Competing Regiochemical Pathways in the Heck Arylation of 1,2-Dihydronaphthalene

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Abstract: The Heck reaction of aryl iodides with 1,2-dihydronaphthalene has been examined. Two separate reaction pathways are observed under all the conditions tried. Arylation adjacent to the aromatic ring leads to a subsequent double bond shift such that the product is a 1-aryl-1,2-dihydronaphthalene. The alternative regiochemistry leads to production of the corresponding 3-aryl-1,2-dihydronaphthalene, and labelling studies with specifically deuterated alkenes demonstrate that this is most likely to be the result of a *trans* Pd-H elimination pathway. The ratio always varies between 75:25 in favour of the 3-aryl product (Jeffery conditions) to 70:30 in favour of the 1-aryl product.

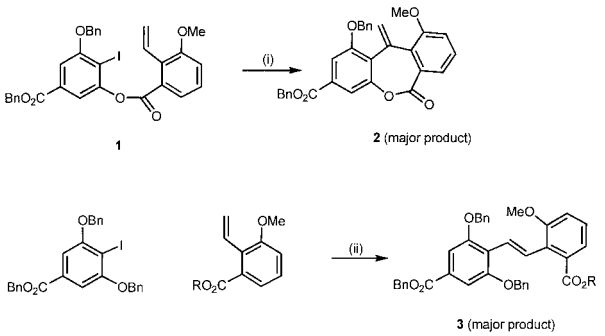
Keywords: deuterated alkenes; dihydronaphthalene; *trans*-elimination; Heck reaction; palladium catalysts.

Introduction

The Heck electrophilic arylation of alkenes has many meritorious features for synthetic chemistry.[1] A new C–C bond is formed under conditions that are tolerant of most functional groups, frequently with predictable regiochemistry. A remarkable range of Pd complexes catalyses the reaction through cationic,[2] neutral,[3] or anionic intermediates.[4] Efficient protocols for asymmetric inter- or intramolecular catalysis have been developed.[5] Much recent effort has been devoted to catalysts which operate with high turnover frequencies and impressive productivity.[6] A healthy debate on the details of mechanism, the structure of reactive intermediates and the role of ligands is underway.[7] Aspects of the reaction pathway have been subject to DFT computational analysis.[8]

In Heck reactions of styrenes and other vinylarenes, the question of regioselectivity arises, the options being formation of a stilbene or a 1,1-diphenylethylene product. In practice the result varies with reaction conditions in a manner that is not clearly defined. With cationic intermediates, the stoichiometric reaction occurs only in a linear direction; the branched intermediate is not observed.[9,10] Nevertheless, related studies indicate that a mixture of the two possible regioisomers of alkene product is formed when $PhPd(dppp)^+X^-$ is reacted with styrene.[10] The main variable is the solvent, which can change the reaction course from 95% linear in 1:9 DMF:CH_2Cl_2 to only 65% linear in pure DMF (X = OTf). In addition, with X = I or OAc, increasing the likelihood of covalent intermediates, the proportion of linear isomer increases to ca. 80%. Catalytic Heck reactions of styrenes under cationic catalyst control typically lead to 40% branched product.[2a] In other cases the formation of branched product is less pronounced,[11] or even absent.[12] It is clearly a general feature of the arylation of vinylarenes, since the cyclisation of compound **1** under the conditions indicated gives rise to the linear branched cyclic product **2**, whilst the linear product **3** (Scheme 1) is preferred when the reactants are not tethered.[13]

At the onset of this work we were interested in the potential of the Heck reaction for introducing substituents in the 1- and 4- positions of a tetrahydronaphthalene in a stereocontrolled manner, starting with 1,2-dihydronaphthalene. A potential short and stereocontrolled synthesis of the antidepressant Sertraline provided an additional incentive for the work.[14] The expectation was that an initial Heck reaction occurring in branched fashion with aryl bonding to the α-position, would generate an unstable alkylpalladium species likely to isomerise to the remote benzylic position by a double Pd-H elimination/readdition.[15] The alternative linear mode of addition would be most likely unproductive, since the intermediate formed lacks a *cis*-Pd-H elimination pathway. The investigation of different catalysts to probe the regioselectivity, and the unexpected outcome of linear addition forms the basis of this investigation.



Scheme 1. Conditions: (i) 10 mol % $Pd(OAc)_2$, 20% PPh_3; (ii) $Cl_2Pd(PPh_3)_2$, NaOAc, MeCN, 90 °C.

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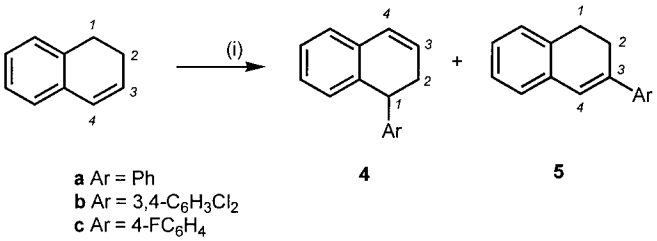
Results and Discussion

The Regiochemistry of Heck Reactions of 1,2-Dihydronaphthalene

At the outset of the work, two distinct palladium catalyst types were identified; the phosphopalladocycles introduced by Herrmann and co-workers and shown to be highly active in the Heck chemistry of simple alkenes,[16] and alternatively the phosphine-free catalysts used in the presence of phase-transfer reagents and pioneered through Jeffery's work.[17] The literature offers interesting examples where the latter elicits unusual regiochemistry in the product compared to phosphine-containing catalysts.[18]

When the Heck reactant is an aryl halide or triflate and the substrate is a styrene, the product may be a stilbene (linear pathway) or 1,1-diarylethylene (branched pathway). If the alkene is monosubstituted, then the product of an intermolecular reaction is normally the *E*-stilbene,[19] with the exception of an unusual reductive arylation under base-free conditions where the *Z*-isomer dominates.[20] The cases where significant amounts of 1,1-diarylethylene have been reported tend to involve cationic palladium intermediates.[2a] Success requires that the branched pathway is enjoined, but preliminary experiments with preformed cationic catalysts and aryl triflates were discouraging. Thus, a mixture of PhOTf and 3,4-dihydronaphthalene reacted with $Pd(OAc)_2$, *(S)*-BINAP and different bases in toluene at 40 °C gave no evidence of reaction after several days. Attention was then shifted to neutral palladium catalysts.

In common with other 1,2-disubstituted alkenes, the Pd-catalysed reaction of 1,2-dihydronaphthalene with aryl halides proceeds much more sluggishly than the reaction of monosubstituted alkenes. Two catalytic systems were discovered that proved to be effective. First, the palladocycle catalysts popularised through Herrmann's work were investigated.[16] Reactions with two different aryl electrophiles and varying conditions (Scheme 2) are reported in Table 1. The desired product **4a** or **4b** arising from a branched pathway is evident in all cases, and is indeed the anticipated result of double isomerisation. It is accompanied, however, by a significant competing pathway leading to the corresponding 3-aryl-1,2-dihydronaphthalenes **5a** and **5b**, the formal linear pathway. The proportion of the two products varies somewhat as the reaction conditions are altered, so that it was never possible to achieve complete dominance of product **4.** The best results were obtained with a ten-fold excess of alkene, when the proportion of branched product was significantly higher, and the yield better. When the reaction was carried out under the alternative phosphine-free conditions developed by Jeffery,[17] the proportion of linear isomer **5c** over branched isomer **4c** was dramatically higher when the alkene was present in substantial excess. Closer examination indicates that this is only in part due to changed regiospecificity, but also to partial disproportionation of the branched product to compounds **6** and **7** under the reaction conditions. At low alkene concentrations, more branched product is formed but the overall yield drops considerably. There is good evidence that Pd nanoparticles formed under turnover conditions are the active catalytic species in the Jeffery phosphine-free catalysts.[21] Their presence could explain the tendency of the doubly benzylic product **4** to disproportionate following well-established heterogeneous or homogeneous Pd-catalysed pathways.[22] Hence the two methods are complementary; under optimal conditions the Jeffery method leads predominantly to **5**, whilst the Herrmann protocol leads to a significant excess of the branched product **4.**



Scheme 2. (i) Heck reaction; conditions as in Table 1.

The Stereochemistry of the Linear Pathway Leading to Compound 5

It is long established that Pd-Ar addition in the initial addition step of the Heck reaction is *cis*-stereospecific.[23] Given that, it is not immediately obvious how a Pd-H elimination leading to **5** can occur. Three possibilities need to be considered; firstly, the process occurs by a *trans*-elimination pathway, secondly, an α-elimination giving a Pd-carbene complex is followed by 1,2-hydride migration and thirdly the configuration of the initially formed Pd insertion product is inverted before elimination. All three of these routes have been suggested in other palladium catalyses. The circumstance that a Heck reaction cannot be completed without a formal *trans*-elimination is not uncommon, and Ikeda has reviewed examples recorded up to 1999 in heterocycle synthesis.[24] There are two substantial categories in his review, one where the final Pd alkyl is adjacent to a carbonyl group (and can therefore epimerise by reversible keto-enol tautomerism), and a second where the Pd alkyl is benzylic. Whilst there is no direct mechanistic evidence in these cases, Pd benzyls can access an η^3-coordination geome-

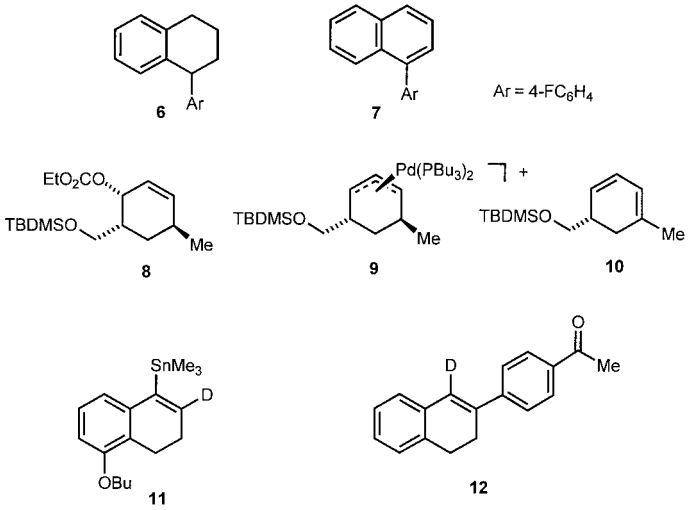
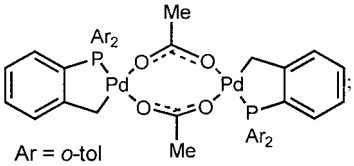


Figure 1.

Table 1.

Entry	Amount of Dihydronaphthalene	Solvent (temp)	Catalyst[e] (mol % as Pd)	Combined yield of 1- and 3-	Ratio of 1- to 3-
1	3.0 eq.	CH_3CN reflux	A (1 mol %)	36	33:67
2	3.0 eq.	CH_3CN[b] reflux	A (1 mol %)	35	36:64
3	3.0 eq.	CH_3CN[c] reflux	B (2 mol %)	13	29:71
4	3.0 eq.	Toluene[b] reflux	B (2 mol %)	36	62:38
5[a]	10.0 eq.	None (110 °C)	B (2 mol %)	32	75:25
6[a]	10.0 eq.	None (110 °C)	B (8 mol %)	59	72:28

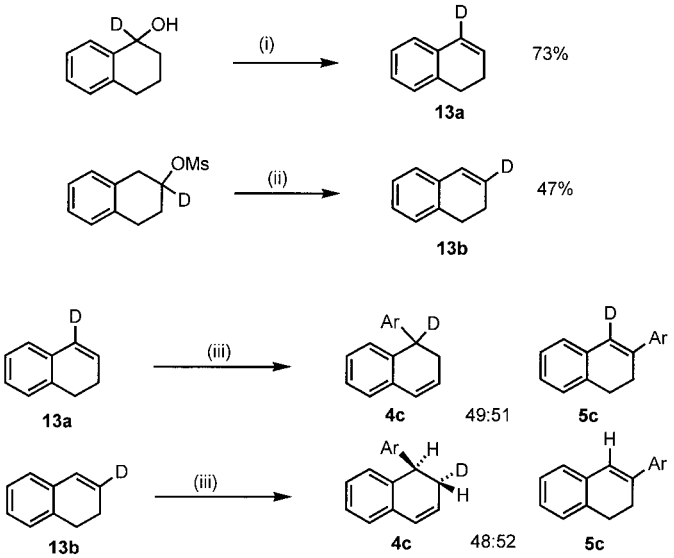
[a] Pr_3N was used instead of Et_3N.
[b] Distilled under nitrogen.
[c] Degassed under reduced pressure (commercial anhydrous grade).
[d] Commercial anhydrous grade.
[e] A: Prepared *in situ* from $Pd(OAc)_2$ and $(o\text{-tol})_3P$. 

; B: Commercial palladacycle from STREM.

try,[25] and a good analogy exists. Takacs and co-workers have shown that the near-symmetrical allylpalladium complex **9** formed from the allylic carbonate precursor **8** is transformed into the corresponding diene **10** by exclusive *trans*-elimination, precluding Pd inversion.[26] An alternative possibility is indicated by studies of *cine*-substitution in organotin cross-couplings. Farina and co-workers have proposed a palladium carbene mechanism to explain the formation of the rearranged product **12** from stannane **11.**[27] The closeness of these structures to potential intermediates in the present chemistry indicates that an experimental distinction between *trans*-elimination and carbene mechanisms is necessary.

The synthesis of the two regioisomeric deuterium-labelled alkenes **13a** and **13b** was carried out as shown in Scheme 3. In separate experiments, they were subjected to coupling with 4-FC_6H_4Br under the Herrmann-type conditions applied earlier. No attempt was made to separate the two reaction products **4c** and **5c** from one another, analysis by ^1H and ^2H NMR being carried out on the TLC-purified mixture. As far as the linear isomer **5c** is concerned, the results were unequivocal since the label at the 4-position (employing **13a**) was completely retained (peak in ^2H NMR, $CHCl_3$ at 6.8 ppm; absence of this peak in ^1H NMR). The label at the 3-position (employing **13b**) was completely removed in the product within experimental error (MS *m/z* 224, full retention of 6.8 ppm peak in the ^1H NMR) (Scheme 2). The carbene mechanism delineated by Farina can be ruled out on this evidence, since it would result in an observable deuterium migration from the 3- to the 4-position when **13b** is the reactant. Further information stems from the deuterium distribution in the branched product **4c**, where the deuterium label is completely retained in both experiments. When **13a** is the reactant, the ^2H NMR shows only a signal at 4.1 ppm; the corresponding H-1 signal of **5c** is absent from the ^1H NMR spectrum. When **13b** is the reactant, the ^2H NMR spectrum of **4c** ($\delta = 2.66$ ppm, $CHCl_3$) demonstrates that deuterium is retained in the product, and exclusively associated with a single site. This is corroborated by the ^1H NMR spectrum showing that the low-field component of the diastereotopic CH_2 at C-2 is absent. By nOe and COSY calibration of the ^1H NMR spectrum of protonated **4c,** this is indicated to be H-2 *trans* to the aryl group. The fact that deuterium is not present at *cis*-H-2 or any other site in **4c** demonstrates that the classical mechanism of *cis*-PdAr addition to the alkene followed by Pd migration is upheld; the Pd migrates much faster than inversion of configuration at C-2.

Experiments with **13a** or **13b** under Jeffery's conditions uphold the interpretation. The fact that 3-arylation occurs with comparable facility using two widely different Pd catalyst systems, and the deuterium is completely lost from C-2 in both cases, indicates that the *trans*-elimination pathway is at the very least more likely than Pd inversion followed by *cis*-elimination.[27e] It can be envisaged to occur through an E_2 reaction of the base, present in stoichiometric amount, with a Pd benzyl that has an enhanced lifetime compared to related alkyls because of partial or complete η^3-association with the arene. The regioisomer ratio is comparable for the two deuterated reactants at comparable alkene concentrations. This indicates the absence of significant reversibility in the Pd-aryl addition step, given that a primary isotope effect on the elimination step would bias the reaction towards 4-arylation in the 3-d reactant **13b.**



Scheme 3. Conditions: (i) DMSO, 170 °C, 1 h; (ii) 100 °C, toluene, 2 h; (iii) Bu_4NCl, KOAc, $Pd(OAc)_2$ [5 mol %], DMF, 80 °C, 18 h.

Mechanistic Conclusions

Here we endeavour to address why the regiochemical course should depend on the reaction conditions, and why two distinct procedures for the Heck reaction give the opposite regiochemical preference, when run under the optimum condition using excess alkene. This is counterintuitive, since expectation is that the course of arylation should be relatively weakly influenced by ligands. Delivery of palladium to the 3-position and formation of the 1-aryl isomer will be expected, in any *ionic* mechanism because of benzylic charge stabilisation irrespective of charge. In experimentally defined cases, the Pd acts as the nucleophilic partner in addition of Pd-Ar to the alkene.[28] As a counterforce, the benzyl formed by Pd delivery to the 4-position will be preferred if the stability of the oxidative addition product is important. Broadly speaking, an early transition state favours 1-arylation but a late transition state favours 3-arylation on this basis.

How this should relate to the two catalytic protocols is unclear. For the Jeffery catalyst case Pd nanoparticles formed under turnover conditions are likely to be the active catalysts.[21] The reactivity of these particles will be affected by association of reactants at active surface sites, hence the effect of alkene concentration (high [alkene] masking the most reactive early TS sites and leading to an increased proportion of 3-arylation?) on the regioselectivity is reasonable. With the Herrmann catalyst system, the trend is towards increasing 1-arylation at higher alkene concentration. That implies a change in the nature of the catalyst, although other than indicating that a higher coordination state of alkene is increasingly involved, the details remain elusive.

Experimental Section

General

See previous papers on related topics for full protocols of spectroscopic and experimental procedures.[29]

1-Phenyl-1,2-dihydronaphthalene[30] and 3-Phenyl-1,2-dihydronaphthalene[31] (4a and 5a)

Palladium acetate (45 mg, 0.2 mmol) and tri-*o*-tolylphosphine (243 mg, 0.8 mmol) were dissolved in acetonitrile (20 mL) under argon. The solution was heated under reflux for 15 min, then iodobenzene (4.080 g, 2.24 mL, 20 mmol), freshly distilled 1,2-dihydronaphthalene (7.812 g, 7.84 mL, 60 mmol) and triethylamine (2.192 g, 4 mL, 29 mmol) were added to the solution and the solution was heated under reflux for 48 h. The cooled reaction mixture was diluted with diethyl ether (100 mL), poured into HCl (aq, 1.0 M, 100 mL), then extracted with diethyl ether (2×100 mL). The combined organic layer was washed with brine (100 mL) and dried ($MgSO_4$), filtered and evaporated. Removing 1,2-dihydronaphthalene under vacuum, then purification by flash column chromatography (Biotage® cartridge silica gel, pentane only) gave 0.325 g of 1-phenyl-1,2-dihydronaphthalene,[30] 0.368 g of 3-phenyl-1,2-dihydronaphthalene,[31] and 0.839 g of their unseparated mixture (37% yield, combined coupling products). The ratio of 1-phenyl-1,2-dihydronaphthalene and 3-phenyl-1,2-dihydronaphthalene was determined to be 33:67 by comparison of ^{1}H NMR area (before purification) of 8-H of 1-phenyl-1,2-dihydronaphthalene ($\delta = 6.97$, 0.33H, d, $J = 7.4$ Hz) and 4-H of 3-phenyl-1,2-dihydronaphthalene ($\delta = 6.96$, 0.67H, s).

1-Phenyl-1,2-dihydronaphthalene: a clear colourless oil; ^{1}H NMR (200 MHz; $CDCl_3$): $\delta = 7.50-7.19$ (8H, m), 6.97 (1H, d, $J = 7.4$ Hz), 6.70 (1H, d, $J = 9.7$ Hz), 6.19–6.10 (1H, m), 4.28 (1H, t, $J = 8.7$ Hz), 2.82–2.74 (2H, m); ^{13}C NMR (200 MHz; $CDCl_3$): $\delta = 144.8$, 138.2, 134.5, 128.8, 128.8, 128.4, 128.2, 127.5, 127.5, 127.1, 126.8, 126.5, 43.9, 32.0; MS (CI$^+$): $m/z = 207$ ($M^+ + 1$).

3-Phenyl-1,2-dihydronaphthalene: white needles; mp 62–64 °C, (lit. 62–64 °);[31] ^{1}H NMR (200 MHz; $CDCl_3$): $\delta = 7.68-7.61$ (2H, m), 7.52–7.32 (3H, m), 7.29–7.21 (4H, m), 6.96 (1H, s), 3.05 (2H, t, $J = 8.2$ Hz), 2.83 (2H, t, $J = 7.9$ Hz); ^{13}C NMR (200 MHz; $CDCl_3$): $\delta = 141.4$, 139.0, 135.1, 135.1, 128.7, 127.6, 127.5, 127.2, 126.9, 125.4, 125.4, 124.6, 28.1, 26.3; MS (CI$^+$): $m/z = 207$ ($M^+ + 1$, 34%), 206 (100), 128 (9).

1- and 3-(3,4-Dichlorophenyl)-1,2-dihydronaphthalene (4b and 5b)

As above, but with 3,4-dichloroiodobenzene (2.729 g, 10 mmol) and freshly distilled 1,2-dihydronaphthalene (3.906 g, 3.92 mL, 30 mmol) to yield 0.960 g of a mixture of 1-(3,4-dichlorophenyl)-1,2-dihydronaphthalene and 3-(3,4-dichlorophenyl)-1,2-dihydronaphthalene (35% yield, combined coupling products). The ratio of 1-(3,4-dichlorophenyl)-1,2-dihydronaphthalene and 3-(3,4-dichlorophenyl)-1,2-dihydronaphthalene was determined to be 36:64 by same method as above.

1-(3,4-Dichlorophenyl)-1,2-dihydronaphthalene: clear colourless oil; ^{1}H NMR (300 MHz; $CDCl_3$): $\delta = 7.36-7.01$ (6H, m), 6.82 (1H, d, $J = 7.2$ Hz), 6.54 (1H, d, $J = 9.6$ Hz), 5.98–5.92 (1H, m), 4.08 (1H, t, $J = 8.1$ Hz), 2.71–2.64 (1H, m), 2.58–2.53 (1H, m); ^{13}C NMR (300 MHz; $CDCl_3$): $\delta = 144.9$, 136.4, 133.8, 132.3, 130.3, 130.3, 130.2, 128.1, 127.8, 127.8, 127.5, 127.3, 126.4, 126.4, 42.8, 31.7; MS (CI$^+$): $m/z = 275(M^+ + 1)$; HRMS: m/z calcd. for $C_{16}H_{12}Cl_2$ (M^+) 274.0316, found 274.0334.

3-(3,4-Dichlorophenyl)-1,2-dihydronaphthalene; white needles; mp 79–80 °C; ^{1}H NMR (300 Hz; $CDCl_3$): $\delta = 7.58$ (1H, d, $J = 2.1$ Hz), 7.41–7.31 (2H, m), 7.21–7.07 (4H, m), 6.82 (1H, s), 2.93 (2H, t, $J = 8.1$ Hz), 2.66 (2H, t, $J = 7.9$ Hz); ^{13}C NMR (300MHz; $CDCl_3$): $\delta = 141.1$, 136.1, 134.7, 134.0, 132.5, 130.8, 1302, 127.5, 127.3, 126.9, 126.9, 126.7, 125.7, 124.3, 27.9, 26.0; MS (CI$^+$): $m/z = 275(M^+ + 1)$; HRMS: m/z calcd for $C_{16}H_{12}Cl_2$ (M^+) 274.0316, found 274.0300.

3-(4-Fluorophenyl)-1,2-dihydronaphthalene[32] (5c)

To a well-stirred suspension of *tert*-butylammonium chloride (933.5 mg, 3.35 mmol) and potassium acetate (330 mg, 3.35 mmol) in dry DMF over 4 Å molecular sieves were successively added 1-bromo-4-fluorobenzene (235 mg, 1.35 mmol), 1,2-dihydronaphthalene (1.75 g, 13.45 mmol) and palladium acetate (15.1 mg, 0.013 mmol). The reaction mixture was stirred at 80 °C for 18 hours under argon. Diethyl ether was added and the reaction mixture was filtered through a Celite bed to remove palladium salts. The organic phase was washed with water (2×20 mL) followed by drying over $MgSO_4$ and the solvent and starting materials removed under vacuum. The crude product purified by column chromatography using pentane as the eluent. The clear liquid produced was identified as >96% 3-(4-fluorophenyl)-1,2-dihydronaphthalene (151 mg, 50%). The proton NMR, mass spectrum and GC trace of the product corresponded with those of an authentic sample, prepared from β-tetralone by reaction with 4-fluorophenylmagnesium bromide and acid-catalysed dehydration of the product: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.81$ [2H, t, $CH_2CH=$, $^3J(H,H) = 8.0$ Hz], 3.04 [2H, t, $CH_2CH_2CH=$, $^3J(H,H) = 8.0$ Hz], 6.89 [1H, s, $CH=C(Ar)$], 7.26 (6H, m, H_{ar}), 7.58 (2H, m, H_{ar}); MS (EI$^+$): $m/z = 224.19$ (M^+).

4-Deuterio-1,2-dihydronaphthalene[34] (13a)

1-Deuterio-2,3,4-trihydro-1-naphthol (3.3 g, 22.1 mmol) and DMSO (25 mL) were placed in a dry Schlenk tube under argon and heated to 170 °C for 1 h. The product was partitioned between water (100 mL) and pentane and the organic layer separated, dried ($MgSO_4$) and solvent removed under vacuum. After purification by Kugelrohr distillation the

resulting clear liquid (2.12 g, 73%) was identified as 4-deuterio-1,2-dihydronaphthalene; bp 32 °C/0.2 torr; IR (thin film): $\nu_{max} = 3052$, 3014 (sp^2CH), 2251 cm^{-1} (sp^2C-D); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.49$ [2H, td, $CH_2CH=$, $^3J(H,H) = 8.2$ Hz, $^3J(H,H) = 4.4$ Hz], 2.98 [2H, t, $CH_2CH_2CH=$, $^3J(H,H) = 8.2$ Hz], 6.20 [1H, tt, CD=CH, $^3J(H,H) = 4.4$ Hz, $^3J(H,D) = 1.4$ Hz], 7.20, 7.33 (4H, m, C_{Ar}); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 25.8$, 30.2 (C_{sat}), 130.1 [CD=, t, $^1J(C,D) = 24$ Hz], 128.5, 129.1, 129.5, 130.2, 131.2 (C_{Ar},C_{sp2}), 136.7, 138.1 (C_{Ar}); MS (CI^+): $m/z = 131$ (M^+).

3-Deuterio-1,2-dihydronaphthalene[34] (13b)

A dry Schlenk tube was charged with 2-deuterio-1,3,4-trihydro-2-naphthol[33] (3.78 g, 25.4 mmol), ethylamine (3.54 mL, 25.4 mmol) and dichloromethane (75 mL). Mesyl chloride (2.06 mL , 26.6 mmol) was then added over a period of 15 minutes at 0 °C. A white precipitate was formed, and the reaction stirred for a further 90 min. The organic layer was washed with water (3×200 mL), dried over $MgSO_4$ and solvent was removed under vacuum. **Mesylate** (yield: 5.14 g, 83%) mp 58 – 59.5 °C; IR (KBr): $\nu_{max} =$ 3024.5, 2972.0, 2936.3, 2892.5, 2192.8 (C – D), 1340.1 (vs), 1166.3 cm^{-1} (vs); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.20$ [2H, t, $CH_2CH_2CD(OMs)$, $^3J(H,H) =$ 6.5 Hz], 2.98 [2H, ABqt, $CH_2CH_2CD(OMs)$ $^2J(H,H) = 17.0$ Hz, $^3J(H,H) =$ 6.5 Hz], 3.06 (3H, s, CH_3SO_2), 3.18 [2H, ABq, $C_{arom}CH_2CD(OMs)$, $^2J(H,H) = 17.0$ Hz], 7.16 (4H, m, H_{ar}); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta =$ 26.38, 29.30, 35.77, 39.20, 77.83 [CD(OMs), t, $^1J(C,D) = 23.4$ Hz], 126.66, 126.89, 129.10, 129.70, 132.74 (q), 135.30 (q); MS (EI^+): $m/z = 131$ ($M^+ - CH_3SO_3H$). The mesylate (5.14 g, 22.5 mmol) was placed in a dry Schlenk tube under argon and dissolved in toluene (150 mL). To this solution was added 1,8-diazabicyclo[5.4.0]undec-7-ene (13.5 mL, 90.0 mmol) – the mixture immediately went green. The reaction was stirred for 2 hours at 100 °C. After cooling, the crude mixture was washed with 2 M HCl (3×150 mL) and dried over $MgSO_4$. After removal of solvent under vacuum, the crude product was purified by distillation. The clear liquid isolated was identified as 3-deuterio-1,2-dihydronaphthalene; yield:1.67 g (56%); bp 31 °C/0.2 mbar; IR (thin film): $\nu_{max} = 3064.7$, 3028.7, 3014.0, 2254.9 cm^{-1} (C=C – D); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.41$ [2H, td, $CH_2CH=$, $^3J(H,H) = 8.2$ Hz, $^4J(H,H) =$ 2.0 Hz], 2.90 [2H, t, $CH_2CH_2CH=$, $^3J(H,H) = 8.2$ Hz], 6.57 [1H, m, CH= CD, $^4J(H,H) = 2.0$ Hz, $^3J(H,D) = 1.5$ Hz], 7.13, 7.21 (4H, m, H_{ar}); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 23.2$, 29.7, 128.4 [CD=, t, $^1J(C,D) = 24.2$ Hz], 125.9, 126.5, 126.9, 127.6, 127.7,134.2 (q), 135.5 (q); MS (EI^+): $m/z = 131$ (M^+).

Coupling of 4-Deuterio-1,2-dihydronaphthalene with 4-Fluorobromobenzene under Jeffery Conditions

To a well-stirred suspension of tetrabutylammonium chloride (208 mg, 0.75 mmol) and potassium acetate (73 mg, 0.75 mmol) in 3 mL of dry DMF with 4 Å molecular sieves were successively added 4-fluorobromobenzene (37 µL, 0.30 mmol), 4-deuterio-1,2-dihydronaphthalene (391 µL, 3.0 mmol) and palladium acetate (3.5 mg, 5 mol %). The reaction mixture was stirred under argon at 80 °C for 18 hours. After cooling, 5 mL of diethyl ether were added and the mixture filtered through Celite. After removal of the solvent and the starting material under vacuum, the crude product was purified by preparative TLC (pentane) to afford 3-(4-fluorophenyl)-4-deuterio-1,2-dihydronaphthalene; IR (thin film): $\nu_{max} = 3015.2$, 2939.9, 2828.2, 2167.3 (C=C – D), 1650.1 (C=C), 1223.5 cm^{-1}(C – F, s); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.73$ [2H, t, $CH_2CH=$, $^3J(H,H) = 8.0$ Hz], 2.97 [2H, t, $CH_2CH_2CH=$, $^3J(H,H) = 8.0$ Hz], 7.07, 7.17 (6H, m, H_{ar}), 7.51 (2H, m); ^{13}C NMR (500 MHz, $CDCl_3$): $\delta = 26.40$, 28.1, 115.29 [d, $^2J(C,F) = 21.3$ Hz], 126.50, 126.64, 126.72, 127.02, 127.22, 137.50, 134.57 [d, $^4J(C,F) = 1.7$ Hz], 137.19 [d, $^3J(C,F) =$ 3.9 Hz], 162.19 [d, $^1J(C,F) = 245.0$ Hz]; MS (EI^+): $m/z = 225.19$ (M^+).

Coupling of 4-Deuterio-1,2-dihydronaphthalene with 1-Bromo-4-fluorobenzene under Herrmann Conditions

1-Bromo-4-fluorobenzene (55 µL, 0.51 mmol), 4-deuterio-1,2-dihydronaphthalene (100 mg, 0.76 mmol), Herrmann's catalyst (4 mg, 1%), sodium acetate (46 mg, 0.56 mmol) and 4 Å molecular sieves were added in a Schlenk tube under argon. DMF (1 mL) was then added and the reaction mixture was stirred at 80 °C for 18 hours. The crude product was purified as before.

Attempts at Asymmetric Heck Coupling Reactions

Following Hayashi's conditions,[15a] palladium acetate (2.2 mg, 0.01 mmol) and (*R*)-BINAP (12.5 mg, 0.02 mmol) were dissolved in toluene (2 mL) under argon. The solution was stirred at room temperature for 10 min, then phenyl triflate (0.226 g, 162 µL, 1.0 mmol), freshly distilled 1,2-dihydronaphthalene (0.651 g, 653 µL, 5.0 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (0.616 g, 3.0 mmol) or triethylamine (0.506 g, 697 µL, 5.0 mmol) were added to the solution and stirred at 40 °C for 24 – 48 h. The same procedure of work-up as above gave no coupling, and starting materials were recovered.

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