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Magnetite (Fe_3O_4) Nanoparticles-Catalyzed Sonogashira–Hagihara Reactions in Ethylene Glycol under Ligand-Free Conditions

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Abstract: A novel application of nanoparticles of paramagnetic magnetite (Fe_3O_4) as an efficient catalyst for carbon-carbon bond formation *via* the Sonogashira–Hagihara reaction under heterogeneous ligand-free conditions in ethylene glycol (EG) is described. By using this catalyst, arylalkynes are produced from the reaction of aryl iodides and activated heteroaryl bromides with alkynes. The results are reproducible using the catalyst, which was prepared from different sources. The catalyst is easily separated by an external magnetic field from the reaction mixture. The separated catalyst can be recycled for several consecutive runs without appreciable loss of its catalytic activity.

Keywords: ethylene glycol; iron oxide; magnetite (Fe_3O_4); nanoparticles; Sonogashira–Higahara reaction

Introduction

Transition metal salts play an important role as efficient catalysts in organic reactions. In the last decade, transition metal-catalyzed cross-coupling reactions have grown into an essential and highly important class of reactions in modern organic chemistry.[1] In this line, group VIIIB metals demonstrate astonishing effectiveness for the formation of carbon-carbon and carbon-heteroatom bonds by the reactions of organic electrophilic substrates with suitable nucleophiles. Over the past decades, enormous efforts have been committed to the reactions catalyzed by palladium- and nickel-based catalysts.[2] This huge effort has somewhat laid down its shadows upon the reports of alternative metal complexes and metal-free protocols in this showground.[2] Toxicological features in parallel with high prices related to utilizing palladium and nickel catalysts have somewhat placed limitations on their general use for large-scale operations.[3]

In contrast, iron is one of the most plentiful metals on our globe, and consequently, one of the most economical and environmentally well-suited ones.[4] Moreover, iron is not toxic and additionally, many different preparations of iron salts are in readily found in the literature and in addition, some of the iron complexes are commercially accessible. In spite of the aforementioned advantages, unexpectedly, in comparison with some other transition metals until lately, iron has been relatively ignored as a potential catalyst in the science of organic synthesis. However, in the last few years, intensive attention has been paid to iron as a catalyst for different organic transformations such as hydrogenation,[5] oxidation,[6] epoxidation,[7] etc. In recent years, the search for catalysts other than the widely used palladium and nickel species for cross-coupling reactions has been under attention. Along this line, immense efforts have started with the especial focus on the use of iron as catalyst. The recently published articles by Furstner,[8] Knochel,[9] Nakamura and Bedford,[10] Cahiez,[11] Bolm,[12] and others[13] all contain some of the examples for cross-coupling protocols using cheap and non-toxic iron catalysts. However, iron salt/amine pre-catalysts have been also used for organomagnesium reactants in large-scale carbon-carbon bond formation.[4]

A new discussion by Buchwald and Bolm has raised a fundamental and interesting question about

the role of metal contaminants in $FeCl_3$ when it is used as a catalyst for carbon-carbon and carbon-heteroatom bond formation in cross-coupling reactions.[12i] They have claimed, in their discussion, that the addition of a trace amount of copper oxide to the reaction mixture has facilitated the cross-coupling reaction.

Since the olden times, magnetite with the chemical formula Fe_3O_4 has been engaged and recognized as a permanent magnet. Because of the unique physical properties of magnetite, in recent years, there is growing interest in using magnetite as a privileged support in organic synthesis.[14] Palladium and ruthenium supported on Fe_3O_4 are reported for the oxidation of alcohols[14a–c] and a recoverable palladium-supported magnetite Fe_3O_4-ionic liquid catalyst for Suzuki–Miyaura and Heck-Mizoroki coupling reaction was also reported.[14d,e] Recently, Yus and co-workers have used impregnated copper on magnetite for the addition of alkoxydiboron reagents to C=C double bonds and for multicomponent preparations of propargylamines.[14f,g] Direct coupling of sulfonamides and alcohols was also reported using a nano-Ru/Fe_3O_4 catalyst.[14h]

Superparamagnetic nanoparticles of Fe_3O_4 have been extensively developed and studied for basic scientific considerations and also for manifold technological purposes.[15,16] All the technical and biomedical applications require that the nanoparticles have high magnetization values, a size smaller than 100 nm, and a narrow particle size distribution.[15]

The Sonogashira–Hagihara reaction is a rapidly rising protocol in organic synthesis, which results in bond formation between C(sp^2) and C(sp) atoms by the catalysis of palladium in the presence or absence of Cu(I) as a co-catalyst to produce arylalkynes and conjugated enynes, which are important predecessors for the preparation of natural products, pharmaceuticals and useful organic materials.[17] Replacement of palladium with other transition metals, which are more abundant and cheaper, for catalysis of this reaction is of concern for academia and industries.

A recent publication by Bolm et al. presents an iron-catalyzed Sonogashira–Hagihara reaction using $FeCl_3$/*N*,*N*-dimethylethylenediamine (dmeda) in toluene at 135 °C.[12h] This is the first report regarding a Sonogashira–Hagihara reaction catalyzed by an iron-based catalyst. Moreover, in a subsequent publication, the use of a similar catalytic system for the cross-coupling reaction of terminal alkynes with vinyl iodides was presented.[13b]

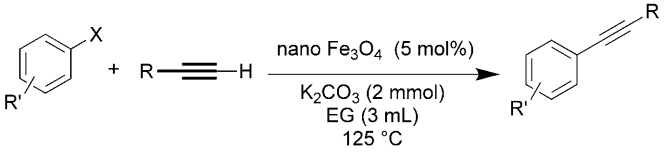
Easy and not time-consuming separation of the catalysts from the reaction mixtures is a subject of interest for investigation, especially for large-scale operation in industries. Moreover, in the past few years, attention has been paid to the use of nanoparticles in comparison with the corresponding bulk materials, because of their potential applications in a variety of fields and their size-dependent evolution properties. They can have different heat capacity, vapour pressure, melting point, and optical, magnetic and electronic properties. Also owing to their high surface area, application of these particles as catalysts results in a high concentration of reactive sites leading to higher reactivity and selectivity.[15]

Result and Discussion

Now in this article, we want to report the use of nanoparticles of paramagnetic magnetite (Fe_3O_4) (< 30 nm) as an efficient catalyst for carbon-carbon bond formation *via* the Sonogashira-Hagihara reaction under ligand-free conditions using ethylene glycol (EG) as a solvent and K_2CO_3 as a base (Scheme 1).

This nanocatalyst can be easily prepared from different chemical sources with reproducible results and also its separation from the reaction mixture by an external magnetic field is an easy task and not a time-consuming process. Use of Fe_3O_4 as a catalyst in organic reactions is as yet limited to a few reports. Recently, the three-component coupling reaction of aldehyde, alkyne and amine, the synthesis of α-amino nitriles catalyzed directly by nanoparticles of Fe_3O_4, and intramolecular C–N cross-coupling reactions catalyzed by nanoparticles of Fe_3O_4 were reported in the literature.[18] Also very recently magnetite nanoparticle-supported gel nanofibers have been used for the Suzuki–Miyaura coupling reaction.[19]

In order to establish the reproducibility of the catalyst, we have prepared the nanoparticles of Fe_3O_4 (< 30 nm) from three different sources according to the literature. For this purpose, a powder bulk sample of Fe_3O_4 (Sigma–Aldrich 99.99%) and another powder bulk sample of Fe_3O_4 (Aldrich, 98%),[20] were employed for the preparation of the nanoparticles of Fe_3O_4. In addition, the catalyst was prepared from the reaction of $Fe_2(SO_4)_3{\cdot}(H_2O)_X$ [Merck, contains 80% of $Fe_2(SO_4)_3$] with $FeSO_4$ (Merck, 99%)[14a] while the last sample of the catalyst was prepared by the reaction of $FeCl_2{\cdot}4H_2O$ with $FeCl_3{\cdot}6H_2O$[21] (Merck > 99%). The amounts of the contaminations of the produced Fe_3O_4 nanoparticles from the above sources with respect to Pd, Ni, Cu, and Co were determined by ICP analysis. The results of the analysis are tabu-



Scheme 1. Nanoparticles of Fe_3O_4: catalyzed Sonogashira–Hagihara coupling reaction of aryl iodides and activated heteroaryl bromides in ethylene glycol.

Table 1. Contamination (ppb) of nanoparticles of Fe_3O_4 prepared from different sources with respect to Pd, Cu, Ni and Co.

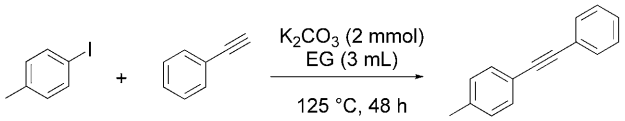
Nano iron sources[a]	Pd	Cu	Ni	Co
Fe_3O_4 (A)	450	34	80	440
Fe_3O_4 (B)	485	45	95	448
Fe_3O_4 (C)	416	63	239	764
Fe_3O_4 (D)	850	3	65	563

[a] A: nanoparticles of Fe_3O_4 produced from bulk powder of Fe_3O_4 (Sigma–Aldrich, 99.99%); B: nanoparticles of Fe_3O_4 produced from bulk powder of Fe_3O_4 (Aldrich, 98%); C: nanoparticles of Fe_3O_4 produced from the reaction of $Fe_2(SO_4)_3{\cdot}(H_2O)_X$ with $FeSO_4$ (Merck, 80% and 99%, respectively); D: nanoparticles of Fe_3O_4 produced from the reaction of $FeCl_2{\cdot}4H_2O$ and $FeCl_3{\cdot}6H_2O$ (Merck, both 99%).

lated in Table 1. Contamination of K_2CO_3 with respect to the above-mentioned metals was also resolved to be Pd (130 ppb), Ni (45 ppb), Cu (24 ppb) and Co (21 ppb). Moreover, the contamination of ethylene glycol by Pd, Cu, Ni and Co has been also determined by ICP analysis to be Pd (20 ppb), Cu (33 ppb), Ni (27 ppb) and Co (24 ppb).

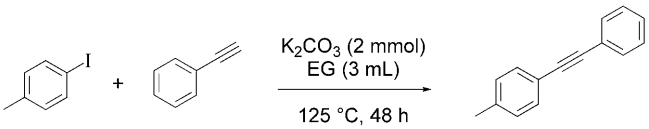
In order to ascertain or negate the role of nanoparticles of Fe_3O_4 as the catalyst and also the reproducibility of the results, we have studied the reaction of 4-iodotoluene with phenylacetylene as a model reaction in the presence of the nanoparticles of Fe_3O_4 (prepared from the abovementioned sources) using K_2CO_3 as a base in ethylene glycol at 125 °C. We noticed that the desired arylalkyne was produced in 75–88% yields. This observation shows that the catalyst, which was prepared from different chemical sources, gives reproducible results. However, for resolving the effect of the size of the catalyst particles plus its essentiality for the reaction, first the reaction of 4-iodotoluene with phenylacetylene in the presence of the powder bulk Fe_3O_4 (Aldrich, 98%) under similar reaction conditions was investigated. Under these conditions, the reaction proceeded sluggishly and the desired alkyne was produced in a low yield (40% GC) after 48 h. The similar reaction in the presence of nanoparticles of Fe_3O_4 proceeded smoothly with excellent isolated yield (88–90%) of the desired product after 48 h. Moreover, in the absence of the nanomagnetite catalyst, the reaction was a low-yielding process and the desired arylalkyne (GC) was produced in $<8\%$ after 48 h. Nevertheless, the effect of the separate addition of Pd, Ni, Cu and Co to the reaction mixture in the absence of the nanocatalyst was also studied. For this aim, Pd, Ni, Cu and Co as their salts (1000 ppb) were added independently to the reaction mixture. The results of this investigation are tabulated in Table 2.

Table 2. The effect of the addition of Pd, Cu, Ni and Co in the reaction of 4-iodotoluene with phenylacetylene after 48 h.



Entry	Added metal	GC yield [%]
1	$Pd(OAc)_2$ (1000 ppb)	42
2	$NiCl_2$ (1000 ppb)	14
3	CuCl (1000 ppb)	10
4	$CoCl_2$ (1000 ppb)	15
5	No addition	<10

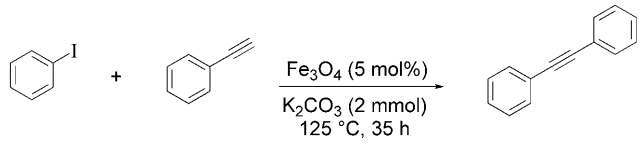
Table 3. Study of reaction of 4-iodotoluene with phenylacetylene in the presence of different ratios of Pd and Cu impurities and different amount of Fe_3O_4 nanoparticles.



Entry	Added metal	Concentration	GC yield [%]
1	$Pd(OAc)_2$	200 ppb	35
2	$Pd(OAc)_2$	500 ppb	41
3	$Pd(OAc)_2$	1000 ppb	42
4	$Pd(OAc)_2$	1200 ppb	42
5	CuCl	500 ppb	10
6	CuCl	1000 ppb	10
7	CuCl	1500 ppb	12
8	Fe_3O_4 nanocatalyst	1 mol%	40
9	Fe_3O_4 nanocatalyst	2.5 mil%	67
10	Fe_3O_4 nanocatalyst	5 mol%	88

For demonstrating the major role of Fe_3O_4 nanoparticles as catalysts, we have studied the reaction of 4-iodotoluene with phenylacetylene using different ratios of Pd and Cu impurities and also by applying different ratios of Fe_3O_4 nanocatalyst. The results of this study clearly confirm the role of Fe_3O_4 nanocatalyst. Increasing or decreasing the amounts of Pd and Cu impurities to the reaction mixture in the absence of the nanocatalyst did not affect the yield of the product noticeably. The addition of different amounts of Pd to the reaction mixture resulted in the production of the desired product in only 35-42% yields, whereas, the addition of extra amounts of Cu to the mixture was even less effective and only 10–12% formation of the desired product was observed. However, we have observed that the addition of different amounts of Fe_3O_4 nanocatalyst to the reaction mixture affects the yield of the product noticeably. These results clearly show that Fe_3O_4 nanoparticles play a

Table 4. Solvent screening for nanoparticles of paramagnetic magnetite (Fe_3O_4) catalysis for the coupling reaction of iodobenzene with phenylacetylene in different solvents.

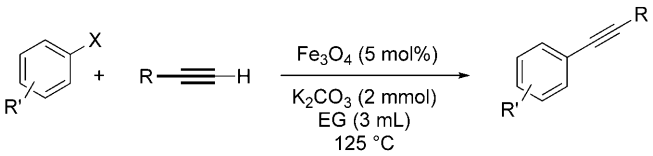


Entry	Solvent	Isolated yield [%]
1	DMF	67
2	NMP	40
3	EG	92
4	toluene	trace
5	water	trace

major role as catalysts for the reaction in spite of their contamination with Pd and Cu impurities. The results are shown in Table 3.

The effect of different solvents upon the reaction of iodobenzene (1 mmol) with phenylacetylene (2 mmol) as a model reaction in the presence of K_2CO_3 (2 mmol) and 5 mol% of the nanocatalyst (Fe_3O_4) at 125 °C was studied (Table 4). The results show that ethylene glycol (EG) is a suitable solvent for the reaction. EG possesses negligible vapour pressure, is thermally stable, is not so expensive with a low toxicity (oral rat LD_{50}: 4700 mg kg^{-1}; skin rabbit LD_{50}: 9530 mg kg^{-1}).[22] Ethylene glycol is highly soluble in water, and can be easily separated from the organic phase by addition of water to the reaction mixture.

Table 5. Sonogashira-Hagihara coupling reactions of phenylacetylenes/alkynes with aryl iodides catalyzed by nanoparticles of paramagnetic magnetite (Fe_3O_4) in ethylene glycol (EG) at 125 °C.



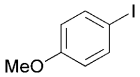
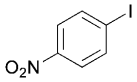
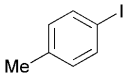
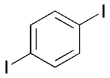
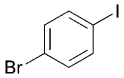
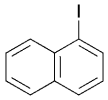
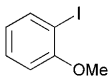
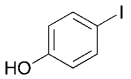
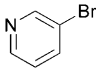
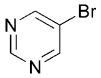
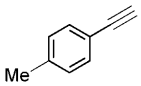
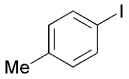
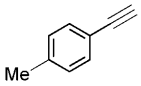
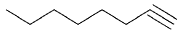
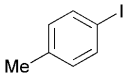
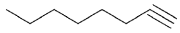
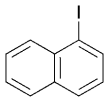
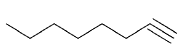
Entry	ArI	Alkyne	Time [h]	Product	Isolated yield [%]
1			35	**1a**	92
2			60	**1b**	90
3			40	**1c**	82
4			48	**1d**	88
5			30	**1e**	85
6			28	**1f**	86
7			40	**1g**	82[a]
8			20	**1h**	86
9			45	**1i**	90
10			30	**1j**	91
11			72	**1k**	76
12			30	**1l**	79

Table 5. (Continued)

Entry	ArI	Alkyne	Time [h]	Product	Isolated yield [%]
13			72	**1m**	80
14			72	**1n**	76
15			30	**1d**	90
16			42	**1o**	86
17			35	**1p**	86
18			48	**1q**	81
19			48	**1r**	78

[a] This reaction shows the selectivity of the catalyst, which discriminates bromo from iodo compounds.

Evaporation of the aqueous phase results in reusable EG for the subsequent reaction. EG can also be separated from the reaction mixture by distillation. We have applied both procedures for the isolation and recycling of the solvent for the semi large-scale reaction of iodobenzene with phenylacetylene. In addition, we have also shown that the hydroxy groups in EG play a determinant role to improve the catalytic activity of iron nanoparticles by stabilizing the lower oxidation states of iron. For this statement, we have studied the model reaction (4-iodotoluene with phenylacetylene) in EG, which carries two hydroxy groups, 3-methoxy-1-propanol, which has one hydroxy group, and 1,2-dimethoxyethane without hydroxy groups.The results show that when the reaction was conducted in the solvent with more hydroxy groups a higher yield of the desired product is obtained. We were able to isolate the enyne from EG in 85% whereas, from 3-methoxy-1-propanol, and 1,2-dimethoxyethane, the desired product was isolated in 75 and 58% yields , respectively

Therefore, the subsequent reactions were performed in EG in which the coupling reactions of phenylacetylene with both electron-rich and electron-deficient aryl iodides furnished the desired enynes in 76–90% isolated yields (Table 5). Nevertheless, in the presence of this catalyst, the reaction of phenyl bromide with phenylacetylene was very sluggish and the unreacted substrates were observed by GC analysis. However, we observed that activated aryl bromides such as 5-bromopyrimidine and 3-bromopyridine reacted smoothly in the presence of this catalyst and the desired alkynes were obtained in 76% and 80% isolated yields, respectively (Table 5). In order to show the general applicability of the method, we have also sudied the reaction of 1-octyne and 4-ethynyltoluene with some aryl iodides. The reactions proceeded well with high yields. The results are presented in Table 5, entries 15–19.

Comparison of the reactions of iodobenzene, 4-iodonitrobenzene and 2-iodoanisole with phenylacetylene catalyzed by Fe_3O_4 nanocatalyst and the $FeCl_3$/*N*,*N*-dimethylethylenediamine system,[12h] shows that the Fe_3O_4 nanocatalyst is a more efficient promoter as tabulated in Table 6.

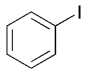
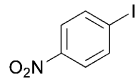
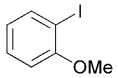
Finally, the separation of the nano-particles of paramagnetic Fe_3O_4 is a highly simple process, which is achieved by using a magnetic rod or by an external electrically induced magnetic field as shown in Figure 1.

Recyclability of the catalyst was tested upon the reaction of iodobenzene with phenylacetylene in ethylene glycol (EG). We observed that the catalytic activity of the catalyst was restored within the limits of the experimental errors for five successive runs as presented in Table 7, Very lately, such a restoration of catalytic activity for nanoparticles of Fe_3O_4 has been also reported for the synthesis of α-amino nitriles,[18b] propargylamines,[18c] and intramolecular C–N cross-coupling reactions.[18d]

Studies on other applications of this catalyst for the related Sonogashira–Hagihara reactions and also the other carbon-carbon and carbon-heteroatom bond formation reactions are underway in our laboratories.

In conclusion, in this study we have presented a novel protocol in which paramagnetic nanoparticles

Table 6. Comparison between catalyst activity of $FeCl_3$/*N,N*-dimethylethylenediamine (dmeda) and Fe_3O_4 nanoparticles.

Entry	ArX	Time [h] with Fe_3O_4 (with $FeCl_3$/dmeda)[12h]	Isolated yield [%] with Fe_3O_4 (with $FeCl_3$/dmeda)[12h]
1		35 (72)	92 (68)
2		40 (72)	82 (74)
3		60 (72)	76 (60)

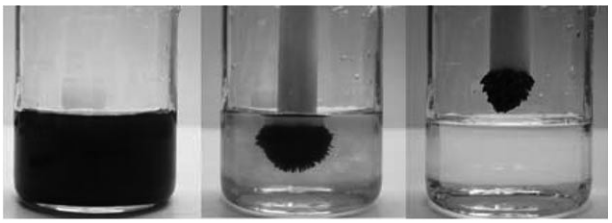


Figure 1. a: Nanoparticles of paramagnetic Fe_3O_4 dispersed in the reaction mixture at the beginning of the reaction, **b:** accumulation of the nanoparticles of paramagnetic Fe_3O_4 around the magnetic bar after completion of the reaction, and **c:** complete accumulation and separation of the catalyst particles from the reaction mixture by the magnetic bar.

Table 7. Recycling of the Fe_3O_4 nanoparticle catalyst for the reaction of iodobenzene with phenylacetylene.

Run	Time [h]	Isolated yield [%]
1	35	92
2	35	90
3	35	89
4	35	89
5	35	90

of magnetite (Fe_3O_4) with the average size <30 nm have been used as catalyst for the important Sonogashira–Hagihara reaction in ethylene glycol (EG) using aryl iodides and activated heteroaryl bromides with phenylacetylene. Our investigation shows that Fe_3O_4 nanoparticles are responsible for the catalytic activities for the reactions investigated and presented in this article, rather than its contamination with minute amounts of Pd, Ni, Cu and Co. The reactions proceeded in the air without any precautionary measures. The catalyst functions under heterogeneous conditions and its separation from the reaction mixture is easily achieved by an external magnetic field, which is of interest for large-scale operations for industrial purposes. The catalyst is also recyclable with retention of catalytic activity for several runs without markedly observable signs for loss of its catalytic activity.

Experimental Section

Procedure for Preparation of Arylalkynes using Fe_3O_4 Nanoparticles as Catalyst

To a 5-mL flask, which contained ethylene glycol (3 mL) were added nanoparticales of magnetite (Fe_3O_4, 0.05 mmol, 11 mg), K_2CO_3 (2 mmol, 276 mg), aryl halide (1 mmol) and phenylacetylene (2 mmol) and the mixture was heated at 125 °C for the appropriate reaction times. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate or diethyl ether (5×1 mL) and the upper organic phase was separated and evaporated. Further purification was performed by column chromatography (EtOAc/*n*-hexane) to obtain the desired coupling product (Table 5).

Typical Procedure for Large-Scale Preparation of Diphenylacetylene using Fe_3O_4 Nanoparticles as Catalyst

The catalyst was easily employed for the large-scale operation. For this aim, the reaction of iodobenzene (30 mmol, 6.12 g) with phenylacetylene (60 mmol, 7.2 g) and the catalyst (15 mmol, 3.48 g) under similar optimized reaction conditions (see preceding paragraph). The reaction proceeded well and the desired diphenylacetylene was obtained in a high isolated yield after 40 h; yield: 4.5 g (86%) (Table 5, entry 1).

Reaction of 4-Iodotoluene with Phenylacetylene in the Presence of Different Ratios of Fe_3O_4 Nanocatalyst

The reactions of 4-iodotoluene with phenylacetylene under conditions mentioned in the preceding section with 5, 2.5 and 1 mol% of the catalyst were performed. Work up of the reaction mixture after 48 h resulted the isolation of the desired compound in 88, 67 and 40% yields, respectively (Table 3, entries 8–10).

1a: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.43$–7.47 (m, 3H), 7.28–7.23 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta=132.5$, 128.3, 128.2, 123.2, 89.3.

1b: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.37$–7.43 (m, 4H), 7.22–7.25 (m, 3H), 6.79 (d, 2H, $J=8.2$), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=159.6$, 133.1, 131.5, 128.1 128.0, 123.6, 115.4, 114.0, 89.5, 88.1, 55.3.

1c: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=8.23$–8.20 (m, 2H), 7.68–7.54 (m, 4H), 7.40–7.36 (m, 3H).

1d: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.42$–7.44 (m, 2H), 7.30–7.36 (m, 2H), 7.20–7.25 (m, 3H), 6.99–7.08 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.4$, 131.6, 131.5, 129.1, 128.3, 128.1, 123.5, 120.2, 89.6, 88.8, 21.5.

1e: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.41$–6.88 (m, 8H).

1f: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.48$–7.43 (m, 8H), 7.30–7.26 (m, 6H).

1g: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.44$–7.37 (m, 4H), 7.31–7.24 (m, 5H).

1h: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.42–7.45$ (m, 2H), 6.91–7.27 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 132.8$, 131.7, 129.9, 129.3, 128.7, 128.5, 125.5, 123.3, 89.1, 84.7.

1i: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.37–8.34$ (m, 2H), 7.75–7.25 (m, 10H); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 133.2$, 131.7, 130.4, 129.1, 128.6, 128.4, 128.3, 128.0, 126.8, 126.4, 126.2, 125.3, 123.4, 120.9, 94.4, 87.6.

1j: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.48–7.41$ (m, 2H), 7.28–7.15 (m, 7H); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 140.2$, 131.8, 131.5, 129.5, 128.4, 128.3, 128.2 125.6, 123.5, 123.0, 93.4, 88.4, 20.8.

1k: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.60–7.51$ (m, 2H), 7.40–7.28 (m, 5H), 6.99–6.92 (m, 2H), 3.94 (s, 3H).

1l: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.60–7.23$ (7H, m), 6.74–6.71 (m, 2H), 5.20 (s, 1H).

1m: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.69$ (s, 1H), 8.46–8.47 (m, 1H), 7.71–7.74 (m, 1H), 7.45–7.51 (m, 2H), 7.31–7.28 (m, 4H).

1n: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 9.05$ (s, 1H), 8.76 (s, 2H), 7.31–7.26 (m, 3H), 7.48–7.42 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 158.5$, 156.6, 131.2, 129.3, 128.5, 122.6, 119.8, 96.3, 82.3.

1o: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.46–7.43$ (m, 2H), 7.18–7.16 (m, 2H), 2.39 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 138.1$, 131.4, 129.0, 120.4, 88.8, 21.4.

1p: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.46–7.41$ (m, 2H), 7.35–7.28 (m, 3H), 2.47–2.42 (m, 2H), 1.67–1.34 (m, 6H), 0.98–0.93 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 131.5$, 128.1, 127.4, 124.0, 90.4, 80.5, 31.3, 28.7, 28.6, 22.5, 19.4, 14.0.

1q: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.35–7.28$ (m, 2H), 7.14–7.04 (m, 2H), 2.50–2.31(m, 5H), 1.64–1.34 (m, 8H), 0.98–0.93 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.3$, 131.4, 128.9, 121.0, 89.6, 80.6, 31.4, 28.8, 28, 6, 22.6, 21.3, 19.4, 14.0.

1r: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.42–8.39$ (m, 1H), 7.89–7.41 (m, 6H), 2.64–2.59 (m, 2H), 1.78–1.38 (m, 8H), 0.99–0.95 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 133.5$, 133.2, 129.9, 128.2, 127.8, 126.4, 126.3, 126.2, 125.2, 121.8, 95.6, 78.6, 31.4, 28.9, 28.7, 22.6, 19.7, 14.1.

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