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PALLADIUM-CATALYZED 8-EXO TRIG INTRAMOLECULAR HECK REACTION UNDER MICROWAVE IRRADIATION IN THE PRESENCE OF BASIC ALUMINA

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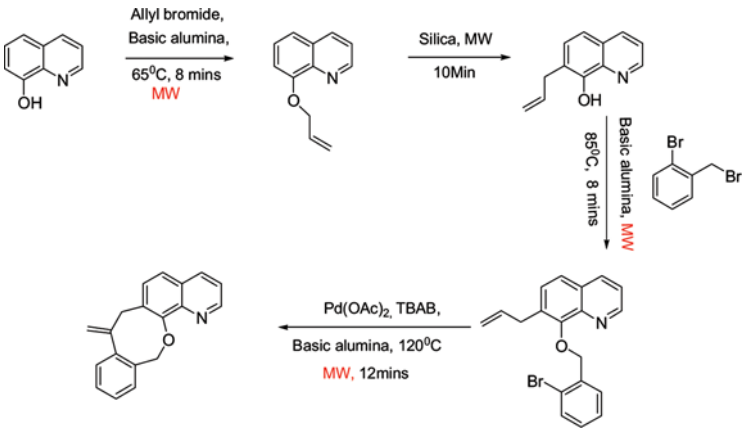
GRAPHICAL ABSTRACT



Abstract *The Heck cross-coupling reaction has been employed for efficient conversion of quinolines to benzoxocinoquinoline through a microwave-assisted palladium-catalyzed intramolecular cyclization in the presence of basic alumina.*

Keywords Basic alumina; benzoxocinoquinoline; Heck cross-coupling reaction; microwave irradiation; solid-phase synthesis

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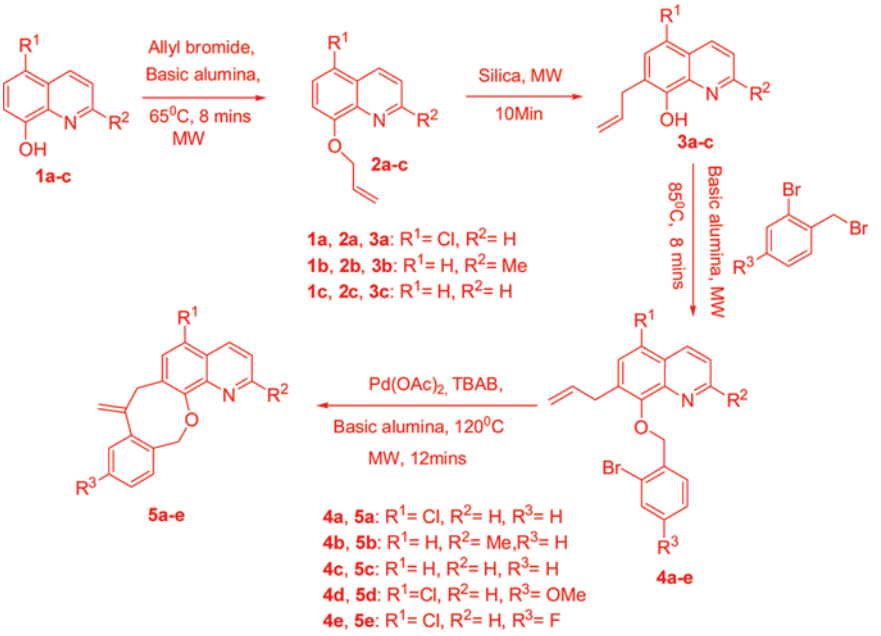
INTRODUCTION

Palladium-catalyzed C-C and C-heteroatom bond-forming reactions have gained enormous interest nowadays in organic synthesis for the construction of small to medium-sized heteroaromatics[1,2] because many natural products, drugs, and preclinical leads contain medium-sized heterocycles fused to aryl rings, which are used as antipsychotic drugs.[2c] Among several palladium-catalyzed reactions, the use of the Heck reaction[3] in the synthesis of organic molecules through C-C bond formation is quite significant. Also, the use of methodological tools such as microwave-assisted solid-phase organic synthesis provides powerful means for the preparation of compound libraries[4] and is well known for achieving energy efficiency and enhancing the rate of reaction as well as product yields.[5] Moreover, the possibility of using a solid-supported reaction is particularly attractive. It is well documented that organic compounds get adsorbed on the surface of inorganic oxides such as alumina or silica, which themselves do not absorb or restrict the transmission of microwave irradiation.[6] This is also the case with reagents immobilized on porous solid supports, which have an advantage over the conventional solution-phase reactions because of the good dispersion of active sites, associated selectivities, and easier workup.[6] Our recent success in establishing a basic alumina-supported, Suzuki[7a] and Sonogashira[7b] reaction for C-C bond formation coupled with the biological importance of oxa-heterocycles[8] prompted us to apply the methodology for rapid and efficient synthesis of oxa-aza heterocyclic moieties by intramolecular Heck reaction. It is worth mentioning that several groups[9] have reported the formation of medium-sized heterocycles by palladium-catalyzed Heck reaction,[10] where harsh reaction conditions were used. Some groups performed the synthesis through sequential changes in catalysts, bases, ligands, and solvents or through a radical pathway[11] in the conventional heating process. The Heck precursor was also synthesized through Wittig olefination[12] or *O*-allylation and *O*-benzylation pathways in organic solvent, and these intramolecular Heck reactions sometimes produced eight-membered or nine- membered compound or even both. None have used microwave as a tool and solid support in reactions for synthesizing heterocycles either as Heck precursor or in Heck reaction. In this communication, we describe palladium-catalyzed synthesis of exclusively eight-membered oxa-aza heterocycles by microwave-assisted basic alumina–supported Heck reaction without use of any external base. To the best of our knowledge, this is the first report of benzoxocinoquinoline synthesis through the application of Heck reaction.

RESULTS AND DISCUSSION

The easy availability of 8-hydroxyquinolines (**1a–c**) prompted us to synthesize oxa-aza heterocycles from these starting materials employing the Heck reaction. We planned to insert an allyl group ortho to the phenolic group exploiting the Claisen rearrangement. Conversion of the C-allyl phenol to its 2-bromobenzylether should be easy, furnishing the substrate for our Heck cyclization step. At the outset, we chose 5-chloro-8-hydroxyquinoline (**1a**) and allyl bromide as model reaction partners to produce *O*-allyl-quinoline (**2a**). The basic property of basic alumina[7] was utilized for the synthesis of **2a** under a microwave environment. The



Scheme 1. Synthesis of benzoxocinoquinoline through microwave-assisted palladium-catalyzed intramolecular Heck reaction. (Figure is provided in color online.)

O-allyl-quinoline (**2a**) was then subjected to Claisen rearrangement utilizing silica gel as the solid support as the acidic nature of the silica surface promotes the rearrangement leading toward the synthesis of C-allyl product (**3a**).[13] The physisorption of reactants on the silica surface leads to an increase in local concentration, which in turn enhances the rate of reaction. Compounds **3a** was then reacted with 2-bromo benzylbromide for the preparation of the *O*- benzoylated product **4a**, the desired substrate for Heck reaction, as shown in Scheme 1.

To optimize the yield of the Heck reaction products, a systematic study was performed on our model precursor **4a**, varying the catalysts, bases, solvents, solid supports, temperature, and time period. The results of the systematic studies revealed that the reactions catalyzed by different palladium catalysts like $PdCl_2$ and $Pd(PPh_3)_2Cl_2$ with different bases like K_2CO_3, Ag_2CO_3, Et_3N, and NaOAc in different solvents like dimethylformamide (DMF), toluene or dioxane in the presence of tetrabutylammonium bromide (TBAB) at 120 °C (oil bath) for 4–6 h were either ineffective or gave poor (20%) to moderate (48%) yield of **5a.** However, when the reaction was carried out in DMF in the presence of $Pd(OAc)_2$ using TBAB as moderator and KOAc as base under microwave irradiation (120 °C) for 45 min, an increase in yield (57%) was observed. The efficacy of $Pd(OAc)_2$ as catalyst prompted us to extend the study to evaluate the effect of various solid supports under microwave irradiation. The results are summarized in Table 1.

The results showed that the use of magnesium oxide, titanium dioxide, or montmorillonite K-10 as a solid support was unsatisfactory. There was some improvement in yield using activated carbon (50%, entry 9), silica gel (56%, entry

Table 1. Optimization of catalyst [$Pd(OAc)_2$] loading on different solid supports[a]

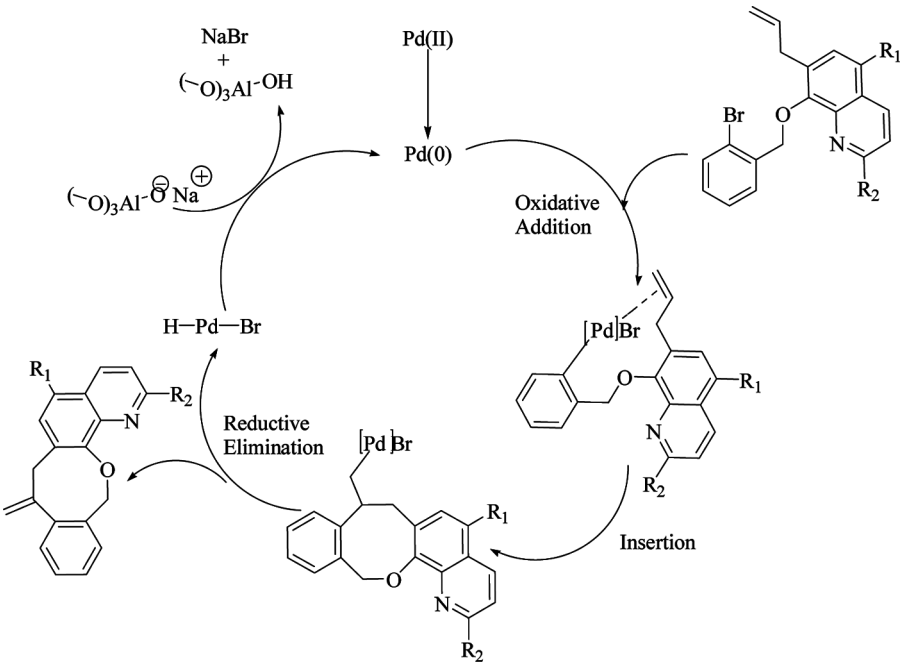
Entry	Solid support	Catalyst (mol %)	Temperature (°C)	Time (min)	Yield[b] (%)
Using KOAc as base					
1	MgO	10	120	30	NR[c]
2	MgO	20	120	30	NR
3	TiO_2	10	120	20	33
4	TiO_2	20	120	20	33
5	Montmorillonite K10	10	120	20	39
6	Montmorillonite K10	20	120	20	39
7	Activated carbon	10	90	17	43
8	Activated carbon	10	110	17	48
9	Activated carbon	10	120	15	50
10	Activated carbon	20	120	15	50
11	Silica gel	10	120	15	56
12	Silica gel	20	120	15	56
13	Acidic alumina	10	120	15	59
14	Acidic alumina	20	120	15	59
15	Neutral alumina	10	120	15	68
16	Neutral alumina	20	120	15	68
17	Basic alumina	10	120	12	87
18	Basic alumina	20	120	12	87
Without KOAc:					
19	Basic alumina	10	120	12	87
20	Basic alumina	20	120	12	87
21	Basic alumina	6	120	12	87
22	Basic alumina	3	120	12	64

[a]All the studies were performed by using **4a**, $Pd(OAc)_2$ catalyst under microwave irradiation at 250 W.
[b]Isolated yield.
[c]No reaction.

11), acidic alumina (59%, entry 13), or neutral alumina (68%, entry 15), but the best results were obtained using basic alumina, which gave the product in 87% yield (entry 17) even in the absence of KOAc as a base (entries 19, 20, and 21).

The good performance of basic alumina,[6] for the synthesis of benzoxocinoquinoline by the Heck reaction, may be attributed to its role as a base that leads to the regeneration of palladium(0) by base-induced proton abstraction from the H-[Pd]-Br species (Scheme 2). The reaction proceeds in the 8-*exo trig* mode, which is far less sterically demanding, whereas the endo trig mode of cyclization requires the olefinic bond to be positioned inside the intermolecular л complex. Because of geometry, it is improbable to have flexible tether between the olefin bond and bending of aromatic ring in proper conformation.[14]

To rationalize the applicability of this method for the synthesis of eight-membered oxa-heterocycles, we extended the study by varying the functional groups in the Heck precursors (**4b–e**) (Table 2). Here also we observed the formation of the eight-member *exo trig* ring products rather than the nine-*endo trig* mode of cyclization, probably because of the less sterically demanding environment in the eight-*exo trig* product.[15,16] The results are summarized in Table 2.



Scheme 2. Plausible pathway for basic alumina-mediated Heck reaction.

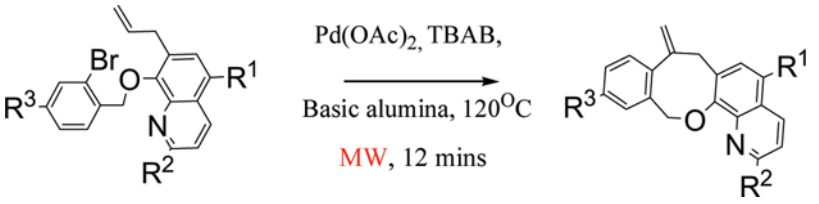
We then investigated the reusability of basic alumina for the reaction of **4a**. It was found that the recovered basic alumina could be recycled three to four times with insignificant change in its activity. The recycling process involves proper washing, first with acetone and then with water, and calcination in an oven for 5 h at 150 °C. To examine the advantage of using microwave irradiation, we also performed the reaction with **4a** in an oil bath at 120 °C under otherwise identical reaction conditions. It is noteworthy that only 18% yield of **5a** was obtained after 15 h of reaction, whereas 87% yield was obtained in 12 min under microwave irradiation.

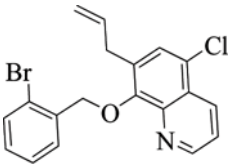
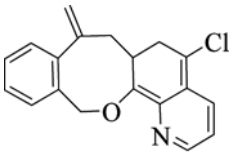
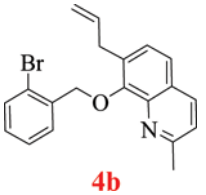
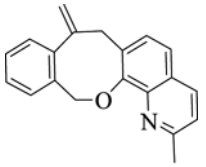
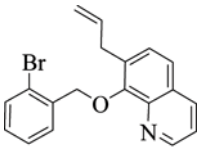
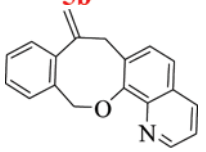
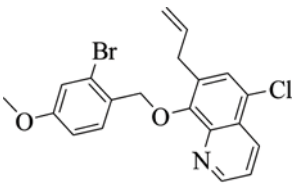
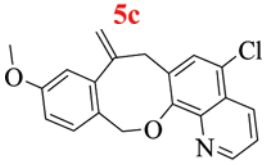
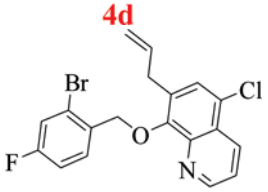
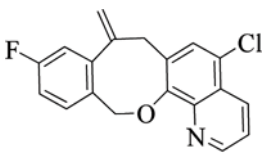
EXPERIMENTAL

Representative Procedure for o-Allyl-quinoline (2a–c)

Chloroform was added to a mixture of 8-hydroxyquinoline derivatives (**1a–c**) (1 equiv.) and basic alumina (500 mg) in a round-bottomed flask. The organic layer was evaporated to dryness under reduced pressure. The solid mixture was stirred at room temperature for an additional 10–15 min to ensure efficient mixing, followed by subsequent addition of allyl bromide (1.1 equiv.). The flask was then fitted with a septum, and the mixture was subjected to irradiation in a microwave reactor (CEM, Discover, USA) at 65 °C (250 W) for 8 min (as monitored by thin-layer chromatography, TLC). After cooling, ethyl acetate was added, and the slurry stirred at

Table 2. Intramolecular Heck cross-coupling reaction of 8-hydroxyquinolines for the synthesis of benzoxocinoquinolines under microwave irradiation



Entry[a]	Substrate	Product	Yield[b]%
1	 **4a**	 **5a**	87
2	 **4b**	 **5b**	83
3	 **4c**	 **5c**	86
4	 **4d**	 **5d**	84
5	 **4e**	 **5e**	81

[a]Reaction conditions: basic alumina (250 mg), Heck precursor (1 equiv.), $Pd(OAc)_2$ (6 mol%), and TBAB, under microwave irradiation (250 W), reaction time 12 min, temperature 120 °C.

[b]Isolated yield. The products were characterized by MS and ^1H and ^{13}C NMR spectroscopy.

room temperature for 10 min. The mixture was vacuum filtered through a sintered glass funnel, and the product was isolated via flash chromatography to yield the desired *O*-allyl-quinolines (**2a–c**)compound.

Representative Procedure for Heck Precursor (4a–e)

Chloroform was added to a mixture of C-allyl-quinoline derivatives (**3a–c**) (1 equiv.) and basic alumina (500 mg) in a round-bottomed flask. The organic layer was evaporated to dryness under reduced pressure. The solid mixture was stirred at room temperature for an additional 10–15 min to ensure efficient mixing, followed by subsequent addition of 2-bromo benzylbromide (1.2 equiv.). The flask was then fitted with a septum, and the mixture was subjected to irradiation in a microwave reactor (CEM, Discover, USA) at 85 °C (250 W) for 8 min (as monitored by TLC). After cooling, ethyl acetate was added, and the slurry was stirred at room temperature for 10 min. The mixture was vacuum filtered through a sintered glass funnel and the product was isolated via flash chromatography to yield the desired Heck precursors (**4a–e**).

Representative Procedure for Heck Reaction

Chloroform was added to a mixture of Heck precursors (**4a–e**) (1 equiv.) and basic alumina (250 mg) in a round-bottomed flask. The organic layer was evaporated to dryness under reduced pressure. The solid mixture was stirred at room temperature for an additional 10–15 min to ensure efficient mixing, followed by subsequent addition of $Pd(OAc)_2$ (6 mol%). The flask was then fitted with a septum, and the mixture was subjected to irradiation in a microwave reactor (CEM, Discover, USA) at 120 °C (250 W) for 12 min (as monitored by TLC). After cooling, ethyl acetate was added, and the slurry was stirred at room temperature for 10 min. The mixture was vacuum filtered through a sintered glass funnel, and the product was isolated via flash chromatography to yield the benzoxocinoquinolines (**5a–e**). In the recycling experiment, the residue obtained was washed with acetone and water (three or four times) and subjected to calcination at 150 °C. The calcinated material could be further be utilized in the coupling reaction.

Data for Compound 4a

R_f(30% petroleum ether–EtOAc) 0.38. Grey solid; mp 92–94°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.54 (2H, d, $J = 6.6$ Hz), 5.06 (2H, m), 5.49 (2H, s), 5.86 (1H, m), 7.20 (1H, t, $J = 7.8$ Hz), 7.37 (1H, t, $J = 7.2$ Hz), 7.47 (1H, s), 7.50 (1H, q, $J = 4.2$ Hz), 7.58 (1H, d, $J = 7.8$ Hz), 7.77 (1H, d, $J = 7.2$ Hz), 8.54 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 1.2$ Hz), 8.98 (1H, dd, $J_1 = 3.0$ Hz, $J_2 = 1.2$ Hz) ; ^{13}C NMR ($CDCl_3$, 150 MHz): δ 34.2 (CH_2), 75.6 (CH_2), 116.7 (CH_2), 121.4 (CH), 122.7 (CH), 125.9 (C), 126.2 (C), 127.5 (CH), 128.5 (CH), 129.2 (CH), 129.7 (CH), 132.4 (CH), 133.1 (C), 133.2 (C), 136.0 (CH), 137.3 (C), 143.5 (C), 150.0 (CH), 151.0 (C). ESI-MS: m/z 388 $[M + H]^+$, 410 $[M + Na]^+$.

Data for Compound 4b

R_f(30% petroleum ether–EtOAc) 0.40. Yellowish brown solid; mp 102–104°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.61 (3H, s), 3.50 (2H, d, $J = 7.8$ Hz), 4.98 (2H, m), 5.36 (2H, s), 5.74 (1H, m) 7.07 (1H, m), 7.14 (1H, d, $J = 7.2$ Hz), 7.20 (1H, d, $J = 6.6$ Hz), 7.28 (1H, t, $J = 6.6$ Hz), 7.37 (1H, s), 7.43 (1H, m), 7.53 (1H, d, $J = 7.2$ Hz), 8.41 (1H, m) ; ^{13}C NMR ($CDCl_3$, 150 MHz): δ 22.3 (CH_3), 34.2 (CH_2), 75.1 (CH_2), 116.1 (CH_2), 121.9 (CH), 122.2 (C), 125.7 (C), 125.9 (C), 127.1 (CH), 127.5 (CH), 128.8 (CH), 129.4 (CH), 133.0 (CH), 133.1 (CH), 135.8 (CH), 137.1 (C), 138.8 (C), 142.7 (C), 150.8 (C), 155.6 (CH). ESI-MS: m/z 368 $[M + H]^+$, 390 $[M+Na]^+$.

Data for Compound 4c

R_f(30% petroleum ether–EtOAc) 0.40. Yellowish brown solid; mp 112–114°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.50 (2H, d, $J = 7.2$ Hz), 4.93 (2H, m), 5.40 (2H, s), 5.78 (1H, m), 7.05 (1H, t, $J = 7.8$ Hz), 7.16 (1H, d, $J = 7.2$ Hz), 7.20 (1H, d, $J = 7.2$ Hz), 7.30 (1H, t, $J = 7.2$ Hz), 7.39 (1H, s), 7.43 (1H, m), 7.52 (1H, d, $J = 7.2$ Hz), 8.44 (1H, dd, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz), 8.80 (1H, dd, $J_1 = 2.4$ Hz, $J_2 = 1.2$ Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 33.9 (CH_2), 76.8 (CH_2), 115.8 (CH_2), 116.0 (C), 118.5 (CH), 120.4 (CH), 122.0 (C), 125.7 (C), 127.0 (CH), 127.8 (CH), 128.0 (CH), 132.9 (CH), 133.0 (CH), 133.8 (CH), 135.6 (C), 139.1 (C), 142.5 (C), 148.5 (CH), 153.2 (CH). ESI-MS: m/z 354 $[M + H]^+$.

Data for Compound 4d

R_f(30% petroleum ether–EtOAc) 0.45. Grey solid; mp 82–84°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.51 (2H, d, $J = 7.2$ Hz), 3.70 (3H, s), 4.98 (2H, m), 5.42 (2H, s), 5.82 (1H, m), 7.29 (1H, t, $J = 6.6$ Hz), 7.42 (1H, m), 7.44 (1H, d, $J = 7.2$ Hz), 7.56 (1H, d, $J = 7.8$ Hz), 7.72 (1H, d, $J = 7.2$ Hz), 8.53 (1H, m), 8.90 (1H, m) ; ^{13}C NMR ($CDCl_3$, 150 MHz): δ 34.0 (CH_2), 56.6 (CH_3), 75.8 (CH_2), 112.7 (CH_2), 116.4 (CH), 117.2 (CH), 121.0 (CH), 121.8 (C), 125.3 (C), 126.4 (C), 128.0 (CH), 129.6 (CH), 132.2 (CH), 133.1 (C), 135.4 (CH), 137.5 (C), 137.9 (C), 150.3 (CH), 151.0 (C), 158.5 (C). ESI-MS: m/z 418 $[M + H]^+$, 440 $[M + Na]^+$.

Data for Compound 4e

R_f(30% petroleum ether–EtOAc) 0.43. Light yellow solid; mp 88–90°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.53 (2H, d, $J = 6.6$ Hz), 4.95 (2H, m), 5.40 (2H, s), 5.85 (1H, m), 7.32 (1H, d, $J = 7.2$ Hz), 7.42 (1H, d, $J = 6.0$ Hz), 7.52 (1H, m), 7.57 (1H, d, $J = 7.2$ Hz), 7.70 (1H, d, $J = 7.2$ Hz), 8.49 (1H, m), 8.93 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 34.0 (CH_2), 74.6 (CH_2), 111.5 (CH_2), 116.0 (CH), 116.9 (CH), 121.0 (CH), 121.8 (C), 124.8 (C), 125.9 (C), 128.4 (CH), 129.2 (CH), 132.5 (CH), 133.1 (C), 135.2 (CH), 136.9 (C), 137.3 (C), 150.1 (CH), 151.6 (C), 155.8 (C). ESI-MS: m/z 406 $[M + H]^+$.

Data for Compound 5a

R_f(30% petroleum ether–EtOAc) 0.50. Grey solid; mp 80-82°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.00 (2H, s), 5.19 (1H, d, $J = 0.6$ Hz), 5.37 (1H, d, $J = 1.2$ Hz), 5.60 (2H, s), 7.10 (2H, m), 7.20 (2H, m), 7.33 (1H, s), 7.43 (1H, m), 8.41 (1H, dd, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz), 8.97 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 1.2$ Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 41.3 (CH_2), 75.7 (CH_2), 114.8 (CH_2), 121.4 (CH), 125.0 (CH), 126.1 (C), 127.6 (CH), 128.5 (CH), 128.7 (CH), 132.4 (CH), 132.9 (CH), 133.1 (C), 134.1 (C), 142.2 (C), 143.4 (C), 148.5 (C), 150.1 (CH), 150.3 (C), 151.2 (C). ESI-MS: m/z 308 $[M + H]^+$, 330 $[M + Na]^+$, HRMS: calcd. 308.0842 $[M + H]^+$; found 308.0836.

Data for Compound 5b

R_f(30% petroleum ether–EtOAc) 0.42. Greenish yellow solid; mp 72–74°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.78 (3H, s, $J = 3.6$ Hz), 3.98 (2H, s), 5.11 (1H, s), 5.32 (1H, d, $J = 1.2$ Hz), 5.57 (2H, s), 7.07 (1H, m), 7.09 (1H, m), 7.18 (4H, m), 7.33 (1H, d, $J = 8.4$ Hz), 7.90 (1H, d, $J = 8.4$ Hz). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 25.7 (CH_3), 41.5 (CH_2), 75.7 (CH_2), 114.0 (CH_2), 121.6 (CH), 122.5 (CH), 126.6 (C), 127.2 (CH), 127.9 (CH), 128.0 (CH), 128.2 (CH), 128.5 (CH), 132.8 (C), 135.1(C), 135.9 (CH), 142.5 (C), 142.6 (C), 149.6 (C), 151.8 (C), 158.5 (C). ESI-MS: m/z 288 $[M + H]^+$, HRMS: calcd. 288.1388 $[M + H]^+$; found 288.1383.

Data for Compound 5c

R_f(25% petroleum ether–EtOAc) 0.40. Pale yellow solid; mp 94–96°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.02 (2H, s), 5.19 (1H, s), 5.37 (1H, s), 5.62 (2H, s), 7.11 (2H, m), 7.19 (2H, m), 7.43 (3H, m), 8.07 (1H, d, $J = 7.8$ Hz), 8.96 (1H, brs). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 41.4 (CH_2), 75.6 (CH_2), 114.6 (CH_2), 120.7 (CH), 120.8 (CH), 122.6 (CH), 127.5 (C), 127.7 (CH), 127.9 (CH), 128.7 (CH), 128.9 (CH), 129.4 (CH), 132.4 (C), 136.4 (C), 137.9 (CH), 142.5 (C), 149.1 (C), 149.5 (C), 151.8 (C). ESI-MS: m/z 274 $[M + H]^+$, HRMS: calcd. 274.1232 $[M + H]^+$; found 274.1227.

Data for Compound 5d

R_f(30% petroleum ether–EtOAc) 0.52. Grey solid; mp 76–78°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.79 (3H, s), 4.10 (2H, s), 5.23 (1H, d, $J = 1.2$ Hz), 5.42 (1H, d, $J = 1.8$ Hz), 5.68 (2H, s), 7.06 (2H, m), 7.27 (1H, s), 7.39 (1H, s), 7.47 (1H, m), 8.32 (1H, dd, $J_1 = 7.2$ Hz, $J_2 = 0.6$ Hz), 8.92 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 1.2$ Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 42.4 (CH_2), 56.5 (CH_3), 75.9 (CH_2), 115.4 (CH_2), 121.0 (CH), 122.2 (CH), 127.1 (CH), 128.9 (CH), 129.4 (CH), 132.7 (CH), 133.3 (C), 133.9 (CH), 134.6 (C), 143.0 (C), 143.9 (C), 148.7 (C), 150.0 (C), 150.9 (C), 151.8 (C), 159.4 (C). ESI-MS: m/z 338 $[M + H]^+$, 360 $[M + Na]^+$.

Data for Compound 5e

R_f(30% petroleum ether–EtOAc) 0.58. Light brown solid; mp 94–96°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.09 (2H, s), 5.27 (1H, d, $J = 0.6$ Hz), 5.50 (1H, s),

5.73 (2H, s), 7.20 (1H, s), 7.23 (1H, m), 7.31 (1H, s), 7.45 (1H, s), 7.51 (1H, m), 8.32 (1H, m), 8.96 (1H, dd, $J_1 = 2.4$ Hz, $J_2 = 0.6$ Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 42.5 (CH_2), 75.7 (CH_2), 115.0 (CH_2), 120.3 (CH), 122.6 (CH), 127.7 (CH), 128.7 (CH), 129.0 (CH), 132.5 (CH), 133.0 (CH), 133.7 (C), 134.3 (C), 143.2 (C), 144.0 (C), 148.5 (C), 150.4 (C), 152.0 (C), 152.8 (C), 159.9 (C). ESI-MS: m/z 326 $[M + H]^+$, 348 $[M + Na]^+$.

CONCLUSION

In conclusion, we have developed a new methodology for basic alumina-supported microwave-assisted intramolecular Heck reaction and exemplified it by the synthesis of eight-membered benzoxocinoquinoline. The operational simplicity, energy efficiency, and general applicability of the strategy coupled with the reusability of basic alumina ensure the development of green methodology for further syntheses of other heterocyclic compounds of interest.

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