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Benzylic C–H activation and C–O bond formation via aryl to benzylic 1,4-palladium migrations

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Abstract

A procedure for benzylic C–H activation has been developed using a palladium 1,4-aryl to benzylic migration as a key step. Carboxylates and phenoxides readily trap the resulting benzylic palladium intermediates obtained from palladium 'through space' migration. Aryl bromides and iodides have been successfully employed in this reaction, furnishing moderate to good yields. The mechanism of this reaction has been studied by deuterium-labeling experiments, which suggest that the migration of palladium from an aryl to a benzylic position occurs reversibly. The reaction conditions developed for the migration process also oxidize the neighboring benzylic alcohols to the corresponding aldehydes and ketones.

1. Introduction

Metal-catalyzed C–C bond forming reactions and C–H activation are well studied areas of growing interest.[1] These reactions have been increasingly applied to the synthesis of natural products.[1e–h] Among all of the transition metals known to undergo such processes, the C–C bond forming reactions of palladium have received the most attention. In recent years, palladium-catalyzed C–H activation has been used extensively in organic synthesis.[2] Many examples of cyclopalladation proceeding through alkyl/aryl palladacycles have been reported. They have proven to be a good model for C–H activation.[3] Lautens, Catellani, and others have successfully employed these reactions for the formation of a variety of heterocyclic ring systems.[3]

Transition metal-catalyzed intramolecular C–H activation via 'through space' migration of a metal has been recently disclosed.[1b,2b,c,4] It appears that the 'through space' migration is quite a general reaction in the case of palladium, examples of vinylic to aryl,[5] aryl to aryl,[6] alkyl to aryl,[7] vinylic to aryl to allylic,[8] benzylic to aryl,[9] and aryl to imidoyl[10] migration having been recently reported. We have earlier demonstrated that in *o*-iodobiaryls, palladium can migrate from one ring to the other and the resulting palladium intermediate can be trapped by Heck, as well as Suzuki, cross-coupling reactions or direct arylation.[6] The aryl palladium intermediate formed by alkyl to aryl palladium migration can also be trapped by Heck olefination or arylation.[7] Cesium pivalate, a crucial base for these Pd migration reactions, can also be used for the trapping, as we have demonstrated in vinylic to aryl to allylic migrations to form the corresponding allylic esters.[8]

Metal migration reactions provide an alternate way to introduce a palladium moiety into a specific position in an organic molecule, which has proven to be a useful tool for the synthesis of many heterocyclic ring systems. Vinylic to aryl migrations have been employed for the synthesis of alkylidene fluorenes,[5a,b] dibenzofurans,[5c,d] carbazoles,[5c,d] and indoles,[5d] whereas alkyl to aryl and aryl to aryl migrations have proven useful for the synthesis of fused polycycles.[6,7] Recently, we have also utilized aryl to imidoyl palladium migrations for the synthesis of fluoren-9-ones and xanthones.[10] Dyker has successfully applied the C–H activation of a methoxy group for the synthesis of 6*H*-dibenzo[*b*,*d*]pyrans.[11]

The reported palladium migration reactions are presumed to proceed through a five- or six-membered palladacycle.

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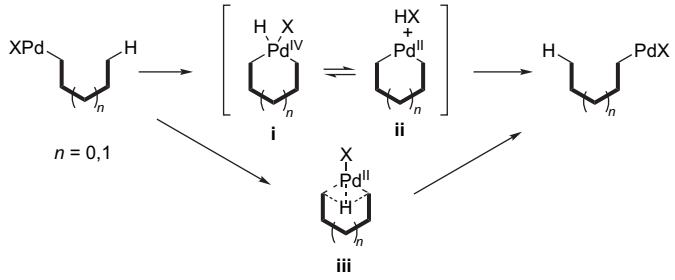
The mechanism suggested for these Pd migrations by our group involves a palladacycle(IV) hydride **i** or a palladacycle(II) intermediate **ii** (Scheme 1).[5a–d,6a,b,d,7,8] In contrast to our observations, a theoretical study published by Bour and co-workers suggests the possibility of intermediate **iii**, which they suggest is energetically favored.[5e,f] However, this mechanism fails to account for H–D exchange processes observed in our present work as well as many of our earlier migration reactions.[6a,8]



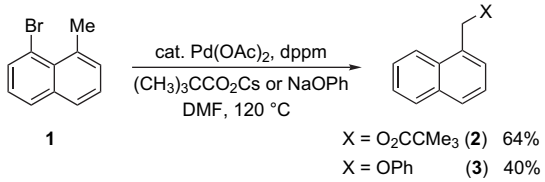
Scheme 1.

Wang and co-workers have reported the migration of palladium from a benzylic to an aryl position and subsequent trapping of the resulting intermediates by a Heck reaction.[9] Their reaction conditions required that relatively electron-rich alkenes be employed in order for the Pd migration to take place prior to the Heck reaction. A mixture of isomeric olefins was produced, reducing the synthetic utility of the overall process. Moreover, they did not demonstrate the actual migration of the palladium from an aryl to a benzylic position. Herein, we report a number of aryl to benzylic palladium migrations and subsequent trapping of the benzylic palladium intermediate by oxygen nucleophiles to form benzylic esters and ethers. The advantage of our methodology is that the benzylic position can be selectively activated, resulting in good clean reactions, producing a single product in good yields.

2. Results and discussion

2.1. Benzylic C–H activation

We have found that 1-bromo-8-methylnaphthalene (**1**), prepared by the reduction of commercially available (8-bromonaphthalen-1-yl)methanol using $NaBH_3CN$ and $BF_3\cdot Et_2O$,[12] when subjected to our standard palladium migration conditions employing cesium pivalate as a base furnished the corresponding benzylic ester **2** in 64% yield (Scheme 2 and Table 1, entry 1). The reaction requires a shorter reaction time (6 h)



Scheme 2.

Table 1
Effect of the nucleophile on the reaction in Scheme 2[a]

Entry	Nucleophile	Time (h)	Product	Yield (%)
1	$(CH_3)_3CCO_2Cs$	6	**2**	64
2	PhONa	12	**3**	40
3	EtONa	24	**4**	0
4	Ph_2NH	24	**5**	0
5	*n*-Bu_2NH	24	**6**	0
6	NaN_3	24	**7**	0
7	Diethyl sodium malonate	24	**8**	0
8	Sodium phthalimide	24	**9**	0

[a] Reaction conditions: all reactions were performed using 0.25 mmol of aryl halide **1a**, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, 3 equiv of the nucleophile, and 4 mL of DMF at 120 °C.

compared with our earlier reported migration reactions and is very clean. Only a trace amount of the protodehalogenated by-product 1-methylnaphthalene was observed.

To study the scope of this migration process, different nucleophiles other than cesium pivalate have been employed as potential traps for the presumed benzylic palladium intermediate. It seemed most reasonable to try nucleophiles, which have been used to trap π-benzylic[13] and π-allylic[14] intermediates. As mentioned earlier, cesium pivalate has proven crucial for migration of the palladium in our earlier work. However, we were surprised to observe that sodium phenoxide also allows the migration of palladium. Nucleophilic displacement of palladium by this nucleophile gave a 40% yield of the corresponding benzylic aryl ether **3** (Scheme 2 and Table 1, entry 2). However, most other nucleophiles examined failed to give the desired product, including an alkoxide, amines, azide, malonate, and a phthalimide anion (Table 1, entries 3–8).

Since the cation present in such reactions can often have a profound effect on the overall yield, we have examined the effect of various alkali metal pivalates on the process shown in Scheme 2 (see Table 2). In contrast to cesium pivalate, sodium pivalate gave a poor yield of 27% (Table 2, compare entries 1 and 2). We also tried the corresponding potassium and lithium salts, but they also failed to give better yields when compared with cesium. Potassium pivalate only gave a 15% yield of the desired product and lithium pivalate failed to give any of the desired product even after 1 day (entries 3 and 4). No correlation is observed between the size of the cation and the yield of the reaction.

To further study the scope of this methodology, other aryl halides along with several other phenoxides and carboxylates have been subjected to our migration reaction conditions (Table 3). In the pivalate reactions, we have found that

Table 2
Effect of the cation on the reaction in Scheme 2[a]

Entry	Base	Time (h)	Yield (%)
1	$(CH_3)_3CCO_2Cs$	6	64
2	$(CH_3)_3CCO_2Na$	12	27
3	$(CH_3)_3CCO_2K$	12	15
4	$(CH_3)_3CCO_2Li$	24	0

[a] Reaction conditions: all reactions were performed using 0.25 mmol of aryl halide **1a**, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, 3 equiv of the base, and 4 mL of DMF at 120 °C.

Table 3
Scope of the benzylic C–H activation[a]

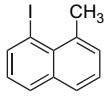
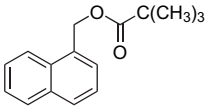
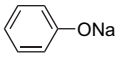
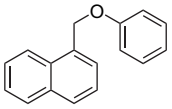
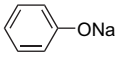
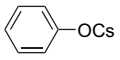
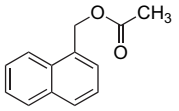
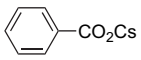
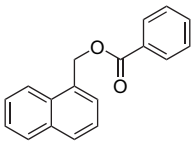
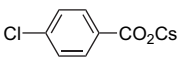
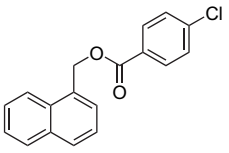
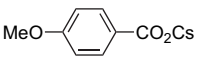
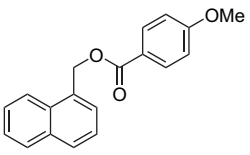
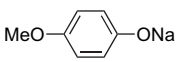
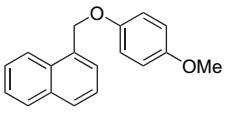
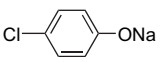
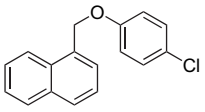
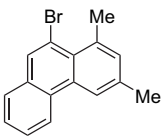
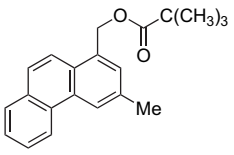
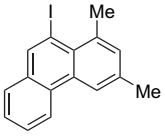
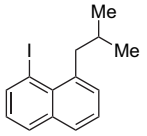
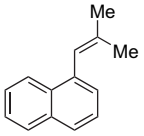
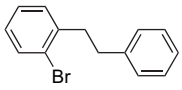
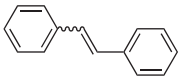
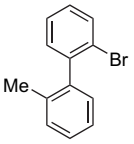
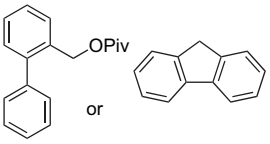
Entry	Aryl halide		Base	Time (h)	Product		Yield[b] (%)
1		**1**	$(CH_3)_3CCO_2Cs$	6		**2**	64
2		**10**	$(CH_3)_3CCO_2Cs$	4		**2**	81
3		**1**		12		**3**	40
4		**10**		12		**3**	52
5		**1**		12		**3**	39
6		**10**	CH_3CO_2Cs	4		**11**	64
7		**10**		4		**12**	61
8		**10**		4		**13**	38[c]
9		**10**		4		**14**	67
10		**10**		12		**15**	57
11		**10**		12		**16**	44
12		**17**	$(CH_3)_3CCO_2Cs$	6		**18**	37
13		**19**	$(CH_3)_3CCO_2Cs$	4		**18**	66

Table 3 (*continued*)

Entry	Aryl halide		Base	Time (h)	Product		Yield[b] (%)
14		**20**	$(CH_3)_3CCO_2Cs$	4		**21**	75[c]
15		**22**	$(CH_3)_3CCO_2Cs$	24		**23**	0
16		**24**	$(CH_3)_3CCO_2Cs$	24		**25** or **26**	0

[a] Unless otherwise stated, all reactions were performed using 0.25 mmol of the aryl halide, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, 3 equiv of the base, and 4 mL of DMF at 120 °C.

[b] Isolated yield.

[c] The yield was determined by quantitative ^1H NMR spectroscopic analysis.

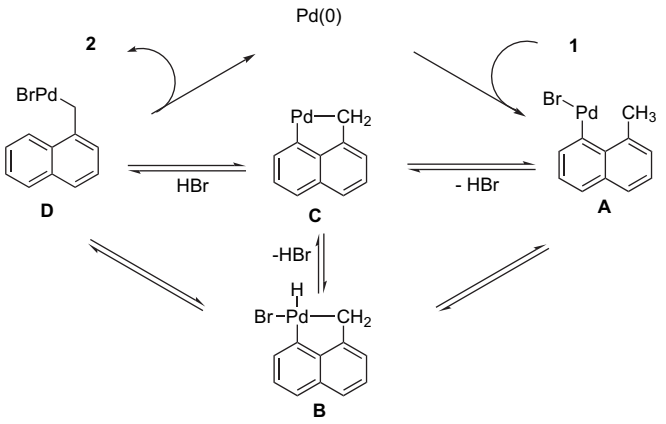
1-iodo-8-methylnaphthalene (**10**) gives a better yield and a cleaner reaction than the corresponding bromide (Table 3, entries 1 and 2). Similar results have been obtained with phenoxide as the nucleophile. Thus, iodoarene **10** gave aryl ether **3** in a 52% yield, while the corresponding aryl bromide furnished the desired product in only a 40% yield (entries 3 and 4). Surprisingly, aryl bromide **1** when subjected to our migration conditions using cesium phenoxide as the nucleophile failed to give a higher yield of the desired aryl ether **3** (entry 5).

When cesium acetate was employed, instead of cesium pivalate, the yield of the reaction dropped from 81% to 64% (compare entries 2 and 6). Substituted cesium benzoates have also been successful in these benzylic C–H activation processes (entries 7–9). However, the yields are lower than those obtained using pivalate anion. Cesium *p*-chlorobenzoate (entry 8) produced a lower yield than cesium benzoate (entry 7). However, cesium *p*-methoxybenzoate resulted in a higher yield (entry 9). This observation can be attributed to the relative nucleophilicity of the corresponding anions. The nucleophilicity of the phenoxides has also been found to be a crucial factor in the yields of the reactions (compare entries 4, 10, and 11). Phenoxide gave a lower yield of ether **3** than *p*-methoxyphenoxide, which gave a 57% yield of the desired product **15** (entry 10) whereas *p*-chlorophenoxide gave **16** in only a 44% yield (entry 11).

Our methodology has an advantage over typical benzylic oxidations or brominations as these latter reactions are usually not very selective if more than one benzylic group is present. Our methodology can be used for selective C–H activation as observed in the case of aryl halides **17** and **19**, where the benzylic C–H, which is in close proximity to the halide is selectively activated and furnishes only the corresponding ether (entries 12 and 13). Analogous to our earlier observation, aryl bromide **17** furnished the corresponding ester **18** in a lower yield (37%) than aryl iodide **19**, which gave a 66% yield of ester **18** (entries 12 and 13).

The benzylic palladium intermediate formed after palladium migration can also undergo facile β-hydride elimination when such hydrogens are available, as observed in the case of aryl iodide **20**, where the expected product **21** was formed in a good yield of 75% (entry 14). Our efforts to extend this methodology to a limited number of other systems have failed. For example, no migration/hydride elimination product **23** was observed when bibenzyl **22** was subjected to the usual migration reaction conditions (entry 15). In similar systems, Olivier and co-workers have demonstrated the C–H activation of an alkyl position.[15] However, the presence of a benzylic *gem*-dialkyl group in their systems reduces the bond angle and enhances the possibility of forming the necessary five-membered ring palladacycle. Our one attempt to activate a benzylic C–H bond by a 1,5-palladium migration also failed, as biphenyl derivative **24** failed to furnish any of the desired product **25** or **26**, instead producing only protodehalogenated product (entry 16).

Possible mechanisms for these reactions are depicted in Scheme 3. After oxidative addition of the aryl halide to Pd(0), the resulting intermediate **A** can insert into the neighboring C–H bond to form palladium(IV) intermediate **B** or a palladium(II) intermediate **C**. Intermediate **C** can also be produced by loss of HBr from palladacycle **B**. Palladacycles **B** and **C** both can form



Scheme 3.

D, which results in migration of the palladium to the benzylic position. Previous work on benzylic to aryl palladium migrations reported by Wang and co-workers[9] suggested that the steps to obtain **D** from **A** could be reversible.

To study the mechanism in detail, we decided to employ a deuterated version of compound **1** (**1a**) under our standard reaction conditions, since such reactions should result in the migration of deuterium from the benzylic position to the aryl position (Scheme 4). To our surprise, we did not see any deuterium incorporation in the aromatic ring when **1a** was allowed to react with cesium pivalate in DMF straight from the bottle (Scheme 4, Eq. 1). This observation might be attributed to H–D exchange between the palladium(IV) deuteride or DBr formed in the reaction with spurious H_2O present in the reaction system. However, we observed 100% deuterium incorporation into one aryl position when the same reaction was performed with 10 equiv of D_2O added to anhydrous DMF (Scheme 4, Eq. 2). The outcome of the above studies strongly suggests that the H–D exchange reactions arise by the equilibria indicated in Scheme 3. This encouraged us to check the reversibility of the steps that might exist between intermediates **D** and **A**.

To do this, we decided to carry out the reaction with non-deuterated 1-bromo-8-methylnaphthalene in the presence of 10 equiv of D_2O using anhydrous DMF (Scheme 4, Eq. 3). Proton NMR spectroscopic analysis of the product showed that incorporation of the deuterium occurs not only in the aryl position (30% of one aromatic hydrogen), but also in the benzylic position (70% of two benzylic hydrogens). This provides strong evidence that the palladium migration occurs reversibly between the aryl and benzylic positions. Increasing the amount of D_2O from 10 to 20 equiv did not change the amount of deuterium incorporation in either the aryl or the benzylic position. Interestingly, we have found that not only an M^+ (MW=242) peak was observed in the GC–MS, but also M+1, M+2 and M+3 peaks were present in significant amounts.

These four peaks in the GC–MS suggest that six possible compounds have been formed as illustrated in Figure 1. Out of the six possible products formed, the mechanism for the formation of **2e** and **2c** is outlined in Scheme 5. As discussed earlier, palladacycles **B** and **C** could be obtained from **A** via cyclopalladation. These two cyclic intermediates can undergo H–D exchange to form **E**. Benzylic intermediate **F** can be obtained from reductive elimination of **E** or from palladium(II) palladacycle **C** directly. Nucleophilic substitution of **F** ultimately produces the deuterated compound **2e**. Similar steps can be written for the formation of **2c** starting from **G**. The formation of **G** can take place from **E** via reductive elimination. **G**, which can also be obtained from **C** directly, can undergo benzylic C–H activation similar to that of **A**. The steps for the formation of **2c** from **G** are expected to be similar to those required for the formation of **2e**. Again, they may proceed through palladium(II) intermediate **H** or palladium(IV) intermediate **I**. Equivalent processes can be written starting from **H** and **J** for the formation of the other deuterated products.

The deuterated compound **1a** used for the mechanistic study was prepared in two steps. We started from 8-bromo-1-naphthoyl chloride (**27**) (Scheme 6), which was prepared

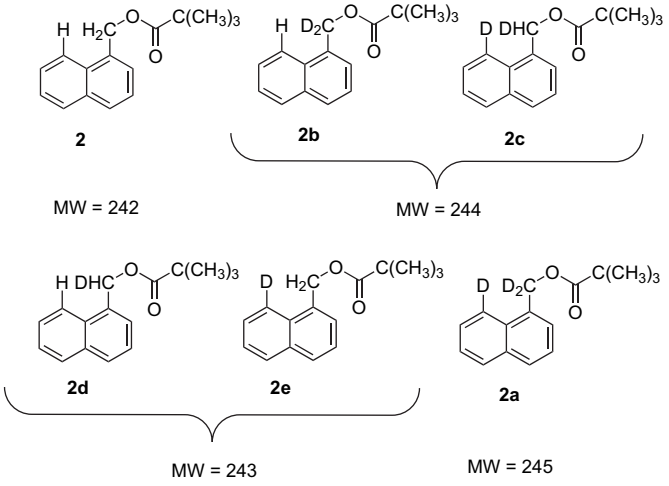
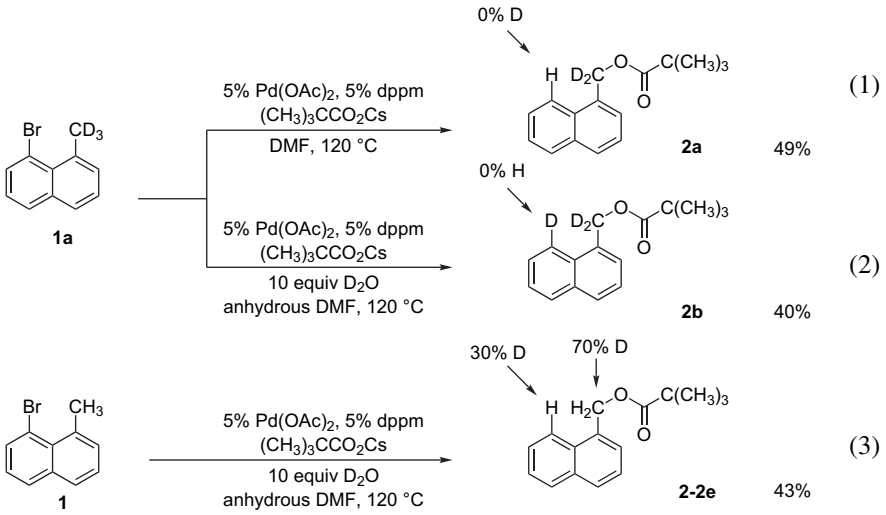
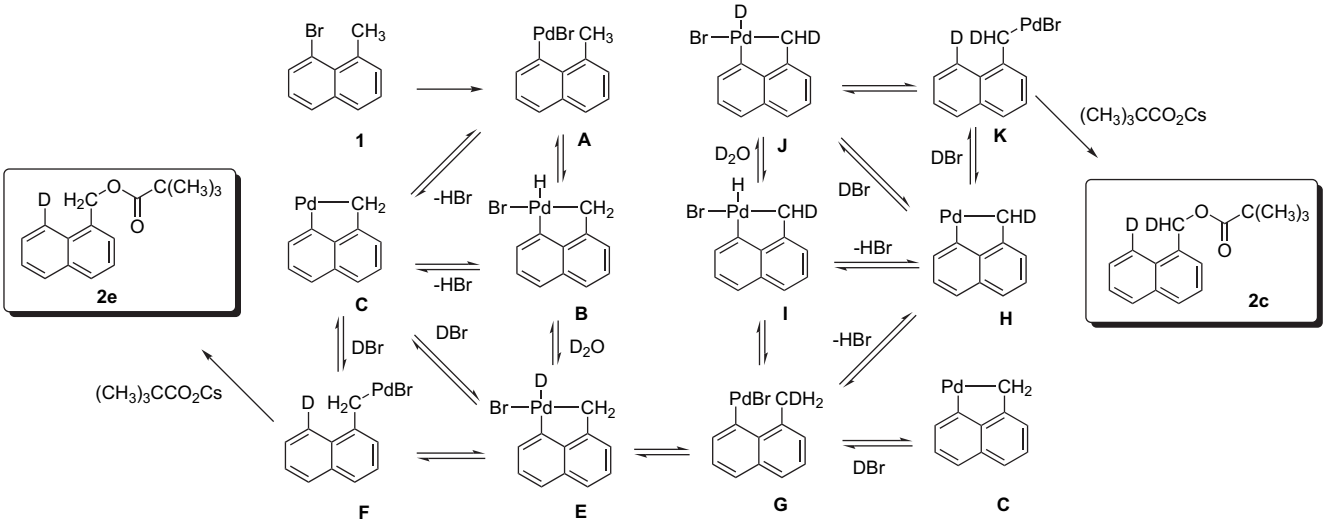


Figure 1.

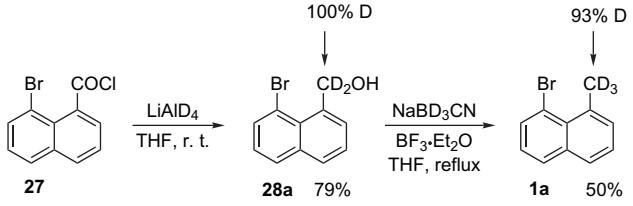


Scheme 4.



Scheme 5.

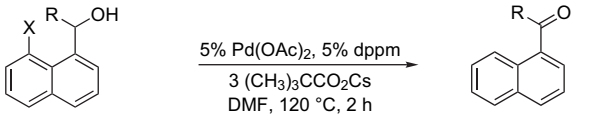
from 8-bromo-1-naphthoic acid using a literature procedure.[16] Reduction of the acid chloride **27** to the corresponding benzylic alcohol **28a** using $LiAlD_4$ resulted in a 79% yield of **28a** with 100% deuterium incorporation in both of the benzylic positions. The reduction of **28a** with $NaBD_3CN$ and $BF_3{\cdot}Et_2O$ gave the desired deuterated compound **1a** in a 50% yield with 93% deuterium incorporation in the three benzylic positions.



Scheme 6.

2.2. Oxidation of benzylic alcohols

The palladium-catalyzed oxidation of alcohols has been well studied.[17] Generally, these reactions require a palladium catalyst with an aryl halide or O_2 as the oxidant.[17b–i] When aryl halide **28** was subjected to our standard palladium migration conditions, 1-naphthaldehyde (**29**) was obtained in a 71% yield (Scheme 7). Since the reaction was performed under argon, the absence of O_2 suggests that the aryl bromide present in the starting material must be acting as an oxidant. To check the involvement of the aryl bromide in the reaction, we performed the same reaction using 1-naphthylmethanol (**30**) (Scheme 7, entry 2), which did not give any aldehyde product. Aryl iodide **31** gave a cleaner reaction than **28** and a slightly higher yield of aldehyde when compared with the corresponding bromo derivative **28** (compare entries 1 and 3). We have also found that aryl halide-containing secondary benzylic alcohols can be oxidized to the corresponding ketones in good yields (entries 4 and 5). The relatively hindered alcohol



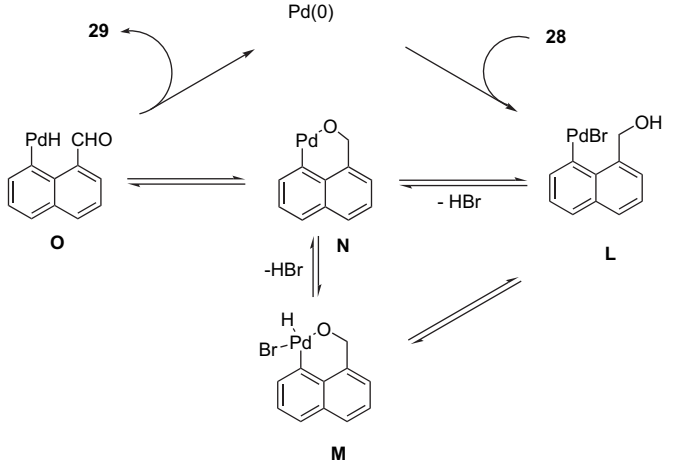
entry	aryl alcohol	X	R	product	yield (%)
1	**28**	Br	H	**29**	71
2	**30**	H	H	**29**	0
3	**31**	I	H	**29**	73
4	**32**	I	$PhCH_2CH_2$	**33**	70
5	**34**	Br	*n*-Hex	**35**	67
6	**36**	Br	Ph	**37**	52

Scheme 7.

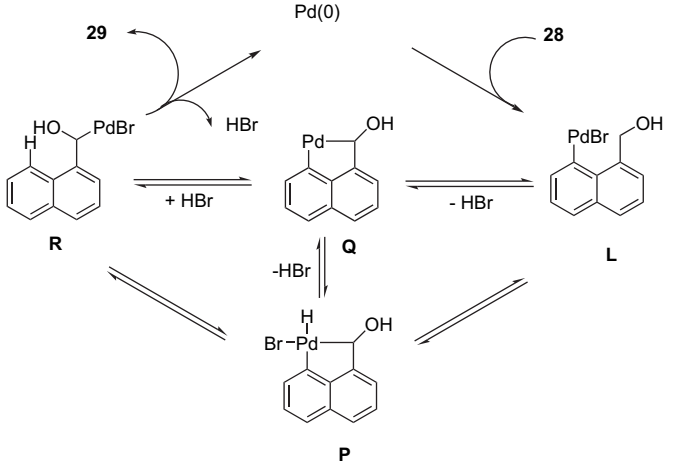
36 was also successfully oxidized, but in a lower yield of 52% (entry 6).

This redox chemistry could potentially occur via two different pathways. One possible route to the product could be the usual oxidation mechanism suggested by Turner and co-workers (Scheme 8).[17c] Palladacycle **L**, obtained after oxidative insertion of palladium into aryl halide **28**, can react with the neighboring alcohol group to form the Pd(IV) palladacycle **M** or Pd(II) intermediate **N**. Aryl palladium intermediate **O** can then be obtained via β-hydride elimination from **N** and can undergo reductive elimination to form the corresponding product **29**. A second possible route based upon a methoxy C–H activation process reported by Dyker[11] and our present aryl to benzylic palladium migration is outlined in Scheme 9. Aryl palladium intermediate **L** could also undergo benzylic C–H activation to form palladacycles **P** or **Q**. Intermediate **P** can also lead to the formation of **Q** via loss of HBr. Benzylic palladium intermediate **R**, which might be obtained from **P** and/or **Q** could easily undergo β-hydride elimination to give aldehyde **29**.

If the reaction proceeds through the pathway mentioned in Scheme 8, then it should also be possible to oxidize aryl iodide



Scheme 8.

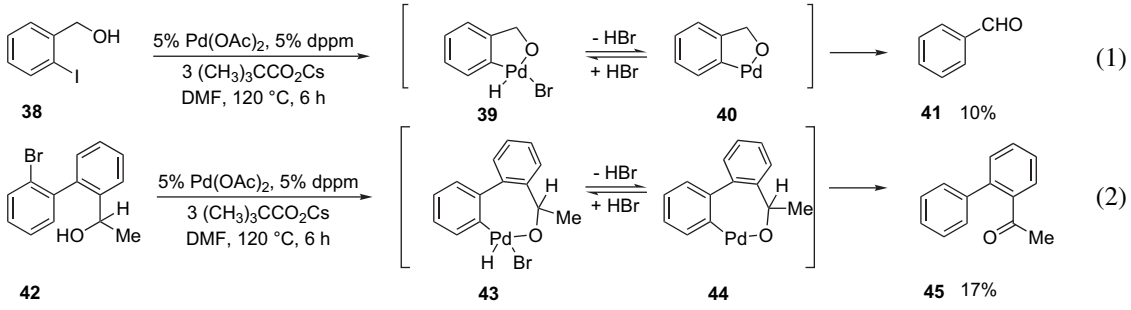


Scheme 9.

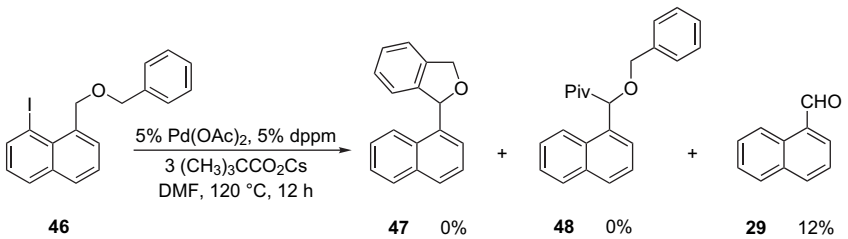
38 under these conditions (Scheme 10, Eq. 1). Moreover, the formation of five-membered ring palladacycles similar to **M** and **N** might be favored. However, we observe only a 10% yield of benzaldehyde (**41**) from this reaction. Even though the formation of five-membered rings is more favorable than six-membered ring formation, it is not a favorable geometry for the β-hydride elimination. Analogous to our above observation, the aryl bromide **42** also failed to furnish the desired product in a good yield, affording only a 17% yield of ketone **45** (Scheme 10, Eq. 2). In this case, the formation of a seven-membered ring palladacycle is not very favorable, even though it is probably a more favorable geometry for β-hydride elimination.

We have also subjected aryl halide **46** to our standard migration conditions hoping to perhaps see heterocycle **47** or pivalate **48**, the formation of which would suggest the possibility of benzylic C–H activation next to the electron-withdrawing oxygen (Scheme 11). Cyclization of the resulting benzylic palladium intermediate onto the remote aryl group would lead to heterocycle **47**, whereas nucleophilic substitution of the benzylic palladium by pivalate anion should produce compound **48**. To our surprise, only 1-naphthaldehyde (**29**) was formed in a poor 12% yield. This observation suggests the possible formation of **48**, which has hydrolyzed to give the observed aldehyde or perhaps Pd-benzyl elimination from an intermediate formed by benzylic C–H activation. However, all attempts to isolate **48** have failed.

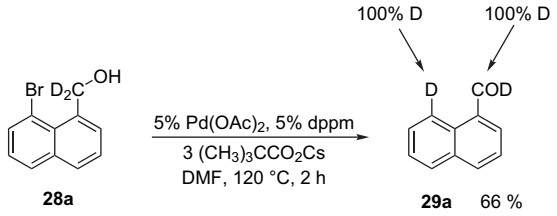
When the deuterium-labeled compound **28a** was subjected to our usual palladium migration conditions, 100% migration of one deuterium to the aryl position was observed (Scheme 12). This reaction was unaffected by H–D exchange with solvent, even when H_2O is added. This would presumably not be the case if the reaction is taking place by the mechanism depicted in Scheme 9. The deuterium-labeling experiments and the possibility of strong coordination between



Scheme 10.



Scheme 11.



Scheme 12.

palladium and oxygen suggest that the pathway outlined in Scheme 8 is more favorable for this particular reaction.

3. Conclusions

A benzylic C–H activation procedure has been developed using 'through space' migration of palladium as a key step. This process is not only very interesting from the point of view of mechanism, but it is also very useful for selective C–H activation. Carboxylates and phenoxides have been employed to prepare the corresponding benzylic esters and ethers in moderate to good yields. It is observed that the more nucleophilic aromatic phenoxides and carboxylates give better yields. The mechanism of the reaction involving palladium(II) or palladium(IV) intermediates has been discussed. Deuterium-labeling experiments suggest that the key step is reversible. That is aryl to benzylic and benzylic to aryl migrations are both possible. The reaction conditions developed for these migration processes also oxidize aryl-containing benzylic alcohols to the corresponding aldehydes and ketones in good yields with simultaneous reduction of halogen. Two possible mechanisms for the oxidation of these alcohols are discussed.

4. Experimental section

4.1. General

The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz, respectively. All melting points are uncorrected. High-resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. (8-Bromonaphthalen-1-yl)methanol (**28**), **30**, (8-iodonaphthalen-1-yl)methanol (**31**), and **38** were obtained commercially. All reagents were used directly as-obtained commercially unless otherwise noted. The following starting materials were made according to literature procedures: 8-bromo-1-naphthoyl chloride (**27**),[16] 10-bromo-1,3-dimethylphenanthrene (**17**),[18] 1-bromo-2-(phenethyl)benzene (**22**),[19] and 1,8-diiodonaphthalene.[20]

4.1.1. Preparation of 1-bromo-8-methylnaphthalene (*1*)

To a stirred solution of (8-bromonaphthalen-1-yl)methanol (472 mg, 2.0 mmol) and $BF_3 \cdot Et_2O$ (2.39 mL, 6.0 mmol) in dry THF (10 mL), sodium cyanoborohydride (240 mg, 4.0 mmol) was added. The reaction mixture was allowed to reflux for 2 days and was monitored by TLC. After completion of the reaction, 20 mL of ether was added and the solution was washed with saturated aqueous $NaHCO_3$ and brine. The resulting mixture was dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the crude mixture on silica gel afforded the desired product **1** (234 mg, 53%) as a white solid: mp 78–80 °C (lit.[21] 79–80 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.14 (s, 3H), 7.23 (t, J=7.6 Hz, 1H), 7.34–7.41 (m, 2H), 7.70–7.76 (m, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.86 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 120.0, 125.6, 126.0, 128.1, 129.3, 131.0, 131.3, 133.4, 135.4, 136.6; IR (neat, cm^{-1}) 3055, 2968, 2930, 2861, 1563, 1497, 1441, 1381, 1357, 1248, 1192, 1070, 893, 807, 756; HRMS calcd for $C_{11}H_9Br$: 219.98876, found: 219.98916.

4.1.2. 1-Bromo-8-(trideuteromethyl)naphthalene (*1a*)

8-Bromo-1-naphthoyl chloride[16] (525 mg, 2.0 mmol) in anhydrous THF (2 mL) was added to lithium aluminum hydride (92.4 mg, 2.2 mmol) suspended in anhydrous THF (3 mL). After the addition was complete, the mixture was stirred at room temperature for 1 h and hydrolyzed with saturated aqueous sodium sulfate. The resulting solution was extracted with ethyl ether (2×10 mL). The ether layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was obtained as a pale yellow solid, which was further purified using column chromatography to furnish deuterated alcohol **28a** (376 mg, 79%) as a white solid: mp 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (br s, 1H), 7.25 (t, J=7.6 Hz, 1H), 7.44 (t, J=7.2 Hz, 1H), 7.66 (dd, J=1.6, 7.2 Hz, 1H), 7.77–7.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 64.4 (m), 118.1, 125.9, 126.2, 129.8, 129.9, 130.2, 130.3, 133.8, 136.7, 136.8; IR (neat, cm^{-1}) 3048, 2961, 1738, 1364, 1227, 1023, 798, 776; HRMS calcd for $C_{11}H_7D_2BrO$: 237.99623, found: 237.99655. The deuterated aryl bromide **1a** was prepared using the procedure described for the preparation of **1**, but using alcohol **28a** and $NaBD_3CN$, and was obtained as a white solid: mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, J=7.6 Hz, 1H), 7.32–7.42 (m, 2H), 7.68–7.75 (m, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.85 (d, J=7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6 (m), 120.0, 125.7, 126.0, 128.1, 129.4, 131.0, 131.3, 133.4, 135.3, 136.6; IR (neat, cm^{-1}) 3055, 2968, 2930, 2861, 1563, 1497, 1441, 1381, 1357, 1248, 1192, 1070, 893, 807, 756; HRMS calcd for $C_{11}H_9D_3Br$: 223.00759, found: 223.00802.

4.1.3. 1-Iodo-8-methylnaphthalene (*10*)

Trifluoroacetic acid (1.3 g, 12 mmol) was added to a solution of (8-iodonaphthalen-1-yl)methanol (568 mg, 2.0 mmol) and 5 mL of dry CH_2Cl_2 at 0 °C. A solution of triethylsilane (277 mg, 4.4 mmol) in 1 mL of anhydrous CH_2Cl_2 was added to the reaction mixture. The reaction mixture was allowed to reach room temperature and stirred overnight under nitrogen. After completion of the reaction, the CH_2Cl_2 was removed under reduced pressure and the resulting solution was diluted with 20 mL of ether and washed with saturated aqueous sodium bicarbonate solution. The resulting organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure and purification of the crude mixture using column chromatography furnished the

desired product **10** (219 mg, 41% yield) as a white solid: mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.21 (s, 3H), 7.03 (t, J=7.6 Hz, 1H), 7.32–7.44 (m, 2H), 7.72 (d, J=7.6 Hz, 1H), 7.81 (d, J=8.0 Hz, 1H), 8.31 (d, J=7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.6, 90.4, 125.8, 126.2, 128.7, 130.3, 131.0, 133.1, 135.0, 135.9, 142.2; IR (neat, cm^{-1}) 3051, 2964, 2927, 2860, 1558, 1494, 1440, 1380, 1191, 1038, 805, 756; HRMS calcd for $C_{11}H_9I$: 267.97490, found: 267.97553.

4.1.4. 10-Iodo-1,3-dimethylphenanthrene (*19*)

To a stirred solution of **17**[18] (284 mg, 1.0 mmol) in THF (5 mL) at −78 °C, *n*-BuLi (2.5 M in hexanes, 0.4 mL, 1.0 mmol) was added. The resulting solution was stirred for 15 min. To the resulting solution, I_2 (508 mg, 2.0 mmol) in THF (1 mL) was slowly added by syringe over a period of 5 min. The solution was then allowed to reach room temperature and treated with a saturated aqueous $Na_2S_2O_3$ solution. The resulting mixture was extracted with diethyl ether (2×10 mL). The extracted organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by flash chromatography to provide **19** as a brown solid (209 mg, 63%): mp 65–67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 3.19 (s, 3H), 7.32 (s, 1H), 7.54 (t, J=7.6 Hz, 1H), 7.62 (t, J=7.2 Hz, 1H), 7.68 (d, J=7.6 Hz, 1H), 8.41 (s, 1H), 8.55–8.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 27.1, 88.8, 121.8, 123.3, 127.0, 127.2, 127.4, 128.7, 130.3, 132.5, 132.7 133.6, 135.8, 136.2, 142.1; IR (neat, cm^{-1}) 3076, 3052, 2966, 2926, 1613, 1566, 1453, 1378, 1164, 1033, 901, 874, 779; HRMS calcd for $C_{16}H_{13}I$: 332.00620, found: 332.00662.

4.1.5. 1-Iodo-8-isobutylnaphthalene (*20*)

A 100 mL round bottom flask containing 1,8-diiodonaphthalene[20] (1.14 g, 3.0 mmol) was flushed with argon and charged with 50 mL of anhydrous Et_2O. The pale yellow solution was cooled to −30 °C and *n*-BuLi (1.2 mL of 2.5 M solution in hexane, 3.0 mmol) was added over a period of 3 min. After 30 min, isobutyraldehyde (324 mg, 4.5 mmol) in 5 mL of anhydrous Et_2O was added by a syringe. The reaction mixture was allowed to warm to room temperature overnight and was then poured into 30 mL of 10% aqueous HCl. The aqueous layer was separated and extracted with three 10 mL portions of Et_2O. The combined organic layer was washed with 30 mL of aqueous NaCl. After drying over Na_2SO_4, the organic layer was concentrated to afford a yellow oil. Without purification this crude alcohol was added to a stirred solution of trifluoroacetic acid (975 mg, 9.0 mmol) and 5 mL of dry CH_2Cl_2 at 0 °C. A solution of triethylsilane (415 mg, 6.6 mmol) in 1 mL of anhydrous CH_2Cl_2 was added to the reaction mixture. The reaction mixture was allowed to warm to room temperature and stirred overnight under nitrogen. After completion of the reaction, the CH_2Cl_2 was removed under reduced pressure. The resulting solution was diluted with 30 mL of ether and washed with saturated aqueous sodium bicarbonate solution. The separated organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure and purification of the crude mixture using column chromatography furnished the desired product **20** (130 mg, 14%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, J=6.8 Hz, 6H), 2.08 (q, J=6.4 Hz, 1H), 3.44 (d, J=7.2 Hz, 2H), 7.03 (t, J=7.6 Hz, 1H), 7.33–7.45 (m, 2H), 7.74 (dd, J=2.0, 7.6 Hz, 1H), 7.84 (d, J=8.0 Hz, 1H), 8.56 (dd, J=1.2, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 31.0, 44.5, 89.9, 125.5, 126.1, 129.0, 130.8, 131.9, 132.4, 136.5, 138.4, 142.9; IR (neat, cm^{-1}) 3054, 2951, 2927, 2864, 1558, 1364, 1191, 1009, 801, 762; HRMS calcd for $C_{14}H_{15}I$: 310.021845, found: 310.02887.

4.1.6. 2-Bromo-2′-methylbiphenyl (*22*)

2-Bromophenylboronic acid (220 mg, 1.1 mmol) was added to a solution of *o*-iodotoluene (218 mg, 1.0 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol), K_2CO_3 (276 mg, 2.0 mmol), 4 mL of DMF, and 1 mL of H_2O. The reaction vial was sealed and flushed with argon and then allowed to stir at room temperature for 24 h. The resulting reaction mixture was diluted with 20 mL of Et_2O and washed several times with water to remove DMF. The resulting organic solution was dried over Na_2SO_4, concentrated in vacuum, and purified by column chromatography using hexanes as the eluent to furnish the desired product **22** (189 mg, 77%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 7.12 (d, J=7.6 Hz, 1H), 7.17–7.40 (m, 6H), 7.66 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 123.8, 125.5, 127.2, 127.9, 128.8, 129.3, 129.8, 130.9, 132.6, 136.0, 141.2, 142.7; IR (neat, cm^{-1}) 3055, 3017, 2941, 2882, 1466, 1403, 1119, 1064, 1004, 779; HRMS calcd for $C_{11}H_9D_3Br$: 246.00441, found: 246.00481.

4.1.7. 1-(8-Iodonaphthalen-1-yl)-3-phenylpropan-1-ol (*32*)

A 100 mL round bottom flask containing 1,8-diiodonaphthalene[20] (1.14 g, 3.0 mmol) was flushed with argon and charged with 50 mL of anhydrous Et_2O. The pale yellow solution was cooled to −30 °C and *n*-BuLi (1.2 mL of 2.5 M solution in hexane, 3.0 mmol) was added over a period of 3 min. After 30 min, a solution of 3-phenylpropanal (603 mg, 4.5 mmol) in 5 mL of anhydrous Et_2O was added by a syringe. The reaction mixture was allowed to warm to room temperature overnight and then poured into 30 mL of 10% aqueous HCl. The aqueous layer was separated and extracted with three 10 mL portions of Et_2O. The combined organic layer was washed with 30 mL of H_2O and 30 mL of saturated aqueous NaCl. After drying over Na_2SO_4, the organic layer was concentrated and the crude product was purified by column chromatography to give the desired alcohol **32** (453 mg, 39%) as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98–2.10 (m, 1H), 2.11–2.25 (br s, 1H), 2.28–2.41 (m, 1H), 2.95 (t, J=8.8 Hz, 2H), 7.84 (dd, J=2.8, 9.6 Hz, 1H), 7.04 (t, J=8.0 Hz, 1H), 7.13–7.32 (m, 5H), 7.53 (t, J=7.6 Hz, 1H), 7.74 (dd, J=1.2, 8.0 Hz, 1H), 7.85 (d, J=8.0 Hz, 1H), 8.04 (d, J=7.2 Hz, 1H), 8.29 (dd, J=1.2, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.5, 41.8, 67.6, 87.7, 125.8, 125.9, 126.0, 126.1, 128.4, 128.6, 129.6, 130.7, 131.2, 136.0, 141.3, 142.2, 143.0; IR (neat, cm^{-1}) 3320, 3056, 2951,

2924, 2854, 1563, 1463, 1035, 802, 761; HRMS calcd for $C_{19}H_{17}IO$: 388.03242, found: 388.03309.

*4.1.8. 1-(8-Bromonaphthalen-1-yl)heptan-1-ol (**34**)*

Manganese(IV) oxide (352 mg, 4.0 mmol) was added to a solution of the alcohol (8-bromonaphthalen-1-yl)methanol (470 mg, 2.0 mmol) in chloroform (10 mL) and the stirred mixture was allowed to reflux for 24 h. The suspension was filtered through Celite and washed with chloroform. The filtrate was washed with water (5 mL), dried over Na_2SO_4, and concentrated in vacuum to give 8-bromo-1-naphthaldehyde (369 mg, 79% yield) as a white solid: mp 81–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, J=8.0 Hz, 1H), 7.50 (t, J=8.0 Hz, 1H), 7.81–7.96 (m, 3H), 8.22 (d, J=7.6 Hz, 1H), 11.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 89.9, 126.0, 127.8, 129.8, 130.2, 133.7, 134.3, 135.7, 136.5, 141.4, 191.7; IR (neat, cm^{-1}) 2878, 2861, 1672, 1609, 1553, 1493, 1335, 1234, 1197, 1063, 824, 790, 747; HRMS calcd for $C_{11}H_7BrO$: 233.96803, found: 233.96836. At 0 °C, a 1 M solution of hexylmagnesium bromide (1.5 mL, 1.5 mmol) was added dropwise to a solution of 8-bromo-1-naphthaldehyde (233 mg, 1.0 mmol) in THF (10 mL). The mixture was stirred for 4 h at room temperature and then hydrolyzed with H_2O (3 mL). The organic phase was separated and the water phase was extracted with ether (2×10 mL). The combined extracts were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was further purified by flash chromatography on silica gel to give the required alcohol **34** (153 mg, 48% yield) as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J=6.8 Hz, 3H), 1.20–1.45 (br m, 6H), 1.50–1.75 (m, 3H), 1.98–2.18 (m, 2H), 6.60–6.67 (m, 1H), 7.23 (t, J=7.6 Hz, 1H), 7.51 (t, J=7.6 Hz, 1H), 7.76 (d, J=7.6 Hz, 1H), 7.79–7.88 (m, 2H), 8.02 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 22.8, 26.5, 29.6, 32.0, 40.7, 69.8, 117.9, 125.6, 125.8, 126.2, 129.2, 129.3, 129.9, 134.4, 136.7, 142.5; IR (neat, cm^{-1}) 3388 (br), 3056, 2951, 2924, 2854, 1563, 1463, 1192, 1059, 818, 761; HRMS calcd for $C_{17}H_{21}BrO$: 320.07758, found: 320.07806.

*4.1.9. (8-Bromonaphthalen-1-yl)(phenyl)methanol (**36**)*

Compound **36** was prepared as described for the synthesis of **34** using 8-bromo-1-naphthaldehyde and phenylmagnesium bromide and was obtained as a colorless liquid (240 mg, 77% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50–2.80 (br s, 1H), 7.25–7.32 (m, 2H), 7.33–7.42 (m, 4H), 7.46 (t, J=7.6 Hz, 1H), 7.68 (dd, J=1.2, 7.2 Hz, 1H), 7.80–7.94 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.9, 117.9, 125.9, 126.1, 127.4, 127.6, 128.4, 129.5, 130.0, 130.1, 130.2, 134.7, 136.7, 140.1, 144.1; IR (neat, cm^{-1}) 3319, 3083, 3057, 3028, 1561, 1450, 1193, 1035, 761; HRMS calcd for $C_{17}H_{13}BrO$: 312.01498, found: 312.01548.

*4.1.10. 1-(2′-Bromobiphenyl-2-yl)ethanol (**42**)*

2-Bromophenylboronic acid (440 mg, 2.2 mmol) was added to a solution of *o*-iodobenzaldehyde (462 mg, 1.0 mmol), $Pd(PPh_3)_4$ (48 mg, 0.04 mmol), K_2CO_3 (552 mg, 4.0 mmol), 8 mL of DMF, and 2 mL of H_2O. The reaction vial was sealed and flushed with argon and allowed to stir at room temperature for 24 h. The resulting reaction mixture was diluted with 30 mL of Et_2O and washed several times with water to remove DMF. The resulting organic solution was dried over Na_2SO_4 and concentrated in vacuum. The crude product was further purified by column chromatography using hexanes as the eluent to furnish the desired product 2′-bromobiphenyl-2-carbaldehyde (848 mg, 82%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.38 (m, 3H), 7.42 (dt, J=1.2, 7.6 Hz, 1H), 7.56 (t, J=7.6 Hz, 1H), 7.63–7.73 (m, 2H), 8.05 (dd, J=1.2, 8 Hz, 1H), 9.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.0, 127.5, 127.6, 128.7, 130.0, 131.0, 131.8, 132.9, 133.8, 133.9, 139.0, 144.6, 191.7; IR (neat, cm^{-1}) 3058, 2916, 2847, 2750, 1693, 1597, 1464, 1393, 1268, 1196, 1003, 826, 754; HRMS calcd for $C_{13}H_9BrO$: 259.98368, found: 259.98402. At 0 °C, a 1 M solution of methylmagnesium bromide (1.5 mL, 1.5 mmol) was added dropwise to a solution of 2′-bromobiphenyl-2-carbaldehyde (259 mg, 1.0 mmol) in THF (10 mL). The mixture was stirred for 4 h at room temperature and then hydrolyzed with H_2O (3 mL). The organic phase was separated and the water phase was extracted with ether (2×10 mL). The combined extracts were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was further purified by flash chromatography on silica gel to give alcohol **42** (184 mg, 67% yield) as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, J=6.4 Hz, 3H), 1.42 (d, J=6.4 Hz, 3H), 2.01 (br s, 2H), 4.64–4.78 (m, 2H), 7.09 (d, J=7.6 Hz, 1H), 7.13 (d, J=7.6 Hz, 1H), 7.20–7.42 (m, 8H), 7.44–7.53 (m, 2H), 7.63–7.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 24.6, 66.9, 67.2, 123.7, 124.2, 125.3, 125.4, 127.2, 127.3, 127.3, 127.5, 128.7, 128.9, 129.2, 129.2, 129.3, 129.9, 131.1, 131.5, 132.6, 132.8, 138.8, 139.4, 141.6, 141.7, 143.0, 144.0; IR (neat, cm^{-1}) 3350 (br), 3055, 3023, 2971, 2924, 1464, 1444, 1080, 1001, 754; HRMS calcd for $C_{14}H_{13}BrO$: 276.01498, found: 276.01531.

*4.1.11. 1-(Benzyloxymethyl)-8-iodonaphthalene (**46**)*

NaH (54 mg, 2.2 mmol) was added in small portions to a stirred solution of (8-iodonaphthalen-1-yl)methanol (566 g, 2.0 mmol) in dry DMF (50 mL) at 0 °C. After 20 min, benzyl bromide (0.42 mL, 4.0 mmol) was added dropwise to the solution at 0 °C and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl and the resulting mixture was diluted with Et_2O (30 mL). The organic layer was washed with water and brine, and then dried over $MgSO_4$. Evaporation of the solvent in vacuum afforded a residue, which was purified by column chromatography to furnish ether **46** (658 mg, 88%) as a yellow solid: mp 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.73 (s, 2H), 5.50 (s, 2H), 7.07 (t, J=7.6 Hz, 1H), 7.28–7.53 (m, 6H), 7.74–7.84 (m, 2H), 7.85 (d, J=8.0 Hz, 1H), 8.33 (d, J=7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.6, 72.3, 125.6, 126.3, 127.6, 128.0, 128.4, 129.6, 130.3, 130.3, 132.7, 133.9, 136.2, 138.3, 142.6; IR (neat, cm^{-1}) 3055,

3024, 2971, 2868, 1495, 1483, 1451, 1351, 1212, 1193, 1064, 1001, 815, 767, 757; HRMS calcd for $C_{18}H_{15}IO$: 374.01676, found: 374.01709.

4.2. General procedure for the C–H activation chemistry

To a stirred solution of 0.25 mmol of the aryl halide, $Pd(OAc)_2$ (2.8 mg, 0.012 mmol), dppm (4.8 mg, 0.012 mmol), and 4 mL of DMF, 3 equiv of the desired base was added. The reaction vial was sealed, flushed with argon, heated at 120 °C, and monitored by TLC. After completion of the reaction, the mixture was diluted with 20 mL of Et_2O and washed several times with small amounts of water to remove DMF. The resulting organic solution was dried over Na_2SO_4, concentrated in vacuum, and purified by column chromatography using hexanes and ethyl acetate as the eluent.

4.2.1. Naphthalen-1-ylmethyl pivalate (**2**)

The product was obtained as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 5.58 (s, 2H), 7.47 (t, J=7.2 Hz, 1H), 7.51–7.60 (m, 3H), 7.83–7.94 (m, 2H), 8.01 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.4, 39.2, 64.8, 123.8, 125.4, 126.1, 126.6, 127.2, 128.9, 129.2, 131.8, 132.0, 133.9, 178.6; IR (neat, cm^{-1}) 3049, 2972, 2934, 2871, 1726, 1599, 1479, 1397, 1281, 1148, 963, 795; HRMS calcd for $C_{16}H_{18}O_2$: 242.13068, found: 242.13116.

4.2.2. 1-(Phenoxymethyl)naphthalene (**3**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (s, 2H), 7.03 (t, J=7.2 Hz, 1H), 7.05 (d, J=8.0 Hz, 2H), 7.36 (t, J=7.6 Hz, 2H), 7.45–7.62 (m, 3H), 7.63 (d, J=6.8 Hz, 1H), 7.85–7.96 (m, 2H), 8.09 (d, J=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.8, 115.1, 121.3, 123.9, 125.5, 126.1, 126.6, 126.8, 128.9, 129.2, 129.8, 131.7, 132.5, 134.0, 159.1; IR (neat, cm^{-1}) 3053, 2986, 1598, 1495, 1421, 1265, 1173, 1029, 739; HRMS calcd for $C_{17}H_{14}O$: 234.10447, found: 234.10483.

4.2.3. Naphthalen-1-ylmethyl acetate (**11**)

The product was obtained as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 3H), 5.59 (s, 2H), 7.47 (t, J=8.0 Hz, 1H), 7.51–7.64 (m, 3H), 7.87 (d, J=8.4 Hz, 1H), 7.90 (d, J=8.4 Hz, 1H), 8.03 (d, J=8.4 Hz, 1H). Other physical and spectral data are consistent with those reported in the literature.[22]

4.2.4. Naphthalen-1-ylmethyl benzoate (**12**)

The product was obtained as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (s, 2H), 7.43 (t, J=7.6 Hz, 2H), 7.47–7.63 (m, 4H), 7.67 (d, J=6.8 Hz, 1H), 7.90 (d, J=9.6 Hz, 1H), 7.93 (d, J=9.6 Hz, 1H), 8.08 (d, J=8.0 Hz, 2H), 8.15 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.3, 123.8, 125.5, 126.2, 126.8, 127.7, 128.6, 128.9, 129.5, 129.9, 130.3, 131.7, 131.9, 133.2, 133.9, 166.7; IR (neat, cm^{-1}) 3061, 3010, 2961, 2900, 1923, 1719, 1600, 1511, 1451, 1314, 1270, 957, 710; HRMS calcd for $C_{18}H_{14}O_2$: 262.09938, found: 262.09974.

4.2.5. Naphthalen-1-ylmethyl 4-chlorobenzoate (**13**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (s, 2H), 7.38 (d, J=8.8 Hz, 2H), 7.47–7.63 (m, 3H), 7.65 (d, J=6.8 Hz, 1H), 7.87–7.95 (m, 2H), 8.00 (d, J=8.8 Hz, 2H), 8.13 (d, J=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.5, 123.7, 125.4, 126.2, 126.8, 127.8, 128.6, 128.8, 128.9, 129.6, 131.3, 131.4, 131.9, 133.9, 139.6, 165.7; IR (neat, cm^{-1}) 3048, 2962, 1720, 1594, 1478, 1400, 1268, 1171, 1100, 1014, 792, 758; HRMS calcd for $C_{17}H_{13}ClO$: 296.06041, found: 296.06080.

4.2.6. Naphthalen-1-ylmethyl 4-methoxybenzoate (**14**)

The product was obtained as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 5.81 (s, 2H), 6.90 (d, J=8.8 Hz, 2H), 7.45–7.62 (m, 3H), 7.65 (d, J=6.8 Hz, 1H), 7.89 (d, J=8.4 Hz, 1H), 7.92 (d, J=8.4 Hz, 1H), 8.13 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 64.9, 113.7, 122.5, 123.7, 125.4, 126.0, 126.6, 127.4, 128.8, 129.3, 131.8, 131.8, 133.8, 163.5, 166.3; IR (neat, cm^{-1}) 3050, 3007, 2960, 2934, 2838, 1710, 1605, 1511, 1256, 1167, 1100, 1028, 770; HRMS calcd for $C_{19}H_{16}O_3$: 292.10994, found: 292.11036.

4.2.7. 1-[(4-Methoxyphenoxy)methyl]naphthalene (**15**)

The product was obtained as a white solid: mp 72–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 5.46 (s, 2H), 6.89 (d, J=8.8 Hz, 2H), 7.01 (d, J=8.8 Hz, 2H), 7.48 (t, J=7.2 Hz, 2H), 7.52–7.65 (m, 3H), 7.84–7.94 (m, 2H), 8.08 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 69.6, 114.9, 116.1, 123.9, 125.5, 126.0, 126.6, 126.7, 128.8, 129.1, 131.7, 132.7, 133.9, 153.2, 154.3; IR (neat, cm^{-1}) 3051, 3001, 2954, 2911, 2834, 1507, 1465, 1265, 1227, 1037, 826, 738; HRMS calcd for $C_{18}H_{16}O_2$: 264.11503, found: 264.11547.

4.2.8. 1-[(4-Chlorophenoxy)methyl]naphthalene (**16**)

The product was obtained as a pale yellow solid: mp 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (s, 2H), 5.58 (s, 2H), 6.99 (d, J=8.2 Hz, 2H), 7.28 (d, J=9.2 Hz, 2H), 7.48 (t, J=7.2 Hz, 1H), 7.52–7.63 (m, 3H), 7.85–7.95 (m, 2H), 8.05 (dd, J=2.4, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 69.2, 116.4, 123.8, 125.5, 126.2, 126.7, 126.8, 128.9, 129.4, 129.6, 131.6, 132.1, 134.0, 157.6; IR (neat, cm^{-1}) 3055, 2924, 2872, 1592, 1509, 1468, 1377, 1279, 1236, 1007, 917, 797; HRMS calcd for $C_{17}H_{13}ClO$: 268.06549, found: 268.06583.

4.2.9. (3-Methylphenanthren-1-yl)methyl pivalate (**18**)

The product was obtained as a brown solid: mp 74–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 9H), 2.63 (s, 3H), 5.57 (s, 2H), 7.49 (s, 1H), 7.55–7.70 (m, 2H), 7.76 (d, J=8.8 Hz, 1H), 7.85–7.95 (m, 2H), 8.52 (s, 1H), 7.78 (d, J=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 27.4, 39.1, 65.2, 122.3, 123.0, 123.4, 126.7, 126.7, 126.8, 128.5, 128.7, 130.0, 130.4, 131.0, 131.9, 132.4, 135.8, 178.6; IR (neat, cm^{-1}) 2967, 2920, 2852, 1725, 1478, 1281, 1147, 1033,

950, 864, 819, 750; HRMS calcd for $C_{21}H_{22}O_2$: 306.16198, found: 306.16244.

4.2.10. 1-(2-Methylprop-1-enyl)naphthalene (**21**)

The product was obtained as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74 (s, 3H), 2.04 (s, 3H), 6.68 (s, 1H), 7.30 (d, J=7.0 Hz, 1H), 7.48–8.05 (m, 6H). The other physical and spectral data are consistent with those reported in the literature.[23]

4.3. General procedure for the alcohol oxidations

To the stirred solution of 0.25 mmol of the aryl halide, $Pd(OAc)_2$ (2.8 mg, 0.012 mmol), dppm (4.8 mg, 0.012 mmol), and 4 mL of DMF, cesium pivalate (175 mg, 0.75 mmol) was added. The reaction vial was sealed, flushed with argon, heated at 120 °C, and monitored using TLC. After completion of the reaction, the mixture was diluted with 20 mL of Et_2O and washed several times with small amounts of water to remove the DMF. The resulting organic solution was dried over Na_2SO_4, concentrated in vacuum, and purified by column chromatography using hexanes and ethyl acetate as the eluent.

4.3.1. 1-Naphthaldehyde (**29**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (m, 2H), 7.67 (t, J=8.5 Hz, 1H), 7.90 (d, J=8.5 Hz, 1H), 7.95 (d, J=8.2 Hz, 1H), 8.06 (d, J=8.2 Hz, 1H), 9.25 (d, J=8.5 Hz, 1H), 10.36 (s, 1H). The other physical and spectral data are consistent with those reported in the literature.[24]

4.3.2. (8-Deuteronaphthalen-1-yl)deuterocarbaldehyde (**29a**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.68 (m, 2H), 7.71 (d, J=6.8 Hz, 1H), 7.94 (dd, J=1.2, 8.0 Hz, 1H), 8.01 (dd, J=1.2, 6.8 Hz, 1H), 8.11 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.6, 124.9, 127.0, 128.5, 129.0, 130.5, 131.3 (m), 133.7, 135.4, 136.7, 193.3 (m); IR (neat, cm^{-1}) 3054, 2951, 2927, 2864, 1558, 1364, 1191, 1009, 801, 762; HRMS calcd for $C_{11}H_6D_2O$: 158.07007, found: 158.07033.

4.3.3. 1-(Naphthalen-1-yl)-3-phenylpropan-1-one (**33**)

The product was obtained as a light brown liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (t, J=7.6 Hz, 2H), 3.37 (t, J=7.6, Hz, 2H), 7.10–7.36 (m, 6H), 7.45 (t, J=8.0 Hz, 1H), 7.48–7.60 (m, 2H), 7.80 (d, J=7.2 Hz, 1H), 7.85 (d, J=7.6 Hz, 1H), 7.96 (d, J=8.4 Hz, 1H), 8.54 (d, J=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 44.0, 124.5, 125.9, 126.3, 126.6, 127.6, 128.1, 128.6, 128.6, 128.7, 130.3, 132.7, 134.1, 136.1, 141.3, 203.7; IR (neat, cm^{-1}) 3056, 3020, 2937, 2908, 1679, 1497, 1362, 1275, 1156, 1100, 945, 782; HRMS calcd for $C_{19}H1_6O$: 260.12012, found: 260.12055.

4.3.4. 1-(Naphthalen-1-yl)heptan-1-one (**35**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J=6.8 Hz, 3H), 1.20–1.45 (m, 6H), 1.79 (quintet, J=7.2 Hz, 2H), 3.05 (t, J=7.2 Hz, 2H), 7.46–7.65 (m, 3H), 7.81–7.92 (m, 2H), 7.98 (d, J=8.0 Hz, 1H), 8.55 (d, J=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.8, 29.1, 31.7, 42.4, 124.4, 125.8, 126.4, 127.2, 127.8, 128.4, 130.1, 132.3, 134.0, 136.5, 205.2; IR (neat, cm^{-1}) 2953, 2926, 2855, 1677, 1507, 1462, 1278, 1233, 1171, 1086, 799, 775; HRMS calcd for $C_{17}H_{20}O$: 240.15142, found: 240.15173.

4.3.5. Naphthalen-1-yl(phenyl)methanone (**37**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.51 (m, 2H), 7.51–7.56 (m, 3H), 7.56–7.63 (m, 2H), 7.86–7.89 (q, J=3.3 Hz, 2H), 7.92–7.94 (t, J=4.8 Hz, 1H), 8.00–8.02 (d, J=8.0 Hz, 1H), 8.09–8.11 (d, J=8.0 Hz, 1H). The other physical and spectral data are consistent with those reported in the literature.[25]

4.3.6. 1-(Biphenyl-2-yl)ethanone (**45**)

The product was obtained as a pale yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 7.35–7.47 (m, 7H), 7.53 (dt, J=1.4, 7.5 Hz, 1H), 7.58 (dd, J=1.2, 7.6 Hz, 1H). The other physical and spectral data are consistent with those reported in the literature.[26]

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