 5-aryloxy-1-aryltetrazole ethers has revealed for the first time for heterogeneous, liquid-phase, catalytic transfer reduction, a mechanism whereby after an initial burst of one product, a steady-state rate is achieved, controlled by the rate of release of catalyst sites as the other product desorbs slowly from the catalyst surface. The evidence suggests strongly that the initial complexation of the phenolic tetrazole ethers to the catalyst surface is effected largely through the tetrazolyl part of the molecule but that steric effects in the aryl ring can be important also. Recent work conducted at this laboratory[22] has involved the preparation of a complex between $PdCl_2$ and 5-phenoxy-1-phenyltetrazole the structure of which was determined by *X*-ray crystallography; the Pd atom was shown to be co-ordinated to nitrogen in the tetrazole nucleus.

The work presented here shows also that the rate of catalytic transfer hydrogenolysis of 5-(4-methoxyphenoxy)-1-phenyltetrazole is dependent on the pH of the system and on the degree of doping of the catalyst with Pb. For mechanisms proposed in this paper, no attempt has been made to develop a detailed kinetic model on the basis of rate constants. No conclusive information has been revealed on the exact nature of binding of the tetrazole ring to the catalyst or on quantitative distributions of catalytic active sites. For example, it is not clear how many Pd atoms comprise an active site.

Experimental

Compounds were identified by three or more of the following: m.p., mass, i.r., and ^1H n.m.r. spectroscopy, and elemental analysis. For known compounds only selected spectroscopic data are quoted, sufficient to verify identification. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Mass spectra were recorded on an AEI MS 12 mass spectrometer or a VG 11/250 mass spectrometer, operating at 70 eV. Infra red spectra were recorded on either a Perkin Elmer or a Pye Unicam SP 200 spectrophotometer, liquids as films and solids as Nujol mulls. ^1H N.m.r. spectra were recorded on a Perkin Elmer R34 (220 MHz) or a Bruker (250 MHz) instrument. Unless otherwise stated, the solvent was $CDCl_3$, with tetramethylsilane as the internal standard. G.l.c. analyses were obtained with a DANI 3800 gas chromatograph instrument equipped with a flame ionisation detector.

Capillary columns with the stationary-phase coated on the internal wall were used with nitrogen as carrier gas. An Autolab Vidar 6300 digital integrator was employed to estimate peak areas. Product yields were calculated by reference to an internal standard after precalibration. High performance liquid chromatographic analyses were carried out on a Spectra-Physics SP 8440 instrument. Tubular stainless steel columns were used with a reversed-phase (C_{18}) packing and methanol–water as the eluant. Metal catalysts were obtained from commercial sources (Koch–Light) and, unless otherwise stated, received no pre-treatment.

Preparation of 5-Aryloxy-1-phenyltetrazole Ethers.—The following example is typical.

5-(4-*Methoxyphenoxy*)-1-*phenyltetrazole.* To a solution of 4-methoxyphenol (1.37 g, 11.07 mmol) in dry dimethylformamide (25 ml) was added potassium t-butoxide (1.25 g, 11.14 mmol) with stirring. When all the base had dissolved (approximately 15 min), 5-chloro-1-phenyltetrazole (2.0 g, 11.07 mmol) was added. The mixture was stirred at room temperature for a further 1 h and then poured into a large excess of ice–water. The solid formed was collected by filtration and dried in air at room temperature. Purification by recrystallisation (from aqueous ethanol) gave the required product (2.57 g, 87%) as white plates, m.p. 79—80 °C (Found: C, 62.3; H, 4.5; N, 20.6. $C_{14}H_{12}N_4O_2$ requires C, 62.7; H, 4.5; N, 20.9%); $\nu_{max.}$ 1 590, 1 545, 1 500, 1 450, 1 250, 835, and 760 cm^{-1}; δ_H 3.76 (3 H, s, OMe), 6.89 (2 H, d, *J* 8.9 Hz, ArH), 7.35 (2 H, d, *J* 8.9 Hz, ArH), 7.4—7.6 (3 H, m, ArH), and 7.7—7.8 (2 H, m, ArH); *m/z* 268 ($M^{+\cdot}$).

Similarly prepared were the following compounds, all of which gave satisfactory elemental analyses, i.r. and ^1H n.m.r. data and mass spectra (with a well-characterised molecular ion, $M^{+\cdot}$).

5-*Aryloxy*-1-*aryltetrazoles*, $YC_6H_4{\cdot}N_4C{\cdot}OC_6H_3X$. (*a*) Y = H, X = H: m.p. 132—133 °C (from aqueous ethanol) (lit.,[23] 132—133 °C); (*b*) Y = H, X = 4-CF_3: m.p. 70—71 °C (aqueous ethanol); (*c*) Y = H, X = 4-NH_2, 172—174 °C (ethanol); (*d*) Y = H, X = 3-CN: m.p. 125—127 °C (aqueous ethanol); (*e*) Y = H, X = 4-CN: m.p. 124—125 °C (aqueous ethanol); (*f*) Y = H, X = 3-Me: m.p. 66—68 °C (aqueous ethanol); (*g*) Y = H, X = 3,5-dimethyl: m.p. 104—106 °C (aqueous ethanol); (*h*) Y = H, X = 4-Bu^t: m.p. 112—114 °C (ethanol); (*i*) Y = H, X = 4-Ph: m.p. 150—152 °C (ethanol); (*j*) Y = H, X = 3-CF_3: m.p. 49—51 °C (ethanol); (*k*) Y = H, X = 4-MeCO, m.p. 98—101 °C (aqueous ethanol); (*l*) Y = H, X = 2-Pr^i: 86—87 °C (aqueous ethanol); (*m*) Y = H, X = 2,6-dimethyl: 126—128 °C (aqueous ethanol); (*n*) Y = H, X = 3-NH_2: m.p. 118—121 °C (ethanol); (*o*) Y = H, X = 3-OMe, m.p. 72—74 °C (ethanol); (*p*) Y = H, X = 2-Me, m.p. 88—89 °C (aqueous ethanol); (*q*) Y = H, X = 2,6-di-isopropyl: m.p. 132—133 °C (ethanol); (*r*) Y = H, X = 4-Me, 91—92 °C (ethanol) (lit.,[23] 91—92 °C); (*s*) Y = H, X = 4-SMe: m.p. 83—85 °C (ethanol); (*t*) Y = 4-NO_2, X = 4-OMe: m.p. 161—164 °C (ethanol); (*u*) Y = 4-NH_2, X = 4-OMe: m.p. 135—138 °C [ethyl acetate–light petroleum (b.p. 60—80 °C)]; (*v*) Y = 3-CF_3, X = 4-OMe: m.p. 90—93 °C [ethyl acetate–light petroleum (b.p. 60—80 °C)]; (*w*) 5-(4-methoxyphenoxy)-1-methyltetrazole: m.p. 132—134 °C [ethyl acetate–light petroleum (b.p. 60—80 °C)]; (*x*) 3-(4-methoxyphenoxy)-5,6-diphenyl-1,2,4-triazine: m.p. 139—142 °C [ethyl acetate–light petroleum (b.p. 60—80 °C)]. 5-(4-Phenoxycarbonylphenoxy)-1-phenyltetrazole was provided.[8]

5-(4-*Methylsulphonylphenoxy*)-1-*phenyltetrazole.*—A solution of *m*-chloroperbenzoic acid (1.58 g, 7.2 mmol) in dichloromethane (30 ml) was added dropwise, with ice-cooling, to a solution of 5-(4-methylthiophenoxy)-1-phenyltetrazole (1.0 g, 3.5 mmol) in dichloromethane (10 ml). The reaction was then allowed to stir at room temperature overnight. The resulting white precipitate (*m*-chlorobenzoic acid) was filtered off and washed with dichloromethane. The dichloromethane washings and filtrate were combined and washed with aqueous potassium carbonate, and then dried ($MgSO_4$). The solvent was removed

under reduced pressure to give a colourless oil that solidified on standing. Recrystallisation from ethyl acetate–light petroleum (b.p. 60—80 °C) yielded the required compound (1.69 g, 96%) as white needles, m.p. 110—113 °C (Found: C, 53.3; H, 4.0; N, 17.8. $C_{14}H_{12}N_4O_3S$ requires C, 53.2; H, 3.8; N, 17.7%); $\nu_{max.}$ 1 590, 1 533, 1 490, 1 310 (>SO_2), 1 296, 1 146 (>SO_2), and 760 cm^{-1}; δ_H 3.08 (3 H, s, Me), 7.55—7.85 (5 H, m, ArH), 8.05—8.10 (2 H, d, *J* 8.95 Hz, ArH), and 7.7 (2 H, d, *J* 8.95 Hz, ArH); *m/z* 316 ($M^{+\cdot}$).

5-*Hydroxy*-1-*phenyltetrazole*.—5-Chloro-1-phenyltetrazole (1.0 g, 5.54 mmol) was added to a mixture (3:1 v/v; 20 ml) of 2M aqueous sodium hydroxide and ethanol and warmed to 70 °C with stirring for 1 h, when all the starting material had disappeared (t.l.c.). The resulting clear solution was cooled and made just acidic by the slow, dropwise addition of concentrated hydrochloric acid, to afford a thick white precipitate which was filtered off, washed thoroughly with water and dried in air at room temperature. The crude product was recrystallised from benzene to give white crystals (0.7 g, 80%), m.p. 185—187 °C (lit.,[24] 187—188 °C); $\nu_{max.}$ 2 550—3 300br (OH), 1 714 (C=O), 1 600, 1 500, 1 466, 1 363, and 754 cm^{-1}. (5-Hydroxy-1-phenyltetrazole exists as a tautomeric mixture with 1-phenyltetrazolone[17]).

5-*Chloro*-1-(4-*nitrophenyl*)*tetrazole*.—5-Chloro-1-phenyl-1*H*-tetrazole (10.0 g, 56 mmol) was added to fuming nitric acid (s.g. 1.42; 30 ml) in a 500 ml flask. The reaction was heated at 100 °C for 5 min and then poured onto a large excess of ice. After allowing it to stand for 2 h, the thick yellow precipitate was filtered off, washed with water, and dried in air at room temperature. Recrystallisation from ethanol gave the desired heterocycle (11.7 g, 94%) as yellow plates, m.p. 93—96 °C (lit.,[15] 98—99 °C); $\nu_{max.}$ 1 640 (NO_2), 1 592, 1 520, 1 493, 1 350, 1 243, and 760 cm^{-1}; δ_H 8.53 (2 H, d, *J* 9.0 Hz, ArH), 7.94 (2 H, d, *J* 9.0 Hz, ArH); *m/z* 225/227 ($M^{+\cdot}$).

1-(4-*Aminophenyl*)-5-*chlorotetrazole*.—A solution of 5-chloro-1-(4-nitrophenyl)tetrazole (2.0 g, 8.9 mmol) in ethanol (300 ml) containing hydrochloric acid (9M; 2 ml) and platinum oxide catalyst (0.6 g) was hydrogenated in a sealed bomb at 2.8×10^3 kg m^2 hydrogen pressure for 2 h. The catalyst was filtered and the ethanol evaporated. The residue was dissolved in water and brought to pH 9 with aqueous 2M-sodium hydroxide to give a thick white precipitate which was filtered off, washed with water, and dried in air at room temperature. Purification by recrystallisation from ethyl acetate–light petroleum (b.p. 60—80 °C) yielded the required compound (0.85 g, 52%) as pale plates, m.p. 142—144 °C, $\nu_{max.}$ 3 485 (NH_2), 3 370 (NH_2), 3 300 (NH_2), 1 628 (NH_2), 1 540, 1 512, 1 430, 1 241, and 832 cm^{-1}; δ_H[$(CD_3)_2SO$] 5.16 (2 H, br s, exchanges in D_2O, NH_2), 6.80 (2 H, d, *J* 8.9 Hz, ArH), and 7.2 (2 H, d, *J* 8.9 Hz, ArH); *m/z* 195/197 ($M^{+\cdot}$).

5,6-*Diphenyl*-3-*hydroxy*-1,2,4-*triazine*.[25]—A solution of semicarbazide hydrochloride (14.0 g, 0.125 mol) in distilled water (20 ml) was added to benzil (21.0 g, 0.1 mol) in acetic acid (190 ml). The mixture was heated under reflux for 3 h when the dark yellow solution was poured into distilled water (400 ml). The creamy-coloured solid that precipitated was collected by filtration, washed with water, and dried in air at room temperature. Purification by recrystallisation from ethanol gave the required compound (21.2 g, 85%, m.p. 225—226 °C (lit.,[25] 224—226 °C); $\nu_{max.}$ 3 230 (OH), 3 090 (OH), 1 705 (C=O), 1 670 (C=O), 1 220, 1 065, 770, and 700 cm^{-1}; δ_H[$(CD_3)_2SO$] (this compound exists as a tautomeric mixture) 7.10—7.64 (10 H, m, ArH), 8.63 (0.5 H, s, exchanges in D_2O), and 10.93 (0.5 H, s, exchanges in D_2O); *m/z* 249 ($M^{+\cdot}$).

3-*Chloro*-5,6-*diphenyl*-1,2,4-*triazine*.—Freshly distilled *N*,*N*-dimethylaniline (10 ml) was added dropwise with stirring, to freshly distilled phosphorus oxychloride (50 ml, 0.55 mol) at 0 °C. To the resulting solution was added finely ground 5,6-diphenyl-3-hydroxy-1,2,4-triazine (10.0 g, 40.2 mmol) and the mixture was heated under reflux for 3 h. After having been cooled, the reaction mixture was poured onto a large excess of ice. The resulting brown oil gradually solidified to give a yellow solid which was collected by filtration and washed with water. To prevent viscous oils forming during recrystallisation the crude product was scrupulously dried over phosphorus pentaoxide. The finely ground crude product was purified by recrystallisation from benzene–light petroleum (b.p. 60—80 °C) to yield 3-chloro-5,6-diphenyl-1,2,4-triazine (7.1 g, 66%), m.p. 155—156 °C (lit.,[26] 157—157.5 °C), $\nu_{max.}$ 1 330, 1 180, 715, and 695 cm^{-1}; δ_H[$(CD_3)_2CO$] 7.30—7.65 (10 H, m, ArH); *m/z* 267/269 ($M^{+\cdot}$).

3-*Trifluoromethylformanilide*.—A solution of 3-trifluoromethylaniline (50.0 g, 0.31 mol) and formic acid (100%; 15 ml; 0.4 mol) in benzene (150 ml) was heated under reflux for 2.5 h. The excess of water and formic acid was azeotroped away using a Dean–Stark apparatus. The benzene was removed under reduced pressure to yield a colourless liquid that slowly solidified, (58.0 g, 98%), m.p. 46—48 °C, $\nu_{max.}$ 3 260 (CONH), 2 950 (CONH), 1 675 (CONH), 1 540, 1 150, 1 068, and 738 cm^{-1}; δ_H 7.2—8.9 (4 H, m, ArH), 8.49 (0.6 H, d, CHO), 8.75 (0.4 H, d, CHO), 8.96 (0.6 H, br s, exchanges in D_2O, CONH), and 9.46 (0.4 H, br d, exchanges in D_2O, CONH) (the ^1H n.m.r. spectrum indicates that 3-trifluoromethylformanilide exists as a mixture of rotamers); *m/z* 189 ($M^{+\cdot}$).

Dichloro-N-(3-*Trifluoromethylphenyl*)*azomethine*.—3-Tri fluoromethylformanilide (25.0 g, 0.13 mol) was melted and, over a period of 30 min, was added in portions to a solution of sulphuryl chloride (20.0 g, 0.15 mol) in thionyl chloride (50 ml). The reaction was stirred at room temperature for 1 h and then at 30 °C for 1 h; and for a further 1 h at 50 °C. The thionyl chloride was removed under reduced pressure and the residual oil was fractionally distilled to give a colourless liquid (22.0 g, 70%), b.p. 42 °C/0.1 mmHg, $\nu_{max.}$ 1 657, 1 326, 1 125, and 905 cm^{-1}; δ_H 7.05—7.55 (4 H, m, ArH); *m/z* 241/243/245 ($M^{+\cdot}$).

5-*Chloro*-1-(3-*trifluoromethylphenyl*)*tetrazole*.—Dichloro-*N*-(3-Trifluoromethylphenyl)-azomethine (10.0 g, 40.8 mmol) and activated sodium azide[17] (2.65 g, 40.8 mmol) were stirred together in dimethoxyethane (50 ml) at room temperature overnight. The resultant cloudy suspension was poured into a large excess of ice–water and the solid was collected by filtration and dried in air at room temperature. Purification by recrystallisation from ethyl acetate–light petroleum (b.p. 60—80 °C) gave the required product (8.5 g, 83% yield) as white crystals, m.p. 42—44 °C, $\nu_{max.}$ 1 492, 1 470, 1 460, 1 427, 1 230, 810, and 707 cm^{-1}; δ_H 7.75—8.00 (4 H, m, ArH); *m/z* 248/250 ($M^{+\cdot}$).

Preparation of Modified Palladium–Charcoal Catalyst.[27]—The following procedure is typical.

10% *Palladium–charcoal catalyst with* 0.1 *mol equiv. of lead*. To a calculated amount of lead acetate (19.0 mg, 50 μmol) and commercially available palladium–charcoal catalyst (10% m/m, Koch–Light; 0.53 g, 0.5 mmol) in water (10 ml), was slowly added, with vigorous stirring, a solution of sodium borohydride (0.38 g; 0.01 mol) in distilled water (10 ml). The mixture was stirred vigorously for 1 h when the catalyst was filtered off, washed with water (200 ml), and dried in air at 50 °C overnight.

Other modified 10% Pd–charcoal catalysts were similarly prepared by varying the amount of lead acetate so that samples

containing 0.05, 0.2, 0.3, 0.5, and 0.7 mol equiv. of lead were obtained.

Competitive Reductions of Pairs of Substituted 5-Aryloxy-1-aryltetrazole Ethers in a Two-phase Solvent System (Benzene–Ethanol–Water), Using Pd–C Catalyst and Sodium Phosphinate as Hydrogen Donor.—The following procedure is typical.

5-(4-Methoxyphenoxy)-1-phenyltetrazole and 5-(4-trifluoromethylphenoxy)-1-phenyltetrazole. To a solution of 5-(4-methoxyphenoxy)-1-phenyltetrazole (150 mg, 0.56 mmol), 5-(4-trifluoromethylphenoxy)-1-phenyltetrazole (171 mg, 0.56 mmol), and durene * (internal standard; 75 mg, 0.56 mmol), in benzene (11 ml), was added Pd–charcoal catalyst (10% m/m; 30 mg; Koch–Light), all samples were drawn from only one batch of catalyst, followed by sodium phosphinate (200 mg, 2.3 mmol) in water (3.5 ml). The whole was refluxed (80 °C) with vigorous stirring. Samples of the reacton mixture were quenched by cooling to room temperature and analysed for the arenes, anisole, and α,α,α-trifluorotoluene, by g.c. on an OV 351 capillary column. The relative sensitivity for detection of each arene was obtained from a gas chromatogram of a standard solution comprised of the internal standard (durene) and the expected reaction products, anisole and α,α,α-trifluorotoluene. Quantities of arenes were obtained after correcting the observed peak area for the relative sensitivity of detection of each arene. For separate experiments results were reproducible to *ca.* ±6%.

Competitive Adsorption of Pairs of 5-Aryloxy-1-phenyltetrazoles onto Pd–C *Catalysts.*—The following example is typical.

5-(4-Methoxyphenoxy)-1-phenyltetrazole and 5-(4-cyanophenoxy)-1-phenyltetrazole. A 20 ml portion of a standard solution of 5-(4-methoxyphenoxy)-1-phenyltetrazole (13.4 mg, 50 μmol) and 5-(4-cyanophenoxy)-1-phenyltetrazole (13.2 mg, 50 μmol) in benzene (100 ml), was stirred with Pd–C catalyst (10% m/m; 30 mg) for 1 h at room temperature. The catalyst was filtered off, rinsed quickly with a little benzene and the filtrate removed under reduced pressure to give a residue which was dissolved in methanol (20 ml) and analysed by h.p.l.c. The peak areas for the two aryloxytetrazole ethers were compared with the areas obtained by h.p.l.c. before the solution had been stirred with catalyst. The relative decrease in peak area gave the relative adsorption of the aryloxytetrazole ethers onto the catalyst. The experiment was repeated using Pd–C catalyst (10% m/m; 100 mg) to check that the relative adsorption of the aryloxytetrazole ethers correlated linearly with amount of catalyst used.

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