Highly Regioselective Heck Coupling Reactions of Aryl Halides and Dihydropyran in the Presence of an NHC-Pyridine Ligand

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Abstract: The Heck coupling reactions of aryl halides and 3,4-dihydro-2*H*-pyran facilitated the regioselective synthesis of arylated cyclic enol ethers. Good yields were obtained using 5 mol% of an NHC-ligand–Pd-catalyst complex in the presence of K_2CO_3 in DMF at 100 °C. The use of this catalytic system broadens the substrate scope and improves the selectivity for this cross-coupling process.

Key words: Heck reaction, N-heterocyclic carbine, pyridine ligand, palladium, cyclic enol ether

N-Heterocyclic carbenes (NHC) have become one of the most popular ligand classes for transition metals.[1] The stability of nitrogen-containing ligands and the use of carbenes bearing appended N-heterocycles, such as pyridine, have attracted particular attention and have shown promising potential in catalytic applications such as in Heck coupling reactions.[2] A ligand comprised of a benzimidazolium carbene tethered to pyridine by a short alkyl group was expected to create a robust catalyst, which could withstand high-temperature reaction conditions. Also, since NHC are good σ-donors, this could enhance the rate of oxidative addition.[3] Additionally, the steric bulk of this type of ligand could assist with reductive elimination and therefore be useful for Heck-type reactions.

The Heck reaction, a powerful carbon–carbon bond-forming reaction, is the palladium-catalyzed cross-coupling of an aryl halide with an olefin and has been widely used by chemists.[4] The Heck reaction employing cyclic enol ethers could serve as a route to synthetically important glycosides, and the cyclic enol ether motif is one found in different toxins, such as ciguatoxin, and other natural products that display bioactivity.[5] However, to our knowledge, the scope of this particular reaction has been relatively under-explored. Although there are examples of reactions employing 2,3-dihydrofuran, previous studies using 3,4-dihydro-2*H*-pyran (DHP) gave only modest yields and mixtures of regioisomers and only one enantioselective reaction was reported.[6] Therefore, we believed that the development of a more versatile catalyst system to expand the substrate scope of the Heck reaction using DHP would be worthwhile, and our progress towards this goal is presented herein.

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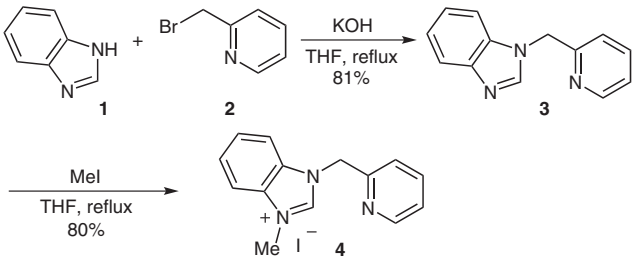
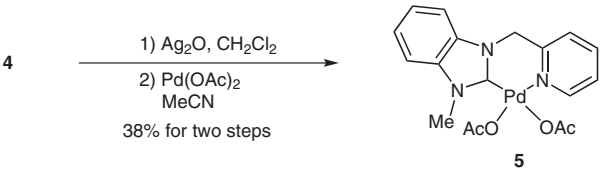
The preparation of the NHC-ligand precursor **4** is shown in Scheme 1. The N-alkylation of benzimidazole **1** and 2-bromomethyl pyridine **2** in the presence of KOH in THF gave the corresponding pyridinyl benzimidazole compound **3** as a brown solid in 81% yield. N-Methylation of **3** with iodomethane while refluxing in THF for 12 hours then gave **4** in 80% yield. Although synthesis of ligand **4** was previously reported, the synthetic route used was not as efficient as that employed by our group.[7]



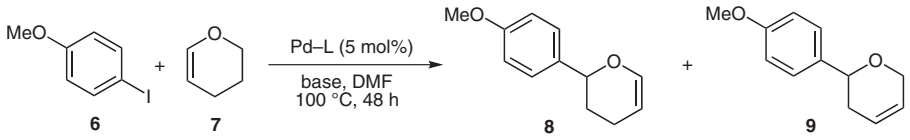
Scheme 1 Synthesis of ligand precursor

To form the NHC–palladium complex **5**, as shown in Scheme 2, NHC precursor **4** was treated with silver(I) oxide in predried dichloromethane at room temperature to afford the silver–NHC complex. This was then followed by metal exchange with $Pd(OAc)_2$ in acetonitrile to give the palladium(II)–NHC-ligand complex **5** as a pale orange solid in 38% yield over two steps. The structure was confirmed by the complete disappearance of the imidazole proton (δ = 9.14 ppm) of **4**, as well as the ^{1}H NMR resonance of the pyridine *ortho*-proton, which was observed to have a downfield shift (δ = 8.48 ppm to 8.98 ppm) upon coordination to palladium. In addition, broadening of the methylene at δ = 5.96 ppm was observed in the coordinated complex **5**. Attempts to form **5** by direct palladation using potassium *tert*-butoxide led to the formation of a mixture of compounds, which were not separable.



Scheme 2 Synthesis of palladium complex **5**

Table 1 Effect of Catalyst and Base on the Cross-Coupling Reactions of 4-Iodoanisole and DHP[a]



6 7 8 9

Entry	Pd/ligand	Base	Yield (%)[b] (**8**:**9**)
1	$Pd(OAc)_2$/none	K_2CO_3	50 (88:12)
2	$Pd(OAc)_2$/phen[c]	K_2CO_3	36 (78:22)
3	$Pd(OAc)_2$/dmphen[c]	K_2CO_3	60 (66:3)
4	**5**	K_2CO_3	80 (100:0)
5	**5**	Na_2CO_3	43 (100:0)
6	**5**	Cs_2CO_3	10 (100:0)
7	**5**	Et_3N	41 (100:0)

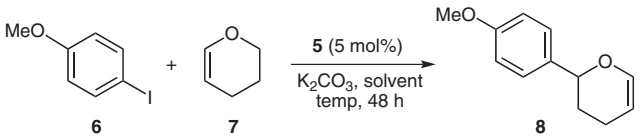
[a] All reactions were carried out with 4-iodoanisole (0.5 mmol), DHP (6 mmol), base (0.75 mmol), and Pd–L (5 mol%) in solvent (1 mL) under argon atmosphere.
[b] Isolated yield.
[c] phen: 1,10-phenanthroline, dmphen: 2,9-dimethylphenanthroline.

After obtaining palladium complex **5**, we then turned our attention to the cross-coupling of 4-iodoanisole with DHP to see if yields and regioselectivity could be improved in comparison with earlier work.[6] As shown in Table 1, we initially investigated the effect of using $Pd(OAc)_2$ with commercially available amine ligands, but a mixture of regioisomers **8** and **9** was obtained with poor to modest yields (entries 1–3).[8] However, when **5** was used, compound **8** was obtained as the exclusive product, and the use of K_2CO_3 as a base led to high yield (entry 4). Consistent with previous results, which demonstrated that an oxygen near an olefin electronically assists with favorable coordination of the Pd(II) center and inverts the polarization of the double bond with respect to the traditional Heck reaction, arylation was observed only at the α-carbon.[6a,b] In the past, double-bond isomerization of the Heck product had been attributed to high-temperature reaction conditions, but Jeffery and David determined that use of an appropriate catalytic system could direct selectivity of the reaction.[6d] We have also found that the use of our NHC-ligand–Pd-catalyst complex allowed for isolation of the arylated vinylic ether as the sole product, and therefore demonstrated that these are selective reaction conditions. This selectivity may be due to the unsymmetrical nature of palladium complex **5**.

After ascertaining that **5**[10] and K_2CO_3 were the best combination of catalytic complex and base for reaction selectivity, we then investigated the role of solvent and temperature as shown in Table 2. In the cases of toluene, benzene, and THF, the reactions were incomplete and the yields were low (entries 2–4). However, in polar aprotic solvent such as DMF, the desired product **8** was obtained in 80% yield (entry 1). The isomeric side product **9** was not detected at all in any of those cases. Independent of bases, the cross-coupling reaction was not efficient at 50 °C or room temperature (entries 5 and 6). Only at high temperature (100 °C) did the coupling reaction proceed well to afford compound **8**. As a result, we determined that the optimal reaction conditions were in polar aprotic solvent, such as DMF, in the presence of K_2CO_3 at 100 °C.

To diversify the scope of the reaction, it was then attempted to use less active aryl halides in the cross-coupling reaction. However, as shown in Table 3, a reduction in yields was observed when aryl bromides (entries 2 and 4) and aryl chlorides (entry 5) were used. This result is consistent with the fact that oxidative addition of aryl

Table 2 Effect of Solvent and Temperature on the Cross-Coupling Reactions of 4-Iodoanisole and DHP in the Presence of Pd–Ligand Complex **5**[a]

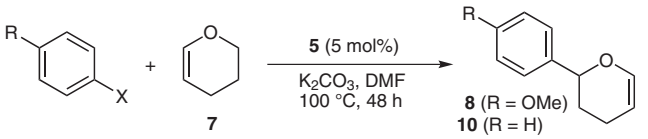


6 7 8

Entry	Solvent	Temp (°C)	Yield (%)[b]
1	DMF	100	80
2	toluene	100	34
3	benzene	100	51
4	THF	100	16
5	DMF	50	41
6	DMF	23	10

[a] All reactions were carried out with 4-iodoanisole (0.5 mmol), DHP (6 mmol), K_2CO_3 (0.75 mmol), and **5** (5 mol%) in solvent (1 mL) under argon atmosphere.
[b] Isolated yield.

Table 3 Effect of Aryl Halide on the Cross-Coupling Reactions with DHP in the Presence of Pd–Ligand Complex **5**[a]



Entry	R	X	Yield (%)[b]
1	OMe	I	80
2	OMe	Br	21
3	H	I	51
4	H	Br	35
5	H	Cl	<5

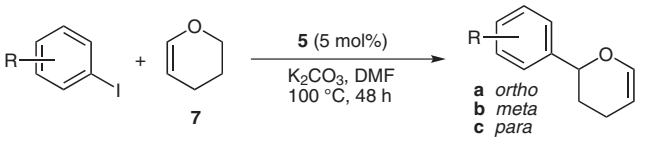
[a] All reactions were carried out with aryl halide (0.5 mmol), DHP (6 mmol), K_2CO_3 (0.75 mmol), and **5** (5 mol%) in solvent (1 mL) under argon atmosphere.
[b] Isolated yield.

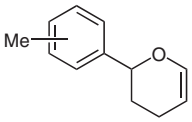
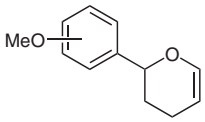
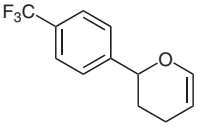
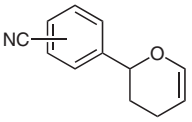
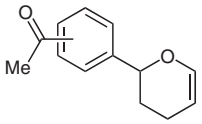
bromides and aryl chlorides to Pd(0) is more difficult due to the greater bond strengths of the Ph–X bond in aryl bromides and aryl chlorides compared to that of aryl iodides.[9]

With the optimized conditions in hand, the functionality of the halide as coupling partner was varied to investigate the range of substrates.[11] As shown in Table 4, cross-coupling proceeded well with electron-donating and neutral substrates (entries 1 and 2); reactions of *ortho*-, *meta*-, and *para*-methyl or methoxy phenyl iodide with DHP took place to provide the desired products **11a** to **11c** (62–75%) and **12a** to **12b** (58–62%), respectively. However, the reactions with trifluoromethyl, cyano, and acetyl phenyl iodides (entries 3–5), substituted with an electron-withdrawing group, showed little reactivity and removal of unreacted starting material proved laborious and caused low yields (<16%). Therefore, aryl iodides including an electron-donating or neutral substituent proved to be the best for the coupling reaction with DHP.

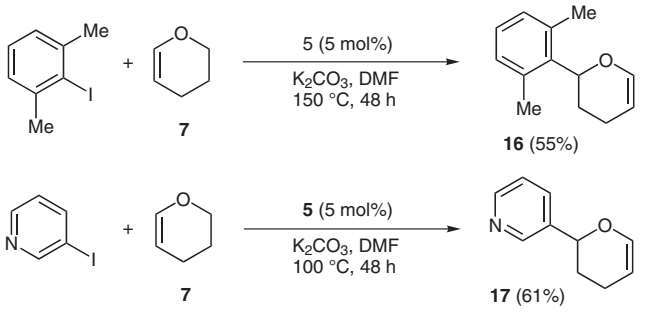
Also, the sterically hindered substrates reacted smoothly, but for the most hindered aryl halide an increase in temperature was necessary to drive the reaction to completion. As shown in Scheme 3, the coupling reaction of 2,6-dimethyl iodobenzene with DHP at 150 °C for 48 hours proceeded to give the corresponding cross-coupling compound **16** in 55% yield. In addition, this methodology is applicable for the use of nitrogen-containing heterocycles as well, as demonstrated by the successful coupling of 3-iodopyridine with DHP to afford the desired product **17** in 61% yield (Scheme 3). The application of this reaction is important because heterocyclic compounds are building blocks for natural products and biologically active target molecules.

Table 4 Effect of Aryl Halide on the Cross-Coupling Reactions with DHP in the Presence of Pd–Ligand Complex **5**[a]



Entry	R	Products	Yield (%)[b]
1	Me		**11a** (71) **11b** (75) **11c** (62)
2	OMe		**12a** (62) **12b** (58)
3	CF_3		**13** (15)
4	CN		**14b** (15) **14c** (trace)
5	COMe		**15a** (trace) **15c** (16)

[a] All reactions were carried out with aryliodine (0.5 mmol), DHP (6 mmol), K_2CO_3 (0.75 mmol), and **5** (5 mol%) in solvent (1 mL) under argon atmosphere.
[b] Isolated yield.



Scheme 3 Coupling reaction with hindered and heterocyclic halides

In summary, we have synthesized an NHC-pyridinyl ligand–palladium complex **5** that was successfully employed in regioselective Heck reactions with DHP. Synthesis of the catalyst is efficient and it may be useful in additional palladium-catalyzed reactions.

Acknowledgment

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References and Notes

(1) (a) Bourissou, D.; Guerret, O.; Gabbai, F.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39. (b) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290. (c) Perry, M. C.; Burgess, K. *Tetrahedron: Asymmetry* **2003**, *14*, 951. (d) Cesar, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619. (e) Sigman, M. S.; Jensen, A. D. *Acc. Chem. Res.* **2006**, *39*, 221. (f) Douthwaite, R. E. *Coord. Chem. Rev.* **2007**, *251*, 702. (g) Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem. Int. Ed.* **2007**, *46*, 2768. (h) Gade, L. H.; Bellemin-Laponnaz, S. In *Top. Organomet. Chem.*, Vol. 21; Glorius, F., Ed.; Springer: Berlin, **2007**, 117–157. (i) Arduengo, A. J. III; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361. (j) Enders, D.; Breuer, K.; Raabe, G.; Runsink, J.; Teles, J. H.; Melder, J. P.; Ebel, K.; Brode, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1021. (k) Herrmann, W. A.; Elison, M.; Fischer, J.; Kocher, C.; Artus, G. R. J. *Chem. Eur. J.* **1996**, *2*, 772.

(2) (a) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (b) Peris, E.; Crabtree, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2239. (c) Grasa, G. A.; Singh, R.; Stevens, E. D.; Nolan, S. P. *J. Organomet. Chem.* **2003**, *687*, 269. (d) Najera, C.; Gil-Molto, J.; Karlstrom, S.; Falvell, L. R. *Org. Lett.* **2003**, *5*, 1451. (e) Chen, W.; Xi, C.; Wu, Y. *J. Organomet. Chem.* **2007**, *692*, 4381. (f) Khramov, D. M.; Rosen, E. L.; Joyce, A. V.; Vu, P. D.; Lynch, V. M.; Bielawski, C. W. *Tetrahedron* **2008**, *64*, 6853. (g) Taige, M. A.; Zeller, A.; Ahrens, S.; Goutal, S.; Herdtweck, E.; Strassner, T. *J. Organomet. Chem.* **2007**, *692*, 1519. (h) Chen, T.; Gao, J.; Shi, M. *Tetrahedron* **2006**, *62*, 6289. (i) Xu, Q.; Duan, W.; Lei, Z.; Zhu, Z.; Shi, M. *Tetrahedron* **2005**, *61*, 11225.

(3) Crabtree, R. H. *J. Organomet. Chem.* **2006**, *691*, 3146.

(4) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P. Jr. *J. Org. Chem.* **1972**, *37*, 2320. (c) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. (d) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (e) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (f) Jeffery, T. In *Advances in Metal-Organic Chemistry*, Vol. 5; Liebeskind, L. S., Ed.; JAI: London, **1996**, 153–260. (g) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*; VCH: New York, **1996**, Chap. 31. (h) Link, J. T.; Overman, L. E. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: New York, **1998**, Chap. 6.

(5) (a) Shimizu, Y. *Chem. Rev.* **1993**, *93*, 1685. (b) Yasumoto, T. *Chem. Rec.* **2001**, *1*, 228. (c) Conway, J. C.; Urch, C. J.; Quayle, P.; Xu, J. *Synlett* **2006**, 776.

(6) (a) Arai, I.; Doyle Daves, G. *J. Org. Chem.* **1978**, *44*, 21. (b) Andersson, C.; Hallberg, A.; Doyle Daves, G. *J. Org. Chem.* **1987**, *52*, 3529. (c) Larock, R. C.; Gong, W. H.; Baker, B. E. *Tetrahedron Lett.* **1989**, *30*, 2603. (d) Loiseleur, O.; Hayashi, M.; Schmees, N.; Pfaltz, A. *Synthesis* **1997**, 1338. (e) Jeffery, T.; David, M. *Tetrahedron Lett.* **1998**, *39*, 5751. (f) Dupont, J.; Gruber, A. S.; Fonseca, G. S.; Monteiro, A. L.; Ebeling, G. *Organometallics* **2001**, *20*, 171.

(7) Barczak, N. T.; Grote, R. E.; Jarvo, E. R. *Organometallics* **2007**, *26*, 4863.

(8) When using a combination of $Pd(OAc)_2$ and 1,10-phenanthroline or 2,9-dimethylphenanthroline, the catalyst and ligand were premixed in DMF at r.t. for 30 min before the addition of substrates.

(9) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.

(10) **General Procedure for the Synthesis of Palladium(II) Complex 5**

To a solution of **4** (0.6 mmol) in anhyd CH_2Cl_2 (20 mL) was added Ag_2O (0.3 mmol), and the reaction mixture was stirred at r.t. for 4 h. The reaction mixture was then gravity filtered and dried under nitrogen to obtain a silver complex as a white solid. The silver complex (0.4 mmol) was then suspended in a solution of MeCN (20 mL) in a foil-covered round-bottom flask. To the reaction mixture was then added $Pd(OAc)_2$ (0.4 mmol), and the reaction mixture was stirred at r.t. for 24 h. The reaction mixture was then gravity filtered, and the filtrate was concentrated in vacuo to obtain **5** (100 mg, 38% over two steps) as an orange solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.98–9.02 (m, 1 H), 7.82–7.90 (m, 1 H), 7.59 (d, *J* = 10.0 Hz, 1 H), 7.49–7.55 (m, 1 H), 7.32–7.45 (m, 4 H), 5.96 (br s, 2 H), 4.06 (s, 3 H), 2.02 (s, 6 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 178.1, 153.5, 153.4, 139.8, 134.5, 132.7, 125.0, 124.9, 124.4, 124.1, 110.9, 110.4, 51.40, 33.40, 22.60.

(11) **General Procedure for the Preparation of Substituted Dihydropyrans**

An oven-dried resealable Schlenk flask was evacuated and filled with argon, then were added 4-iodoanisole (117 mg, 0.5 mmol), 3,4-dihydro-2*H*-pyran (0.55 mL, 6 mmol), K_2CO_3 (104 mg, 0.75 mmol), DMF (1 mL), palladium complex **5** (22 mg, 0.05 mmol). The reaction mixture was stirred at 100 °C. After 48 h the solution was then allowed to cool to r.t. EtOAc (20 mL) was added to the reaction mixture, and then the reaction mixture was washed with H_2O (3 × 10 mL). The organic layer was dried over Na_2SO_4. After filtration, solvent was evaporated and purified by column chromatography (hexanes–EtOAc, 19:1), to afford 2-(4-methoxy-phenyl)-3,4-dihydro-2*H*-pyran (76 mg, 80%) as a light orange oil.

Compound **11a**: yellow oil (62 mg, 71%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.43 (m, 1 H), 7.17–7.26 (m, 3 H), 6.56 (d, *J* = 7.5 Hz, 1 H), 5.00 (dd, *J* = 10.0 Hz, 1 H), 4.80 (m, 1 H), 2.35 (s, 3 H), 2.20–2.32 (m, 2 H), 1.84–2.12 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 144.7, 140.0, 134.6, 130.4, 127.5, 126.3, 125.6, 100.6, 74.37, 29.29, 20.93, 18.95. GC-MS: *m/z* calcd for $C_{12}H_{14}O$: 174.1; found: 173.9. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.56; H, 8.12.

Compound **11b**: yellow oil (65 mg, 75%). ^{1}H NMR (250 MHz, $CDCl_3$): δ: = 7.45–7.48 (m, 1 H), 7.38–7.42 (m, 1 H), 7.31–7.35 (m, 1 H), 7.17–7.27 (m, 1 H), 6.61 (d, *J* = 7.5 Hz, 1 H), 4.87–4.89 (m, 1 H), 4.83–4.87 (m, 1 H), 2.44 (s, 3 H), 2.26–2.36 (m, 2 H), 1.96–2.16 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 144.1, 137.9, 128.5, 127.9, 126.5, 124.2, 122.9, 100.5, 77.06, 30.22, 21.35, 20.29. GC-MS *m/z* calcd for $C_{12}H_{14}O$: 174.1; found: 174.0. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.69; H, 8.11

Compound **11c**: yellow oil (54 mg, 62%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 10.0 Hz, 2 H), 7.22 (d, *J* = 10.0 Hz, 2 H), 6.53 (d, *J* = 7.5 Hz, 1 H), 4.82 (m, 1 H), 4.77 (m, 1 H), 2.35 (s, 3 H), 2.13–2.25 (m, 2 H), 1.90–2.08 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 140.1, 137.0, 129.0, 128.9, 126.8, 125.9, 92.47, 77.50, 32.67, 22.49, 21.10. GC-MS: *m/z* calcd: 174.1; found: 174.0.

Compound **12a**: yellow oil (59 mg, 62%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 10.0 Hz, 1 H), 7.22–7.35 (m, 1 H), 6.98 (t, *J* = 7.5 Hz, 1 H), 6.88 (d, *J* = 7.5 Hz, 1 H), 6.66 (d, *J* = 7.5 Hz, 1 H), 5.21 (d, *J* = 7.5 Hz, 1 H), 4.74–4.80 (m, 1 H), 3.84 (s, 3 H), 1.94–2.30 (m, 2 H), 1.72–1.88 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 158.1, 144.5, 128.1, 128.0, 126.4, 122.5, 111.0, 100.6, 72.47, 56.26, 29.58, 20.50. GC-MS: *m/z* calcd for $C_{12}H_{14}O_2$: 190.1; found: 190.0.

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.71; H, 7.48.

Compound **13**: yellow oil (17 mg, 15%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 10.0 Hz, 2 H), 7.47 (d, *J* = 10.0 Hz, 2 H), 6.54 (d, *J* = 7.5 Hz, 1 H), 4.90 (d, *J* = 7.5 Hz, 1 H), 4.75–4.84 (m, 1 H), 1.65–2.15 (m, 2 H), 1.55–1.64 (m, 2 H). GC-MS: *m/z* calcd: 230.1; found: 229.7.

Compound **16**: orange oil (52 mg, 55%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.98–7.11 (m, 3 H), 6.51 (d, *J* = 7.5 Hz, 1 H), 5.20 (d, *J* = 10.0 Hz, 1 H), 4.76–4.82 (m, 1 H), 2.39 (s, 6 H), 2.02–2.30 (m, 2 H), 1.80–1.94 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 143.9, 137.1, 136.0, 129.2, 127.2, 100.2, 75.11, 26.03, 20.80, 20.51. GC-MS: *m/z* calcd for $C_{13}H_{16}O$: 188.1; found: 188.0. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.89; H, 8.59.

Compound **17**: a yellow oil (49 mg, 61%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.61 (s, 1 H), 8.53–8.57 (m, 1 H), 7.67–7.73 (m, 1 H), 7.27–7.33 (m, 1 H), 6.53 (d, *J* = 7.5 Hz, 1 H), 4.88 (d, *J* = 10.0 Hz, 1 H), 4.78–4.84 (m, 1 H), 2.18–2.30 (m, 2 H), 1.88–2.14 (m, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 149.1, 147.8, 143.9, 133.6, 123.4, 101.0, 74.82, 30.14, 20.02. GC-MS: *m/z* calcd for $C_{10}H_{11}NO$: 161.1; found: 161.0. Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.39; H, 6.91; N, 8.61.

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