ELSEVIER

Journal of Molecular Catalysis A: Chemical 196 (2003) 65–81

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

From 2,3-dihydrofuran to 2,2-dialkyl-2,3-dihydrofurans: new substrates for the intermolecular asymmetric Heck reaction

Tim G. Kilroy, Alan J. Hennessy, David J. Connolly, Yvonne M. Malone, Annette Farrell, Patrick J. Guiry*

Centre for Synthesis and Chemical Biology, Conway Institute of Biomolecular and Biomedical Research, Department of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland

Received 9 July 2002; accepted 22 September 2002

Abstract

Palladium complexes of heterobidentate ferrocene-containing ligands were tested as catalysts in asymmetric intermolecular Heck reactions employing 2,3-dihydrofuran as the substrate and afforded a mixture of products in various ratios depending on the choice of ligand and the conditions employed. The favoured kinetic isomer was obtained in enantioselectivities of up to 99%. Dihydrofurans disubstituted at the 2-position were postulated as new substrates as they form a single regioisomeric product, thus providing a true comparative test of enantioselectivity of a range of palladium complexes. The synthesis of 2,2-dimethyl-2,3-dihydrofuran and 2,2-diethyl-2,3-dihydrofuran and their application in the intermolecular asymmetric Heck reaction with both diphosphine and phosphinamine ligands is also described. For both phenylation and cyclohexenylation of 2,3-dihydrofuran and 2,2-dimethyl-2,3-dihydrofuran the *t*-Bu substituted diphenylphosphinoferrocenyloxazoline ligand gave best results. The use of 2,2-diethyl-2,3-dihydrofuran as substrate demonstrated that the increased bulk at the 2-position had a deleterious effect on both the chemical yields and ees in phenylations and cyclohexenylations although enantioselectivities of 94 and 93% were obtained, respectively.

Keywords: Intermolecular asymmetric Heck; Chiral heterobidentate ligands; New 2,3-dihydrofuran substrates

1. Introduction

The Heck reaction is a versatile and useful palladium-catalysed elaboration of substituted alkenes by direct C–C bond formation at a vinylic carbon centre [1–3]. Its potential has been exploited in the key steps of many total syntheses [4] and a better understanding of the reaction mechanism continues to emerge [5–8]. Both intramolecular and intermolecular asymmetric variants have been extensively studied and have been the subject of numerous reviews [9–13]. The initial substrate employed by Ozawa et al. [14] in asymmetric intermolecular arylation studies was the cyclic olefin, 2,3-dihydrofuran **1** [14]. The asymmetric induction obtained was due to Pd complexes of (*R*)-BINAP **2** and a mixture of regioisomers **3** and **4** were obtained, with the thermodynamic product **4** being formed in 96% ee, favoured over the kinetic product **3** in a 71:29 ratio when 1,8-bis(dimethylamino)naphthalene (proton sponge) was used as the base (Scheme 1). Since that initial report a range of diphosphine ligands have been employed and two of the more recent examples include the application of BINAPFu by Andersen et al. [15]

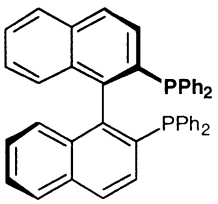
* Corresponding author. Tel.: +353-1-716-2309; fax: +353-1-716-2127.
E-mail address: p.guiry@ucd.ie (P.J. Guiry).

1381-1169/02/$ – see front matter © 2002 Elsevier Science B.V. All rights reserved.
PII: S1381-1169(02)00635-0

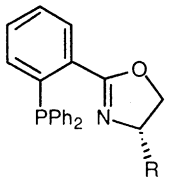
and BITIANP by Tietze et al. [16]. Palladium complexes of the former outperformed BINAP although mixtures of regioisomeric products were still obtained whilst in contrast, complexes of the latter afforded the 2,3-dihydrofuran **4** with complete regioselectivity and high enantioselectivity.

Pfaltz and co-workers [17,18] described the application of diphenylphosphinooxazoline ligands of type **5** to the arylation and alkenylation of substrate **1** with complexes of the *t*-butyl-substituted oxazoline **5b** affording both the best enantioselectivities and catalyst activity. In contrast to the regioisomer problem observed by Hayashi, the phenylation of dihydrofuran **1** produced only (*R*)-**3** in 97% ee. Since that study a range of oxazoline-containing phosphinamine ligands have been applied to this reaction with similar levels of regioselectivity and high enantioselectivities by the groups of Gilbertson and co-workers [19,20] Hashimoto et al. [21]. Related (phosphinophenyl)benzoxazine ligands from Kündig and Meier [22] and *iso*-PINPHOS ligands from Malkov et al. [23] followed the same pattern of both high regioselectivity and enantioselectivity.

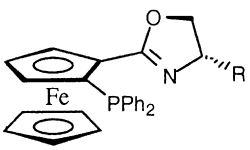
Metal complexes of ferrocene-based planar chiral ligands have proven to be highly effective in a range of catalytic asymmetric transformations [24]. Diphenylphosphinoferrocenyloxazolines **6** were first reported by the groups of Nishibayashi and Uemura [25] and Richards et al. [26]. These ligands have been successfully applied in the ruthenium- and iridium-catalysed hydrosilylation of imines and ruthenium-catalysed hydrosilylation of ketones with ees up to 97% [27,28]. We had independently synthesised these ligands and achieved ees of up to 92% using ligand **6b** in the palladium-catalysed allylic alkylation of 1,3-diphenyl-propenylacetate [29] and up to 72% ee in the allylic amination of ethyl (2*E*)-1,3-diphenylprop-2-enyl carbonate [30]. This led us to believe that these ligands would have potential in the Pd-catalysed asymmetric intermolecular Heck reaction. We wished to compare ligands **6** with those of Pfaltz and co-workers as both have the same amino-alcohol derived oxazoline chiral directing group with ligands **6** possessing the extra element of planar chirality on the ferrocene group. Whilst our work was underway, Deng et al. [31] successfully applied the related 2′-substituted 1,1′-P,N-ferrocene ligand **7** to the phenylation of 2,3-dihydrofuran in THF but reported that ligands **6** were inactive in this solvent after 24 h [31]. We first reported our initial findings on the application of ligands **6** in the intermolecular asymmetric Heck [32] subsequent to a similar preliminary report from Soulsby and Sammakia [33]. In addition, we recently reported the preparation of a novel planar chiral ferrocene-containing ligand **8** which possesses a C2-symmetric *trans*-2,5-dimethylpyrrolidine unit and its application in the palladium-catalysed allylic alkylation of 1,3-diphenyl-propenylacetate [34]. We now wish to report in full our results on the application of palladium complexes of ligands **6a** and **6b** and **8** to the phenylation of 2,3-dihydrofuran **1** and on the synthesis and employment of new substrates for the asymmetric intermolecular Heck reaction.



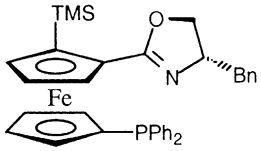
2



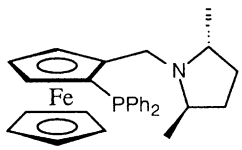
5a: R = *i*-Pr
5b: R = *t*-Bu



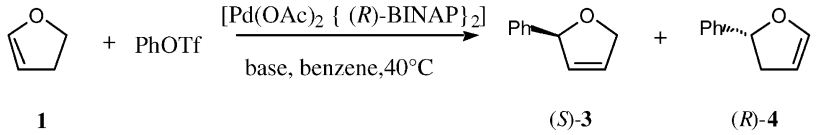
6a: R = *i*-Pr
6b: R = *t*-Bu



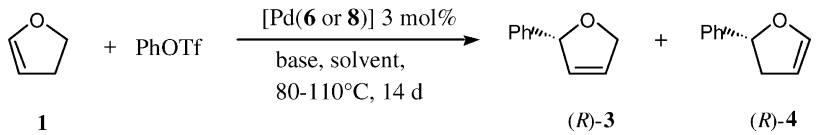
7



8



Scheme 1.



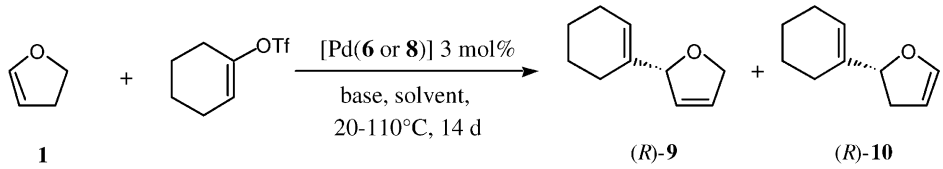
Scheme 2.

The results of our investigations on the phenylation of 2,3-dihydrofuran **1** are given in Table 1. Using palladium complexes (3 mol%) formed in situ from $Pd(dba)_2$ and diphenylphosphinoferrocenyloxazoline ligands **6a** and **6b** and ligand **8**, phenylation gave (*R*)-5-phenyl-2,5-dihydrofuran **3** as the major product in consistently good to excellent ees but only in reasonable to moderate yields (Scheme 2). After variation of solvent and base our optimal results were achieved using ligand **6b,** which gave enantioselectivities of up to 99%. Carrying out the reaction in benzene at reflux with the palladium complex of the *i*-Pr-substituted ligand **6a** gave poor yields (9–20%) with high enantioselectivities of 90–92% (entries 1 and 2). A change of solvent to toluene at reflux led to an increase of chemical yields (70–72%) of the kinetic product **3** with minor amounts of product **4** also being formed (4–6%). However, the increase in chemical yields was accompanied by a decrease in enantioselectivities to 59 and 69% (entries 3 and 4) using proton sponge and Hünig's base, respectively. Changing the ligand to the bulkier *t*-butyl-substituted analogue **6b** led to an increase in both reactivity and enantioselectivity, a feature already noted in the original work of Pfaltz and co-workers [17]. Employing benzene as solvent and proton sponge as base gave a mixture of regioisomers with the more favoured product **3** being obtained in 99% ee (entry 5). Using Hünig's base led to **3** as the

Table 1
Asymmetric phenylation of 2,3-dihydrofuran **1** catalysed by Pd complexes of **6** or **8**

Entry	Ligand	Solvent	Base	Temperature (°C)	Yield (%)[a] (*R*)-**3** ((*R*)-**4**)	Ee (%)[b] (*R*)-**3**
1	**6a**[c]	Benzene	Proton sponge	80	20 (1)	92
2	**6a**[c]	Benzene	*i*-Pr_2NEt	80	9 (–)	90
3	**6a**[c]	Toluene	Proton sponge	110	70 (4)	59
4	**6a**[c]	Toluene	*i*-Pr_2NEt	110	72 (6)	69
5	**6b**[c]	Benzene	Proton sponge	80	38 (12)	99
6	**6b**[c]	Benzene	*i*-Pr_2NEt	80	19 (–)	99
7	**6b**[c]	Benzene	Et_3N	80	40 (–)	98
8	**6b**[c]	Toluene	Proton sponge	110	61 (–)	98
9	**6b**[c]	Toluene	*i*-Pr_2NEt	110	52 (21)	99
10	**6b**[c]	Toluene	Et_3N	110	57 (6)	98
11	**8**[c]	Benzene	Proton sponge	80	17 (7)	16 (*S*)
12	**8**[c]	Toluene	Proton sponge	110	24 (10)	17 (*S*)

[a] Conversions by GC (SE-30, 30 m, 11 psi He).
[b] Enantiomeric excesses were determined by GC on a Chiraldex γ-cyclodextrin TFA capillary column (30 m × 0.25 m, 15 psi He); 80 °C, 0.3 °C/min up to 90 °C, 5 °C/min up to 130 °C, (t_R = 31.80 (*S*) and 34.0 (*R*) min) for **3** and t_R = 23.30 (*S*) and 24.6 (*R*) min) for **4**).
[c] Pd^0 complexes formed in situ from $Pd(dba)_2$ and phosphinamines **5**, **6** and **8**.



Scheme 3.

single product, again with excellent enantioselectivity (99%), albeit in a low yield of 19% (entry 6). A change to triethylamine afforded similar regio- and enantioselectivity and an increase in yield to 40% (entry 7). Reaction conditions of toluene at reflux, using proton sponge as base gave our best result of 61% yield of **3** alone in 98% ee (entry 8). The use of other bases such as Hünig's or triethylamine led to mixtures of regioisomeric products **3** and **4** with high ees of **3** being consistently observed (entries 9 and 10). The use of the novel ligand **8** in this transformation gave disappointingly poor regioselectivities, yields and enantioselectivites. The best result using this ligand was a 24% yield of **3** in 17% ee, with 10% yield of **4** also being obtained (entry 12). The poor reactivity of this ligand, even after 14 days, is typical of P–N ligands containing a basic nitrogen donor [10] and the poor enantioselectivity can be attributed to a mismatch between the planar and central elements of chirality [34].

The asymmetric cyclohexenylation of 2,3-dihydrofuran **1** was also studied employing palladium complexes of ligands **6** and **8** (Scheme 3) and the results obtained are given in Table 2.

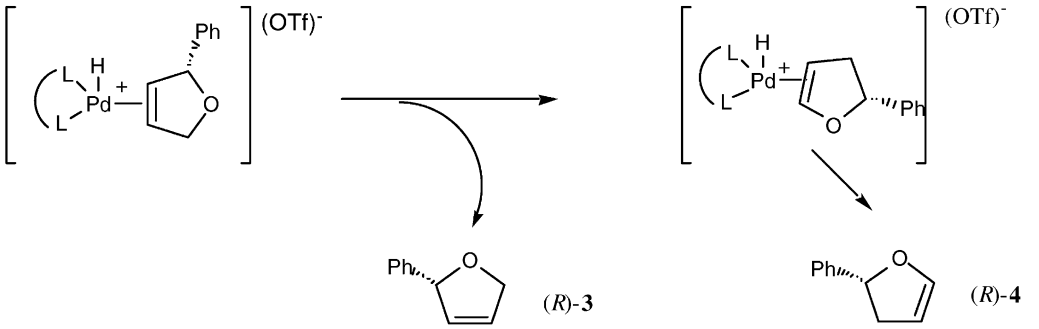
Typically, the cyclohexenylation of **1** is a slower process than the corresponding phenylation and this is also true in our study where poorer yields in general were obtained. The optimal result employing ligand **6a** was in toluene at reflux with Hünig's base where both regioisomeric products **9** and **10** were obtained with the former being the favoured product in an ee of 68% (entry 3). As in the phenylation of **1**, the change to the bulkier ligand **6b** led to a more reactive catalyst system with both regioisomeric products being formed in higher yields and enantioselectivities (entries 5–7). Use of the more forcing conditions of toluene at reflux was required for the obtention of reasonable yields and the use of proton sponge as base gave an 85% ee of the favoured (*R*)-enantiomer of product **9** in 75% yield. The minor product **10** was formed in 18% yield and in an ee of 77%, again favouring the (*R*)-enantiomer (entry 6). As in the phenylation studies detailed in Table 1, the use of catalyst systems derived from ligand **8** gave disappointing yields and enantioselectivities (entries 8 and 9).

One explanation for the difference in product distribution between catalyst systems derived from

Table 2
Asymmetric cyclohexenylation of 2,3-dihydrofuran **1** catalysed by Pd complexes of **6** or **8**

Entry	Ligand	Solvent	Base	Temperature (°C)	Yield (%)[a] (*R*)-**9** ((*R*)-**10**)	Ee (%)[b] (*R*)-**9** ((*R*)-**10**)
1	**6a**[c]	Benzene	Proton sponge	80	51 (7)	35 (20)
2	**6a**[c]	Toluene	Proton sponge	110	21 (2)	65 (–)
3	**6a**[c]	Toluene	*i*-Pr_2NEt	110	24 (9)	68 (11)
4	**6a**[c]	Toluene	Et_3N	110	20 (–)	43 (–)
5	**6b**[c]	Benzene	Proton sponge	80	49 (18)	76 (82)
6	**6b**[c]	Toluene	Proton sponge	110	75 (18)	85 (77)
7	**6b**[c]	Toluene	Et_3N	80	31 (20)	64 (32)
8	**8**[c]	Benzene	Proton sponge	20	7 (–)	12 (*S*) (–)
9	**8**[c]	Benzene	Proton sponge	40	3 (8)	8 (*S*) (6 (*S*))

[a] Conversions by GC (SE-30, 30 m, 11 psi He).
[b] Enantiomeric excesses were determined by GC on a Chiraldex γ-cyclodextrin TFA capillary column (30 m × 0.25 m, 15 psi He); 80 °C, 0.3 °C/min up to 90 °C, 5 °C/min up to 130 °C, (t_R = 22.20 (*S*) and 24.9 (*R*) min) for **9** and t_R = 18.0 (*S*) and 18.3 (*R*) min) for **10**).
[c] Pd^0 complexes formed in situ from $Pd(dba)_2$ and phosphinamines **5**, **6** and **8**.



Scheme 4.

diphosphines and phosphinamines is that the initial olefin-bound complex, formed after migratory insertion and β-elimination, is more prone to dissociation to give **3** in Pd{P-N} catalyst systems than in the Pd{P-P} catalyst system, where a reverse β-elimination followed by β-elimination and dissociation affords **4** (Scheme 4).[1]

Mechanistically, it is clear that product **4** can only be formed when there is a H-substituent at C-2. A dihydrofuran disubstituted at this position would be a substrate which would provide a true comparative test of reactivity and enantioselectivity for a range of Pd complexes. This is not the case using substrate **1** as the final isomer ratio and enantioselectivities are complicated by kinetic resolution processes [35].

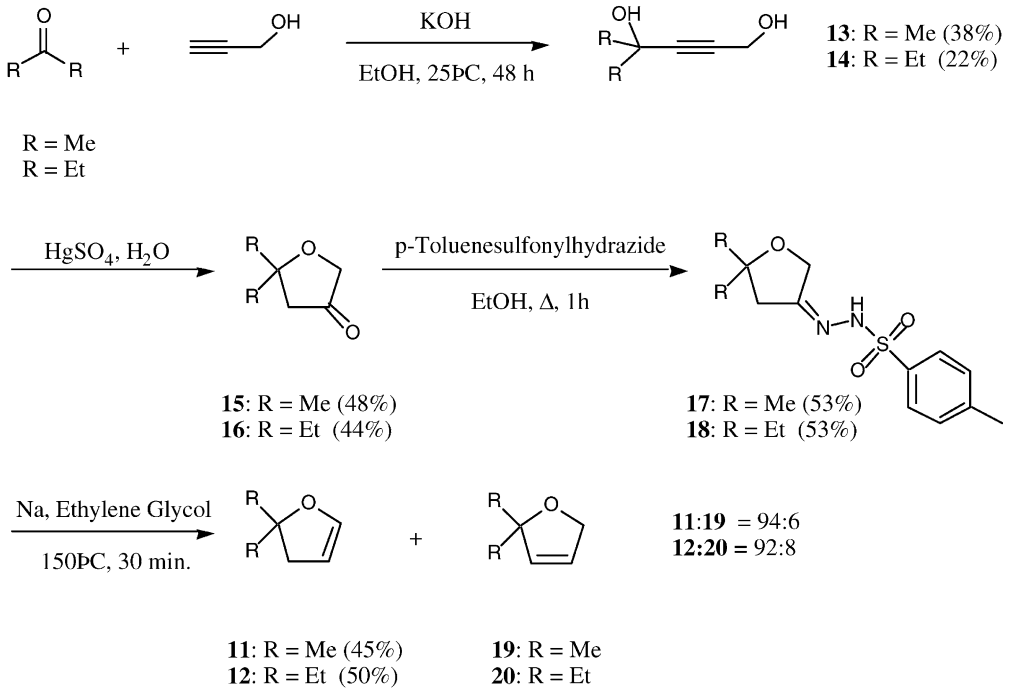
Therefore, 2,2-dimethyl-2,3-dihydrofuran **11** and its 2,2-diethyl analogue **12** were chosen as new substrates for the intermolecular asymmetric Heck reaction as such disubstituted substrates would allow for a simple and direct comparison of various ligands in this reaction as only one regioisomeric product can be formed.

2. Synthesis of new heck reaction substrates

The required 2,3-dihydrofurans **11** and **12** were prepared in four steps from propargylic alcohol and acetone and pentan-3-one, respectively, using a method of dihydrofuran preparation reported by Gianturco et al. [36] (Scheme 5).

The first step in their synthesis was the base-promoted addition of propargylic alcohol to either acetone or pentan-3-one which gave the corresponding diols **13** and **14** in low yields of 38 and 22%, respectively, after distillation [37]. The next step involved the mercuric sulfate-catalysed hydration of these diols and subsequent cyclisation. After work-up, which included steam distillation, extraction and distillation, furanones **15** and **16** were obtained in 48 and 44% yields, respectively. These furanones were subsequently converted to their tosylhydrazones **17** and **18**, by treatment with *p*-toluenesulfonylhydrazide, in 53% yield after recrystallisation from ethanol. The final step involved a Bamford–Stevens reaction in which base, generated from sodium and ethylene glycol, eliminated the tosylhydrazone group to form dihydrofurans as product [38]. The regioisomeric dihydrofurans **11** and **19** were distilled from the reaction mixture in 45% yield with the desired 2,2-dimethyl-2,3-dihydrofuran isomer **11** being formed in a 94:6 ratio over 2,2-dimethyl-2,5-dihydrofuran **19**. This ratio was calculated from the ^{1}H NMR integration of the alkene protons of the two products. The H-4 and H-5 alkene protons of **11** resonate at 4.62 and 6.20 ppm, respectively. The H-5 methylene protons of **19** resonate at 4.64 ppm while its alkene protons appear at 5.50 ppm. In a similar fashion, the 2,2-diethyl analogues **12** and **20** were obtained although with slightly higher regioselectivity of 92:8 favouring the required dihydrofuran **12**. As the experimental conditions employed in the intermolecular Heck reaction uses a five-fold excess of dihydrofuran and because **11** or **12** is more reactive than **19** or **20** these mixtures were used as substrates without further purification.

[1] One intermediate **9** is shown for clarity and (*S*)-**3** and (*S*)-**4** are formed in a similar manner from the C2-epimer of **9**.

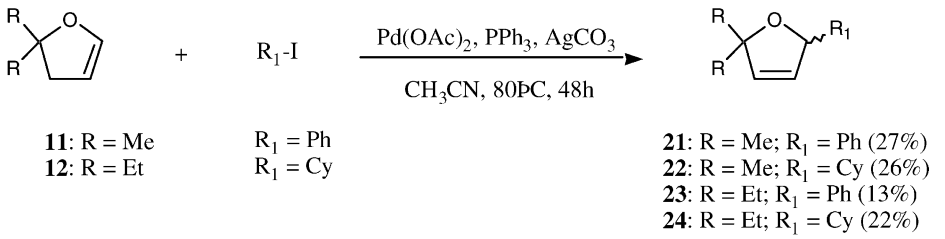


Scheme 5.

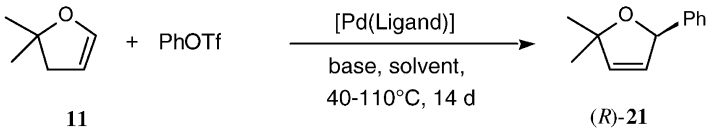
3. Synthesis of racemic Heck reaction products

The Heck reaction products of the phenylation and cyclohexenylation of these new substrates **11** and **12** were synthesised racemically prior to the investigations of asymmetric reactions. Thus, **11** and **12** were phenylated according to Larock's protocol for making 2-phenyl-2,5-dihydrofuran and not the conditions for making the isomeric 2-phenyl-2,3-dihydrofuran (Scheme 6) [39]. Both methods work because only one product can be formed but the work-up and product purification is simpler using the former method. The synthesis of 2,2-dimethyl-5-phenyl-2,5-dihydrofuran **21** and its 2,2-dimethyl-5-cyclohexenyl analogue **22** proceeded in 27 and 26% yields, respectively, after purification by column chromatography. In a similar manner, 2,2-diethyl-5-phenyl-2,5-dihydrofuran **23** and its 2,2-diethyl-5-cyclohexenyl analogue **24** were prepared in 13 and 22% yields, respectively.

These yields are low and unoptimised but nevertheless afforded sufficient quantities of pure compounds for the obtention of baseline separated peaks for each enantiomer by chiral gas chromatography using a γ-cyclodextrin-TFA chiral capillary column.



Scheme 6.



11 (*R*)-**21**

Scheme 7.

4. Asymmetric phenylation of 2,2-dimethyl-2,3-dihydrofuran (11)

We now report in full our findings on the phenylation of 2,2-dimethyl-2,3-dihydrofuran **11** with palladium complexes derived from a range of chiral ligands, from diphosphine BINAP **2**, to the diphenylphosphinoaryl-oxazolines **5** and diphenylphosphinoferrocenyloxazolines **6** (Scheme 7, Table 3) [40].

Using Pd^0 complexes (3 mol%) formed in situ from $Pd(OAc)_2$ and (*R*)-BINAP **2**, phenylation gave (*R*)-2,2-dimethyl-5-phenyl-2,5-dihydrofuran **21** in consistently good ees and in good yield, except when proton sponge was used as base. The chemical yields observed using catalysts prepared in situ from $Pd_2(dba)_3$ and diphenylphosphinoaryloxazoline ligand **5a** were poor although the ees improved to 81% (entry 5). As in the study by Pfaltz and co-workers the more sterically demanding *tert*-butyl substituted ligand **5b** afforded a more reactive catalyst and ees in the range 89–92% were obtained with benzene being the best solvent (entries 6 and 7). A change to diphenylphosphinoferrocenyloxazoline ligand **6a** gave similar ees and chemical yields to **5a** (entries 8 and 9). Our best results were obtained using ligand **6b** although the chemical yields were highly dependent on the base employed. Proton sponge gave poor chemical yields but consistently high ees whereas Hünig's base gave 98% ee in 68% yield and triethylamine gave our optimal result of 98% ee in 90% yield (entry 12). This contrasts with the work of Hayashi and co-workers where proton sponge gave the highest ee and Hünig's base and triethylamine afforded lower ee values (82 and 75%, respectively) [14].

Table 3
Asymmetric phenylation of furan **11** catalysed by Pd complexes of **6** or **8**

Entry	Ligand	Solvent	Base	*T* (°C)	Yield (%)[a]	Ee (%)[b] (configuration)[c]
1	**2**[d]	Benzene	Proton sponge	40	52	76 (*R*)
2	**2**[d]	Benzene	*i*-Pr_2NEt	40	100	76 (*R*)
3	**2**[d]	Benzene	Et_3N	40	95	70 (*R*)
4	**5a**[e]	Toluene	Proton sponge	110	13	76 (*R*)
5	**5a**[e]	Benzene	Proton sponge	80	23	81 (*R*)
6	**5b**[e]	Toluene	Proton sponge	110	37	89 (*R*)
7	**5b**[e]	Benzene	Proton sponge	80	100	92 (*R*)
8	**6a**[e]	Toluene	Proton sponge	110	34	78 (*R*)
9	**6a**[e]	Benzene	Proton sponge	80	42	79 (*R*)
10	**6b**[e]	Benzene	Proton sponge	80	27	95 (*R*)
11	**6b**[e]	Benzene	*i*-Pr_2NEt	80	68	98 (*R*)
12	**6b**[e]	Benzene	Et_3N	80	90	98 (*R*)
13	**6b**[e]	Toluene	Proton sponge	110	57	92 (*R*)
14	**6b**[e]	Toluene	*i*-Pr_2NEt	110	45	92 (*R*)

[a] Conversions by GC (SE-30, 30 m, 11 psi He), 50 °C for 4 min, 15 °C/min up to 170 °C, t_R = 13.5 min for for product **21** and t_R = 14.1 min for tridecane.

[b] Enantiomeric excesses were determined by GC on a Chiraldex γ-cyclodextrin TFA capillary column (30 m × 0.25 m, 15 psi He); 80 °C, 0.3) C/min up to 90 °C, 5 °C/min up to 110 °C, (t_R = 29.6 (*S*) and 30.9 (*R*) min) for **21**.

[c] Absolute configuration shown assumes the same sense of asymmetric induction as with 2,3-dihydrofuran as the optical rotation was also (+) and the (*R*)-isomer had the longer retention time.

[d] Pd^0 complexes formed in situ from $Pd(OAc)_2$ and (*R*)-BINAP.

[e] Pd^0 complexes formed in situ from $Pd_2(dba)_3$ and phosphinamines **5**, **6**.

This work highlights 2,2-dimethyl-2,3-dihydrofuran as a new and useful substrate for the asymmetric Heck reaction which allows easy and direct comparison of a wide range of ligands. Our optimal result in the intermolecular phenylation of 2,2-dimethyl-2,3-dihydrofuran was 98% ee with diphenylphosphinoferrocenyloxazoline ligand **6b**.

5. Asymmetric cyclohexenylation of 2,2-dimethyl-2,3-dihydrofuran

The asymmetric intermolecular Heck alkenylation of 2,3-dihydrofuran **1** was first reported by Hayashi and co-workers who employed palladium complexes of (*R*)-BINAP **2** [41]. In light of the success of 2,2-dimethyl-2,3-dihydrofuran **11** as a substrate for asymmetric phenylation we wished to investigate the use of this substrate in asymmetric cyclohexenylation [42]. The ligands which we screened were (*R*)-BINAP **2**, the diphenylphosphinoaryloxazolines **5** and the diphenylphosphinoferrocenyloxazolines **6**. The results obtained using these ligands in the test reaction of **11** with cyclohex-1-en-1-yl trifluoromethanesulfonate (Scheme 8) are given in Table 4.

The first experiments used palladium complexes of (*R*)-BINAP **2** generated in situ from $Pd(OAc)_2$ and **2**. The yields of (*R*)-5-cyclohex-1′-en-1′-yl-2,2-dimethyl-2,5-dihydrofuran **22** were moderate (34–52%, entries 1–3) and the ees obtained were poor (optimised to 37% using $N(i\text{-}Pr)_2Et$ as base). With the pre-formed Pd(0)-BINAP catalyst yields were even lower (12–15%, entries 4–6) and an optimal ee of 35% was attained using proton sponge as base. These results compare poorly with those obtained by Hayashi and co-workers using 2,3-dihydrofuran **1** as substrate [41]. This lowered enantioselectivity was not observed in the phenylation of 2,2-dimethyl-2,3-dihydrofuran **11** as similar ees in the range 70–76% were observed.

Table 4
Asymmetric cyclohexenylation of **11** catalysed by Pd complexes of **2**, **5** and **6**.

Entry	Ligand	Base	Yield (%)[a]	Ee (%)[b] (configuration)[c]
1	**2**[d]	Proton sponge	34	19 (*R*)
2	**2**[d]	$i\text{-}Pr_2NEt$	44	37 (*R*)
3	**2**[d]	Et_3N	52	18 (*R*)
4	**2**[e]	Proton sponge	12	35 (*R*)
5	**2**[e]	$i\text{-}Pr_2NEt$	15	16 (*R*)
6	**2**[e]	Et_3N	13	18 (*R*)
7	**5a**[f]	Proton sponge	33	83 (*R*)
8	**5a**[f]	$i\text{-}Pr_2NEt$	13	22 (*R*)
9	**5a**[f]	Et_3N	23	22 (*R*)
10	**5b**[f]	Proton sponge	68	97 (*R*)
11	**5b**[f]	$i\text{-}Pr_2NEt$	60	40 (*R*)
12	**5b**[f]	Et_3N	26	38 (*R*)
13	**6a**[f]	Proton sponge	19	76 (*R*)
14	**6a**[f]	$i\text{-}Pr_2NEt$	17	22 (*R*)
15	**6b**[f]	Proton sponge	88	73 (*R*)
16	**6b**[f]	$i\text{-}Pr_2NEt$	73	87 (*R*)

[a] Conversions by GC (SE-30, 30 m, 11 psi He), 50 °C for 4 min, 15 °C/min up to 170 °C, t_R = 13.2 min for product **22** and t_R = 14.1 min for tridecane.

[b] Enantiomeric excesses were determined by GC on a Chiraldex γ-cyclodextrin TFA capillary column (30 m × 0.25 m, 15 psi He); 80 °C, 0.3 °C/min up to 90 °C, 5 °C/min up to 130 °C, (t_R = 22.0 (*S*) and 22.6 (*R*) min) for **22**.

[c] Absolute configuration shown assumes the same sense of asymmetric induction as with 2,3-dihydrofuran by comparison of the optical rotations of **22** and an enantiopure sample of (*R*)-**22** [43].

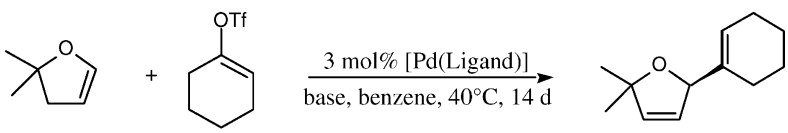
[d] Pd^0 complexes formed in situ from $Pd(OAc)_2$ and (*R*)-BINAP.

[e] Pd^0 BINAP complexes pre-formed.

[f] Pd^0 complexes formed in situ from $Pd_2(dba)_3$ and phosphinamines **5** and **6**.

This may be due to increased ligand–reactant steric interactions in the migratory insertion transition state caused by both a bulkier alkene (**11** versus **1**) and a bulkier nucleophilic component (cyclohexenyl versus phenyl) when BINAP is the ligand.

The next catalysts tested were generated in situ from $Pd(dba)_2$ and the diphenylphosphinoaryloxa-



11 (*R*)-**22**

Scheme 8.

zolines **5** and **6**, respectively. The catalyst derived from the *i*-Pr substituted ligand **5a** exhibited low reactivity (13–33% yield, entries 7–9) but a marked improvement in enantioselectivity of up to 83% when proton sponge was the base (entry 7). With the *t*-Bu substituted ligand **5b** a more reactive catalyst was formed and the chemical yield increased to 68% with an optimal ee of 97% (entry 10). For complexes derived from **5a** and **5b**, proton sponge gave both higher chemical yields and enantioselectivities compared to the trialkylamines tested. These results contrast with the work of Pfaltz and co-workers who reported excellent ees (>98%) and yields (>92%) with a variety of amine bases in the cyclohexenylation of 2,3-dihydrofuran **1** [43].

As palladium complexes of the analogous diphenylphosphinoferrocenyloxazoline ligands **6** gave ees of up to 98% in the phenylation of dihydrofuran **11** it was of interest to test them in asymmetric cyclohexenylations. Complexes derived from the *i*-Pr substituted ligand **6a** once again gave poor yields (17–19%, entries 13 and 14) and an optimum enantioselectivity of 76% when proton sponge was used as base (entry 13). The palladium catalyst prepared from the *t*-Bu substituted ligand **6b** gave improved yields (73–88%) and high ees (73–87%), which were not as dependent upon the choice of base as complexes made from **5a**, **5b** or **6a** were. The highest ee was still lower than that observed when ligand **5b** was employed (87 versus 97%). In addition, the catalyst derived from **6b**, which gave our best ee in the corresponding phenylation of 2,2-dimethyl-2,3-dihydrofuran **11**, was not as successful in the corresponding cyclohexenylation of the same substrate (98 versus 87%).

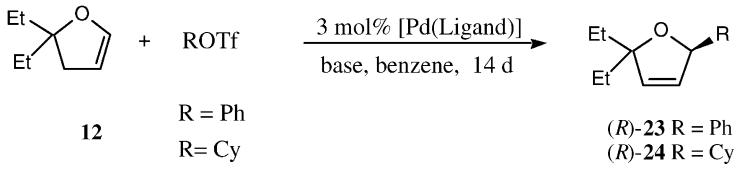
The reasons why complexes derived from ligand **6b** are superior to those from ligand **5b** for the phenylation and not the cyclohexenylation of **11** and the greater reactivity and selectivity of the palladium complexes from *t*-Bu substituted ligands (**5b**, **6b**) compared to the *i*-Pr substituted ligands (**5a**, **6a**) underline how the electronic and steric properties of ligands must be finely tuned for individual substrates. To date a ligand which provides the maximum reactivity and selectivity across a wide range of substrates remains elusive.

In conclusion, catalysts derived from a range of ligands have been directly compared in the asymmetric cyclohexenylation of 2,2-dimethyl-2,3-dihydrofuran **11**. The diphosphine (*R*)-BINAP **2** gave poor results in comparison to use of 2,3-dihydrofuran **1** as substrate, regardless of whether it was made in situ or pre-formed. More reactive and more enantioselective catalysts were derived from phosphinamine ligands and our highest enantioselectivity of 97% was obtained using complexes derived from the *t*-butyl substituted diphenylphosphinoaryloxazoline ligand **5b**. The choice of amine base was also crucial for both diphosphine and phosphinamine chelating ligands with proton sponge giving better results than trialkylamines.

6. Asymmetric phenylation and cyclohexenylation of 2,2-diethyl-2,3-dihydrofuran 12

In light of the success of the phenylation of 2,2-dimethyl-2,3-dihydrofuran **11**, it was of interest to determine whether the extra steric hindrance caused by the larger ethyl groups in the 2-position in 2,2-diethyl-2,3-dihydrofuran **12** would effect the yields and selectivity in its phenylation and cyclohexenylation catalysed by palladium complexes of ligands **2**, **5** and **6** (Scheme 9) [44]. The reactions were carried out using identical reaction conditions to those used for substrate **11** for comparative purposes and the results obtained are given in Table 5.

The yields obtained with palladium complexes of (*R*)-BINAP **2** were low and the enantioselectivities were moderate (54–64%). This compares unfavourably to the yields of 52–100% and ees of 70–76% obtained in the phenylation of dihydrofuran **11**. The yield using the *i*-Pr-substituted diphenylphosphinoaryloxazoline ligand **5a** was low (16%) and only a moderate ee was achieved in contrast to when **11** was used as substrate (44 versus 81%). The yield increased when the *t*-Bu-substituted analogue **5b** was tested, as was noted with **11**, and a moderate ee (50%) was achieved with $N(i\text{-}Pr)_2Et$ as base (entry 4). When 1,8-bis(dimethylamino)naphthalene (proton sponge) was used a 74% yield and an optimised ee of 94% was obtained. When the *i*-Pr- or *t*-Bu-substituted diphenylphosphinoferrocenyloxazoline ligands **6a** or **6b** were tested, low yields (7–17%) were observed and the ees were also poor (25–43%). This represents a significant lowering of ee compared to that obtained (92–98%) with the less bulky substrate **11**. Therefore, the optimal ee for the phenylation of dihydrofuran



Scheme 9.

12 was 94%, although in this case it was with the *t*-Bu-substituted diphenylphosphinoaryloxazoline ligand **5b**.

When palladium complexes of (*R*)-BINAP **2** were tested in the cyclohexenylation of **12**, the ees (14–39%) and the yields (32–34%) were low but similar to those obtained with dihydrofuran **11**. The *i*-Pr-substituted diphenylphosphinoaryloxazoline ligand **5a** also gave a low yield (11%) but with a good ee of 87%, again a similar result to that obtained with dihydrofuran **11** (33% yield, 83% ee). With the *t*-Bu-substituted analogue **5b**, somewhat higher yields were obtained (24–34%), although these were lower than with **11** (26–68%).

Good ees of 82–93% were obtained with this ligand and proton sponge as base afforded our optimal result in this series (93%, entry 11) whilst the use of N(*i*-Pr)$_2$Et gave a slightly lowered ee of 82% (entry 12). The yield obtained when the *i*-Pr-substituted diphenylphosphinoferrocenyloxazoline ligand **6a** was used was extremely poor (5%) and the ee decreased from when the less bulky dihydrofuran **11** was used (37 versus 76%). The yield for the *t*-Bu-substituted analogue **6b** was only slightly higher (16%) and the ee was even lower (25%), which represents a large decrease when the same catalyst system was used for the cyclohexenylation of **11** (88% yield, 73% ee).

Table 5
Asymmetric phenylation and cyclohexenylation of **12** catalysed by Pd complexes of **2**, **5** and **6**

Entry	Ligand	Base	*T* (°C)	% Yield[a]	Product (% ee)[b,c]
1	**2**[d]	Proton sponge	40	23	**23** (64)
2	**2**[d]	N(*i*-Pr)$_2$Et	40	47	**23** (54)
3	**5a**[e]	Proton sponge	80	16	**23** (44)
4	**5b**[e]	N(*i*-Pr)$_2$Et	80	33	**23** (50)
5	**5b**[e]	Proton sponge	80	74	**23** (94)
6	**6a**[e]	Proton sponge	80	7	**23** (25)
7	**6b**[e]	Proton sponge	80	17	**23** (43)
8	**2**[d]	Proton sponge	40	32	**24** (14)
9	**2**[d]	N(*i*-Pr)$_2$Et	40	34	**24** (39)
10	**5a**[e]	Proton sponge	40	11	**24** (87)
11	**5b**[e]	Proton sponge	40	24	**24** (93)
12	**5b**[e]	N(*i*-Pr)$_2$Et	40	34	**24** (82)
13	**6a**[e]	Proton sponge	40	5	**24** (37)
14	**6b**[e]	Proton sponge	40	16	**24** (25)

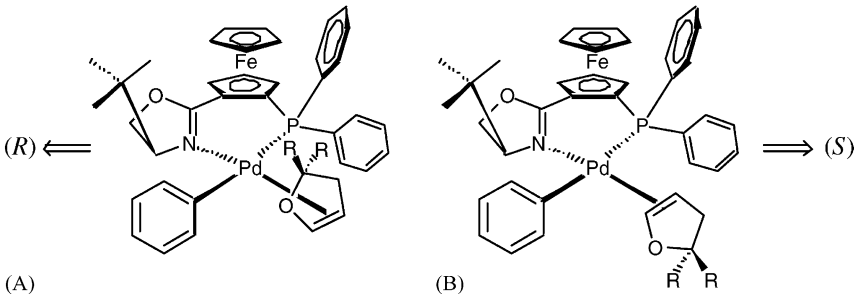
[a] Yields were calculated by GC (SE-30, 30 m, 11 psi He), 50 °C for 4 min, 15 °C/min up to 170 °C, t_R = 13.7 min for product **23**, t_R = 13.5 min for product **24** and t_R = 14.1 min for tridecane.

[b] Enantiomeric excesses were determined by GC on a Chiraldex γ-cyclodextrin TFA capillary column (30 m × 0.25 m, 15 psi He); 80 °C, 0.3 °C/min up to 92 °C, 5 °C/min up to 130 °C, (t_R = 52.0 (*R*) and 52.4 (*S* min) for **23**; 65 °C, 0.3 °C/min up to 95 °C, 5 °C/min, 95 °C, 0.3 °C/min up to 105 °C, 1 °C/min, 5 °C/min up to 130 °C (t_R = 79.3 (*R*) and 79.9 (*S*) min) for **24**.

[c] The absolute configuration was determined to be (*R*) by comparison of the chiral GC retention times and optical rotations of **23** and **24** with optically pure samples of (*R*)-2-phenyl-2,5-dihydrofuran and (*R*)-2-cyclohex-1′-en-1′-yl-2,5-dihydrofuran, respectively.

[d] Pd^0 complexes formed in situ from Pd(OAc)$_2$ and **5a**.

[e] Pd^0 complexes formed in situ from Pd$_2$(dba)$_3$ and phosphinamines **5a** and **6**.



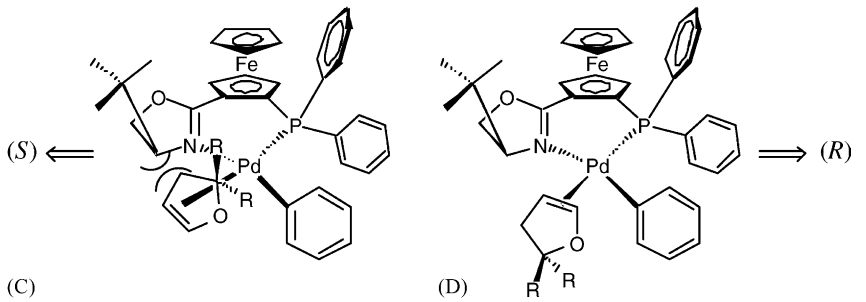
Scheme 10. Alkene approaches *trans* to nitrogen.

Therefore, we have seen that the increased bulk at the 2-position of 2,2-disubstituted-2,3-dihydrofurans does affect both the yields and ees of the asymmetric Heck reactions conducted upon them. In general, a decline in chemical yield was noted for reactions using the diethyl-substituted substrate **12** compared to those using the dimethyl-substituted substrate **11**. This may be due to increased ligand–reactant steric interactions in the migratory insertion transition state caused by the bulkier alkene (**12** versus **1**). Overall, the ees decreased slightly when complexes of BINAP **2** were employed, remained reasonably constant for complexes of ligands **5**, but surprisingly fell dramatically for complexes of the diphenylphosphinoferrocenyloxazolines **6**. The reason for the oxazoline-containing ligands **5** and **6** to behave so differently must lie in their subtle steric and electronic differences.

7. Mechanistic considerations

For the phenylation of 2,3-dihydrofurans **1**, **11** and **12** the possible intermediates prior to migratory insertion in the palladium catalyst derived from ligand **6b** are shown in Schemes 10 and 11. The alkene can be bound to palladium by either of its faces and can bind in a *trans*-fashion to either the nitrogen atom (Scheme 10) or the phosphorous atom (Scheme 11). Similar intermediates have been proposed by Hallberg and Ripa for an intramolecular Heck reaction with ligand **5b** [45].

When the alkene approaches *trans* to nitrogen there seems to be little steric repulsion in binding either face of the alkene. Intermediate (A) would lead to the (*R*) configured product while intermediate (B) would lead to the (*S*) product. If there were little energy difference between either intermediate a low ee would be expected if migratory insertion occurred in this way. When the approach is *trans* to phosphorous intermediate (C) suffers steric repulsion but intermediate (D) does not. This route for migratory insertion would lead to a high ee of the (*R*) product and this is what is seen experimentally in the study completed herein. The same arguments could be used to explain the selectivity of the diphenylphosphinoaryloxazoline ligand **5b** and for the cyclohexenylation of 2,3-dihydrofurans **1**,



Scheme 11. Alkene approaches *trans* to phosphorous.

11 and **12**. The coordination of groups after oxidative addition to Pd complexes containing P-N ligands has received some study by the groups of van Koten, van Leeuwen and Vrieze [46,47].

8. Conclusions

In conclusion, we have tested palladium complexes of diphenylphosphinoferrocenyloxazolines in the intermolecular phenylation and cyclohexenylation of 2,3-dihydrofuran **1**. Phenylations proceeded in moderate to reasonable chemical yields, good to total regioselectivity and in ees up to 99%. Cyclohexenylations gave lower chemical yields and regioselectivities with the optimal result being a 75% yield of the major product in an ee of 85%. For both phenylation and cyclohexenylation the *t*-Bu substituted ligand **6b** gave best results. New 2,2-dialkyl-2,3-dihydrofurans substrates were synthesised and tested as new substrates for the intermolecular Heck as they afford a single regioisomeric product thus providing easier analysis and comparison over a broad range of ligands. The phenylation and cyclohexenylation of 2,2-dimethyl-2,3-dihydrofuran **11** proceeded in excellent yield and ees up to 98 and 97%, respectively, again with palladium complexes of the *t*-Bu substituted ligand **6b** giving optimal results. The use of 2,2-diethyl-2,3-dihydrofuran **12** as substrate demonstrated that the increased bulk at the 2-position had a deleterious effect on both the chemical yields and ees in phenylations and cyclohexenylations. Further studies on related dihydrofuran substrates are in progress and will be reported in due course [49].

9. Experimental

^{1}H and ^{13}C spectra were recorded at 270 (67.5) or 500 (125) MHz at ambient temperature on JOEL JNM-PMX-270 MHz or Varian-Unity 500 MHz spectrometers with tetramethylsilane as the internal standard. Peak assignments were aided by ^{1}H–^{1}H correlation experiments. Coupling constants are given as absolute values. Low resolution electron-impact MS spectra were measured on a VG Analytical spectrometer with attached INCOS 2400 data system at an ionization potential of 70 eV. Isomers were assumed to have the same response factors. Elemental analyses were performed by Ms. Anne Connolly, Department of Chemistry, University College Dublin. Infra-red spectra were recorded on a Perkin-Elmer Paragon 1000 Infra-red FT spectrometer. Optical rotation values were measured on a Perkin-Elmer 241 polarimeter. Melting points were determined in open capillary tubes in a Gallenkamp melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on aluminum sheets pre-coated with silica gel 60 F 254 (0.25 mm, Macherey-Nagel). Column chromatography separations were performed using Merck Kieselgel 60 (Art. 7734), Merck Alumina (Art. 1097) or Merck Alumina (Art. 1104) as stated. Solvents were dried immediately prior to use by distillation from standard drying agents.

9.1. Preparation of 2,2-dimethyl-2,5-dihydrofuran (*11*)

4-Methyl-pent-2-yne-1,4-diol (**13**): Crushed KOH pellets were added to a three-necked flask containing Et_2O (100 ml). Propargylic alcohol (10.0 g, 0.18 mol) was added whilst taking care to keep the temperature below 15 °C. A mixture of propargylic alcohol (24.9 g, 0.44 mol), acetone (88.1 ml, 1.20 mol) and Et_2O (100 ml) was then added over 2 h, again keeping the temperature below 25 °C. The orange coloured mixture was stirred for 48 h. It was then quenched with 50 ml of ice and Et_2O (200 ml) was added. The aqueous layer was acidified with concentrated HCl and extracted with Et_2O (2×500 ml). The combined organic fractions were then dried with K_2CO_3, filtered and the solvent removed in vacuo. Unreacted propargylic alcohol was distilled off (40 °C, 15 mmHg) and then 4-methyl-pent-2-yne-1,4-diol (22.3 g, 38%) was obtained as a viscous yellow oil, bp (90 °C, 1 mbar) (literature [37] 126 °C, 20 mbar). ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.52 (6H, s, $2 \times CH_3$), 3.79 (2H, br. s, $2 \times$ OH) and 4.29 (2H, s, $H_2C(1)$); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 31.18 ($2 \times CH_3$), 50.45 ($H_2C(1)$), 60.03 (C(4)), 80.30 (C(3)) and 90.26 (C(2)); ν_{max} (film) 3517 (s) (–OH), 2950 (s) ($-CH_3$) and 1059 cm^{-1} (s) (C–O).

5,5-Dimethyl-tetrahydrofuran-3-one (**15**): To a solution of mercuric sulphate (5.58 g, 18.80 mol) in H_2O (150 ml) was added 4-methyl-pent-2-yne-1,4-diol (26.51 g, 0.23 mol). The reaction was steam distilled until no further organic material appeared in the

distillate. The organic layer was separated and the aqueous layer was saturated with brine and extracted with Et_2O (200 ml). The combined organic layers were then dried with $MgSO_4$, filtered and the solvent removed in vacuo. The crude product was then distilled to give 5,5-dimethyl-tetrahydrofuran-3-one (12.42 g, 48%) as a colourless oil, bp (59–62 °C, 15 mbar) (literature [37] 143 °C). ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.26 (6H, 2 × CH_3), 2.36 (2H, s, H_2C(4)) and 4.03 (2H, s, H_2C(2)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 27.21 (2 × CH_3), 49.62 (H_2C(4)), 70.16 (H_2C(2)), 80.25 (C(5)) and 160.41 (C(3)); ν_{max} (film) 1761 cm^{-1} (s) (C=O); *m*/*z* (eims 70 eV) 114 (M^+, 3%), 101 (10), 85 (16), 59 (70) and 43 (100).

5,5-Dimethyl-tetrahydrofuran-3-one-tosylhydrazone (**17**): *p*-Toluenesulfonylhydrazide (8.28 g, 44.46 mmol) was added to a solution of 5,5-dimethyl-tetrahydrofuran-3-one (5.06 g, 44.33 mmol) in EtOH (44 ml) and the solution was refluxed for 1 h. After cooling to room temperature overnight the resulting solid was filtered, dried and recrystallised from EtOH to give 5,5-dimethyl-tetrahydrofuran-3-one-tosylhydrazone (6.64 g, 53%) as a white crystalline solid, mp 132–135 °C (decomp.). Found: C, 54.9; H, 6.2; N, 9.7; S, 11.2. $C_{13}H_{18}N_2O_3S$ requires C, 55.3; H, 6.4; N, 9.9 S, 11.4%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.26 (6H, 2 × CH_3), 2.30 (2H, s, H_2C(4), 2.44 (3H, s, Me-Ar), 4.31 (2H, m, H_2C(2), 7.27–7.35 (2H, m, *m*-Ar) and 7.77–7.86 (2H, m, *o*-Ar); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 26.50 (CH_3–Ph), 26.96 (2 × CH_3), 40.51 (H_2C(4)), 67.94 (H_2C(2)), 81.47 (C(5)), 128.03 (2 × *m*-Ar), 129.79 (2 × *o*-Ar), 135.15 (*p*-Ar), 144.39 (*ipso*-Ar) and 163.29 (C(3)); ν_{max} (CH_2Cl_2) 1164 cm^{-1} (s) (–SO_2); *m*/*z* (eims 70 eV) 282 (M^+, 1%), 267 (3), 71 (8), 171 (5), 157 (19), 139 (23), 127 (75) and 91 (100).

2,2-Dimethyl-2,3-dihydrofuran (**11**): According to the procedure of Gianturco et al. [36] sodium metal (0.61 g, 26.53 mmol) was dissolved over a 10 min interval in ethylene glycol (27 ml) and to this was added 5,5-dimethyl-tetrahydrofuran-3-one-tosylhydrazone (4.02 g, 14.17 mmol). The solution was then heated to 150 °C and 2,2-dimethyl-2,3-dihydrofuran (0.63 g, 45%) was distilled off over 30 min under a low stream of nitrogen as a colourless liquid, bp (77–79 °C) (literature [48] 77–82 °C). The ratio of 2,2-dimethyl-2,3-dihydrofuran (**11**) to 2,2-dimethyl-2,5-dihydrofuran (**19**) was seen to be 94:6 by ^{1}H NMR. Found: C, 73.6; H, 11.5. $C_6H_{10}O$ requires C, 73.4; H, 11.3%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.36 (6H, s, 2 × CH_3), 2.41 (2H, app t, *J* 2.38, H_2C(3), 4.62 (1H, m, HC(4)) and 6.20 (1H, m, HC(5)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 28.22 (2 × CH_3), 42.27 (H_2C(3)), 84.49 (C(2)), 98.43 (HC(4)) and 144.01 (HC(5)); ν_{max} (film) 1620 cm^{-1} (w) (C=C); *m*/*z* (eims 70 eV) 98 (M^+, 3%), 97 (11), 71 (8), 57 (10), 43 (29), 32 (36), 31 (29) and 28 (100). Minor isomer (**19**); ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.31 (6H, s, 2 × CH_3), 4.64 (m, 2H, H_2C(5)) and 5.50 (m, 2H, HC(3), HC(4)).

9.2. Preparation of 2,2-diethyl-2,5-dihydrofuran (12)

4-Ethyl-hex-2-yne-1,4-diol (**14**): 4-Ethyl-hex-2-yne-1,4-diol was synthesised in the same way as **13** with the exception that the solution was also refluxed for 3 h. After distillation 4-ethyl-hex-2-yne-1,4-diol (48.50 g, 21%) was obtained as a viscous yellow oil, bp (110 °C, 1 mbar) (literature [37] 140 °C, 20 mbar). ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.03 (6H, t, *J* 7.59, 2 × CH_3), 1.66–1.75 (4H, q, *J* 7.60, 2 × H_2C), 2.30–2.38 (2H, br s, 2 × OH) and 4.31 (2H, s, H_2C(1)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 8.56 (2 × CH_3), 34.12 (2 × CH_2), 50.81 (H_2C(1)), 72.07 (C(4)), 82.67 (C(3)) and 88.06 (C(2)); ν_{max} (CH_2Cl_2) 3602 (m) (O–H) and 2250 cm^{-1} (w) (alkyne).

5,5-Diethyl-tetrahydrofuran-3-one (**16**): Using the same method as for **15**, 5,5-diethyl-tetrahydrofuran-3-one (22.02 g, 44%) was obtained as a colourless liquid, bp (110 °C, 15 mmHg). Found: C, 68.2; H, 10.1. $C_8H_{14}O$ requires C, 67.6; H, 9.9%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.92 (6H, t, *J* 7.33, 2 × CH_3), 1.64 (4H, q, *J* 7.32, 2 × CH_2), 2.33 (2H, s, H_2C(4)), 4.01 (2H, s, H_2C(2)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 8.06 (2 × CH_3), 29.52 (2 × H_2C), 45.92 (H_2C(4)), 70.12 (H_2C(2)), 85.15 (C(5)), 163.58 (C(3)); ν_{max} (film) 1760 cm^{-1} (s) (C=O); *m*/*z* (eims 70 eV) 142 (M^+, 2%), 141 (2), 129 (7), 117 (14), 99 (22), 87 (37), 69 (32) and 57 (100).

5,5-Diethyl-tetrahydrofuran-3-one-tosylhydrazone (**18**): Using the same procedure as for the preparation of (**17**), 5,5-diethyl-tetrahydrofuran-3-one-tosylhydrazone (14.73 g, 53%) was obtained as a white solid, mp 128–130 °C (decomp.). Found: C, 57.8; H, 7.0; N, 8.9; S, 10.3. $C_{15}H_{22}N_2O_3S$ requires C, 58.0; H, 7.1;

N, 9.0 S, 10.4%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.82 (6H, t, J 7.51, 2 × CH_3), 1.52 (4H, q, J 7.51, 2 × H_2C), 2.25 (2H, s, $H_2C(4)$), 2.44 (3H, s, Me–Ar), 4.22 (2H, s, $H_2C(2)$), 7.27–7.34 (2H, m, *m*-Ar) and 7.81–7.85 (2H, m, *o*-Ar); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 8.15 (2 × CH_3) 28.64 (CH_3–Ph), 29.03 (2 × CH2–C(5)), 37.10 ($H_2C(4)$), 68.02 ($H_2C(2)$), 86.10 (C(5)), 129.71 (2 × *m*-Ar), 129.81 (2 × *o*-Ar), 135.10 (*p*-Ar), 144.36 (*ipso*-Ar) and 166.27 (C(3)); ν_{max} (CH_2Cl_2) 1029 cm^{-1} (m) (–SO_2–); *m*/*z* (eims 70 eV) 310 (M^+, 1%), 281 (19), 155 (50), 139 (29), 125 (33) and 91 (100).

2,2-Diethyl-2,3-dihydrofuran (**12**): Using the method employed in the synthesis of **11**, 2,2-diethyl-2,3-dihydrofuran (1.84 g, 50%) was obtained as a colourless liquid, bp (116–119 °C). The ratio of 2,2-diethyl-2,3-dihydrofuran (**12**) to 2,2-diethyl-2,5-dihydrofuran (**20**) was seen to be 92:8 by ^{1}H NMR spectroscopy. Found: C, 76.3; H, 11.4. $C_8H_{14}O$ requires C, 76.1; H, 11.2%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.89 (6H, t, J 7.32, 2×CH_3), 1.61 (4H, q, J 7.31, 2×CH_2), 2.37 (2H, app t, J 2.54 $H_2C(3)$), 4.73 (1H, m, HC(4)) and 6.22 (1H, m, HC(5)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 7.79 (2 × H_3C), 31.51 (2 × H_2C), 37.46 ($H_2C(3)$), 89.41 (C(2)), 98.39 (HC(4)) and 144.63 (HC(5)); ν_{max} (film) 1621 cm^{-1} (w) (C=C); *m*/*z* (eims 70 eV) 126 (M^+, 1%), 125 (1), 97 (3), 69 (2), 32 (38) and 28 (100). Minor isomer 2,2-diethyl-2,5-dihydrofuran (**20**); ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.87–0.92 (6H, 2×CH_3), 1.56–1.64 (4H, 2 × CH_2), 4.62–4.63 (2H, m, $H_2C(5)$), 5.55–5.57 (1H, m, HC(3)) and 5.87–5.89 (1H, m, HC(4)).

9.3. Synthesis of racemic Heck reaction products

2-Phenyl-2,5-dihydrofuran (**3**): $Pd(OAc)_2$ (0.045 g, 0.20 mmol) and triphenylphosphine (0.118 g, 0.45 mmol) were added to a mixture of iodobenzene (1.02 g, 5.00 mmol), 2,3-dihydrofuran (1.75 g, 25.0 mmol), $AgCO_3$ (2.75 g, 9.66 mmol) and acetonitrile (60 ml). This was degassed using three freeze thaw cycles at 0.01 mbar and the reaction was stirred at 80 °C under nitrogen for 48 h. After this the reaction mixture was cooled to room temperature, filtered, the solvent removed in vacuo and the product isolated by column chromatography eluent (pentane:CH_2Cl_2 2:1) to give 2-phenyl-2,5-dihydrofuran (0.25 g, 35%) as a colourless oil. ^{1}H NMR (270 MHz): δ ($CDCl_3$) 4.77 (1H, m, HC(5), 4.86 (1H, m, HC(5)), 5.77–5.82 (1H, m, HC(4), 5.89 (1H, m, HC(2)), 6.04 (1H, m, HC(3)) and 7.24–7.38 (m, 5H, Ph); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 75.87 ($H_2C(5)$), 87.97 (HC(2)), 126.47 (2 × *m*-Ph), 126.67 (*p*-Ph), 127.89 (HC(4)), 128.57 (2 × *o*-Ph), 130.00 (HC(3)) and 142.10 (*ipso*-Ph); ν_{max} (CH_2Cl_2) 1713 cm^{-1} (w) (C=C); *m*/*z* (eims 70 eV) 146 (M^+, 2%), 145 (7), 115 (9) and 105 (100).

2,2-Dimethyl-5-phenyl-2,5-dihydrofuran (**21**): To a mixture of iodobenzene (0.38 g, 1.84 mmol), 5,5-dimethyl-2,3-dihydrofuran (0.58 g, 5.91 mmol) and $AgCO_3$ (1.01 g, 3.55 mmol) in acetonitrile (20 ml) was added $Pd(OAc)_2$ (16.0 mg, 0.071 mmol) and triphenylphosphine (42 mg, 0.16 mmol). This reaction was carried out as for **3** to give 2,2-dimethyl-5-phenyl-2,5-dihydrofuran (0.09 g, 26%) as a colourless oil. ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.40 (3H, s, CH_3), 1.46 (3H, s, CH_3), 5.74 (1H, dd, J 5.9, 1.5, HC(3)), 5.80 (1H, dd, J 2.4, 1.7, HC(5)), 5.90 (1H, dd, J 6.0, 2.6, HC(4) and 7.25–7.36 (5H, m, Ph); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 27.89 (CH_3), 28.86 (CH_3), 86.89 (HC(5)), 88.19 (C(2)), 126.36 (*p*-Ph), 126.67 (2 × *m*-Ph), 127.70 (HC(3)), 128.26 (HC(4), 128.46 (2 × *o*-Ph) and 141.99 (*ipso*-Ph); ν_{max} (CH_2Cl_2) 1650 cm^{-1} (w) (C=C); *m*/*z* (eims 70 eV) 174 (M^+, 10%), 159 (26), 123 (47), 105 (100) and 77 (39); HRMS calculated for $C_{12}H_{14}O$: 174.105, found: 174.096.

2,2-Diethyl-5-phenyl-2,5-dihydrofuran (**23**): To a mixture of iodobenzene (0.40 g, 1.98 mmol), 5,5-diethyl-2,3-dihydrofuran (0.50 g, 3.52 mmol) and $AgCO_3$ (1.90 g, 3.51 mmol) in acetonitrile (10 ml) was added $Pd(OAc)_2$ (39.8 mg, 0.18 mmol) and triphenylphosphine (102.4 mg, 0.39 mmol). The reaction was carried out as for **3** to give 2,2-diethyl-5-phenyl-2,5-dihydrofuran (0.05 g, 13%) as a colourless oil. Found: C, 83.3; H, 8.4. $C_{12}H_{18}O$ requires C, 83.6; H, 8.5%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.88–0.97 (6H, m, 2×CH_3), 1.59–1.81 (4H, m, 2×CH_2), 5.78–5.83 (2H, m, HC(3), HC(5)), 5.88 (1H, dd, J 5.91, 1.69, HC(4)) and 7.24–7.37 (5H, m, Ph); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 8.94 (CH_3), 9.56 (CH_3), 31.88 (H_2C–C(2)), 33.00 (H_2C–C(2)), 87.99 (HC(5)), 94.71 (C(2)), 128.11 (2×*m*-Ph), 128.89 (2×*o*-Ph), 130.15 (HC(3)) and 133.54 (HC(4)), 142.51 (*ipso*-Ph); ν_{max} (CH_2Cl_2) 1640 cm^{-1} (w) (C=C); *m*/*z* (eims 70 eV) 202 (M^+, 1%), 201 (8), 173 (33), 115 (18), 105 (44), 57 (47) and 29 (100).

2-Cyclohex-1′-en-1′-yl-2,5-dihydrofuran (**9**): To a mixture of 1-iodocyclohexene (1.08 g, 5.19 mmol), 2,3-dihydrofuran (1.50 g, 21.40 mmol) and $AgCO_3$ (2.75 g, 9.66 mmol) in acetonitrile (60 ml) was added $Pd(OAc)_2$ (47 mg, 0.21 mmol) and triphenylphosphine (120 mg, 0.46 mmol). The reaction was carried out as for **3** to give 2-cyclohex-1′-en-1′-yl-2,5-dihydrofuran (0.07 g, 9%) as a colourless oil. ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.46–1.69 (4H, m, $H_2C(4')$, $H_2C(5')$), 1.75–2.11 (4H, m, $H_2C(3')$, $H_2C(6')$), 4.59–4.74 (2H, m, $H_2C(5)$), 5.13–5.17 (1H, m, HC(2′)), 5.67–5.72 (2H, m, HC(2), HC(4)) and 5.95 (1H, m HC(3)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 22.45 ($H_2C(4')$, $H_2C(5')$), 23.22 ($H_2C(3')$), 24.98 ($H_2C(6')$), 75.58 ($H_2C(5)$), 90.53 (HC(2)), 124.16 (HC(2′)), 127.00 (HC(4)), 128.70 (HC(3)) and 137.94 (C(1′)); ν_{max} (CH_2Cl_2) 1621 cm^{-1} (w) (C=C); *m/z* (eims 70 eV) 148 (M^+, 10%), 135 (15), 123 (24), 109 (100) and 81 (87).

5-Cyclohex-1′-en-1′-yl-2,2- dimethyl - 2,5-dihydrofuran (**22**): To a mixture of 1-iodocyclohexene (0.88 g, 4.25 mmol), 5,5-dimethyl-2,3-dihydrofuran (0.42 g, 4.25 mmol) and $AgCO_3$ (2.39 g, 8.38 mmol) in acetonitrile (60 ml) was added $Pd(OAc)_2$ (39 mg, 0.17 mmol) and triphenylphosphine (102 mg, 0.39 mmol). The reaction was carried out as for **3** to give 5-cyclohex-1′-en-1′-yl-2,2-dimethyl-2,5-dihydrofuran (0.20 g, 26%) as a colourless oil. Found: C, 80.6; H, 10.3. $C_{14}H_{22}O$ requires C, 80.9; H, 10.2%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 1.30 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.50–1.67 (m, 4H, $H_2C(4')$, $H_2C(5')$), 1.83–2.08 (m, 4H, $H_2C(3')$, $H_2C(6')$), 5.14 (1H, m, HC(2′), 5.56 (1H, dd, *J* 1.46, 6.04, HC(3)), 5.73 (1H, m, HC(5)) and 5.77 (1H, dd, *J* 2.44, 5.86, HC(4)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 22.61 ($H_2C(4')$), 22.64 ($H_2C(5')$), 23.65 ($H_2C(3')$), 25.20 ($H_2C(6')$), 27.91 (CH_3), 28.41 (CH_3), 87.27 (C(2)), 89.80 (HC(5)), 124.93 (HC(2′)), 127.39 (HC(3)), 136.16 (HC(4)) and 137.90 (C(1′)); ν_{max} (CH_2Cl_2) 2910 cm^{-1} (C–H); *m/z* (eims 70eV) 178 (M^+, 3%), 167 (7), 151 (10), 109 (35), 97 (60) and 57 (100).

5-Cyclohex-1′-en-1′-yl-2,2 diethyl-2,5-dihydrofuran (**24**): To a mixture of 1-iodocyclohexene (0.20 g, 0.96 mmol), 5,5-diethyl-2,3-dihydrofuran (0.310 g, 2.18 mmol) and $AgCO_3$ (1.9 g, 6.67 mmol) in acetonitrile (10 ml) was added $Pd(OAc)_2$ (39.3 mg, 0.18 mmol) and triphenylphosphine (102 mg, 0.39 mmol). The reaction was carried out as for **3** to give 5 - cyclohex -1′-en-1′-yl-2,2-diethyl-2,5-dihydrofuran (0.04 g, 22%) as a colourless oil. Found: C, 81.2; H, 10.6; $C_{12}H_{18}O$ requires C, 81.5; H, 10.8%; ^{1}H NMR (270 MHz): δ ($CDCl_3$) 0.84–0.92 (6H, m, 2 × CH_3), 1.47–1.72 (8H, m, 2 × CH2, $H_2C(4')$, $H_2C(5')$), 1.82–2.02 (4H, m, $H_2C(3')$, $H_2C(6')$), 5.09 (1H, m, HC(2′)) and 5.67–5.74 (3H, m, HC(3), HC(4), HC(5)); ^{13}C NMR (67.5 MHz): δ ($CDCl_3$) 8.39 (CH_3), 8.97 (CH_3), 22.61 ($H_2C(4')$), 22.69 ($H_2C(5')$), 24.24 ($H_2C(3')$), 25.19 ($H_2C(6')$), 30.93 (H_2C–C(2)), 32.45 (H_2C–C(2)), 90.42 (HC(5)), 93.14 (C(2)), 124.59 (HC(2′)), 128.92 (HC(3)), 133.19 (HC(4)), 137.83 (C(1′)); ν_{max} (CH_2Cl_2) 2950 (C–H) cm^{-1}; *m/z* (eims 70 eV) 206 (M^+, 5%), 205 (4), 178 (17) and 177 (100).

9.4. Asymmetric Heck reactions—general procedure

According to the procedure reported by Pfaltz and co-workers [17], a solution of phenyl trifluoromethanesulfonate (30.0 mg, 0.13 mmol) and *n*-tridecane (10.0 mg, 0.054 mmol) in benzene (0.5 ml) was added to a schlenk containing $Pd_2(dba)_3$ (2.3 mg, 0.004 mmol) and ligand (0.008 mmol) under nitrogen. To this was then added the 2,3-dihydrofuran (0.65 mmol) and 1,8-bis-(dimethylamino)-naphthalene (proton sponge) (83.58 mg, 0.39 mmol). When BINAP was used as the ligand, it was stirred in degassed benzene with $Pd(OAc)_2$ and base for 10 min prior to addition of triflate, *n*-tridecane and olefin according to the procedure reported by Hayashi [36]. The resulting solution was then degassed by three freeze-thaw cycles at 0.01 mbar and then left to stir under nitrogen at 80 °C for 14 days giving a red solution with precipitation of Base HOTf. Pentane (10 ml) was then added to the reaction mixture and the resulting suspension was filtered through 2 cm of silica with further elution using diethyl ether (10 ml). This solution was then concentrated and the yield calculated using GC (Se-30, 11 psi, 50 °C, 4 min, 15 °C/min, 170 °C, 10 min) by the internal standard method. The yields for all the asymmetric Heck reactions were measured in this way.

Further purification by TLC (a normal sized TLC plate was run and a strip cut off and visualised with $KMnO_4$, the silica of the remainder of the plate at the same Rf as the product was then scraped off and

extracted with CH_2Cl_2) gave product, from which its ee could be determined by chiral GC, (γ-CD-TFA, 30 m, 80–90 °C, 0.3 °C/min, 90–120 °C, 5 °C/min, 10 min, 15 psi, inj 200 °C, det 220 °C).

The enantiomers of **3**, **4**, **9**, **10**, **21** and **22** could also be baseline separated using this temperature program.

9.5. Retention times

2-Phenyl-2,5-dihydrofuran (**3**); RT (*S*)-(**3**) 31.8 min; (*R*)-(**3**) 34.0 min.

2-Phenyl-2,3-dihydrofuran (**4**); RT (*S*)-(**4**) 23.3 min; (*R*)-(**4**) 24.6 min.

2-Cyclohex-1′-en-1′-yl-2,5-dihydrofuran (**9**); RT (*S*)-(**9**) 22.2 min; (*R*)-(**9**) 24.9 min.

2-Cyclohex-1′-en-1′-yl-2,3-dihydrofuran (**10**); RT (*S*)-(**10**) 18.0 min; (*R*)-(**10**) 18.3 min.

2,2-Dimethyl-5-phenyl-2,5-dihydrofuran (**21**); RT (*S*)-(**21**) 29.6 min; (*R*)-(**21**) 30.9 min.

5-Cyclohex-1′-en-1′-yl-2,2-dimethyl-2,5 dihydrofuran (**22**); RT (*S*)-(**22**) 22.0 min; (*R*)-(**22**) 22.6 min.

2,2-Diethyl-5-phenyl-2,5-dihydrofuran (**23**) was separated using a longer oven temperature program (80–92 °C, 0.3 °C/min, 92–130 °C, 5 °C/min, 20 min); RT (*S*)-(**23**) 52.0 min; (*R*)-(**23**) 52.4 min.

5-Cyclohex-1′-en-1′-yl-2,2-diethyl-2,5 dihydrofuran (**24**); required an even longer program for base line separation (65–95 °C, 0.3 °C/min, 95–105 °C, 1 °C/min, 105–130 °C, 5 °C/min, 10 min); RT (*S*)-(**24**) 79.3 min; (*R*)-(**24**) 79.9 min.

Acknowledgements

This Asymmetric Heck project and AH have been supported by an Enterprise Ireland Basic Research Award (SC/96/435) and a President's Research Award (RP100) to PG, YM, DJC and TGK received financial support from Enterprise Ireland Research Scholarships BR/94/024, BR/99/238 and BR/99/240, respectively. The award of the BOC Gases Postgraduate Bursary to YM and AH in 1997 and 1998, respectively, is gratefully acknowledged. We thank Merck Sharpe & Dohme (Ireland Ltd.) for their support of and interest in our Heck research, Schering Corporation (USA) for their support of DJC and Johnson Matthey for a loan of Pd salts. Many thanks to Miss Helen McManus for a critical reading of this manuscript.

References

[1] A. de Meijere, F.E. Meyer, Angew. Chem. Int. Ed. Engl. 33 (1994) 2379.
[2] W. Cabri, I. Candiani, Acc. Chem. Res. 28 (1995) 2.
[3] T. Jeffery, in: L.S. Liebeskind (Ed.), Advances in Metal-Organic Chemistry, Vol. 5, JAI Press, Greenwich, 1996, pp. 153–260.
[4] J.T. Link, L.E. Overman, in: F. Diederich, P.J. Stang (Eds.), Metal-Catalysed Cross-coupling Reactions, Wiley, Weinheim, 1998, Chap. 6, p. 231.
[5] C. Amatore, G. Broeker, A. Jutand, F. Khalil, J. Am. Chem. Soc. 119 (1997) 5176.
[6] K.K. Hii, T.D.W. Claridge, J.M. Brown, Angew. Chem. Int. Ed. Engl. 109 (1997) 1033.
[7] M. Ludwig, S. Strömberg, M. Svensson, B. Åkermark, Organometallics 18 (1999) 970.
[8] K.K. Hii, T.D.W. Claridge, J.M. Brown, A. Smith, R.J. Deeth, Helv. Chim. Acta 84 (2001) 3043.
[9] M. Shibasaki, C.D.J. Boden, A. Kojima, Tetrahedron 53 (1997) 7371.
[10] P.J. Guiry, A.J. Hennessy, J.P. Cahill, Top. Catal. 4 (1997) 311.
[11] S.E. Gibson, R.J. Middleton, Contemp. Org. Synth. 3 (1996) 447.
[12] M. Shibasaki, E.M. Vogl, J. Organomet. Chem. 576 (1999) 1.
[13] M. Ogasawara, K. Yoshida, T. Hayashi, Heterocycles 52 (2000) 195.
[14] F. Ozawa, A. Kubo, T. Hayashi, Tetrahedron Lett. 33 (1992) 1485.
[15] N.G. Andersen, M. Parvez, B.A. Keay, Org. Lett. 2 (2000) 2817.
[16] L.F. Tietze, K. Thede, F. Sannicolo, Chem Commun. (1999) 1811.
[17] O. Loiseleur, P. Meier, A. Pfaltz, Angew. Chem. Int. Ed. Engl. 35 (1996) 200.
[18] O. Loiseleur, M. Hayashi, M. Keenan, N. Schmees, A. Pfaltz, J. Organomet. Chem. 576 (1999) 16.
[19] S.R. Gilbertson, Z. Fu, Org. Lett. 3 (2001) 161.
[20] S.R. Gilbertson, D. Xie, Z. Fu, J. Org. Chem. 66 (2001) 7240.
[21] Y. Hashimoto, Y. Horie, M. Hayashi, K. Saigo, Tetrahedron: Asymmetry 11 (2000) 2205.
[22] P.E. Kündig, P. Meier, Helv. Chim. Acta 82 (1999) 1360.
[23] A.V. Malkov, M. Bella, I.G. Stara, P. Kocovsky, Tetrahedron Lett. 42 (2001) 3045.
[24] A. Togni, T. Hayashi (Eds.), Ferrocenes, Vheim, 1995 (and references therein).
[25] Y. Nishibayashi, S. Uemura, Synlett, 1995, p. 79.
[26] C.J. Richards, T. Damalidis, D.E. Hibbs, M.B. Hursthouse, Synlett, 1995, p. 74.
[27] Y. Nishibayashi, I. Takai, S. Uemura, M. Hidai, Organometallics 17 (1998) 3420.
[28] I. Takai, Y. Nishibayashi, Y. Arikawa, S. Uemura, M. Hidai, Organometallics 18 (1999) 2271.
[29] Y. Malone, Ph.D. thesis, National University of Ireland, 1998.
[30] Y.M. Malone, P.J. Guiry, J. Organomet. Chem. 603 (2000) 110.

[31] W.-P. Deng, X.-L. Hou, L.-X. Dai, X.-W. Dong, Chem Commun. (2000) 1483.
[32] P.J. Guiry, T.G. Kilroy, in: Proceedings of the 222nd ACS National Meeting, Chicago, 26–30 August 2001 (paper No. 389).
[33] D. Soulsby, T. Sammakia, in: Proceedings of the 221st ACS National Meeting, San Diego, 1–5 April 2001 (paper No. 566).
[34] A. Farrell, R. Goddard, P.J. Guiry, J. Org. Chem. 67 (2002) 4209.
[35] F. Ozawa, A. Kubo, Y. Matsumoto, T. Hayashi, Organometallics 12 (1993) 4188.
[36] M.A. Gianturco, P. Friedel, V. Flanagan, Tetrahedron Lett. 6 (1965) 1847.
[37] J. Colonge, R. Falcotet, R. Gaumont, Bull. Soc. Chim. Fr. 1958, p. 211.
[38] W.R. Bamford, T.S. Stevens, J. Chem. Soc. (1952) 4735.
[39] R.C. Larock, W.H. Gong, J. Org. Chem. 54 (1989) 2047.
[40] A.J. Hennessy, Y.M. Malone, P.J. Guiry, Tetrahedron Lett. 40 (1999) 9163.
[41] F. Ozawa, Y. Kobatake, T. Hayashi, Tetrahedron Lett. 34 (1993) 2505.
[42] A.J. Hennessy, Y.M. Malone, P.J. Guiry, Tetrahedron Lett. 41 (2000) 2261.
[43] O. Loiseleur, M. Hayashi, N. Schmees, A. Pfaltz, Synthesis 11 (1997) 1338.
[44] A.J. Hennessy, D.J. Connolly, Y.M. Malone, P.J. Guiry, Tetrahedron Lett. 41 (2000) 7757.
[45] A. Hallberg, L. Ripa, J. Org. Chem. 62 (1997) 595.
[46] W. de Graaf, Ph.D. Dissertation, University of Utrecht, 1989.
[47] G. Deckker, A. Buijs, C.J. Elsevier, C.K. Vrieze, P.W.N.M. van Leeuwen, W.J. Smeets, A.L. Spek, Y.F. Wang, C.H. Stam, Organometallics 11 (1992) 1937.
[48] J. Huet, Bull. Soc. Chem. Fr. 1964, p. 2677.
[49] T.G. Kilroy, P.J. Guiry, unpublished results.