# The Intermolecular Asymmetric *Heck* Reaction: Mechanistic and Computational Studies[1])

by **K. K. (Mimi) Hii**[2]), **Timothy D. W. Claridge**, and **John M. Brown***

Dyson Perrins Laboratory, South Parks Rd., Oxford, OX1 3QY, UK (phone: (+44)-1865-275642; fax: (+44)-1865-275674; e-mail: john.brown@chem.ox.ac.uk)

and **Andrew Smith** and **Robert J. Deeth***

Department of Chemistry, University of Warwick, Coventry, CV4 7AL, UK (phone: (+44)-24-76-523187; fax: (+44)-24-76-524112; e-mail: mssbq@dredd.csv.warwick.ac.uk)

Dedicated to the memory of Professor *Luigi M. Venanzi*

Reactive intermediates in the asymmetric *Heck* reaction between aryl electrophiles and 2,3-dihydrofuran have been identified by NMR and mass spectrometry, with BINAP or the achiral diphosphanes dppp and dppf as ligands. The major cationic species observed is an alkylpalladium produced by addition of PdAr to the alkene followed by two further PdH-mediated isomerisation steps. This last species has been characterised at $-60°$ by $^{1}$H-, $^{13}$C-, and $^{31}$P-NMR, including HMQC techniques. The regiochemistry of PdAr and PdH addition to the reactant are opposite as defined by the reaction with (2-$^{2}H_{1}$)-2,3-dihydrofuran. DFT Calculations on the reaction pathway between $[CH_2(PH_2)]PdPh^+$ and 2,3-dihydrofuran reveal several structurally interesting intermediates involving agostic $\beta$-H-atom, *ipso*-Ph or reactant O-atom bonded to the Pd-atom, and elucidate the isomerisation pathway.

**Introduction.** – The *Heck* reaction between an unsaturated electrophile and an alkene may be catalysed by several different classes of Pd complexes and has a correspondingly diverse mechanistic basis [2]. The reaction normally proceeds through an addition-elimination pathway such that the reactant and product have $sp^2$-hybridisation at the site of substitution. For asymmetric synthesis to function, there needs to be double-bond isomerisation in the course of reaction. Essentially all the examples of enantioselective *Heck* reactions in the literature involve cationic diphosphinepalladium complexes[3]), and the mechanistic studies reported herein are based on the intermolecular examples discovered by *Hayashi* and co-workers [5], and depicted in *Scheme 1*. In the addition of an aryl- or vinyl-Pd species to a cyclic alkene, the initial addition step enforces PdH elimination away from the new C–C bond, and, in doing so, a new stereogenic centre is generated. Much of the published work has involved aryl additions to 2,3-dihydrofuran (**1**) with BINAP as ligand, and our studies have largely followed that example.

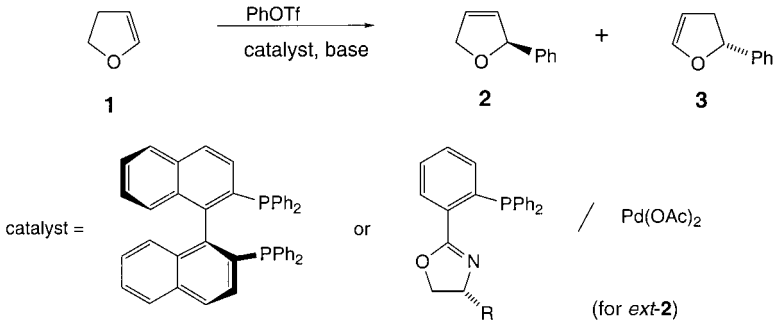
---

[1]) For preliminary communication of part of this work, see [1].

[2]) Present address: Department of Chemistry, King's College, Strand, London, WC2R 2LS, UK.

[3]) For reviews, see [3a][3b]; but for an exception involving neutral intermediates, see [3c]. For more recent examples, see [4].

Scheme 1. *The Intermolecular Asymmetric* Heck *Reaction of 2,3-Dihydrofuran with Phenyl Triflate.* With PP ligands, the 2,3-dihydrofuran isomer predominates, but with PN ligands the 2,5-dihydrofuran isomer predominates.




An interesting mechanistic sidelight emerged from the earliest reports of the specified *Heck* reaction (see [6] and earlier papers cited therein). Depending on the reaction conditions, the product was predominantly the 2,5- or 2,3-dihydro isomer **2** or **3**, respectively, with excess $PPh_3$ providing the latter. This implies an intermediate that can partition between elimination and isomerisation. In the detailed studies carried out by *Hayashi* and co-workers, both were formed with the latter favored; the enantiomer excess (e.e.) of the major product was enhanced by a favorable partition of the diastereoisomers of the first-formed intermediate, minor towards elimination and major towards isomerisation [5]. Subsequently, *Pfaltz* and *Loiseleur* and co-workers demonstrated that catalysis involving a PN ligand in the phosphinoaryldihydrooxazole series provided entirely the 2,5-dihydroisomer in high e.e. [7]; other results obtained were broadly in line with a single double-bond-shift pathway. Subsequent workers have largely confirmed this regiochemical pattern, with diphosphine ligands giving rise mainly to double-isomerisation products and with phosphinamine ligands to single-isomerisation products.

When this work was started, there were no detailed mechanistic studies on the asymmetric *Heck* reaction and, indeed, few on the reaction in general [8]. In the intervening period, there has been an effusion of speculations about the detailed mechanism of simple *Heck* reactions, especially on the role of $Pd^0-Pd^{II}$ *vs.* $Pd^{II}-Pd^{IV}$ cycles [9][4]), and the possible involvement of deligated colloidal Pd or Pd nanoparticles [10]. Direct evidence on the structure of true late intermediates in the catalytic cycle remains limited to the cationic-diphosphine case from our own work [1][7][11] and a related contribution from *Akermark* and co-workers [12]. There are related studies on alkene-Pd polymerisation or alkene/CO copolymerisation [13] in which comparable intermediates have been identified and characterised.

**Results and Discussion.** – *Observation of Reactive Intermediates.* In our original communication on this topic, the observation of a single transient intermediate on the catalytic pathway of the asymmetric *Heck* arylation reaction from compound **1** was

---

[4]) For a theoretical comparison of $Pd^{IV}$ and $Pd^{II}$ pathways, see [9c].

described. This had the surprising structure **4** shown in *Fig. 1*, being formed by a double migration of the original Pd arylation adduct. No evidence for a second diastereoisomer on the alternative enantiomeric pathway was observed, and, at that stage, the distinctive NMR spectrum of 2,5-dihydro-2-phenylfuran (**2**) (or its 2,3-dihydro-isomer **3**) was not present. Its structure was established by a multifaceted NMR approach, in which the key experiments were based on the $^1$H-NMR spectra. The most distinctive feature in the spectrum of complex **4** was the existence of two separate tertiary low-field H-atom signals at 5.3 and 5.5 ppm, assigned by a combination of HMQC, $^{31}$P-decoupling, and COSY experiments; the last of these located adjacent $CH_2$ groups and completed the H-atom connectivity of the ring. The NOE 'map' derived from ROESY experiments is shown in *Fig. 1* and suggestes that the Pd and Ph substituents are *cis* related on opposite flanks of the ether moiety. A definitive choice between these two was made by employing the 2-deuterated analogue of **1**; the $^1$H-resonance at 5.5 ppm was not observed in the spectrum of the intermediate. On the basis of additional information from the ROESY experiment, where a cross-peak between the signal at

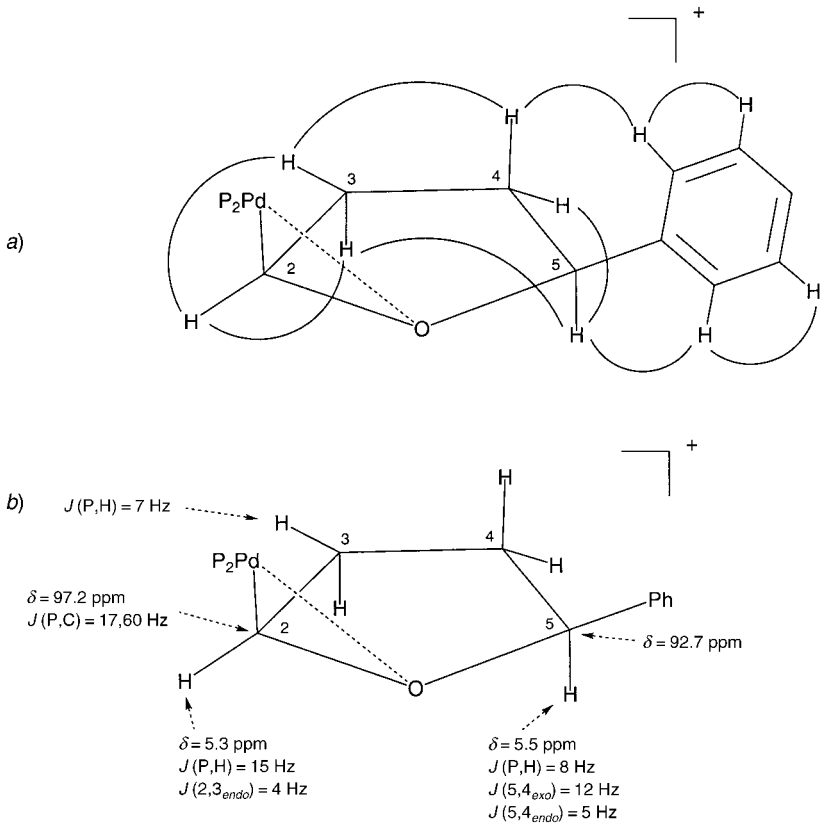


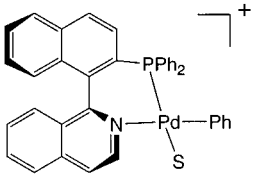

Fig. 1. *NMR characterisation of the intermediate* **4** *observed by NMR in the range of* $-70°$ *to* $-50°$*;* a) *connectivities from NOE data obtained by ROESY experiments;* b) *selected chemical shift and coupling data derived from* ($^1$H,$^1$H)- *and* ($^1$H,$^{31}$P)-*COSY, -TOCSY, and -HMQC experiments that define the solution structure*

5.5 ppm of the $H_{endo}-C(5)$ and the signal at 1.7 ppm associated with $H_{endo}-C(4)$ was observed, a likely geometry for the complex was suggested. In this, the five-membered ring is in a twist conformation where the Ph group is equatorial and the Pd-atom with its ligands is axial. This unusual geometry raised the possibility that the ether O-atom participates in bonding to the Pd-atom. Whilst not proved by the data, the existence of a unique five-bond coupling between the tertiary benzylic H-atom and one of the two P-atoms, provided further support for the postulate. DFT Calculations (*vide infra*) also support this possibility.

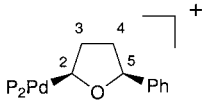
The intermediate **4** observed by NMR is stable at $-60°$ for short periods and decomposes on warming. GC Analysis of the product shows that it is exclusively **2** (< 5% **3**) and is formed in 95% e.e. of the (*S*)-enantiomer, consistent with the catalytic results from the work of *Hayashi* and co-workers [5]. When decomposition of complex **4** was monitored by $^{31}$P-NMR, two new species were observed concurrently. Cross-reference to the $^{1}$H-NMR spectra, and especially the species formed in the $^{1}$H-NMR spectrum of (2-$^{2}H_1$)-**1** indicates that these are the diastereoisomers of the Pd complex **5** formed by the unselective addition of PdH to reactant **1** but with the Pd-atom now adjacent to the heteroatom. Not all low-field $^{1}$H-resonances of the two diastereoisomers of **5** have been uniquely identified, but there is sufficient information to be clear about the regiochemistry of addition. Interestingly, the new intermediate **5** does not react readily with a further molecule of reactant **1** to produce a di- or oligomeric product by multiple *Heck* condensation.

A single experiment was carried out with the corresponding complex **6** derived from the PN-ligand QUINAP. The reaction was considerably slower, and, at 10°, intermediates were not observed. Analysis of the reaction product by GC indicated the formation of (*S*)-**3** in 95% e.e., demonstrating the alternative regiochemistry of reaction to the BINAP case.

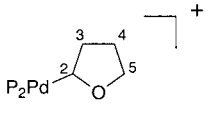
Similar reaction conditions were established for dppp- or dppf-ligated reactant complexes. In the first case, the initial intermediate **7** was unstable at $-50°$, and hence only its $^{31}$P-NMR spectrum was recorded. This species provided the second intermediate **8** cleanly together with product **2**. The $^{1}$H-NMR spectrum augments the evidence for Pd–C(2) bonding since there are three characteristic low-field $^{1}$H-resonances, with the H–C–Pd signal as a broad doublet; the low value of vicinal coupling constants indicates an axial conformation for the C–Pd bond, as in the initial adducts. In the dppf case both **9** and **10** were spectroscopically characterised by $^{31}$P-NMR, the latter exhibiting interesting dynamic behaviour, which precluded interpretation of the $^{1}$H-NMR spectrum. The origin of this process equilibrating P(1) and P(2)




**6** ($OTf^-$); S = thf




**4** $P_2$ = BINAP
**7** $P_2$ = dppp
**9** $P_2$ = dppf




**5** $P_2$ = BINAP
**8** $P_2$ = dppp
**10** $P_2$ = dppf

[**5a, 5b** = (2*S*) or (2*R*)]

is unknown but may indicate rapid reversible $\beta$-hydride transfer to the Pd-atom with an intermediate that equivalences the two P-atoms.

*DFT Studies of Initial Complex and Insertion Step*. The starting point for computation was the cationic complex **11** carrying both the Ph group and the alkene. As in previous work [14], the 'computational' ligand $H_2PCH_2PH_2$ was employed, and the $TfO^-$ counterion involved in the mechanistic studies described above was replaced by $I^-$ ion for ease of computation. With an achiral ligand there are two possible conformations (*exo* or *endo*) linked by rotation about the alkene–metal bond, which is orthogonal to the square plane. The preferred plane of the Ph ring is also orthogonal. Their respective binding energies, and the computed structure of the lower-energy isomer are shown in *Fig. 2*. As expected [15], the $\beta$-C-atom of the enol-ether double-bond is much closer to the square plane than is the $\alpha$-C-atom, and C($\beta$)-Pd at 2.21 Å is much shorter than C($\alpha$)-Pd at 2.38 Å. In contrast to a free vinyl ether [16], the $\beta$-C-atom is essentially neutral (*Mulliken* charge $-0.02$ e) whereas the $\alpha$-C-atom is strongly positive (0.58 e). The Ph group is $\eta^1$-bound to the Pd-atom, and bond lengths within the ring are typically aromatic. Negative charge is essentially localised on the *ipso* C-atom ($-0.35$ e) providing a charge-based rationalisation for the regiochemistry of the *Heck* migration step, since it is transferred exclusively to the positive $\alpha$-C-atom of the vinyl ether. The Pd–Ph bond is very short. This resulting high *trans* influence gives rise to a long *trans* Pd–P bond.

In order for the migration step to occur, the alkene must first rotate into the square plane, and the productive transition state involves charge-matched bonding of the Ph group to C($\alpha$), indicated in *Fig. 2*. A confirmatory frequency calculation was undertaken and generated one negative frequency at $-234$ cm$^{-1}$. This frequency was animated and corresponds to the coupling of C(2) and C(8). The C–C distance is

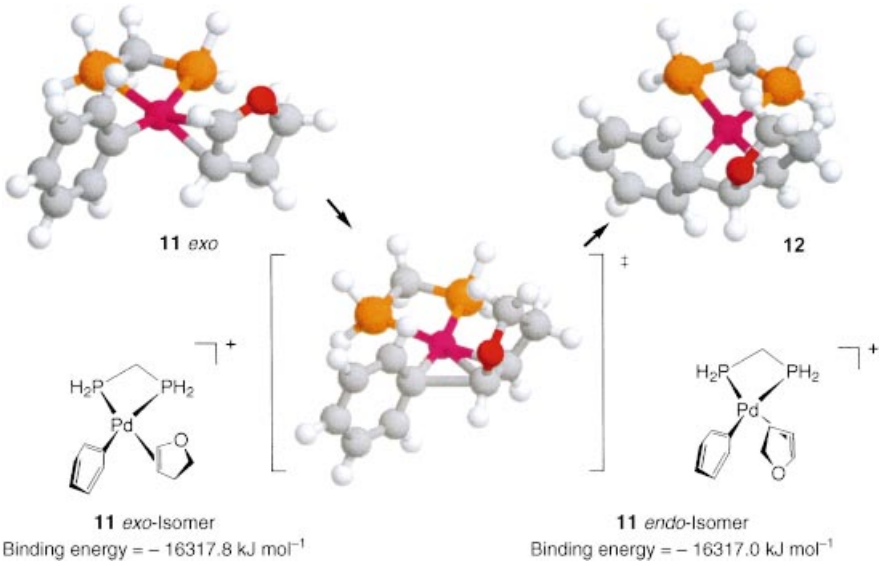



Fig. 2. *The reaction pathway of the first step of the* Heck *phenylation of 2,3-dihydrofuran from complex* **11** *to complex* **12**, *with DFT energies of the different states quoted in kJ mol$^{-1}$*

2.16 Å, significantly longer than in related calculations, and having its likely origin in the electrostatic attraction between the partners, leading to an earlier transition-state (TS). In fact, C(2) is more negative at the TS and compensated by increased positive charge at the *ortho* positions of the aryl ring. The transition-state for the disfavoured transfer to C($\beta$) was also found, and is 6.7 kJ mol$^{-1}$ higher than that for the preferred pathway. If realised in practice, this would correspond to $\geq$95% regioselectivity in the observed direction.

The terminus of the migration step was also subjected to computational analysis, with the new ground-state **12** shown in *Fig. 3*. The most striking feature is the direct $C_{ipso}$–Pd bond. This observation is in contrast to one related computational study of Ph–Pd insertion into ethene by carbene ligands; for the model (bis)diaminocarbene ligand in **13** weak $\eta^2$-Pd *ipso-ortho* bonding was observed at the same stage, whilst the monocarbene complex **14** exhibited only Pd–$C_{ortho}$ bonding [17]. There are, in addition, well-established and X-ray-characterised examples of *ipso* bonding in Pd complexes [18], raising the possibility that this substitution type could be important in Pd catalysis when an aryl ring is in proximity to the catalytic centre. The relative stability of the $C_{ipso}$–Pd bond in the present case can be established by introducing a single $H_2O$ molecule into the coordination sphere. This leads to the displacement of the Ph group and replacement by $H_2O$ at that coordination site. The C–Pd $\sigma$-bond rotates to remove the Ph group from the vicinity of the metal, giving rise to the structure shown boxed in *Fig. 3*. Summing the total energies, however, indicates that the *ipso*-bonded intermediate is lower in energy than the aqua complex **18** (corrected by the energy of a fully dissociated $H_2O$ molecule, $-1357.4$ kJ mol$^{-1}$) by 9.6 kJ mol$^{-1}$.

*DFT Studies of Pd–H Migrations.* To generate the alternative Pd-hydrides required to explain the multiplicity of products in the experimental *Heck* reactions, possible pathways for this step were evaluated empirically. Through a linear transit calculation on structure **12** with constraints on C–H distances designed to enforce hydride migration, the ground-state structure of the next intermediate **15** was obtained in which the integrity of the $C_{ipso}$–Pd bond was maintained. With these constraints an improbably high-energy path was revealed, and structure **15** was indicated to be 7 kJ mol$^{-1}$ above structure **12** in binding energy. To gain more insight into the pathway the transformation was run in reverse, emphasising PdH extraction without explicit migration. The most favorable route discovered revealed a complex multi-minima surface with a calculated energy barrier of 49 kJ mol$^{-1}$. An important feature of this pathway is that the Ph group rotates away from the Pd-atom, weakening the $C_{ipso}$–Pd bond, and that $\beta$-hydride agostic bonding occurs concomitantly, giving structure **16**. This process continues with local minima to the eventual formation of a true $\eta^2$-alkene-Pd hydride **17** (*Fig. 3*), 42 kJ mol$^{-1}$ higher in energy than the original structure **12**. Interestingly, the double bond is in the coordination square plane in this intermediate, such that the Ph group may interact weakly (Pd–$C_{ipso}$ = 2.63 Å) with the $dz^2$ orbital orthogonal to the same plane. The reverse process provides a model for the path of Pd migration that is shown in *Fig. 3*.

If the isomerisation process is repeated once more from complex **15**, the resulting Pd alkyl is adjacent to the ring O-atom. Computation of the ground state of this final intermediate **19** reveals that the Pd–O bond is established in preference to participation of $\beta$-hydride or aryl C-atoms. The calculations support experimental

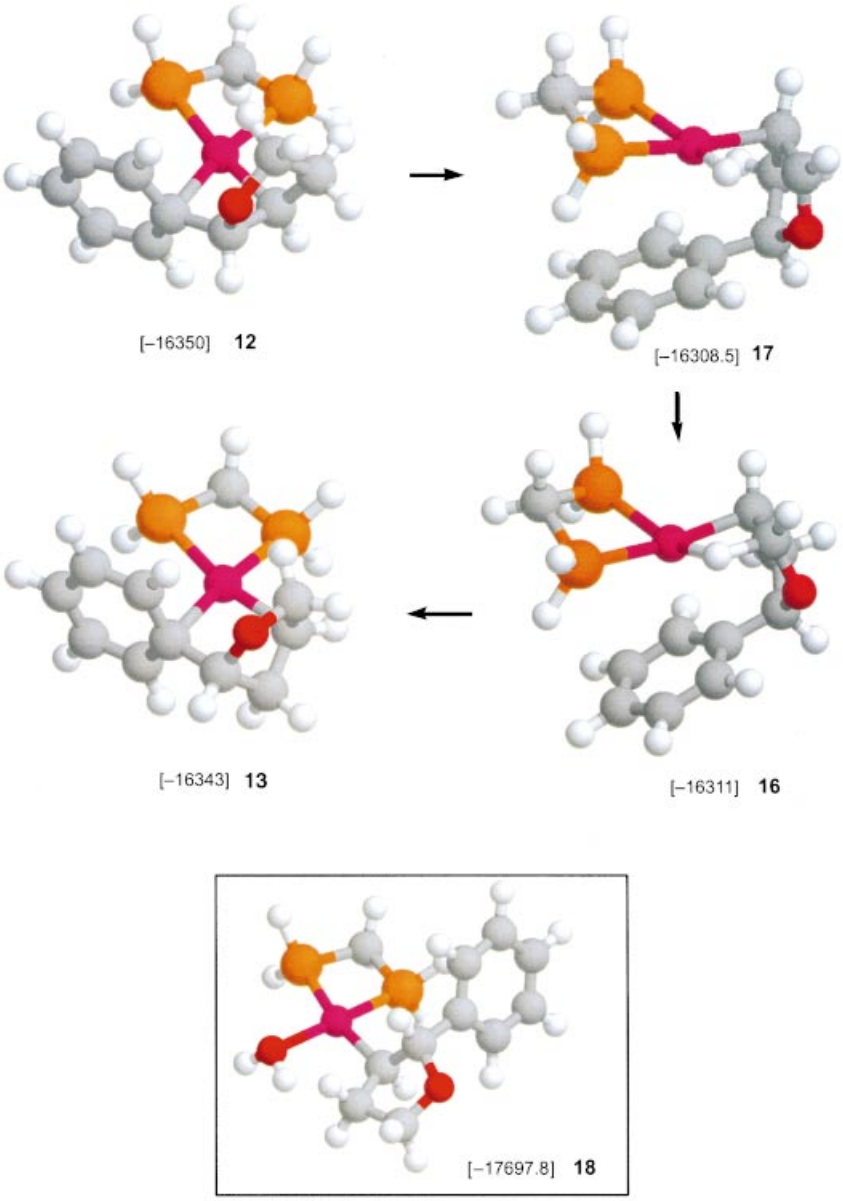



Fig. 3. *The reaction pathway for the first isomerisation step from the alkyl-Pd intermediate.* For ease of computation, the ground states prior to and subsequent to isomerisation (compounds **12** and **16**, resp.) were first established, and then the two further intermediate minimum-energy states **17** and **18** were located by working backwards from **16**. The energy of the aqua complex **15** needs to be corrected for the binding energy of $H_2O$ ($-1457.4$ kJ mol$^{-1}$) in order to facilitate comparisons.

observations in that the ultimate product of the *Heck* reaction of 2,5-dihydrofuran depends on a competition between elimination and migration pathways, the latter governed by a subtle interplay between differing weak ligands and the unsaturated Pd intermediates (for full details of the computational chemistry, see [19]).

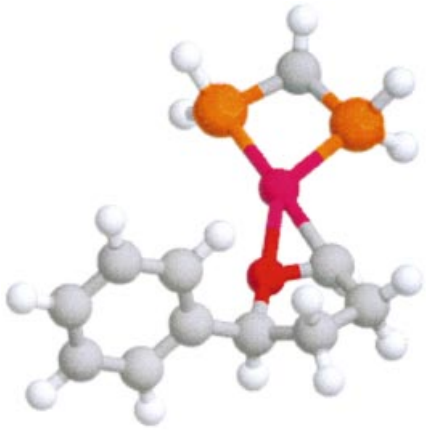
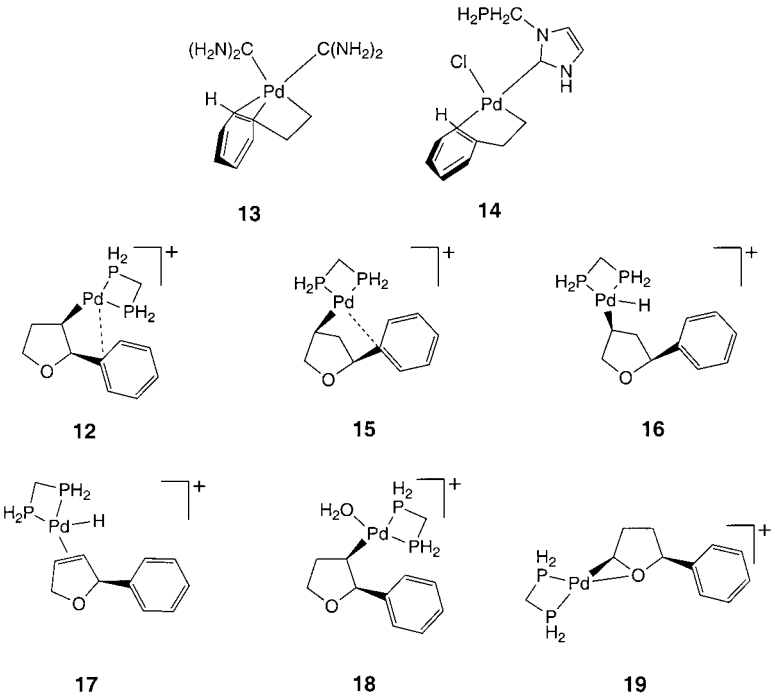



Fig. 4. *The structure and energy of the final alkyl–Pd intermediate* **19** *formed by double Pd–H-mediated rearrangement*



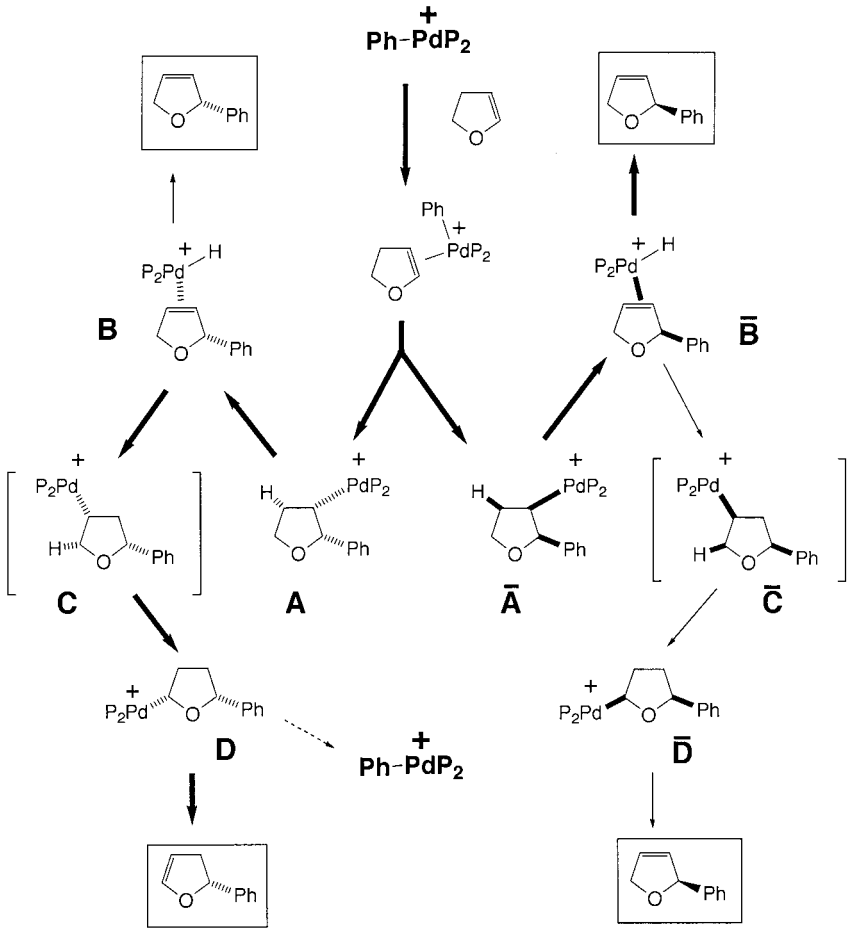
**Conclusions.** – Overall, the work reported herein reinforces and refines previous ideas about the asymmetric *Heck* reaction. The diverse product distributions observed by *Hayashi* and co-workers, in which the proportions of products **2** and **3** are highly sensitive to added AcOH and the nature of the base [5], may be economically explained. Similarly, the preponderance of product **3** when PN ligated catalysts are employed can be explained. The initial observation of *Larock* and co-workers that excess $PPh_3$ diverted the reaction pathway from predominantly **3** to predominantly **2**, can also be explained by the same mechanistic model. The detail is set out in *Scheme 2*, an essential new factor being the easy accessibility and stability of the doubly isomerised Pd–alkyl. With an achiral ligand, the product of the first addition step provides a branching point. The options are direct elimination of Pd–H and release of alkene, or dyotropic rearrangement to give the isomeric Pd–alkyl. If the intermediate Pd–alkene hydride has the capacity to lose a ligand by dissociation (monophosphine not in excess, or PN chelate) then alkene release is the preferred route. If the intermediate is long-lived enough to rearrange (PP chelate), then a second dyotropic step occurs rapidly so that the resting state is the doubly rearranged alkyl. The ultimate product can only be the 2-arylated 2,3-dihydrofuran. For the asymmetric cases, two possible diastereoisomers are formed in the initial step, and both proceed along the pathways described. If the first intermediate is unstable (PN chelate), the product enantiomer ratio is determined only by the stereoselectivity of the initial addition of the Pd–Ar group to the alkene. In cases where further rearrangement occurs (PP chelate), the enantiomer ratio is determined by two factors – the stereoselectivity of the initial addition step, and also the branching of the first intermediate between alkene release and isomerisation. In the stoichiometric NMR experiments, the sole intermediate observed is one diastereoisomer from the double-rearrangement process, without any evidence of product release at that stage. In the catalytic experiments of *Hayashi* and co-workers, the more favored enantiomer of the product is formed *via* more stable intermediates. A consequence of this is that the less-favored diastereoisomeric pathway is more likely to lead to **3** rather than to **2**. Together with our previous work, these observations demonstrate that the Pd–H formed in the *Heck* reaction is efficiently captured by an excess of the alkene in the absence of base. When base is present, however, this pathway is averted [20]. These previous calculations indicate that a Pd-agostic $\beta$-hydride of significant lifetime would also be responsive to base-promoted alkene formation.

The DFT calculations endorse the veracity of this interpretation, and offer insights into the structure and energetics of the intermediates involved. The first-formed alkyl complex is computed to possess strong Pd–$C_{ipso}$ bonding, maintained in the first rearrangement product. This isomerisation is endothermic. The second rearrangement gives rise to the most stable of the three positional isomers of the adduct, whose additional stability is conferred by significant Pd–O bonding. At intermediate stages $\beta$-agostic Pd–H bonding can produce additional shallow minima. The energetics of the various intermediates described in the computational part are summarised in *Scheme 2*. The broad indications from these studies are borne out in practice – the first-formed $\eta^2$-alkene adduct remains unobserved in realistic models for the *Heck* reaction because it has a low-energy migration pathway in which the first alkyl is formed. The initially formed alkyl–Pd cation is higher in energy than the first intermediate by 32 kJ $mol^{-1}$ in

the model calculations so that the migration step is exothermic and probably irreversible. Formation of a Pd hydride by $\beta$-elimination is endothermic by $>35$ kJ mol$^{-1}$. The order of stability of the three alkyl–Pd intermediates in the DFT calculations is final $>$ initial $>$ intermediate, indicating the value of the additional Pd–O stabilisation in the final species.

We thank *EPSRC* for support (to *K. K. H.*), the University of Warwick for provision of computer equipment and financial support (for *A. S.*), and *Johnson-Matthey* for the loan of Pd salts. We thank Prof. *A. Pfaltz* for a useful discussion.

Scheme 2. *Pathways for the Asymmetric Phenylation of 2,3-Dihydrofuran*. The partitioning of the first-formed Pd–H complex **B** determines the course of reaction. With (*S*)-BINAP as ligand, hydride return is the main pathway, giving the transient isomer **C**, which further rearranges to the most stable Pd–alkyl **D**, the precursor of the major product. On the minor enantiomer pathway, Pd–H complex $\bar{\mathbf{B}}$ preferentially partitions to the 2,5-dihydrofuran rather than further rearrangement through **C**. Collapse to product through **B** or $\bar{\mathbf{B}}$ is the exclusive pathway when PN ligands are employed [7].



## Experimental Part

*General*. Experimental protocols and resources are taken from previous papers on this topic [21].

*Computational Details.* The DFT calculations were obtained with the *Amsterdam Density Functional* (ADF) program suite Version 2.3 [22]. Geometries were optimised at the local density approximation level and with binding energies computed subsequently with the *Becke88/Perdew86* gradient-corrected functional [23][24]. The frozen-core approximation [25] was applied with orbitals 1s-3d frozen on Pd-atoms, 1s-2p on P-atoms and the 1 s orbital frozen for O- and C-atoms. Basis sets comprised triply-$\zeta$ + polarisation STO expansions (basis IV) throughout.

*Preparations. General Procedures for the Preparation of [Pd(I)(Ph)P$_2$]. Method A:* A soln. of $Li_2$(COT) [26] (0.26M in $Et_2O$, 1.5 equiv.) was added slowly to a stirred soln. of the corresponding [$PdCl_2P_2$] complex in THF at $-78°$. The resulting dark red soln. was stirred for 30 min followed by the addition of PhI (2 equiv.). The mixture was then allowed to warm to r.t. and stirred overnight. The mixture was evaporated, and petroleum ether (40–60°) was added to precipitate the crude product, which was filtered off and recrystallized from THF/pentane to give the required compound as a creamy solid. Yields were between 65–75%.

*Method B.* A *Schlenk* tube charged with [Pd(I)(Ph)(tmeda)] [27] (150 mg, 0.35 mmol) and the corresponding diphosphine (0.35 mmol) was purged-filled with Ar twice. Degassed toluene (3 ml) was added and the soln. was stirred for 5 h, during which time the required compound precipitated from the soln. as a solid. This was filtered off, washed ($Et_2O$), and dried. A second crop of compound may be recovered by evaporating the mother liquor to dryness, followed by the addition of $Et_2O$. Typical yields are 65–85%.

*[Pd(BINAP)(I)(Ph)]*. The complex decomposes rapidly at r.t. in chlorinated solvents, therefore the NMR spectra were recorded at 243 K. $^1$H-NMR (500 MHz, $CD_2Cl_2$, 243 K): 6.47 (*dd*, *J*(H,H) = 2.2, 9.8, H–C(3)); 6.66 (br. *t*, P*Ph*); 6.71 (*ddd*, *J*(H,H) = 1.5, 3.3, 7.3, 1 H); 6.74 (*ddd*, *J*(H,H) = 1.1, 1.2, 7.2, H–C$_{ortho}$); 6.86–6.97 (*m*, 7 H); 6.95 (*td*, *J*(H,H) = 1.2, 6.8, H–C(4)); 7.04 (*ddd*, *J*(H,H) = 1.0, 1.3, 8.8, H–C(9)); 7.12 (*m*, 2 H); 7.18 (*ddd*, *J*(H,H) = 1.3, 6.8, 8.8, H–C(10)); 7.29 (*ddd*, *J*(H,H) = 1.2, 6.8, 8.1, H–C(5)); 7.34 (*dt*, *J*(H,H) = 8.8, *J*(P,H) = 1.0, H–C(8)); 7.37 (*ddd*, *J*(H,H) = 1.3, 6.8, 8.1, H–C(11)); 7.44 (br. *m*, 4 H, P*Ph*); 7.51–7.55 (*m*, 4 H); 7.58 (*dd*, *J*(H,H) = 1.2, 8.3, H–C(6)); 7.69 (*dd*, *J*(H,H) = 1.3, 8.3, H–C′$_{ortho}$); 7.74 (br. *m*, 4 H, P*Ph*); 7.78 (*dd*, *J*(H,H) = 8.6, *J*(P,H) = 2.2, H–C(2)); 7.93 (*dd*, *J*(H,H) = 8.6, *J*(P,H) = 11.0, H–C(1)). $^{31}$P-NMR (202 MHz, $CD_2Cl_2$, 243 K): 19.8 (*d*, *J* = 39); 24.3 (*d*, *J* = 39). ES-MS (MeOH, 25 eV): 805 ([*M* – I]$^+$ [Pd(BINAP)(Ph)]$^+$).

*[Pd(dppp)(I)(Ph)]*. $^1$H-NMR (500 MHz, $CD_2Cl_2$): 7.1–7.9 (*m*, 20 H, P*Ph*); 6.89 (*td*, *J*(H,H) = 7.8, *J*(P,H) = 2.2, 7.8, 2 H, H–C(3)); 6.53 (*ddd*, *J*(H,H) = 7.3, 7.6, *J*(P,H) = 5.5, 2 H, H–C(2)); 6.45 (*t*, *J*(H,H) = 7.4, H–C(4)); 2.55 (*m*, C*H*$_2$P); 2.44 (*m*, C*H*$_2$P); 1.80 (*m*, C*H*$_2$). $^{13}$C-NMR (125.7 MHz, $CD_2Cl_2$): 19.5 (*d*, *J*(P,C) = 4, *C*H$_2$); 27.6 (*dd*, *J*(P,C) = 3, 19, *C*H$_2$P); 29.1 (*dd*, *J*(P,C) = 7, 25, *C*H$_2$P); 122.0 (*s*, C(4)); 127.3 (*d*, *J*(P,C) = 9, C(2)); 138.0 (*d*, *J*(P,C) = 3, C(3)); 156.7 (*dd*, *J*(P,C) = 3, 128, C(1)). $^{31}$P-NMR (202 MHz, $CD_2Cl_2$): –8.8 (*d*, *J* = 52), 12.2 (*d*, *J* = 52).

*[Pd(I)(Ph)(*R*)-(QUINAP)]. Super Hydride®* (1M soln. in THF, 0.5 ml, 0.5 mmol) was added to a stirred suspension of [$PdCl_2$(*R*)-(QUINAP)] (117 mg, 0.2 mmol) and 1,5-cyclooctadiene (0.1 cm$^3$) in THF (5 ml) at $-78°$. When effervescence ceased after 15 min, PhI (0.1 ml) was added and the soln. was warmed to r.t. very slowly (over 5 h). The solvents were then removed completely, and the addition of pentane precipitated the crude product as a brown solid, which was recrystallized from toluene/pentane to give the required complex as a buff-coloured solid (50 mg, 35%). $^1$H-NMR (500 MHz, ($D_6$)acetone): 6.52 (*tt*, *J*(H,H) = 1.2, 7.2, 1 H); 6.62 (br. *t*, *J*(H,H) = 7.5); 6.91 (*dddd*, *J*(H,H) = 1.0, 1.0, 1.9, 8.7, H–C(3)); 6.96 (*ddd*, *J*(H,H) = 1.3, 8.5, *J*(P,H) = 11.4, 1 H); 7.07 (*ddd*, *J*(H,H) = 1.0, 1.5, 8.6, H–C(9)); 7.17 (*dd*, *J*(H,H) = 7.4, *J*(P,H) = 2.6, 1 H); 7.16–7.26 (*m*); 7.18 (*ddd*, *J*(H,H) = 1.5, 6.8, 8.3, H–C(11)); 7.30–7.50 (*m*); 7.33 (*ddd*, *J*(H,H) = 1.0, 6.8, 8.7, H–C(4)); 7.40 (*ddd*, *J*(H,H) = 1.1, 6.8, 8.6, H–C(10)); 7.42 (*m*, H–C(7)); 7.68 (*ddd*, *J*(H,H) = 1.0, 6.8, 8.1, 1 H); 7.71 (*ddd*, *J*(H,H) = 1.9, 6.8, 8.3, H–C(5)); 7.76–7.80 (*m*); 7.89 (*ddd*, *J*(H,H) = 1.0, 1.0, 8.3, H–C(6)); 7.92 (*dd*, *J*(H,H) = 1.0, 6.3, H–C(2)); 8.04 (*ddd*, *J*(H,H) = 0.8, 8.5, 8.5, 1 H); 8.17 (*dd*, *J*(H,H) = 1.0, 8.3, H–C(12)); 8.27 (*ddd*, *J*(H,H) = 1.0, 8.6, *J*(P,H) = 1.8, H–C(8)); 9.65 (*d*, *J*(H,H) = 6.3, H–C(1)). $^{31}$P-NMR (202 MHz, ($D_6$)acetone): 27.5.

*Preparation of (2-$^2H_1$)-2,3-Dihydrofuran by a Modified Procedure* [28]. In a dry *Schlenk* tube, BuLi (2.5M in hexane, 13 ml) was added rapidly to a mixture of freshly distilled 2,3-dihydrofuran (2 g, 28.5 mmol) and tmeda (0.6 g), whereupon vigorous effervescence and precipitation occurred. The mixture was then cooled (water bath) and the addition was completed with stirring. The solid was allowed to settle before the liquid was decanted. The residue was washed with dry pentane (3 × 6 ml), and dried *in vacuo* (***Caution:*** highly pyrophoric solid). The solid was subsequently suspended in dry toluene (2 ml) and cooled to $-30°$. $D_2O$ was added

dropwise very slowly, and the soln. was allowed to warm to r.t. gradually. The deuterated 2,3-dihydrofuran was obtained in 60% yield by distillation of the mixture over a 4″ *Vigreux* column. $^1$H-NMR ($CDCl_3$): 2.33 (*dt*, *J* = 2.5, 9.5, $CH_2$); 4.03 (*t*, *J* = 9.5, $CH_2O$); 4.68 (*t*, *J* = 2.5, =C*H*).

*Reactions with 2,3-Dihydrofuran. Typical Procedure for the Reaction of [Pd(P$_2$)(Ph)(S)]TfO with 2,3-Dihydrofuran.* AgOTf (1.1 equiv.) was added to a soln. of the corresponding [Pd(Ar)(diphosphane)(I)] (0.02 mmol) in ($D_8$)THF (0.5 ml) at −78°. After 10 min of vigorous stirring, the mixture was centrifuged at −60°. The pale yellow soln. was decanted quickly into a NMR tube containing the dihydrofuran (6 µl). The mixture was transferred into the NMR spectrometer cooled at −60°. The first intermediate was observed as a single diastereoisomer **4**, which was converted to the diastereoisomeric second intermediates **5a** and **5b** by raising the probe temp. gradually to −20°, where it decomposed to give the turnover product and a mixture of two diastereoisomers. When the mixture was analysed, the turnover product (*S*)-2,3-dihydro-2-phenylfuran was found in 95% e.e. (chiral GC).

*P$_2$ = (*S*)-BINAP:* $^1$H-NMR (500 MHz, 238 K): 5.50 (*ddd*, *J*(P,H) = 8.5, 12.0, *J*(H,H) = 4.8, H−C(5)); 5.30 (*dd*, *J*(P,H) = 15.5, *J*(H,H) = 3.6, H−C(2)); 2.70 (*dddd*, *J*(H,H) = 5, 7, 12, 18, H−C(4)); 2.20 (*ddd*, *J*(H,H) = 4.8, 11, 18, H−C(4)); 1.70 (*ddddd*, *J*(P,H) = 1.0, *J*(H,H) = 3.6, 5, 11, 14.7, H−C(3)); 1.0 (*ddd*, *J*(P,H) = 7.3, *J*(H,H) = 7.0, 14.7, H−C(3)). $^{13}$C-NMR (125.7 MHz, 238 K): 28.6 (*s*, C(3)); 32.5 (*s*, C(4)); 92.7 (*s*, C(2)); 97.2 (*d*, *J*(P,C) = 17, 60, C(5)). $^{31}$P-NMR (202 MHz, 238 K): 22.5 (*d*, *J*(P,P) = 35); 37.0 (*d*, *J*(P,P) = 35). ES-MS, MeOH, 20 eV): 878 ([*M* + 1]), 800 (M−Ph).

*P$_2$ = dppf:* $^1$H-NMR (500 MHz, ($D_8$)THF, 238 K): 1.02 (*ddd*, *J*(H,H) = 6.6, 15, *J*(P,H) = 7, H−C(4)); 1.51 (*m*, H−C(4′)); 2.17 (br. *m*, H−C(3)); 2.46 (br. *m*, H−C(3′)); 4.12 (*m*, 1 H of Cp); 4.17 (*m*, 2 H of Cp); 4.41 (*m*, 1 H of Cp); 4.45 (*m*, 1 H of Cp); 4.50 (*m*, 1 H of Cp); 4.55 (*m*, 1 H of Cp); 4.72 (*m*, 2 H of Cp); 4.76 (*m*, 1 H of Cp); 4.97 (*dd*, *J*(P,H) = 20, *J*(H,H) = 3.7, H−C(5)); 5.57 (*ddd*, *J*(P,H) = 12, *J*(H,H) = 4, 12, H−C(2)). $^{13}$C-NMR (125.7 MHz, 238 K): 32.5 (*s*, C(4)); 92.7 (*s*, C(2)); 98.8 (*s*, C(5)). $^{31}$P-NMR (202 MHz, ($D_8$)-THF, 228 K): 13.1 (*d*, *J*(P,P) = 18); 36.0 (*d*, *J*(P,P) = 18.

*P$_2$ = dppp:* unstable with respect to product elimination at 233 K. $^{31}$P-NMR (202 MHz, 213 K): −0.7 (*J*(P,P) = 60); 31.7 (*J*(P,P) = 60). ES-MS (MeOH, 40 eV): 807 ([$PdP_2$(Ph) + $C_4H_6O$]), 731 ([$PdP_2$ + $C_4H_6O$]).

*Product Characterisation: P$_2$ = (*S*)-BINAP:* Formation of two diastereoisomers was observed at 243 K. Diastereoisomer A. $^1$H-NMR (500 MHz, ($D_8$)THF, 243 K): 5.14 (*dd*, *J* = 3.5, *J*(P,H) = 17.3, 1 H); 4.75 (br. *t*, *J*(H,H) = 7.9).

Diastereoisomer B. $^1$H-NMR (500 MHz, ($D_8$)THF, 243 K): 4.68 (*t*, *J*(H,H) = 8.5, 1 H); 4.60 (*dd*, *J*(H,H) = 3.9, *J*(P,H) = 15.8). $^{31}$P-NMR (202 MHz): 19.6 (*J*(P,P) = 27); 22.4 (*J*(P,P) = 34); 37.7 (*J*(P,P) = 27); 38.8 (*J*(P,P) = 34).

*P$_2$ = dppf:* $^{31}$P-NMR (202 MHz, 233 K): 14.4 (*d*, *J*(P,P) = 22), 36.0 (*d*, *J*(P,P) = 22).

*P$_2$ = dppp:* $^1$H-NMR (500 MHz, ($D_8$)THF, 233 K): 1.20 (*m*, H−C(4)); 1.31 (*m*, H−C(4)); 1.81 (*m*, H−C(3)); 2.05–2.30 (br. *m*, C*H*$_2$); 2.48 (*m*, H−C(3)); 2.73 (*m*, 1 H, C*H*$_2$P); 2.82 (*ddd*, *J*(H,H) = 8.0, 15.3, *J*(P,H) = 15.3, 1 H, C*H*$_2$P); 2.94 (br. *t*, 1 H, C*H*$_2$P); 3.30 (br. *m*, 1 H, C*H*$_2$P); 3.92 (br. *m*, H−C(2)); 4.11 (br. *t*, *J*(H,H) = 8.0, H−C(2)); 4.62 (*dd*, *J*(H,H) = 3.8, *J*(P,H) = 16.1, H−C(5)). $^{31}$P-NMR (202 MHz, 233 K): 2.2 (*J*(P,P) = 47), 31.4 (*J*(P,P) = 47).

*Reaction of [Pd(Ph)(*R*)-(QUINAP)(S)][TfO] with 2,3-Dihydrofuran.* AgOTf (3.5 mg) was added to a soln. of the aryl-Pd halide complex (10 mg, 0.01 mmol) in ($D_8$)THF (0.75 ml) at −78°. $^{31}$P-NMR revealed the formation of a new species (25.0 ppm) which was stable up to 10°, whereupon slow decomposition took place. In the presence of 2,3-dihydrofuran, this was also found to be the reaction temp. Analysis of the org. product formed *in situ* was found to be the (*S*)-2,5-dihydro product in 95% e.e., as analysed by chiral GC.

*Catalytic Studies.* **1a** (*P$_2$ = (*S*)-BINAP*) (5 mol-%) was generated by the addition of AgOTf (6 mg) to a soln. of [Pd(I)($P_2$)(Ph)] (20 mg, 0.02 mmol) in THF at −78°. 2,3-Dihydrofuran (155 mg, 2.2 mmol), $Et_3N$ (135 mg, 1.3 mmol) and PhOTf (100 mg, 0.44 mmol) were added sequentially. The mixture was gradually warmed to r.t., then warmed to 40°. The reaction progress was monitored by GC-MS, which indicated the formation of one single regioisomer. After 22 h (99% consumption of PhOTf), the mixture was poured into pentane (20 ml) and filtered through a short column of silica gel. The filtrate was evaporated to yield a yellow oily residue, which was found to be the 2,3-regioisomer only ($^1$H-NMR) and the (*S*)-enantiomer in 74% e.e. (chiral GC; lit.: 74% e.e. (*S*)).

*[Pd(*S*)-(BINAP)(Ph)(S)]TfO* was generated as before from the addition of AgOTf (7 mg) to a stirred soln. [Pd(*S*)-(BINAP)(I)(Ph)] in THF (1.5 ml) at −78°. After the removal of the precipitated Ag salt by centrifugation, the pale yellow soln. was transferred cold to a *Schlenk* tube containing PhOTf (113 mg, 0.5 mmol) 2,3-dihyrofuran (0.21 ml) and $Bu_4NOAc$ (450 mg, 1.5 mmol). The mixture was warmed slowly to r.t., then warmed at 40° for 72 h. The reaction only achieved 31% conversion as indicated by GC, with the exclusive

formation of one regioisomer. The mixture was poured into $Et_2O$, and washed with $H_2O$. The org. layer was separated, dried ($MgSO_4$), and brought to dryness. Analysis of the residue revealed the presence of only 2,5-dihydro-2-phenylfuran (**3**), racemic by *Cydex-B* GC analysis.

## REFERENCES


[1] K. K. Hii, T. D. W. Claridge, J. M. Brown, *Angew. Chem., Int. Ed.* **1997**, *36*, 984.
[2] I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; G. T. Crisp, *Chem. Soc. Rev.* **1998**, *27*, 427; A. Demeijere, F. E. Meyer, *Angew. Chem., Int. Ed*. **1995**, *33*, 2379.
[3] a) P. J. Guiry, A. J. Hennessy, J. P. Cahill, *Top. Catal*. **1997**, *4*, 311; b) M. Shibasaki, E. M. Vogl, *J. Organomet. Chem*. **1999**, *576*, 1; c) L. E. Overman, D. J. Poon, *Angew. Chem., Int. Ed*. **1997**, *36*, 518.
[4] N. G. Andersen, R. McDonald, B. A. Keay, *Tetrahedron: Asymmetry* **2001**, *12*, 263; A. V. Malkov, M. Bella, I. G. Stara, P. Kocovsky, *Tetrahedron Lett*. **2001**, *42*, 3045; S. R. Gilbertson, Z. Fu, *Org. Lett*. **2001**, *3*, 161; S. R. Gilbertson, Z. C. Fu, D. J. Xie, *Tetrahedron Lett*. **2001**, *42*, 365; K. Yonehara, K. Mori, T. Hashizume, K. G. Chung, K. Ohe, S. Uemura, *J. Organomet. Chem*. **2000**, *603*, 40; N. G. Andersen, M. Parvez, B. A. Keay, *Org. Lett*. **2000**, *2*, 2817; T. Benincori, E. Cesarotti, O. Piccolo, F. Sannicolo, *J. Org. Chem*. **2000**, *65*, 2043; W. P. Deng, X. L. Hou, L. X. Dai, X. W. Dong, *Chem. Commun*. **2000**, 1483; S. R. Gilbertson, D. G. Genov, A. L. Rheingold, *Org. Lett*. **2000**, *2*, 2885; Y. Hashimoto, Y. Horie, M. Hayashi, K. Saigo, *Tetrahedron: Asymmetry* **2000**, *11*, 2205; A. J. Hennessy, D. J. Connolly, Y. M. Malone, P. J. Guiry, *Tetrahedron Lett*. **2000**, *41*, 7757; A. J. Hennessy, Y. M. Malone, P. J. Guiry, *Tetrahedron Lett*. **2000**, *41*, 2261; M. Ogasawara, K. Yoshida, T. Hayashi, *Heterocycles* **2000**, *52*, 195; K. Selvakumar, M. Valentini, P. S. Pregosin, A. Albinati, F. Eisentrager, *Organometallics* **2000**, *19*, 1299; L. F. Tietze, K. Thede, *Synlett* **2000**, 1470; A. J. Hennessy, Y. M. Malone, P. J. Guiry, *Tetrahedron Lett*. **1999**, *40*, 9163; L. F. Tietze, K. Thede, F. Sannicolo, *Chem. Commun*. **1999**, 1811; M. Tschoerner, P. S. Pregosin, A. Albinati, *Organometallics* **1999**, *18*, 670.
[5] T. Hayashi, A. Kubo, F. Ozawa, *Pure Appl. Chem*. **1992**, *64*, 421; F. Ozawa, T. Hayashi, *J. Organomet. Chem*. **1992**, *428*, 267; F. Ozawa, A. Kubo, T. Hayashi, *Tetrahedron Lett*. **1992**, *33*, 1485; F. Ozawa, A. Kubo, Y. Matsumoto, T. Hayashi, E. Nishioka, K. Yanagi, K. Moriguchi, *Organometallics* **1993**, *12*, 4188.
[6] R. C. Larock, W. H. Gong, *J. Org. Chem*. **1990**, *55*, 407.
[7] O. Loiseleur, M. Hayashi, M. Keenan, N. Schmees, A. Pfaltz, *J. Organomet. Chem*. **1999**, *576*, 16; O. Loiseleur, M. Hayashi, N. Schmees, A. Pfaltz, *Synthesis* **1997**, 1338; O. Loiseleur, P. Meier, A. Pfaltz, *Angew. Chem., Int. Ed.* **1996**, *35*, 200.
[8] J. M. Brown, K. K. Hii, *Angew. Chem., Int. Ed.* **1996**, *35*, 657; C. Amatore, E. Carre, A. Jutand, M. A. Mbarki, G. Meyer, *Organometallics* **1995**, *14*, 5605; W. A. Herrmann, C. Brossmer, K. Ofele, M. Beller, H. Fischer, *J. Organomet. Chem*. **1995**, *491*, C 1.
[9] a) B. L. Shaw, *New J. Chem*. **1998**, *22*, 77; b) B. L. Shaw, S. D. Perera, E. A. Staley, *Chem. Commun*. **1998**, 1361; Milstein; c) A. Sundermann, O. Uzan, J. M. L. Martin, *Chem. – Eur. J.* **2001**, *7*, 1703.
[10] A. Biffis, M. Zecca, M. Basato, *Eur. J. Inorg. Chem*. **2001**, 1131; F. Y. Zhao, M. Shirai, M. Arai, *J. Mol. Catal., A* **2000**, *154*, 39; J. H. Ding, D. L. Gin, *Chem. Mater.* **2000**, *12*, 22; M. T. Reetz, E. Westermann, *Angew. Chem., Int. Ed*. **2000**, *39*, 165.
[11] J. M. Brown, J. J. Perez-Torrente, N. W. Alcock, H. J. Clase, *Organometallics* **1995**, *14*, 207.
[12] M. Ludwig, S. Stromberg, M. Svensson, B. Akermark, *Organometallics* **1999**, *18*, 970.
[13] C. S. Shultz, J. Ledford, J. M. DeSimone, M. Brookhart, *J. Am. Chem. Soc*. **2000**, *122*, 6351; D. J. Tempel, L. K. Johnson, R. L. Huff, P. S. White, M. Brookhart, *J. Am. Chem. Soc*. **2000**, *122*, 6686.
[14] R. J. Deeth, A. Smith, K. K. Hii, J. M. Brown, *Tetrahedron Lett*. **1998**, *39*, 3229.
[15] D. W. Price, M. G. B. Drew, K. K. Hii, J. M. Brown, *Chem.–Eur. J.* **2000**, *6*, 4587.
[16] L. R. Domingo, *Eur. J. Org. Chem*. **2000**, 2265; L. R. Domingo, M. Arno, J. Andres, *J. Org. Chem*. **1999**, *64*, 5867.
[17] K. Albert, P. Gisdakis, N. Rosch, *Organometallics* **1998**, *17*, 1608.
[18] W. Lesueur, E. Solari, C. Floriani, A. Chiesi-Villa, C. Rizzoli, *Inorg. Chem*. **1997**, *36*, 3354.
[19] A. Smith, Ph.D. Thesis, Warwick University, 2001.
[20] K. K. Hii, unpublished work.
[21] A. Jutand, K. K. M. Hii, M. Thornton-Pett, J. M. Brown, *Organometallics* **1999**, *18*, 5367.
[22] ADF version 2.3.0, Theoretical Chemistry, Vrije Universiteit, Amsterdam, Netherlands, 1997.
[23] A. D. Becke, *Phys. Rev. A: At., Mol., Opt. Phys.* **1988**, *38*, 3098.
[24] J. P. Perdew, *Phys. Rev. B: Condens. Matter* **1986**, *33*, 8822.
[25] E. J. Baerends, D. E. Ellis, P. Ros, *Theor. Chim. Acta* **1972**, *27*, 339.

[26] J. L. Spencer, *Inorg. Synth*. **1976**, *19*, 214.
[27] P. L. Alsters, J. Boersma, G. van Koten, *Organometallics* **1993**, *12*, 1629.
[28] F. T. Oakes, J. F. Sebastian, *J. Org. Chem*. **1980**, *45*, 4959.

*Received June 14, 2001*