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Palladium-catalyzed heteroannulation of cyclic alkenes by functionally substituted aryl iodides

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Abstract

Indolines and 2,3-dihydrobenzofurans are produced in good yields by the Pd(0)-catalyzed heteroannulation of cyclic and bicyclic alkenes by *o*-amino- and *o*-hydroxyaryl iodides. These processes are only successful with cyclic olefins in which the key alkylpalladium intermediate cannot undergo facile palladium β-hydride elimination. These reactions appear to involve: (1) oxidative addition of the aryl iodide to the palladium catalyst, (2) arylpalladation of the olefin, (3) possible coordination of the internal nucleophile to the palladium, (4) formation of a six-membered palladacycle, and (5) reductive elimination of the organopalladium intermediate to give the heteroannulation product and regenerate Pd(0).

Keywords: Palladium catalysis; Heteroannulation; Indolines; Dihydrobenzofurans; Cyclic alkenes

1. Introduction

Heteroannulation processes allow for the rapid construction of a wide variety of heterocycles [1]. Our group has shown that the Pd(0)-catalyzed annulation of 1,2-, 1,3-, and 1,4-dienes and alkynes can be employed for the synthesis of indoles [2], benzofurans [3], benzopyrans [3], isocoumarins [3], α-pyrones [3], indenones [4], polycyclic aromatic hydrocarbons [5], pyridines [6], isoquinolines [6], isoindoloindoles [7], and carbolines [8]. We hope to extend these annulation processes to cyclic and bicyclic alkenes to produce a variety of indoline [9] and benzofuran [10] derivatives due to their importance in pharmaceuticals and their appearance in a large number of natural products. Typically, synthetic routes to these derivatives have involved multi-step procedures or relatively harsh reaction conditions [11].

We anticipated that to be successful, we would have to employ cyclic olefins with no allylic hydrogens or bicyclic alkenes whose constrained geometry would prevent palladium *syn*-β-hydride elimination in the key alkylpalladium intermediate and thus the formation of Heck-type products. One such alkene is norbornene. Norbornylpalladium species have been previously synthesized and their chemistry has been well-studied [12]. They readily insert CO to produce acylpalladium intermediates, which can be trapped by various nucleophiles [12a–d]. The direct intermolecular intermolecular displacement of the palladium from the norbornyl group by various nucleophiles generates carboxylic acid derivatives [12e,f], nitriles [12g,h], and cross-coupled hydrocarbons [12i–o]. Intramolecular coupling between the palladium and neighboring aryl groups has produced hexahydromethanobiphenyls [13]. After our own work was well underway, Catellani and Del Rio [14] reported several examples of the formation of oxygen- and nitrogen-containing heterocycles by the palladium-catalyzed heteroannulation of norbornene, norbornadiene and bicyclo[2.2.2]octene by *o*-halophenols and -anilines Eq. (1), thus encouraging us to report the full details of our own heteroannulation efforts using a broader range

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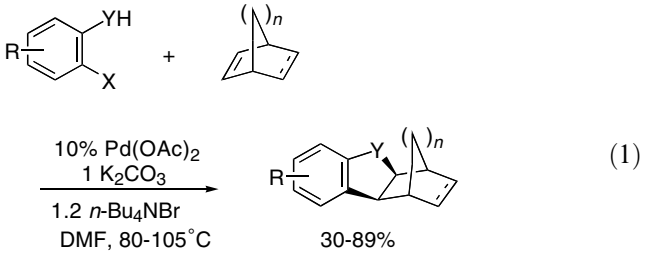
of functionally substituted aromatic halides on various cyclic and bicyclic olefins.

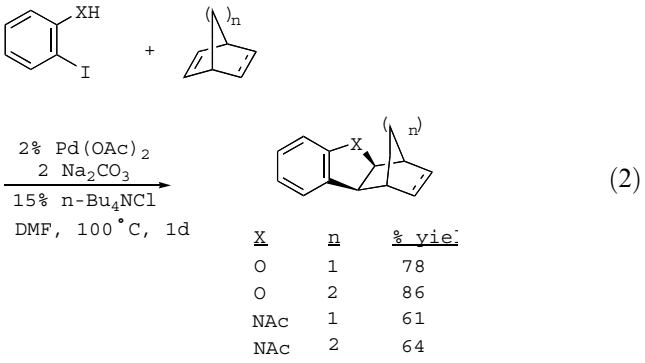


(1)

X=Br,I;Y=OH,NH;*n*=1,2

2. Results and discussion

Like Catellani and Del Rio [14], our initial results on the heteroannulation of norbornene and bicyclo[2.2.2]octene by *o*-iodophenol and *o*-iodoacetanilide were quite promising (Eq. (2)).

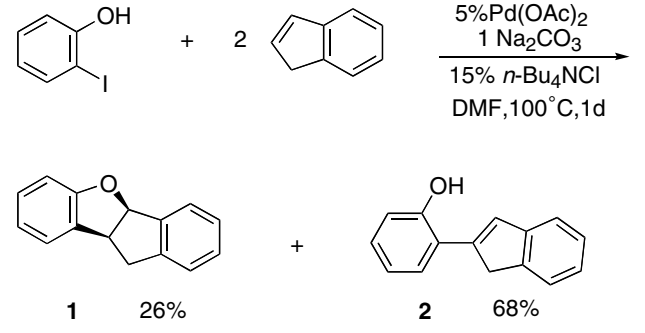


X	n	% yie
O	1	78
O	2	86
NAc	1	61
NAc	2	64

(2)

The base Na_2CO_3 provided excellent results and, unlike much of our earlier annulation chemistry and Catellani's procedure [14], we only needed to use catalytic amounts of *n*-Bu_4NCl to get high yields.

The reaction conditions used on norbornene produced only marginal success when applied to the reaction of 2-iodophenol and the bicyclic alkene indene



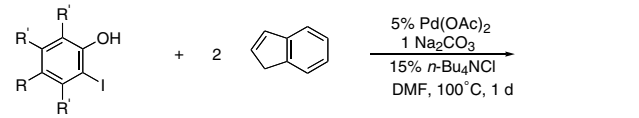
(3)

(Eq. (3)). Two products resulted, the desired heteroannulation product **1** and the undesired Heck-type product **2**. The heteroannulation product is produced by a mechanism to be discussed later. The mechanism for the formation of the olefin **2** is not so clear. After oxidative addition of the aryl iodide to Pd(0) and subsequent carbopalladation of the double bond of indene, the resulting indanylpalladium species apparently either solvolyzes in an S_N1 fashion to regenerate Pd(0) and the relatively stable benzylic cation, which loses a proton to form Heck product **2**, or perhaps the palladium moiety undergoes an *anti* palladium β-hydride elimination or it epimerizes and subsequently undergoes a *syn*-β-hydride elimination to produce olefin **2**.

We have attempted to optimize the reaction conditions to favor formation of the heteroannulation product **1** over the Heck product **2** by employing different solvents and different bases in the reaction. DMF in lower amounts than we have normally used (1 ml versus 8 ml) gave the highest yields of products **1** (26%) and **2** (68%). All other solvents employed gave lower overall yields, although a number of them gave a better ratio of **1** to **2**: DMA (11% of **1**, 22% of **2**), DMSO (10%, 15%), NMP (12%, 18%), toluene (12%, 30%), DME (9%, 24%), THF (11%, 37%), dioxane (14%, 22%), *t*-amyl alcohol (25%, 27%), *t*-butanol (10%, 15%). Our optimization work also determined that 1 equiv. of base was sufficient, rather than the 2 equiv. used previously with norbornene. When a series of different bases were employed in the reaction, none increased the yield over that obtained using Na_2CO_3 (26% of **1**, 68% of **2**): K_2CO_3 (8%, 22%), KOAc (10%, 39%), $KHCO_3$ (15%, 28%), Li_2CO_3 (20%, 48%), LiOAc (21%, 45%), Ag_2CO_3 (10%, 9%), *i*-Pr_2NEt (11%, 23%). We were also curious to see how additives other than *n*-Bu_4NCl [15] might affect the yield of heteroannulation product **1** under our new "optimized" conditions. The chloride salts LiCl, $CuCl_2 \cdot 2H_2O$, CuCl and $ZnCl_2$, and the quarternary ammonium salts *n*-Bu_4NOAc, *n*-Bu_4NI and *n*-Bu_4NBr (all 15 mol%) all gave lower yields than *n*-Bu_4NCl. When 10 mol% of the additive PPh_3 was employed using our new "optimized" procedure, only unreacted starting materials were recovered.

One reason for the poor yields of the heteroannulation product may be failure of the phenol to form a palladacyclic intermediate (see the later mechanistic discussion). Thus, we have examined the effect on the yield of heteroannulation product of varying the nature of the substitutents on the *o*-iodophenol (Eq. (4)). When *o*-iodophenols possessing electron-withdrawing acetyl and chloro groups *para* to the hydroxy group were allowed to react with indene using our "optimized" phenol procedure, the Heck indene

product **4** remained the favored isomer and a decrease in the yield of heteroannulation product **3** was observed.

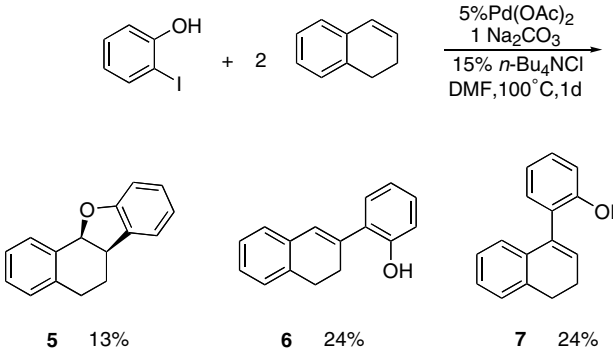


		3	4
a	R = Ac, R′ = H	15%	44%
b	R = Cl, R′ = H	17%	37%
c	R = *t*-Bu, R′ = H	15%	51%
d	R = OMe, R′ = H	17%	0%
e	R = OH, R′ = Me	61%	0%

(4)

A more nucleophilic oxygen atom should favor coordination to the palladium in the presumed alkylpalladium intermediate, and thus facilitate ring-closure to form the heteroannulation product **3**. While *o*-iodophenols with *t*-butyl and methoxy groups *para* to the hydroxy group did not increase the yield (**3c** = 15%; **3d** = 17%) of annulation product, the latter reaction gave none of the indene product. The analogous reaction of 2-iodo-3,5,6-trimethyl-*p*-hydroquinone gave a 61% yield of only the heteroannulation product **3e**. However, this reaction had to be run under an N_2 atmosphere to get this high yield. Because derivatives with electron-donating groups *para* to the hydroxy group give better yields of heteroannulation products than those with electron-withdrawing groups, it appears that an electron-rich internal nucleophile favors formation of the desired product. Furthermore, stronger electron-donating groups produce better selectivity for formation of the heteroannulation product than weaker electron-donating groups.

Next we allowed 2-iodophenol to react with the cyclic alkene 1,2-dihydronaphthalene (Eq. (5)).



5 13% **6** 24% **7** 24%

(5)

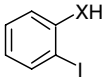
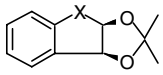
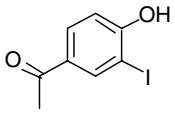
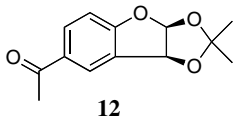
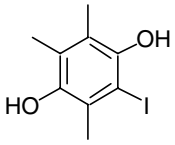
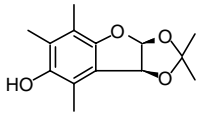
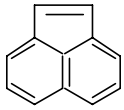
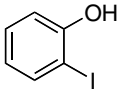
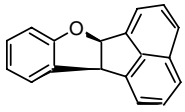
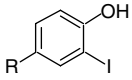
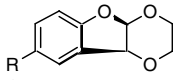
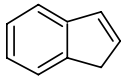
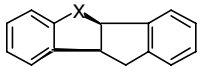
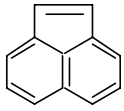
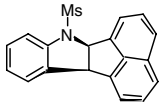
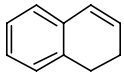
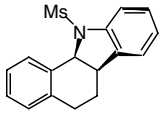
A low 13% yield of heteroannulation product **5** was observed, alongside two Heck regioisomers **6** (24%) and **7** (24%) formed in equal amounts. The lack of regioselectivity in this case may be due to conformational changes brought about by the larger six-membered ring of 1,2-dihydronaphthalene. Increasing and decreasing the amount of 1,2-dihydronaphthalene employed neither improved the yield of **5** nor improved the regioselectivity.

We next sought to apply our ''optimized'' phenol reaction conditions to other alkenes (Table 1). Fortunately, these other alkenes generally have given good yields of annulation products and did not form Heck-type products. Furthermore, we have been able to employ aniline derivatives in this annulation process quite successfully. While the reaction of *o*-iodoaniline and 2,2-dimethyl-1,3-dioxole using our ''optimized'' phenol procedure failed to afford any annulation product, reactions with the nitrogen-containing aryl iodides *N*-(2-iodophenyl)acetamide, *N*-(2-iodophenyl)-*p*-toluenesulfonamide, and *N*-(2-iodophenyl)methanesulfonamide afforded the anticipated heteroannulation products in moderate to good yields (Table 1, entries 1–3). The stronger the electron-withdrawing group present on the nitrogen, the better the yield of annulation product observed. This suggests that the stability of the corresponding nitrogen anion is important to the success of the overall annulation process with these nitrogen-containing substrates.

The phenols 2-iodophenol, 4-hydroxy-3-iodoacetophenone and 2-iodo-3,5,6-trimethyl-*p*-hydroquinone also reacted with 2,2-dimethyl-1,3-dioxole to generate the anticipated heteroannulation products in good yields (entries 4–6). Similarly, the cyclic alkene acenaphthalene gave the expected heteroannulation product in a reasonable yield when allowed to react with 2-iodophenol (Entry 7). The phenols 2-iodophenol, 4-hydroxy-3-iodoacetophenone, and 4-*tert*-butyl-2-iodophenol also reacted with 1,4-dioxene to give the desired products in reasonable yields, although 5 equivs. of the alkene had to be employed to obtain good yields and the reaction had to be run under N_2(entries 8–10). Running the reaction under N_2 allowed us to employ our usual elevated reaction temperature, while apparently limiting decomposition of this relatively unstable alkene.

Although the nitrogen-containing aryl iodides worked well with 2,2-dimethyl-1,3-dioxole (entries 1–3), they failed to produce reasonable yields of annulation products with various other cyclic alkenes. By further optimizing our procedure, we have subsequently developed the following ''optimized'' amide reaction conditions, which do give good yields of heteroannulation products: the nitrogen-containing aryl iodide (0.45 mmol), the olefin (0.90 mmol), NaOAc (0.90 mmol), *n*-Bu_4NCl (0.45 mmol), dimethylglycine (DMG) (0.45 mmol), 5 mol% of $Pd(OAc)_2$ (0.023 mmol) and 1 mL of ethylene glycol at 100 °C for 1 day. The role of the DMG is uncertain. However, Reetz [16] has observed that DMG is an excellent additive in the Heck reaction of aryl bromides. He has hypothesized that DMG may stabilize colloidal palladium, which may be the catalyti-

Table 1
Palladium(0)-catalyzed heteroannulation of cyclic alkenes[a]

Entry	Alkene	Aryl iodide	Product	% Yield
1		 X = NAc	 **8** X = NAc	38
2		X = NTs	**9** X = NTs	64
3		X = NMs	**10** X = NMs	74
4		X = O	**11** X = O	61
5			 **12**	64
6			 **13**	46
7[b]			 **14**	47
8[c]		 R = H	 **15** R = H	64
9[c]		R = Ac	**16** R = Ac	32
10[c]		R = *t*-Bu	**17** R = *t*-Bu	43
11[d]		 X = NMs	 **18** X = NMs	64
12[d]		X = NTs	**19** X = NTs	44
13[d]		X = NMs	 **20**	80
14[d]		X = NMs	 **21**	70

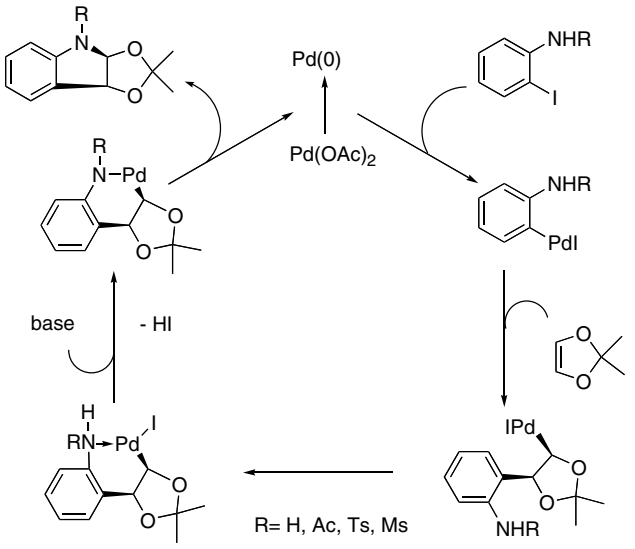
[a] The aryl iodide (0.45 mmol), the olefin (0.90 mmol), Na_2CO_3 (0.45 mmol), 15 mol% of *n*-Bu_4NCl (19.0 mg, 0.068 mmol), and 5 mol% of $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were reacted in 1 mL of DMF at 100 °C for 1 day.

[b] The solvent was ethylene glycol.

[c] 5 equivs of olefin were employed and the reaction was run under N_2.

[d] The aryl iodide (0.45 mmol), the olefine (0.90 mmol), NaOAc (73.8 mg, 0.90 mmol), *n*-Bu_4NCl (125.0 mg, 0.45 mmol), DMG (43.7 mg, 0.45 mmol), and 5 mol% of $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were reacted in 1 mL of ethylene glycol at 100 °C for 1 d.

cally active species in his reactions. Perhaps DMG is performing the same function here. This "optimal" amide procedure for sulfonamide-containing aryl iodides produces good to excellent yields with the alkenes indene, acenaphthalene and 1,2-dihydronaphthalene (entries 11–14).



Scheme 1.

The mechanism proposed for these reactions (Scheme 1) involves: (1) oxidative addition of the carbon–iodide bond of the *o*-substituted aryl iodide to the palladium catalyst, (2) *syn*-arylpalladation of the olefin carbon–carbon double bond, (3) possible coordination of the internal oxygen or nitrogen nucleophile to the palladium, (4) loss of hydrogen iodide with formation of a six-membered ring palladacycle, and (5) reductive elimination of the palladium intermediate to produce the heteroannulation product and regenerate the Pd(0) catalyst. All of these steps have been reported previously in numerous other palladium-catalyzed processes [17], including many of our own previous annulation processes [2–8].

3. Conclusion

The palladium(0)-catalyzed annulation of cyclic and bicyclic alkenes by oxygen- and nitrogen-substituted aryl halides provides an efficient synthesis of a wide variety of dihydrobenzofuran and indoline derivatives. At present this methodology appears limited to heteroannulation. Cyclic and bicyclic alkenes that produce alkylpalladium intermediates incapable of subsequent palladium β-hydride elimination generally provide good yields of heteroannulation products. An electron-donating group *para* to the hydroxy group of the *o*-iodophenols has been shown to favor formation of the heteroannulation product over the Heck product. The "optimal" phenol process does not work well for all nitrogen-containing aryl halides. However, good to excellent yields of nitrogen heterocycles can be obtained by employing ethylene glycol as the solvent and DMG as an additive (the "optimal" amide procedure).

4. Experimental section

4.1. General methods

All ^{1}H and ^{13}C spectra were obtained at 300 or 400 MHz. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates (Whatman K6F) and visualization was effected with short wavelength UV light (254 nm) or a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O].

4.2. Reagents

All reagents were used directly as obtained commercially unless otherwise stated. LiOAc, NaOAc, KOAc, $KHCO_3$, Li_2CO_3, Na_2CO_3, K_2CO_3, *n*-Bu_4NCl, DMF, DMA, DMSO, toluene, dioxane, methanol, NaCl, NH_4Cl, hexane, ethyl acetate, ethylene glycol, and diethylether were obtained from Fisher Scientific. 2-Iodophenol, 2-iodoaniline, acenaphthene, indene, 1,2-dihydronaphthalene, Ag_2CO_3, diisopropylethylamine, NMP, DME, THF, *t*-amyl alcohol, *t*-butanol and 4-hydroxyacetophenone were obtained from Aldrich Chemical Co. Palladium acetate was obtained from Kawaken Fine Chemicals Co., Ltd. and Johnson Matthey Inc. The cyclic alkenes 2,2-dimethyl-1,3-dioxole [18] and 1,4-dioxene [19], as well as the aryl iodides *N*-(2-iodophenyl)methanesulfonamide [20], *N*-(2-iodophenyl)-*p*-toluenesulfonamide [21], *N*-(2-iodophenyl)acetamide [22], 4-hydroxy-3-iodoacetophenone [22], 4-chloro-2-iodophenol [22], 4-hydroxy-3-iodobenzoic acid [22], and 4-*tert*-butyl-2-iodophenol [22] were prepared by their respective literature procedures.

4.3. General "optimal" phenol heteroannulation procedure

The aryl iodide (0.45 mmol), the olefin (0.90 mmol), Na_2CO_3 (48.0 mg, 0.45 mmol), 15 mol% of *n*-Bu_4NCl (19.0 mg, 0.068 mmol), and 5 mol% of $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were added to a 4 dram vial equipped with a stirring bar and Teflon-lined screw cap. One milliliters of DMF was added by syringe. The vial was placed in a mineral oil bath set at 100 °C for 1 day. The reaction mixture was cooled to room temperature then pipetted into 30 mL of diethylether. The ether was washed sequentially with aq. NH_4Cl and brine, dried over $MgSO_4$ and evaporated. The crude product was further purified by silica gel chromatography using a 91:9 hexane/ethyl acetate solution as the eluent.

4.4. *cis*-**4b,9b**-Dihydro-10H-benz[b]indeno[2,1-d]furan (**1**) Eq. (3)

2-Iodophenol was allowed to react with indene using the "optimal" phenol procedure to form compounds **1**

and **2**. Using a stepwise elution of 97:3, 90:10, and 50:50 hexane/ethyl acetate solutions, the isomers were separated on a silica gel column. Compound **1** was isolated as a yellow oil (26% yield): R_f = 0.50 (silica, 91:9 Hex/EtOAc); IR (neat) 3067, 3024, 2920, 2848, 1608, 1476, 1016 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.18 (dd, J = 8.0, 16.0 Hz, 1H), 3.50 (dd, J = 8.0, 16.0 Hz, 1H), 4.28 (dd, J = 8.0, 8.0 Hz, 1H), 6.19 (d, J = 8.0 Hz, 1 H), 6.74 (d, J = 8.0 Hz, 1H), 6.84 (dd, J = 6.0, 13.0 Hz, 1H), 7.06 (dd, J = 6.0, 13.0 Hz, 1H), 7.24 (m, 4H), 7.55 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 39.28, 44.83, 90.65, 110.02, 120.77, 124.83, 125.23, 126.05, 127.34, 128.55, 129.34, 131.03, 140. 86, 142.42, 159.01; HRMS calc for $C_{15}H_{12}O$: 208.08882. Found: 208.08909.

4.5. 2-(2′-Hydroxyphenyl)indene (2) Eq. (3)

Compound **2** was isolated as a yellow oil (68% yield): R_f = 0.26 (silica, 91:9 Hex/EtOAc); IR (neat) 3050, 3300, 2904, 1694, 1598, 1459 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.83 (s, 2H), 5.63 (br s, 1H), 6.90 (m, 2H), 7.15 (m, 3H), 7.42 (m, 4H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 38.79, 115.76, 120.49, 120.72, 121.74, 124.23, 125.67, 126.59, 129.44, 129.63, 132.94, 140.67, 143.93, 144.47, 153.26; HRMS calc for $C_{15}H_{12}O$: 208.08882. Found: 208.08889.

4.6. cis-8-Acetyl-4b,9b-dihydro-10H-benz[b]indeno[2,1-d]furan (3a)

4-Hydroxy-3-iodoacetophenone was allowed to react with indene using the optimized phenol procedure to form compounds **3a** and **4a**. Further purification was achieved using preparative TLC. Compound **3a** was isolated as a clear, yellow oil (15% yield): R_f = 0.12 (silica, 91:9 Hex/EtOAc); IR (neat) 3270, 3192, 3017, 2928 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.58 (s, 3H), 3.21 (d, J = 16.3 Hz, 1H), 3.53 (dd, J = 8.4, 16.3 Hz, 1H), 4.29 (t, J = 8.4 Hz, 1H), 6.29 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 7.24 (m, 3H), 7.55 (m, 1H), 7.91 (m, 1H), 7.92 (s, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 26.66, 39.40, 44.34, 92.41, 109.78, 125.48, 125.70, 126.19, 127.65, 129.85, 131.07, 131.24, 132.22, 140.16, 142.42, 163.54, 196.87; HRMS calc for $C_{17}H_{14}O_2$: 250.09938. Found: 250.09952.

4.7. 2-(5′-Acetyl-2′hydroxyphenyl)indene (4a)

Compound **4a** was purified using preparative TLC and was isolated as a dark yellow oil (44% yield): R_f = 0.20 (silica, 91:9 Hex/EtOAc); IR (neat) 3270, 3192, 3017, 2928, 1698, 1653, 1578, 1436 cm^{-1}; ^1H NMR (300 MHz, d^6-acetone) δ 2.57 (s, 3H), 3.97 (s, 2H), 7.06 (d, J = 8.0 Hz, 1H), 7.17 (dd, J = 7.0, 8.0 Hz, 1H), 7.20 (dd, J = 7.0, 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.23 (s, 1H); ^{13}C NMR (300 MHz, d^6-acetone) δ 25.60, 40.42, 116.02, 121.05, 123.09, 123.45, 124.78, 126.47, 128.91, 129.39, 129.97, 131.04, 142.67, 142.87, 145.91, 159.51, 206.38; HRMS calc for $C_{17}H_{14}O_2$: 250.09938. Found: 250.09880.

4.8. cis-8-Chloro-4b,9b-dihydro-10H-benz[b]indeno[2,1-d]furan (3b)

4-Chloro-2-iodophenol was allowed to react with indene using the optimized phenol procedure to form compounds **3b** and **4b**. Using a stepwise elution of 97:3, 90:10, and 50:50 Hex/EtOAc solutions, the two isomers were separated on a silica gel column. Compound **3b** was isolated as a yellow oil (17% yield): R_f = 0.39 (silica, 91:9 Hex/EtOAc); IR (neat) 3067, 2956, 2924, 1436 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.16 (m, 1H), 3.51 (m, 1H), 4.28 (m, 1H), 6.21 (d, J = 9.0 Hz, 1H), 6.64 (d, J = 9.0 Hz, 1H), 7.06 (m, 5H), 7.53 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 39.06, 44.88, 91.37, 110.95, 124.92, 125.21, 125.33, 125.99, 127.46, 128.43, 129.54, 132.97, 140.39, 142.09, 157.69; HRMS calc for $C_{27}H_{14}ClO$: 242.04984. Found: 242.04983.

4.9. 2-(5′-Chloro-2′-hydroxyphenyl)indene (4b)

Compound **4b** was purified using preparative TLC and was isolated as a light yellow oil (37% yield): R_f = 0.14 (silica, 91:9 Hex/EtOAc); IR (neat) 3270, 2925, 1590, 1461 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 2 H), 5.6 (br s, 1 H), 6.75 (m, 2 H), 7.12 (m, 5 H), 7.48 (m, 1 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 41.29, 116.73, 117.54, 121.63, 123.65, 125.37, 125.75, 126.81, 128.12, 128.34, 129.57, 131.17, 141.75, 142.79, 145.11; HRMS calc for $C_{17}H_{14}O_2$: 242.04984. Found: 242.04952.

4.10. Cis-8-(t-Butyl)-4b,9b-dihydro-10H-benz[b]indeno[2,1-d]furan (3c)

4-*t*-Butyl-2-iodophenol was allowed to react with indene using the optimized phenol procedure to form compounds **3c** and **4c**. Using a stepwise elution of 97:3, 90:10, and 50:50 Hex/EtOAc solutions, the two isomers were separated on a silica gel column. Compound **3c** was isolated as a yellow oil (15% yield): R_f = 0.40 (silica, 91:9 Hex/EtOAc); IR (neat) 3070, 2958, 2867, 1436 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 9H), 3.20 (m, 1H), 3.49 (m, 1H), 4.30 (m, 1H), 6.18 (d, J = 6.0 Hz, 1H), 6.66 (d, J = 6.0 Hz, 1H), 7.10 (m, 1H), 7.24 (m, 4H), 7.55 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 31.83, 34.41, 39.28, 45.01, 90.77, 109.13, 121.64, 125.20, 125.44, 126.02, 127.26, 129.25, 130.51, 141.00, 142.44, 143.93, 156.80; HRMS calc for $C_{19}H_{20}O$: 264.15142. Found 264.15152.

4.11. 2-(5′-t-Butyl-2′-hydroxyphenyl)indene (**4c**)

Compound **4c** was purified using preparative TLC and was isolated as a light yellow oil (51% yield): R_f = 0.25 (silica, 91:9 Hex/EtOAc); IR (neat) 3526, 2867, 1607, 1505 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 9H), 3.88 (s, 2H), 5.45 (br s, 1H), 6.85 (d, J = 8.4 Hz, 1H), 7.25 (m, 7H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 31.62, 34.25, 41.47, 115.88, 121.18, 122.70, 123.59, 124.90, 125.57, 125.75, 126.70, 129.79, 142.97, 143.57, 143.80, 145.46, 151.11; HRMS calc for $C_{19}H_{20}O$: 264.15142. Found: 264.15146.

4.12. cis-**4b,9b**-Dihydro-8-methoxy-10H-benz[b]indeno-[2,1-d]furan (**3d**)

4-Methoxy-2-iodophenol was allowed to react with indene using the optimized phenol procedure to form compound **3d**. Further purification was achieved using preparative TLC. Compound **3d** was isolated as a yellow oil (17% yield): R_f = 0.45 (silica, 70:30 Hex/EtOAc); IR (neat) 3020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.17 (m, 1H), 3.47 (m, 1H), 3.74 (s, 3H), 4.28 (m, 1H), 6.16 (d, J = 6.0 Hz, 1H), 6.63 (s, 2H), 6.68 (s, 1H), 7.22 (m, 3H), 7.53 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 39.03, 45.33, 56.11, 90.79, 109.87, 110.97, 113.58, 125.14, 125.96, 127.31, 129.28, 131.88, 140.99, 142.30, 153.09, 154.45; HRMS calc for $C_{16}H_{14}O_2$: 238.0998. Found: 238.0994.

4.13. cis-**4b,9b**-Dihydro-6,7,9-trimethyl-10H-benz[b]indeno[2,1-**d**]furan-8-ol (**3e**)

2-Iodo-3,5,6-trimethylhydroquinone was allowed to react with indene under a nitrogen atmosphere using the optimized phenol procedure to form compound **3e**. Further purification was achieved by using a stepwise elution of 97:3, 90:10, and 50:50 Hex/EtOAc solutions on a silica gel column. Compound **3e** was isolated as a yellow oil (61% yield): R_f = 0.12 (silica, 91:9 Hex/EtOAc); IR (neat) 3570, 2958, 2867, 1436 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 6H), 2.24 (s, 3H), 3.13 (m, 1H), 3.48 (m, 1H), 4.16 (s, 1H), 4.39 (m, 1H), 6.14 (d, J = 6.0 Hz, 1H), 7.21 (m, 3H), 7.56 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 12.09, 12.32, 12.82, 39.08, 45.14, 90.02, 116.16, 117.19, 122.12, 125.14, 126.09, 126.65, 127.18, 129.21, 141.44, 142.66, 145.91, 151.34; HRMS calc for $C_{18}H_{18}O_2$: 266.13076. Found: 266.13119.

4.14. Compound **5**

2-Iodophenol was allowed to react with 1,2-dihydronaphthalene using the optimized phenol procedure to form isomers **5**–**7**. Compounds **5**–**7** were separated on a silica gel column by using 91:9 Hex/EtOAc as the eluent. Further purification was achieved using preparative TLC. Compound **5** was isolated as a clear, yellow oil (13% yield): R_f = 0.39 (silica, 91:9 Hex/EtOAc); IR (neat) 3020, 2926, 2857, 1595, 1458, 1359 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 (m, 1H), 2.05 (m, 1H), 2.63 (m, 2H), 3.66 (m, 1H), 5.65 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.86 (m, 1H), 7.12 (m, 2H), 7.22 (m, 3H), 7.50 (d, J = 8.0 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 27.67, 28.15, 41.18, 81.89, 109.66, 120.67, 124.46, 126.77, 128.36, 128.38, 128.53, 130.29, 131.43, 133.52, 138.99, 159.48; HRMS calc for $C_{16}H_{14}O$: 222.10447. Found: 222.10434.

4.15. 3-(2-Hydroxyphenyl)-1,2-dihydronaphthalene (**6**)

Compound **6** was obtained as a light yellow oil (24% yield): R_f = 0.25 (silica 91:9 Hex/EtOAc); IR (neat) 3305, 2965 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.61 (t, J = 8.6 Hz, 2H), 2.96 (t, J = 8.6 Hz, 2H), 5.53 (s, 1H), 6.71 (s, 1H), 6.92 (d, J = 6.6 Hz, 2H), 7.11 (m, 5H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 28.22, 28.53, 115.82, 120.67, 126.58, 126.81, 127.15, 127.56, 127.63, 128.03, 128.61, 128.74, 133.79, 134.67, 136.64, 159.34; HRMS calc for $C_{16}H_{14}O$: 222.10447. Found: 222.10434.

4.16. 4-(2-Hydroxyphenyl)-1,2-dihydronaphthalene (**7**)

Compound **7** was obtained as a light yellow oil (24% yield): R_f = 0.25 (silica 91:9 Hex/EtOAc); IR (neat) 3305, 2965 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.54 (m, 2H), 4.43 (m, 1H), 4.73 (s, 1H), 5.99 (m, 1H), 6.53 (d, J = 8.5 Hz, 1H), 6.81 (m, 3H), 7.02 (m, 5H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 28.36, 28.67, 115.97, 120.81, 126.73, 126.96, 127.29, 127.70, 127.78, 128.19, 128.75, 128.89, 133.94, 134.81, 136.79, 152.49; HRMS calc for $C_{16}H_{14}O$: 222.10447. Found: 222.10686.

4.17. N-Acetyl-2,2-dimethylindole[1,3-b]dioxole (**8**) (Table 1, Entry 1)

N-(2-Iodophenyl)acetamide was allowed to react with the 2,2-dimethyl-1,3-dioxole using the optimized phenol procedure. Further purification was achieved using preparative TLC. This compound was isolated as a white solid (38% yield): m.p. = 83–88 °C; R_f = 0.24 (silica, 80:20 Hex/EtOAc); IR (neat) 3010, 2995, 2934, 1602, 1115 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 3H), 1.48 (s, 3H), 2.41 (s, 3H), 5.66 (d, J = 6.1 Hz, 1H), 6.07 (d, J = 6.1 Hz, 1H), 7.08 (dd, J = 8.0, 8.0 Hz, 1H), 7.31 (dd, J = 8.0, 8.0 Hz, 1H), 7.44 (m, 1H), 8.18 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 23.98, 27.43, 27.63, 79.67, 90.99, 112.33, 117.01, 124.41, 125.55, 128.99, 130.61, 142.37, 170.06; HRMS calc for $C_{13}H_{15}NO_3$: 233.10519. Found: 233.10453.

4.18. N-Tosyl-2,2-dimethylindole[2,3-b]dioxole (**9**) (Table 1, Entry 2)

N-(2-Iodophenyl)-*p*-toluenesulfonamide and 2,2-dimethyl-1,3-dioxole were allowed to react using the optimized phenol procedure. Compound **9** was obtained and recrystallized from chloroform. This compound was isolated as a clear, colorless, crystalline solid (64% yield): m.p. = 113–118 °C; R_f = 0.30 (silica, 80:20 Hex/EtOAc); IR (neat) 3010, 2929, 2849, 1599, 1161, 1113 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 3H), 1.46 (s, 3H), 2.37 (s, 3H), 5.57 (d, J = 6.0 Hz, 1H), 6.20 (d, J = 6.0 Hz, 1H), 7.01 (m, 1H), 7.06 (m, 5H), 7.87 (d, J = 1.4 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 21.63, 27.24, 27.41, 79.41, 92.46, 112.33, 113.67, 123.94, 126.27, 127.53, 129.38, 129.67, 129.73, 130.70, 140.94, 144.37; HRMS calc for $C_{18}H_{19}NO_4S$: 345.10348. Found: 345.10328. Anal. Calc. for $C_{18}H_{19}NO_4S$: C, 62.59; H, 5.54; N, 4.06; S, 9.28. Found: C, 62.43; H, 5.84; N, 4.33; S, 9.12%.

4.19. N-Mesyl-2,2-dimethylindole[2,3-b]dioxole (**10**) (Table 1, Entry 3)

N-(2-Iodophenyl)methanesulfonamide was allowed to react with 2,2-dimethyl-1,3-dioxole using the "optimal" phenol procedure to form compound **10**. Compound **10** was recrystallized from chloroform. This compound was isolated as a colorless, crystalline solid (74% yield): m.p. = 160–161 °C; R_f = 0.20 (silica 80:20 Hex/EtOAc); IR (neat) 3008, 3001, 2980, 1600, 1150, 1040 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.49 (s, 3H), 3.11 (s, 3H), 5.71 (d, J = 5.9 Hz, 1H), 6.15 (d, J = 5.9 Hz, 1H), 7.10 (m, 1H), 7.34 (m, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 27.44, 27.62, 40.43, 79.54, 92.16, 112.40, 112.82, 123.98, 126.56, 129.08, 130.92, 140.94; HRMS calc for $C_{12}H_{15}NO_4S$: 269.07218. Found: 269.07169. Anal. Calc. for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20; S, 1.91. Found: C, 53.53; H, 5.89; N, 5.45; S, 1.91%.

4.20. 2,2-Dimethylbenzofurano[2,3-b]dioxole (**11**) (Table 1, Entry 4)

2-Iodophenol was allowed to react with 2,2-dimethyl-1,3-dioxole using the optimized phenol procedure to form compound **11**. Further purification was achieved using preparative TLC. Compound **11** was isolated as a clear, colorless oil (61% yield): R_f = 0.41 (silica, 80:20 Hex/EtOAc); IR (neat) 3020, 2938, 1612, 1478, 1317, 1213, 1102 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.21 (s, 3H), 1.49 (s, 3H), 5.66 (d, J = 4.9 Hz, 1H), 6.27 (d, J = 4.9 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 6.94 (m, 1H), 7.25 (m, 1H), 7.42 (d, J = 7.4 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 27.65, 27.80, 81.27, 107.26, 110.48, 113.16, 121.60, 125.85, 125.92, 131.17, 159.01; HRMS calc for $C_{11}H_{12}O_3$: 192.07864. Found: 192.07858.

4.21. 5-Acetyl-2,2-dimethyl-benzofurano[2,3-b]dioxole (**12**) (Table 1, Entry 5)

2-Iodophenol was allowed to react with the 2,2-dimethyl-1,3-dioxole using the optimized phenol procedure to form compound **12**. Further purification was achieved using preparative TLC. Compound **12** was isolated as an off-white solid (64% yield): m.p. = 71–75 °C; R_f = 0.18 (silica, 80:20 Hex/EtOAc); IR (neat) 3013, 3004, 2938, 2849, 1678, 1153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.5 (s, 3H), 2.57 (s, 3H), 5.67 (d, J = 4.8 Hz, 1H), 6.36 (d, J = 4.8 Hz, 1H), 6.89 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 8.06 (s, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 26.51, 27.65, 27.87, 80.56, 108.51, 110.47, 113.99, 126.61, 127.03, 131.78, 132.85, 162.85, 196.32; HRMS calc for $C_{13}H_{14}O_4$: 234.08921. Found: 234.08886. Anal. Calc for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.47; H, 6.12%.

4.22. 2,2-Dimethyl-5-hydroxy-4,6,7-trimethylbenzofurano[2,3-b]dioxole (**13**) (Table 1, Entry 6)

2-Iodo-3,5,6-trimethylhydroquinone was allowed to react with 2,2-dimethyl-1,3-dioxole using the optimized phenol procedure to form compound **13**. Compound **13** was isolated as a clear, yellow oil (46% yield): R_f = 0.22 (silica, 91:9 Hex/EtOAc); IR (neat) 3499, 2995, 2932, 1682, 1604, 1417, 1214, 1151, 3318 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.21 (s, 3H), 1.49 (s, 3H), 2.13 (s, 3H), 2.16 (s, 3H), 2.28 (s, 3H), 4.24 (s, 1H), 5.67 (d, J = 5.0 Hz, 1H), 6.20 (d, J = 5.0 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 12.10, 12.20, 12.38, 27.81, 27.92, 81.77, 106.60, 112.72, 116.93, 118.30, 121.89, 125.29, 146.44, 151.04; HRMS calc for $C_{14}H_{18}O_4$: 250.12051. Found: 250.12065.

4.23. Compound **14** (Table 1, Entry 7)

2-Iodophenol was allowed to react with acenaphthalene using the optimized phenol procedure with the exception that ethylene glycol was used as the solvent. Compound **14** was purified on a silica gel column using 91:9 Hex/EtOAc as the eluent. Further purification was achieved using preparative TLC. Compound **14** was isolated as a red oil (47% yield): R_f = 0.51 (silica, 91:9 Hex/EtOAc); IR (neat) 3045, 2953, 2922, 2850, 1461, 1215 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40 (d, J = 6.0 Hz, 1H), 6.63 (d, J = 6.0 Hz, 1H), 6.77 (m, 1H), 6.87 (m, 1H), 7.09 (m, 1H), 7.47 (m, 4H), 7.70 (m, 2H), 7.79 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 52.15, 88.58, 110.40, 119.12, 120.87, 122.07, 123.67, 124.63, 125.71, 128.14, 128.42, 128.45, 128.80, 131.65, 137.42,

141.85, 144.50, 159.71; HRMS calc for $C_{18}H_{12}O$: 244.08882. Found: 244.08837.

4.24. 2,3-Dihydroethanobenzofuran[1,4]dioxine (**15**) (Table 1, Entry 8)

2-Iodophenol was allowed to react with 1,4-dioxene using the optimized phenol procedure with a 5-fold excess of the alkene under N_2 to form compound **15**. Further purification was achieved using preparative TLC. Compound **15** was isolated as a light yellow solid (64% yield): m.p. = 89–92 °C; R_f = 0.54 (silica, 80:20 Hex/EtOAc); IR (neat) 3013, 3008, 2994, 2890, 1166, 1080, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.70 (m, 3H), 4.06 (m, 1H), 4.73 (d, J = 3.9 Hz, 1H), 5.57 (d, J = 3.9 Hz, 1H), 6.90 (m, 2H), 7.25 (m, 1H), 7.40 (d, J = 0.9 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 60.97, 62.17, 71.19, 101.14, 110.90, 121.55, 125.97, 126.36, 131.26, 158.29; HRMS calc for $C_{10}H_{10}O_3$: 178.06299. Found: 178.06328. Anal. Calc. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.06; H, 5.66; N, 0.09%.

4.25. 5-Acetyl-2,3-dihydroethanobenzofuran[1,4]dioxine (**16**) (Table 1, Entry 9)

4-Hydroxy-3-iodoacetophenone was allowed to react with 1,4-dioxene using the optimized phenol procedure with a 5-fold excess of the alkene under N_2 to form compound **16**. Further purification was achieved using preparative TLC. Compound **16** was isolated as a clear, light yellow oil (32% yield): R_f = 0.34 (silica, 80:20 Hex/EtOAc); IR (neat) 3015, 2919, 1671, 1616, 1358, 1261, 117 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3H), 3.76 (m, 3H), 4.05 (m, 1H), 4.78 (d, J = 3.9 Hz, 1H), 5.66 (d, J = 3.9 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.04 (s, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 26.42, 60.99, 62.11, 70.33, 102.17, 110.70, 126.90, 126.92, 131.49, 132.72, 162.21, 196.24; HRMS calc for $C_{12}H_{12}O_4$: 220.07356. Found: 220.07334.

4.26. Compound **17** (Table 1, Entry 10)

4-*t*-Butyl-2-iodophenol was allowed to react with 1,4-dioxene using the optimized phenol procedure with a 5-fold excess of the alkene under N_2 to form compound **17**. Compound **17** was isolated as a yellow oil (43% yield): R_f = 0.30 (silica, 83:17 Hex/EtOAc); IR (neat) 3012, 2969, 1489 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 3.74 (m, 3H), 3.83 (m, 1H), 4.71 (d, J = 3.8 Hz, 1H), 5.56 (d, J = 3.8 Hz, 1H), 6.84 (d, J = 8.5 Hz, 1H), 7.32 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 16.61, 31.85, 35.02, 61.16, 62.49, 71.87, 101.47, 110.41, 122.80, 126.64, 128.51, 144.90; HRMS calc for $C_{13}H_{18}O_3$: 234.12559. Found: 234.12595.

4.27. General "optimal" amide heteroannulation procedure

The aryl iodide (0.45 mmol), the olefin (0.90 mmol), NaOAc (73.8 mg, 0.90 mmol), n-Bu_4NCl (125.0 mg, 0.45 mmol), DMG (43.7 mg, 0.45 mmol), and 5 mol% of $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were added to a 4 dram vial equipped with a stirbar and Teflon-lined screw cap. One milliliters of ethylene glycol was added and the reaction mixture was heated to 100 °C for 1 day, cooled to room temperature and pippetted into 30 mL of ethyl ether. The ether layer was washed sequentially with aq NaOH and brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was further purified by silica gel using a 91:9 hexane/ethyl acetate solution as the eluent.

4.28. Compound **18** (Table 1, Entry 11)

N-(2-Iodophenyl)methanesulfonamide was allowed to react with indene using the optimal amide procedure to form compound **18** isolated as an off-white solid (64% yield): m.p. 176–180 °C; R_f = 0.10 (silica, 91:9 Hex/EtOAc); IR (neat) 3068, 3025, 2931, 2854, 1488 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.91 (s, 3H), 3.23 (m, 1H), 3.52 (m, 1H), 4.33 (m, 1H), 5.81 (d, J = 8.0 Hz, 1H), 7.10 (m, 2H), 7.25 (m, 4H), 7.40 (d, J = 7.5 Hz, 1H), 7.77 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) 36.85, 38.69, 44.21, 71.72, 116.50, 124.82, 125.09, 125.19, 126.55, 127.62, 128.64, 129.04, 136.18, 140.69, 140.89, 181.16; HRMS calc for $C_{16}H_{15}NSO_2$: 285.08235. Found: 285.08277.

4.29. Compound **19** (Table 1, Entry 12)

N-(2-Iodophenyl)-*p*-toluenesulfonamide was allowed to react with indene using the optimal amide procedure to form compound **19** isolated as an off-white solid (44% yield): m.p. 186–189 °C; R_f = 0.26 (silica, 91:9 Hex/EtOAc); IR (neat) 3050, 2924, 1476 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.08 (m, 1H), 3.33 (m, 1H), 3.65 (m, 1H), 5.68 (d, J = 8.0 Hz, 1H), 7.05 (m, 8H), 7.61 (m, 3H), 7.80 (d, J = 7.0 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 21.62, 38.07, 43.86, 71.48, 118.15, 124.66, 124.71, 125.40, 126.50, 127.21, 127.53, 128.30, 128.89, 129.68, 135.30, 137.23, 140.67, 140.72, 141.08, 143.94; HRMS calc for $C_{22}H_{19}NSO_2$: 361.11358. Found: 361.11310.

4.30. Compound **20** (Table 1, Entry 13)

N-(2-Iodophenyl)methanesulfonamide was allowed to react with acenaphthene using the optimal amide procedure to form compound **20**, isolated as a yellow oil (80% yield): R_f = 0.40 (silica, 80:20 Hex/EtOAc); IR (neat) 3018 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.97

(s, 3H), 5.42 (d, $J=8.3$ Hz, 1H), 6.20 (d, $J=8.3$ Hz, 1H), 7.07 (t, $J=7.5$ Hz, 1H), 7.18 (m, 1H), 7.38 (d, $J=8.1$ Hz, 1H), 7.49 (m, 4H), 7.72 (m, 2H), 7.92 (d, $J=6.5$ Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 36.88, 51.04, 69.60, 115.43, 119.22, 123.03, 123.96, 124.62, 125.04, 125.27, 128.25, 128.78, 128.83, 131.56, 132.87, 137.13, 141.21, 142.05, 143.73; HRMS calc for $C_{19}H_{15}NSO_2$: 321.08351. Found: 321.08354.

4.31. Compound **21** (Table 1, Entry 14)

N-(2-Iodophenyl)methanesulfonamide was allowed to react with 1,2-dihydronaphthalene using the "optimal" amide procedure to form compound **21**, which was isolated as a clear, crystalline solid (80% yield): m.p. 174–177 °C; $R_f=0.10$ (silica, 91:9 Hex/EtOAc); IR (neat) 3050, 2924, 1476 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.31 (m, 2H), 2.57 (m, 2H), 2.83 (s, 3H), 4.05 (m, 1H), 5.55 (d, $J=8.9$ Hz, 1H), 6.97 (d, $J=7.4$ Hz, 1H), 7.15 (m, 5H), 7.40 (d, $J=7.2$ Hz, 1H), 7.84 (d, $J=7.7$ Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 24.68, 25.18, 37.21, 40.35, 64.41, 118.34, 124.05, 125.61, 126.99, 127.53, 128.16, 128.38, 130.60, 134.42, 135.11, 138.05, 141.98; HRMS calc for $C_{17}H_{17}NSO_2$: 299.09800. Found: 299.09838. Anal Calc. $C_{17}H_{17}NSO_2$ C, 68.20; H, 5.72; N, 4.68. Found: C, 68.03; H, 6.05; N, 4.58.

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