

Coupling of aromatic aldehydes with aryl halides in the presence of nickel catalysts with diazabutadiene ligands*

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Nickel catalysts with diazabutadiene ligands promote cross-coupling of benzaldehydes with aryl halides in the presence of zinc as reducing agent, which leads to the corresponding benzhydrols and benzophenones. The benzophenone percentage considerably increases when lithium chloride additive is used.

Key words: cross-coupling, benzaldehydes, aryl halides, benzhydrols, benzophenones, nickel catalysts.

One of the most important reactions in organic synthesis of biologically active compounds and pharmaceutical drugs is preparation of secondary alcohols from aldehydes and available organometallic reagents.¹ The use of popular organolithium compounds and Grignard reagents is limited by their high nucleophilicity and basicity, which in the case of polyfunctional compounds frequently causes side reactions. To overcome these complications, the methods using less active organoelement compounds as nucleophiles and catalysts based on transition metal derivatives were developed. Thus, coupling of aldehydes with organotin compounds in the presence of rhodium and iridium catalysts was studied.^{2,3} Chromium(III) organic derivatives were used in the nickel-catalyzed synthesis of benzhydrols and vinyl aryl carbinols by the Nozaki–Hiyama–Kishi (NHK) reaction.^{4–7} This reaction constitutes a method for the synthesis of structurally varied natural compounds due to its high chemoselectivity, very mild conditions, as well as to the tolerance to molecular fragments prone to elimination, epimerization, or containing labile functional groups. For example, in the last two years this approach was used to obtain micalolid B and its derivatives,⁸ (+)-pericosin B,⁹ 4 α -carba- β -L-luxofuranose,¹⁰ palytoxin,¹¹ and antibiotic pleuromutilin.¹² However, the NHK reaction has a significant disadvantage of the necessity to use a large amount of expensive and toxic Cr^{III} compound. Apart from that, electron deficient aromatic aldehydes reluctantly undergo this reaction, predominantly giving the corresponding pinacones.

In the work,¹³ the authors suggested an alternative strategy for the synthesis of benzhydrols from

aromatic aldehydes and aryl bromides in the presence of 10 mol.% of NiBr₂(dppe) and zinc powder (75 °C, THF, 24 h) in 38–91% yields. The corresponding pinacones and benzophenones were formed as the side products. The screening of different phosphines, as well as nitrogen-containing ligands (for example, 2,2'-bipyridyl and 1,10-phenanthroline) showed that the most active and selective catalyst of this reaction is a nickel complex with dppe, which in the mechanism of action and reaction conditions resembles the catalytic system used in the NHK reaction. The authors of the work,¹³ together with benzhydrol, observed the formation of the corresponding benzophenone as the side product, the synthesis of which is an important issue in organic chemistry. The diaryl ketone fragments are encountered in many natural (kotoin, papaveraldin) and synthetic biologically active molecules, in nonsteroidal antiinflammatory drugs (tiaprofenic acid, ketoprofen, piketoprofen, suprofen, ketorolac, isoxepac, zamepirak), in all the tranquilizer of benzodiazepine group, as well as in many important antibiotics (anthracycline and anthraquinone derivatives).¹⁴ Such structural fragments are parts of the materials for protection from UV radiation, synthetic dyes, plastics, etc.

Straightforward syntheses of ketones from aryl halides are scarce and usually include several steps. A classic Lewis acid-promoted acylation of arenes by the Friedel–Crafts reaction,^{15–17} as well as acylation of organolithium, -magnesium, and -aluminum reagents with acid derivatives¹⁸ are limited by the fact that aromatic substrates containing electron-donating substituents would form stable complexes with Lewis acids. This decreases the substrate reactivity and leads to low yields of the product or even entire stopping of the reaction. The problem can be partially resolved by the use of a Lewis acid as its complex with the

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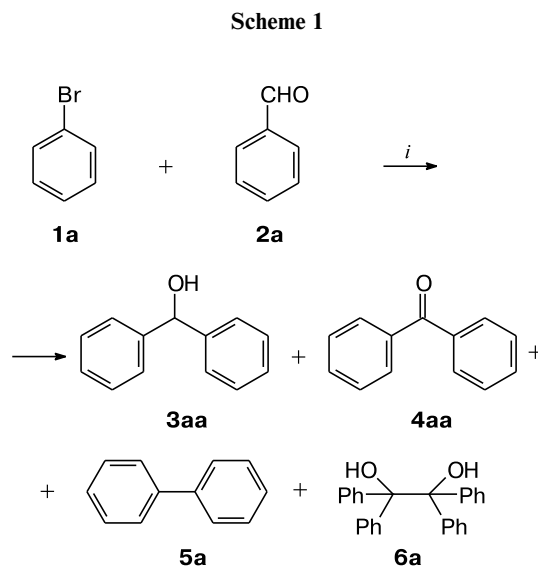
corresponding Lewis base (for example, $\text{AlCl}_3\text{—DMF}$). A principal practical limitation of this approach is the necessity of using much catalyst (up to 10 equiv.) to provide good yield of the product. Another synthetic strategy consists in the use of palladium-catalyzed coupling of $(\text{Ar})_x\text{M}$ ($\text{M} = \text{Cu}^{19}, \text{Sb}^{20}, \text{Ga}^{21}$) with carboxylic acid derivatives. Yet another general approach suggests a transition metal-catalyzed three-component cross-coupling of Ar—X derivatives ($\text{X} = \text{Br}, \text{I}, \text{OTf}, \text{N}_2^+$), carbon monoxide, and arylmetal reagents.^{22–24} It is also necessary to mention the work,²⁵ where benzophenones were successfully obtained by coupling of aromatic aldehydes and aryl iodides on nickel catalysts with phosphine ligands. However, despite of all these methods the problem of the development of new approaches to the preparation of benzophenones remains an actual issue, since the methods mentioned above either do not provide high yields of the products, or require the use of highly active reagents thus limiting the scope of possible substrates or necessitates the use of expensive reagents or catalysts based on platinum group metals.

Recently, we have shown that nickel complexes with diazabutadiene ligands are highly efficient catalysts of aryl halides homocoupling.²⁶ In the present work, we set a goal to study a reaction of aryl halides and benzaldehydes in the presence of similar nickel catalysts and zinc powder as a reducing agent, as well as to investigate a possibility of application of this reaction for the selective preparation of either benzhydrols, or benzophenones, depending on the reaction conditions.

Results and Discussion

At the beginning of our studies we found that bromobenzene (**1a**) reacted with benzaldehyde (**2a**) in the presence of 10 mol.% of $\text{NiBr}_2(\text{DME})$, 10 mol.% of diazabutadiene ligand **L1**, and 1.15 equiv. of zinc powder in THF at 70 °C giving a mixture of benzophenone (**3aa**, 5%), benzhydrol (**4aa**, 55%), biphenyl, as well as a small amount of benzopinacol (Scheme 1).

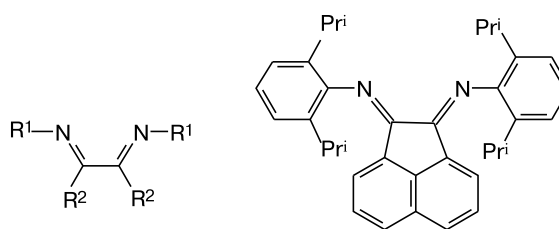
Then, we showed that various diazabutadiene ligands **L1—L12** in the composition of the catalytic system have different effects on its activity in the reaction under study. The nickel complexes with ligands **L8**, **L10**, and **L11** were found to be the least efficient under conditions selected (a conversion of the starting compounds was below 5%). A moderate yield of benzhydrol was obtained when nickel complexes (10 mol.%) based on ligands **L7** (the yields of benzhydrol and benzophenone were 33 and 30%, respectively), **L1** (55 and 5%), and **L2** (68 and 7%) were used. The high yields (85–90%) of benzhydrol were achieved with the catalysts based on ligands **L3**, **L5**, **L6**, **L9**, and **L11**. The activity of these catalysts is high enough, so that a decrease in their amount from 10 to 5 mol.% does not



Reagents and conditions: *i.* 5–10 mol.% of $\text{NiBr}_2(\text{DME})/\text{L}$, 1.15 equiv. of Zn, THF, 70 °C, 24 h.

affect the yield of benzhydrol when running the reaction for 24 h (Table 1). Interestingly that in the case of the nickel complex based on ligand **L1**, a decrease in the amount of the catalyst to 5 mol.% changes the ratio of the reaction products: the yields of benzhydrol and benzophenone are 25 and 30%, respectively.

To sum up, in the first stage of our studies we selected conditions, providing predominantly formation of benzhydrol. In a number of cases, benzhydrol and benzophenone were formed in comparable amounts. Taking this into account, in the next step we decided to find conditions, which would favor a predominant formation of benzophenone.



L1—L11

L12

Ligand	R ¹	R ²
L1	$\text{Me}_3\text{CCH}_2\text{CMe}_2$	H
L2	Bu ^t	H
L3	Bu ^s	H
L4	$\text{MeCH}_2\text{CMe}_2$	H
L5	Cyclohexyl	H
L6	Cyclododecyl	H
L7	Ph_2CH	H
L8	2,6- $\text{Me}_2\text{C}_6\text{H}_3$	H
L9	2,6- $\text{Pr}_2\text{C}_6\text{H}_3$	H
L10	2,6- $\text{Pr}_2\text{C}_6\text{H}_3$	Me
L11	2,6- $\text{Pr}_2\text{C}_6\text{H}_3$	Ph

Table 1. Optimization of reaction conditions of bromobenzene with benzaldehyde (5 mol.% NiBr₂ (DME)/L)

Ligand	Salt additive	Conversion of 1a Yield of 3aa Yield of 4aa		
		(%)		
L1	—	93	25	30
	LiCl	99	15	65
L2	—	96	68	7
	LiCl	98	10	68
L3	—	95	90	5
	LiCl	97	25	50
L5	—	96	90	4
	LiCl	94	25	50
L6	—	95	85	5
	LiCl	97	40	50
L9	—	98	90	4
	LiCl	99	94	4
L12	—	99	90	2
	LiCl	99	90	7

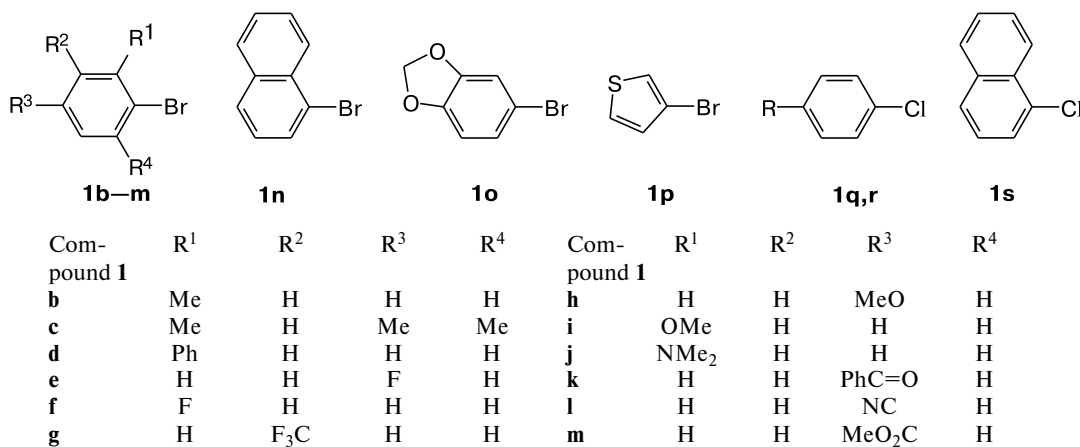
Based on the data,²⁵ when benzophenone was obtained similarly, one can suppose that the yield of this product can be increased by raising temperature to 110 °C. However, it turned out that under our conditions neither increase nor decrease in the temperature had any effect on the ratio of benzhydrol/benzophenone yields, but only affected the reaction rate. Apart from that, a decrease in the temperature to 40 °C allowed us to virtually completely suppress the side homocoupling reaction.

In most cases, the yield of benzophenone can be increased with a simultaneous suppression of the formation of benzhydrol by the addition to the reaction mixture of 0.5 equiv. of the salt LiCl (see Table 1). However, such an effect of the LiCl additive was observed not always. For example, the introduction of LiCl for the catalytic systems containing ligands **L9** or **L12** did not affect the ratio of benzhydrol/benzophenone yields. Thus, all the diazab-

utadiene ligands can be separated into three classes, *i.e.*, the ligands forming catalysts, which allow one to obtain: 1) predominantly benzhydrol (ligands **L9** and **L12**), 2) in the presence of LiCl predominantly benzophenone (ligands **L1** and **L2**), or 3) comparable amounts of benzhydrol and benzophenone (ligands **L3**, **L5**, and **L6**) (see Table 1). It should be noted that the ligands, whose application even in the presence of LiCl additive did not give benzophenone, contain aryl substituents at the nitrogen atoms. All other ligands contain alkyl substituents.

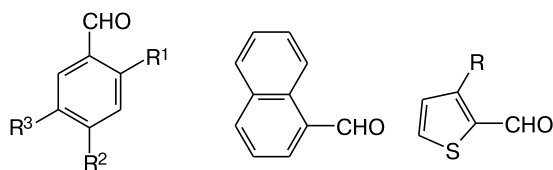
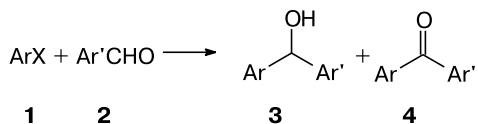
The method developed can be extended to the coupling of benzaldehydes with aryl chloride, which seems useful because of greater commercial availability of aryl chlorides. Under the optimal conditions, *i.e.*, in the presence of 5 mol.% of NiBr₂(DME) and ligand **L12**, 1.15 equiv. of Zn in THF, benzhydrol was obtained from chlorobenzene and benzaldehyde for 24 h at 70 °C in 90% yield. The use of the catalysts based on ligands **L1** and **L9** allowed us under the same conditions to obtain benzhydrol in 80% yield in both cases. In contrast to the reaction of bromobenzene with benzaldehyde, the selectivity of the reaction of chlorobenzene with benzaldehyde depends on temperature. Raising the temperature from 70 to 100 °C leads to a noticeable decrease in the benzhydrol yield, giving larger amount of benzopinacol instead. However, it turned out that the lithium chloride additive exerts the same influence as was observed for similar reaction with bromobenzene, *i.e.*, the use of this additive promotes the formation of benzophenone and decreases the yield of benzhydrol.

As it was noted above, the main advantage of the NHK reaction (using chromium salts) is its tolerance to functional groups, *i.e.*, a possibility to involve in the reaction of various substituted benzaldehydes and aryl halides. To study a synthetic scope of the herein studied procedure, we obtained benzhydrols (**3aa–3ra**, **3ac–3al**) and benzophenones (**4aa–4ra**, **4ac–4al**) containing various functional groups (Scheme 2, Table 2).



R = H (**q**), Me (**r**)

Scheme 2



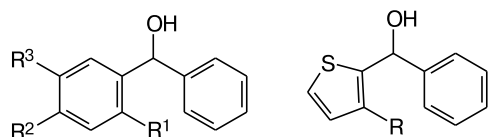
2b–i

2j

2k,l

Compound 2	R ¹	R ²	R ³
b	H	Me	H
c	H	H	F
d	H	H	MeO
e	H	MeO	H
f	MeO	MeO	MeO
g	H	MeO ₂ C	H
h	H	Me ₂ N	H
i	H	MeS	H

R = H (k), Me (l)

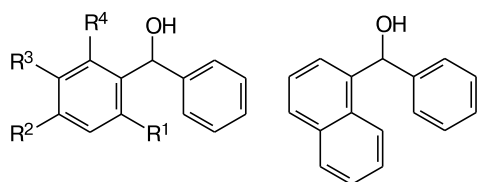


3ab–ai

3ak, 3al

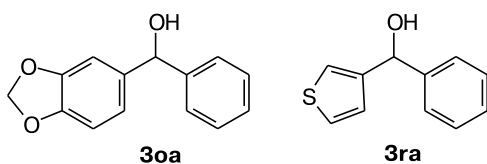
Compound 3	R ¹	R ²	R ³
ab	H	Me	H
ac	H	H	F
ad	H	H	MeO
ae	H	MeO	H
af	MeO	MeO	MeO
ag	H	MeO ₂ C	H
ah	H	Me ₂ N	H
ai	H	MeS	H

R = H (ak), Me (al)



3ba–ma

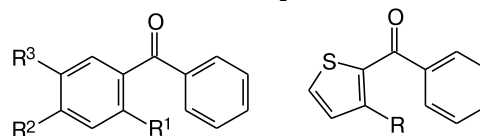
3na



3oa

3ra

Compound 3	R ¹	R ²	R ³	R ⁴
ba	Me	H	H	H
ca	Me	H	Me	Me
da	Ph	H	H	H
ea	H	H	F	H
fa	F	H	H	H
ga	H	F ₃ C	H	H
ha	H	H	MeO	H
ia	OMe	H	H	H
ja	NMe ₂	H	H	H
ka	H	H	PhC=O	H
la	H	Y	NC	H
ma	H	H	MeO ₂ C	H

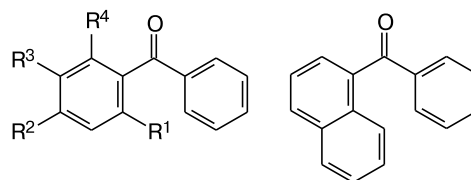


4ac–ai

4ak, 4al

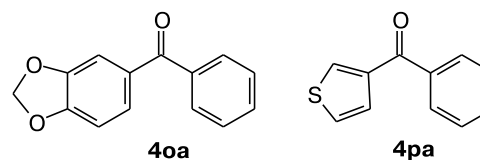
Compound 4	R ¹	R ²	R ³
ab	H	Me	H
ac	H	H	F
ad	H	H	MeO
ae	H	MeO	H
af	MeO	MeO	MeO
ag	H	MeO ₂ C	H
ah	H	Me ₂ N	H
ai	H	MeS	H

R = H (ak), Me (al)



4ba–ma

4n(s)a



4oa

4pa

Compound 4	R ¹	R ²	R ³	R ⁴
ba	Me	H	H	H
ca	Me	H	Me	Me
da	Ph	H	H	H
ea	H	H	F	H
fa	F	H	H	H
ga	H	F ₃ C	H	H
ha	H	H	MeO	H
ia	OMe	H	H	H
ja	NMe ₂	H	H	H
ka	H	H	PhC=O	H
la	H	Y	NC	H
ma	H	H	MeO ₂ C	H

Table 2. Nickel-catalyzed synthesis of diaryl carbinols and diaryl ketones from substrates of various structure (10 mol.% of NiBr₂(DME)/L, 1.15 equiv. of Zn, THF, 70 °C, 24 h; conditions A: L = L12, without salt additive; conditions B: L = L4, 0.5 equiv. of LiCl)^a

Aryl bromide	Aldehyde	Conversion of aryl halide (%)	Yield (%)	
			Benzhydrol 3	Benzophenone 4
1b	2a	96 (100)	3ba , 90 (29)	4ba , 0 (70)
1c	2a	98 (0)	3ca , 93 (0)	4ca , 0 (0)
1d	2a	97 (66)	3da , 90 (0)	4da , 0 (50)
1e	2a	98 (100)	3ea , 93 (47)	4ea , 0 (50)
1f	2a	99	3fa , 93	4fa , 0
1g	2a	100 (98)	3ga , 93 (53)	4ga , 4 (40)
1h	2a	100 (98)	3ha , 94 (53)	4ha , 3 (40)
1i	2a	93	3ia , 85	4ia , 0
1j	2a	93 (94)	3ja , 80 (84)	4ja , 2 (3)
1k	2a	100 (70)	3ka , 90 (10)	4ka , 9 (44)
1l	2a	100	3la , 68	4la , 3
1m	2a	100	3ma , 71	4ma , 1
1n	2a	100 (90)	3na , 70 (10)	4na , 21 (50)
1o	2a	89	3oa , 70	4oa , 10
1p	2a	68 (91)	3pa , 40 (40)	4pa , 10 (30)
1q	2a	97 (78)	3aa , 90 (10)	4aa , 4 (50)
1r	2a	98	3ra , 93	4ra , 3
1s	2a	96 (31)	3na , 77 (15)	4na , 15 (10)
1a	2j	93 (91)	3sa , 85 (17)	4sa , 0 (65)
1a	2b	99 ^b (94)	3ra , 90 (56)	4ra , 5 (28)
1a	2c	100 (81)	3ac , 95 (10)	4ac , 4 (55)
1a	2d	93 (91)	3ad , 78 (26)	4ad , 10 (60)
1a	2e	98 (81)	3ha , 88 (3)	4ha , 7 (70)
1a	2f	100 (91)	3af , 93 (13)	4af , 5 (75)
1a	2g	70	3ma , 30	4ma , 5
1a	2h	98 ^b (97)	3ah , 96 (40)	4ah , 3 (50)
1a	2i	100	3ai , 70	4ai , 15
1a	2k	96 ^b (68)	3ak , 93 (4)	4ak , 0 (40)
1a	2l	95 (84)	3al , 90 (25)	4al , 2 (35)

^a The data obtained under conditions A are given without parentheses, under conditions B in parentheses.^b Chlorobenzene was used instead of bromobenzene.

Generally, the aryl halides containing electron-donating substituents give the corresponding diaryl carbinols in higher yields than the substrates with electron-withdrawing substituents. For example, fluoro- and trifluoromethyl-substituted benzhydrols can be obtained in higher than 90% yields, benzhydrol methoxy and diethylamino derivatives in higher than 80% yields. However, the yield of benzhydrols containing keto, ester, and nitrile functional groups are below 70%. For the reaction involving substituted benzaldehydes, the higher yields of the products can be achieved when using chlorobenzene, rather than bromobenzene. Apparently, this can be explained by the fact that chlorobenzene is less active substrate for the side homocoupling reaction. It should be noted that the synthesis of substituted benzophenones proceeds with lower yields, up to 70%.

In conclusion, catalytic systems based on nickel complexes with diazabutadiene ligands developed by us earlier

for the synthesis of biaryls from the corresponding aryl halides have proved to be efficient in the synthesis of diaryl carbinols from aldehydes and aryl halides, making it possible to completely exclude the use of toxic and expensive chromium salts, as well as for the synthesis of diaryl ketones, which allows one to replace aggressive organometallic substrates and palladium catalysts with more available reagents and catalyst.

Experimental

Ligands L1–L12 were obtained as described earlier.²⁵ To prepare activated zinc powder, commercially available powder of metallic zinc (Acros) was sequentially washed under argon with 2% aqueous hydrochloric acid, anhydrous ethanol, and diethyl ether, then dried *in vacuo* and stored under an inert gas. Tetrahydrofuran was distilled under argon over the mixture of sodium–benzophenone ketyl. ¹H and ¹³C NMR spectra were recorded on a DPX-400 spectrometer (Bruker). Chemical shifts

are given relative to the TMS signal. Elemental analysis was carried out on a CHN-O-Rapid analyzer (Heracus).

Synthesis of benzhydrols by the reaction between aryl halide and benzaldehyde (general procedure). Activated zinc (75 mg, 1.15 mmol), NiBr₂(DME) (15.4 mg, 0.05 mmol), and ligand **L12** (0.05 mmol) were placed into a 8-mL glass vial using an atmosphere-controlled glove box. Then, 0.2 M solution of benzaldehyde (5 mL, 1 mmol) in THF and aryl halide (1.15 mmol) were added to this mixture. The reaction mixture was magnetically stirred at 70 °C, the target product was isolated from the reaction mixture by column chromatography on silica gel 60 Å (40–63 μm).

Benzhydrol (3aa). ¹H NMR (CDCl₃), δ: 7.38–7.31 (m, 8 H); 7.28–7.24 (m, 2 H); 5.83 (s, 1 H); 2.25 (s, 1 H). ¹³C NMR (CDCl₃), δ: 143.8, 128.5, 127.6, 126.5, 76.2. Found (%): C, 84.69; H, 6.56. Calculated (%): C, 84.75; H, 6.57.

(3-Fluorophenyl)(phenyl)methanol (3ac). ¹H NMR (CDCl₃), δ: 7.31–7.19 (m, 6 H); 7.10–7.02 (m, 2 H); 6.95–6.86 (m, 1 H); 5.69 (d, 1 H, *J* = 3.0 Hz); 2.65 (d, 1 H, *J* = 3.3 Hz). ¹³C NMR (CDCl₃), δ: 162.9, 146.3, 143.3, 129.9, 128.6, 127.8, 126.6, 122.0, 114.3, 113.4, 75.6. Found (%): C, 77.48; H, 5.63. Calculated (%): C, 77.21; H, 5.48.

(3-Methoxyphenyl)(phenyl)methanol (3ad). ¹H NMR (CDCl₃), δ: 7.40–7.22 (m, 6 H); 6.97–6.94 (m, 2 H); 6.82–6.79 (m, 1 H); 5.82 (d, 1 H, *J* = 3.3 Hz); 3.79 (s, 3 H); 2.21 (d, 1 H, *J* = 3.3 Hz). ¹³C NMR (CDCl₃), δ: 159.6, 145.3, 143.5, 129.3, 128.3, 127.4, 126.4, 118.7, 112.8, 111.9, 76.0, 55.0. Found (%): C, 78.61; H, 6.72. Calculated (%): C, 78.48; H, 6.59.

(Phenyl)(2,4,5-trimethoxyphenyl)methanol (3af). ¹H NMR (CDCl₃), δ: 7.34–7.23 (m, 3 H); 7.15–7.11 (m, 2 H); 6.91 (s, 1 H); 6.39 (s, 1 H); 6.24 (s, 1 H); 3.88 (s, 3 H); 3.84 (d, 6 H, *J* = 3.8 Hz). Found (%): C, 70.21; H, 6.53. Calculated (%): C, 70.06; H, 6.61.

(4-Dimethylaminophenyl)(phenyl)methanol (3ah). ¹H NMR (CDCl₃), δ: 7.21–7.41 (m, 7 H); 6.69 (d, *J* = 9.3 Hz); 5.78 (s, 1 H); 2.94 (s, 6 H); 2.21 (s, 1 H). ¹³C NMR (CDCl₃), δ: 150.1, 144.2, 131.9, 128.2, 127.6, 127.0, 126.2, 112.4, 75.9, 40.4. Found (%): C, 79.07; H, 7.39; N, 6.22. Calculated (%): C, 79.26; H, 7.54; N, 6.16.

(4-Methylthiophenyl)(phenyl)methanol (3ai). ¹H NMR (CDCl₃), δ: 7.20–7.42 (m, 9 H); 5.78 (s, 1 H); 2.45 (s, 3 H). ¹³C NMR (CDCl₃), δ: 143.6, 140.7, 137.6, 128.5, 127.6, 127.0, 126.6, 126.4, 75.8, 15.8. Found (%): C, 73.14; H, 6.21. Calculated (%): C, 73.01; H, 6.13.

(Phenyl)(2-thienyl)methanol (3ak). ¹H NMR (CDCl₃), δ: 7.46 (d, 2 H, *J* = 6.8 Hz); 7.40 (t, 2 H, *J* = 7.2 Hz); 7.35 (d, 1 H, *J* = 7.2 Hz); 7.28 (d, 1 H, *J* = 5.2 Hz); 6.97 (t, 1 H, *J* = 4.0 Hz); 6.90 (d, 1 H, *J* = 3.2 Hz); 5.98 (s, 1 H); 2.95 (s, 1 H). ¹³C NMR (CDCl₃), δ: 148.1, 143.0, 128.4, 127.8, 126.5, 126.3, 126.2, 125.2, 124.7, 72.2. Found (%): C, 69.58; H, 5.15. Calculated (%): C, 69.44; H, 5.30.

(3-Methyl-2-thienyl)(phenyl)methanol (3al). ¹H NMR (CDCl₃), δ: 7.29–7.20 (m, 5 H); 6.96 (d, 1 H, *J* = 7.0 Hz); 6.59 (d, 1 H, *J* = 6.6 Hz); 5.90 (s, 1 H); 2.27 (s, 3 H). Found (%): C, 70.39; H, 6.00. Calculated (%): C, 70.55; H, 5.92.

(Phenyl)(*o*-tolyl)methanol (3ba). ¹H NMR (CDCl₃), δ: 7.52 (dd, 1 H, *J* = 5.6 Hz, *J* = 1.6 Hz); 7.12–7.36 (m, 8 H); 6.02 (s, 1 H); 2.27 (s, 3 H). ¹³C NMR (CDCl₃), δ: 142.7, 141.3, 135.2, 130.4, 128.3, 127.43, 127.40, 127.0, 126.2, 126.0, 73.4, 19.5. Found (%): C, 84.90; H, 7.31. Calculated (%): C, 84.81; H, 7.12.

(Mesityl)(phenyl)methanol (3ca). ¹H NMR (CDCl₃), δ: 7.28 (s, 5 H); 6.88 (s, 2 H); 6.30 (s, 1 H); 2.28 (s, 3 H); 2.20 (s, 6 H). Found (%): C, 84.98; H, 8.10. Calculated (%): C, 84.91; H, 8.02.

(Biphenyl-2-yl)(phenyl)methanol (3da). ¹H NMR (CDCl₃), δ: 7.56 (d, 1 H, *J* = 7.6 Hz); 7.31–7.41 (m, 5 H); 7.21–7.27 (m, 6 H); 7.17 (d, 2 H, *J* = 7.1 Hz); 5.94 (s, 1 H); 2.04 (s, 1 H). ¹³C NMR (CDCl₃), δ: 143.8, 141.1, 140.9, 140.7, 129.8, 129.2, 128.09, 128.04, 127.7, 127.2, 127.1, 127.0, 126.9, 126.5, 72.1. Found (%): C, 87.75; H, 6.26. Calculated (%): C, 87.66; H, 6.19.

(4-Fluorophenyl)(phenyl)methanol (3ea). ¹H NMR (CDCl₃), δ: 7.28–7.23 (m, 7 H); 6.97–6.93 (m, 2 H); 5.68 (s, 1 H); 2.71 (s, 1 H). ¹³C NMR (CDCl₃), δ: 162.1, 143.6, 139.5, 128.5, 128.2, 127.7, 126.4, 115.2, 75.5. Found (%): C, 77.12; H, 5.26. Calculated (%): C, 77.21; H, 5.48.

(2-Fluorophenyl)(phenyl)methanol (3fa). ¹H NMR (CDCl₃), δ: 7.42 (d, 1 H, *J* = 7.0 Hz); 7.43–7.28 (m, 6 H); 7.19–7.03 (m, 2 H); 6.15 (s, 1 H); 2.47 (s, 1 H). ¹³C NMR (CDCl₃), δ: 158.2, 142.7, 130.8, 129.1, 129.0, 128.4, 127.7, 126.3, 124.3, 115.3, 70.0. Found (%): C, 77.19; H, 5.41. Calculated (%): C, 77.21; H, 5.48.

(Phenyl)(3-trifluoromethylphenyl)methanol (3ga). ¹H NMR (CDCl₃), δ: 7.60 (d, 2 H, *J* = 8.3 Hz); 7.52 (d, 2 H, *J* = 8.3 Hz); 7.37–7.28 (m, 5 H); 5.90 (s, 1 H); 2.36 (s, 1 H). ¹³C NMR (CDCl₃), δ: 147.5, 143.1, 130.8, 129.8, 128.7, 128.0, 126.6, 125.3, 75.7. Found (%): C, 66.83; H, 4.46. Calculated (%): C, 66.66; H, 4.40.

(4-Methoxyphenyl)(phenyl)methanol (3ha). ¹H NMR (CDCl₃), δ: 7.39–7.26 (m, 7 H); 6.89–6.84 (m, 2 H); 5.82 (d, 1 H, *J* = 3.3 Hz); 3.79 (s, 3 H); 2.14 (d, 1 H, *J* = 3.3 Hz). ¹³C NMR (CDCl₃), δ: 159.0, 144.0, 136.2, 128.4, 127.9, 127.3, 126.4, 113.9, 75.8, 55.2. Found (%): C, 78.55; H, 6.43. Calculated (%): C, 78.48; H, 6.59.

(2-Methoxyphenyl)(phenyl)methanol (3ia). ¹H NMR (CDCl₃), δ: 7.19–7.36 (m, 7 H); 6.81–6.92 (m, 2 H); 6.01 (s, 1 H); 7.3 (s, 3 H); 3.14 (s, 1 H). ¹³C NMR (CDCl₃), δ: 156.4, 143.1, 131.8, 128.5, 127.9, 127.6, 126.9, 126.3, 120.6, 110.5, 71.9, 55.3. Found (%): C, 78.67; H, 6.63. Calculated (%): C, 78.48; H, 6.59.

(2-Dimethylaminophenyl)(phenyl)methanol (3ja). ¹H NMR (CDCl₃), δ: 7.46 (s, 1 H); 7.41–7.23 (m, 7 H); 7.13–7.09 (m, 1 H); 7.08–7.02 (m, 1 H); 5.97 (s, 1 H); 2.57 (s, 6 H). ¹³C NMR (CDCl₃), δ: 152.02, 147.67, 130.56, 128.34, 127.73, 126.95, 125.27, 123.53, 83.05, 45.69. Found (%): C, 79.15; H, 7.50; N, 6.30. Calculated (%): C, 79.26; H, 7.54; N, 6.16.

{4-[(Hydroxy)(phenyl)methyl]phenyl}(phenyl)methanol (3ka). ¹H NMR (CDCl₃), δ: 7.2–7.8 (m, 14 H); 5.8 (s, 1 H); 2.8 (s, 1 H). ¹³C NMR (CDCl₃), δ: 196.4, 148.4, 143.3, 137.6, 136.5, 132.3, 130.2, 129.9, 128.6, 128.2, 127.8, 126.6, 126.2, 75.8. Found (%): C, 83.20; H, 5.77. Calculated (%): C, 83.31; H, 5.59.

(4-Cyanophenyl)(phenyl)methanol (3la). ¹H NMR (CDCl₃), δ: 7.53 (d, 2 H, *J* = 8.3 Hz); 7.45 (d, 2 H, *J* = 8.3 Hz); 7.33–7.23 (m, 5 H); 5.78 (s, 1 H); 3.05 (s, 1 H). ¹³C NMR (CDCl₃), δ: 148.9, 142.7, 132.1, 128.7, 128.0, 126.9, 126.5, 118.7, 110.7, 75.3. Found (%): C, 80.25; H, 5.20; N, 6.83. Calculated (%): C, 80.36; H, 5.30; N, 6.69.

Methyl 4-[(hydroxy)(phenyl)methyl]benzoate (3ma). ¹H NMR (CDCl₃), δ: 7.8–7.2 (m, 14 H); 5.8 (s, 1 H); 2.8 (s, 1 H). ¹³C NMR (CDCl₃), δ: 196.4, 148.4, 143.3, 137.6, 136.5, 132.3, 130.2, 129.9, 128.6, 128.2, 127.8, 126.6, 126.2, 75.8. Found (%): C, 74.56; H, 5.99. Calculated (%): C, 74.36; H, 5.82.

(1-Naphthyl)(phenyl)methanol (3na). ¹H NMR (CDCl₃), δ: 7.96 (d, 1 H, *J* = 8.0 Hz); 7.81 (d, 1 H, *J* = 7.0 Hz); 7.75 (d, 1 H, *J* = 8.0 Hz); 7.55 (d, 1 H, *J* = 7.0 Hz); 7.43–7.32 (m, 5 H); 7.28–7.20 (m, 3 H); 6.43 (s, 1 H); 2.60 (s, 1 H). ¹³C NMR (CDCl₃), δ: 143.1, 138.8, 133.9, 130.7, 128.7, 128.41, 128.36,

127.5, 127.0, 126.0, 125.5, 125.3, 124.6, 124.0, 73.5. Found (%): C, 87.02; H, 6.16. Calculated (%): C, 87.15; H, 6.02.

(1,3-Benzodioxol-5-yl)(phenyl)methanol (3oa). ¹H NMR (CDCl₃), δ: 7.26–7.14 (m, 5 H); 6.75–6.64 (m, 3 H); 5.80 (s, 2 H); 5.62 (s, 1 H); 2.30 (s, 1 H). ¹³C NMR (CDCl₃), δ: 148.18, 147.37, 144.19, 140.26, 138.39, 128.89, 127.88, 126.73, 120.38, 108.47, 107.56, 101.41, 76.35. Found (%): C, 73.53; H, 5.39. Calculated (%): C, 73.67; H, 5.30.

(Phenyl)(3-thienyl)methanol (3pa). ¹H NMR (CDCl₃), δ: 7.42–7.26 (m, 6 H); 7.19–7.18 (m, 1 H); 7.01–6.99 (m, 1 H); 5.88 (s, 1 H); 2.34 (s, 1 H). ¹³C NMR (CDCl₃), δ: 145.26, 143.31, 128.46, 127.71, 126.44, 126.35, 126.14, 121.61, 72.75. Found (%): C, 69.24; H, 5.39. Calculated (%): C, 69.44; H, 5.30.

(Phenyl)(*p*-tolyl)methanol (3ra). ¹H NMR (CDCl₃), δ: 7.39–7.28 (m, 5 H); 7.26 (d, 2 H, *J* = 8.0 Hz); 7.15 (d, 2 H, *J* = 8.0 Hz); 5.99 (s, 1 H); 2.36 (s, 3 H); 2.18 (br.s, 1 H). ¹³C NMR (CDCl₃), δ: 143.9, 140.9, 137.4, 129.3, 128.4, 127.5, 126.6, 126.4, 76.2, 21.2. Found (%): C, 84.70; H, 7.33. Calculated (%): C, 84.81; H, 7.12.

Synthesis of benzophenones by the coupling reaction of aryl halides and benzaldehydes (general procedure). Activated zinc (75 mg, 1.15 mmol), LiCl (21.3 mg, 0.05 mmol), NiBr₂(DME) (15.4 mg, 0.05 mmol), and ligand **L4** (0.05 mmol) were placed into a 8-mL glass vial using an atmosphere-controlled glove box. Then, 0.2 *M* solution of benzaldehyde (5 mL, 1 mmol) in THF and aryl halide (1.15 mmol) were added to this mixture. The reaction mixture was magnetically stirred at 70 °C, the target product was isolated from the reaction mixture by column chromatography on silica gel 60 Å (40–60 mesh).

Benzophenone (4aa). ¹H NMR (CDCl₃), δ: 7.47–7.50 (m, 4 H); 7.58–7.61 (m, 2 H); 7.81 (d, 4 H, *J* = 7.5 Hz). ¹³C NMR (CDCl₃), δ: 196.9, 137.8, 132.5, 130.2, 128.4. Found (%): C, 88.70; H, 5.31. Calculated (%): C, 85.69; H, 5.53.

(3-Fluorophenyl)(phenyl)methanone (4ac). ¹H NMR (CDCl₃), δ: 7.88–7.73 (m, 2 H); 7.69–7.55 (m, 2 H); 7.55–7.37 (m, 4 H); 7.29 (tdd, 1 H, *J* = 8.3 Hz, *J* = 2.6 Hz, *J* = 1.1 Hz). ¹³C NMR (CDCl₃), δ: 195.37, 162.55, 139.71, 137.08, 132.88, 130.10, 130.05, 128.51, 125.92, 119.51, 116.81. Found (%): C, 77.73; H, 4.69. Calculated (%): C, 77.99; H, 4.53.

(3-Methoxyphenyl)(phenyl)methanone (4ad). ¹H NMR (CDCl₃), δ: 7.81 (dd, 2 H, *J* = 1.3 Hz, *J* = 8.5 Hz); 7.57–7.60 (m, 1 H); 7.48 (dd, 2 H, *J* = 7.6 Hz, *J* = 7.8 Hz); 7.33–7.39 (m, 3 H); 7.12–7.15 (m, 1 H); 3.86 (s, 3 H). ¹³C NMR (CDCl₃), δ: 196.5, 159.6, 138.9, 137.6, 132.4, 130.1, 129.2, 128.3, 122.9, 118.9, 114.3, 55.5. Found (%): C, 79.01; H, 5.61. Calculated (%): C, 79.22; H, 5.70.

(Phenyl)(2,4,5-trimethoxyphenyl)methanone (4af). ¹H NMR (CDCl₃), δ: 7.77 (dd, 2 H, *J* = 8.0 Hz, *J* = 1.6 Hz); 7.52 (tt, 1 H, *J* = 7.4 Hz, *J* = 1.4 Hz); 7.41 (t, 2 H, *J* = 8.0 Hz); 7.04 (s, 1 H); 6.57 (s, 1 H); 3.95 (s, 3 H); 3.84 (s, 3 H); 3.65 (s, 3 H). ¹³C NMR (CDCl₃), δ: 195.37, 153.17, 152.40, 142.91, 138.73, 132.15, 129.31, 127.81, 119.61, 113.25, 97.28, 56.34, 56.27, 55.94. Found (%): C, 70.39; H, 5.78. Calculated (%): C, 70.57; H, 5.92.

(4-Dimethylaminophenyl)(phenyl)methanone (4ah). ¹H NMR (CDCl₃), δ: 7.83 (d, 2 H, *J* = 8.6 Hz); 7.69 (d, 2 H, *J* = 7.6 Hz); 7.28 (d, 2 H, *J* = 7.1 Hz); 6.70 (d, 2 H, *J* = 8.5 Hz); 3.09 (s, 6 H); 2.46 (s, 3 H). ¹³C NMR (CDCl₃), δ: 194.7, 153.0, 141.5, 136.3, 132.4, 129.5, 128.5, 124.9, 110.4, 39.8, 21.4. Found (%): C, 79.78; H, 6.96; N, 6.02. Calculated (%): C, 79.97; H, 6.71; N, 6.22.

(Phenyl)(2-thienyl)methanone (4ak). ¹H NMR (CDCl₃), δ: 7.87 (d, 2 H, *J* = 7.6 Hz); 7.73 (d, 1 H, *J* = 4.8 Hz); 7.65 (d, 1 H,

J = 3.6 Hz); 7.61 (t, 1 H, *J* = 7.4 Hz); 7.51 (t, 2 H, *J* = 7.8 Hz); 7.17 (t, 1 H, *J* = 4.4 Hz). ¹³C NMR (CDCl₃), δ: 188.2, 143.6, 138.1, 134.8, 134.1, 132.2, 129.1, 128.3, 127.9. Found (%): C, 70.39; H, 4.05. Calculated (%): C, 70.18; H, 4.28.

(3-Methyl-2-thienyl)(phenyl)methanone (4al). ¹H NMR (CDCl₃), δ: 7.78–7.75 (m, 2 H); 7.70–7.66 (m, 1 H); 7.46–7.41 (m, 2 H); 7.32 (d, 1 H, *J* = 7.3 Hz); 6.86–6.84 (d, 1 H, *J* = 7.3 Hz); 2.20 (s, 3 H). Found (%): C, 71.14; H, 5.20. Calculated (%): C, 71.25; H, 4.98.

(Phenyl)(*o*-tolyl)methanone (4ba). ¹H NMR (CDCl₃), δ: 7.78 (d, 2 H, *J* = 8.4 Hz); 7.55–7.62 (m, 1 H); 7.24–7.49 (m, 6 H); 2.32 (s, 3 H). ¹³C NMR (CDCl₃), δ: 198.5, 138.5, 137.7, 136.8, 133.0, 130.9, 130.1, 130.0, 128.4, 128.3, 125.1, 19.9. Found (%): C, 85.49; H, 6.06. Calculated (%): C, 85.68; H, 6.16.

(Biphenyl-2-yl)(phenyl)methanone (4da). ¹H NMR (CDCl₃), δ: 7.64 (d, 2 H, *J* = 7.9 Hz); 7.57–7.56 (m, 1 H); 7.52–7.38 (m, 4 H); 7.28–7.25 (m, 4 H); 7.21–7.14 (m, 3 H). ¹³C NMR (CDCl₃), δ: 198.74, 141.11, 140.13, 138.93, 137.35, 132.76, 130.32, 130.02, 129.86, 128.96, 128.73, 128.20, 128.03, 127.28, 127.02. Found (%): C, 88.50; H, 5.33. Calculated (%): C, 88.34; H, 5.46.

(4-Fluorophenyl)(phenyl)methanone (4fa). ¹H NMR (CDCl₃), δ: 7.72–7.68 (m, 2 H); 7.64–7.62 (m, 2 H); 7.46–7.42 (m, 1 H); 7.35–7.32 (t, 2 H, *J* = 7.3 Hz); 7.02–6.98 (t, 2 H, *J* = 7.0 Hz). ¹³C NMR (CDCl₃), δ: 194.0, 165.5, 163.0, 136.4, 132.7, 132.7, 131.6, 131.5, 131.4, 128.8, 127.3, 114.5, 114.3. Found (%): C, 77.82; H, 4.55. Calculated (%): C, 77.99; H, 4.53.

(Phenyl)(3-trifluoromethylphenyl)methanone (4ga). ¹H NMR (CDCl₃), δ: 7.91–7.89 (d, 2 H, *J* = 7.9 Hz); 7.82–7.80 (m, 2 H); 7.77–7.75 (d, 2 H, *J* = 7.8 Hz); 7.65–7.62 (t, 1 H, *J* = 7.6 Hz); 7.53–7.49 (t, 2 H, *J* = 7.5 Hz). ¹³C NMR (CDCl₃), δ: 195.6, 140.7, 136.7, 133.9, 133.6, 133.1, 130.6, 130.2, 130.1, 128.5, 125.4, 125.3, 125.0, 122.3. Found (%): C, 67.04; H, 3.45. Calculated (%): C, 67.20; H, 3.63.

(4-Methoxyphenyl)(phenyl)methanone (4ha). ¹H NMR (CDCl₃), δ: 7.84 (d, 2 H, *J* = 8.8 Hz); 7.74–7.76 (m, 2 H); 7.55 (d, 1 H, *J* = 7.5 Hz); 7.46 (t, 2 H, *J* = 7.6 Hz); 6.96 (d, 2 H, *J* = 8.8 Hz); 3.87 (s, 3 H). ¹³C NMR (CDCl₃), δ: 195.4, 163.3, 138.4, 132.5, 131.8, 130.1, 129.6, 128.1, 113.5, 55.4. Found (%): C, 79.39; H, 5.81. Calculated (%): C, 79.22; H, 5.70.

1,4-Phenylenebis(phenyl)methanone (4ka). ¹H NMR (CDCl₃), δ: 7.48–7.54 (m, 4 H); 7.60–7.65 (m, 2 H); 7.82–7.86 (m, 4 H); 7.88 (s, 4 H). ¹³C NMR (CDCl₃), δ: 196.1, 140.8, 137.1, 133.1, 130.2, 129.8, 128.6. Found (%): C, 84.06; H, 5.11. Calculated (%): C, 83.90; H, 4.93.

(1-Naphthyl)(phenyl)methanone (4na). ¹H NMR (CDCl₃), δ: 8.10 (d, 1 H, *J* = 8.0 Hz); 8.00 (d, 1 H, *J* = 8.4 Hz); 7.93 (t, 1 H, *J* = 4.8 Hz); 7.87–7.89 (m, 2 H); 7.56–7.63 (m, 2 H); 7.51–7.55 (m, 3 H); 7.45–7.51 (m, 2 H). ¹³C NMR (CDCl₃), δ: 198.0, 138.3, 136.3, 133.7, 133.3, 131.2, 131.0, 130.4, 128.5, 128.4, 127.7, 127.2, 126.5, 125.8, 124.3. Found (%): C, 87.68; H, 5.08. Calculated (%): C, 87.90; H, 5.21.

(Phenyl)(3-thienyl)methanone (4pa). ¹H NMR (CDCl₃), δ: 7.88–7.84 (m, 2 H); 7.68–7.58 (m, 2 H); 7.51–7.46 (m, 2 H); 7.38 (d, 1 H, *J* = 3.3 Hz). ¹³C NMR (CDCl₃), δ: 189.79, 139.21, 137.44, 133.25, 132.26, 130.05, 128.46, 125.08, 110.56. Found (%): C, 70.35; H, 4.19. Calculated (%): C, 70.18; H, 4.28.

(Phenyl)(*p*-tolyl)methanone (4ra). ¹H NMR (CDCl₃), δ: 7.77–7.79 (m, 2 H); 7.72 (d, 2 H, *J* = 8.1 Hz); 7.56 (t, 1 H, *J* = 7.5 Hz); 7.44 (t, 2 H, *J* = 7.5 Hz); 7.27 (d, 2 H, *J* = 8.1 Hz); 2.44 (s, 3 H). ¹³C NMR (CDCl₃), δ: 196.5, 143.2, 137.9, 134.9,

132.2, 130.2, 129.8, 128.8, 128.1, 21.7. Found (%): C, 85.47; H, 6.01. Calculated (%): C, 85.68; H, 6.16.

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