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Arene diruthenium(II)-mediated synthesis of imines from alcohols and amines under aerobic condition

Veerappan Tamilthendral[1] | **Rengan Ramesh**[1] | **Jan Grzegorz Malecki**[2]

[1]Centre for Organometallic Chemistry, School of Chemistry, Bharathidasan University, Tiruchirappalli, India

[2]Department of Crystallography, Institute of Chemistry, University of Silesia, Katowice, Poland

Correspondence
Rengan Ramesh, Centre for Organometallic Chemistry, School of Chemistry, Bharathidasan University, Tiruchirappalli, 620 024 Tamilnadu, India.
Email: rramesh@bdu.ac.in

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The utility and selectivity of the newly synthesized dinuclear arene Ru(II) complex were demonstrated towards the synthesis of imines from coupling of alcohols and amines in the aerobic condition. Analytical and various spectral methods have been used to establish the unprecedented formation of the new thiolato-bridged dinuclear ruthenium complex. The molecular structure of the titled complex was evidenced with aid of X-ray crystallographic technique. A wide range of imines were obtained in good-to-excellent yields up to 98% and water as the by-product through an acceptorless dehydrogenative coupling of alcohols with amines. The catalytic reaction operated a concise atom economical without any oxidant with 1 mol% of the catalyst load. Further, the role of base, solvent and catalyst loading of the coupling reaction has been investigated. A plausible mechanism has been described and was found to proceed via the formation of an aldehyde intermediate. Short synthesis of antibacterial drug *N*-(salicylidene)-2-hydroxyaniline illustrated the utility of the present protocol.

KEYWORDS

aerobic oxidation, imine synthesis, thiolato Ru(II) catalyst, thiourea

1 | INTRODUCTION

Imines are profound important class of nitrogen compounds owing to their high reactivity.[1] They are ubiquitous intermediates in many organic reactions such as cyclization, cycloaddition, multicomponent reactions and condensation.[2] They are adaptable nitrogen sources that find applications in pharmaceuticals, industrial and agriculture.[3] Further, many nitrogen-containing bioactive compounds such as amines, amides and pyrrolines can be constructed from imine functional group (Figure 1).[4] Hence, synthesis and applications of imines are essentially ever-appealing topics in synthetic organic chemistry.

The conventional approach for imine synthesis involves the direct coupling of amines with aldehydes or ketones with Lewis acid or dehydrating agents and higher reaction time are required in many situations.[5] Imines have been also synthesized in different circumstances includes Schmidt reaction, Aza-Wittig reaction[6] and oxidation of secondary amines using oxidizing agents (Scheme 1).[7]

Although a number of methods are known for imine synthesis in the literature, they largely suffer from drawbacks like use of toxic reagents, poor atom economy, harsh synthetic process and low level of selectivity.[8]

To overcome the aforementioned limitations, the metal-catalyzed direct synthesis of imines from alcohols with amines through acceptorless dehydrogenation coupling mechanism is an alternative approach. The strategy consists of two steps: (i) aerobic oxidation of alcohol in the presence of a transition metal catalyst and (ii) generation of imine. More advantageously, the acceptorless dehydrogenative methodology is a greener protocol

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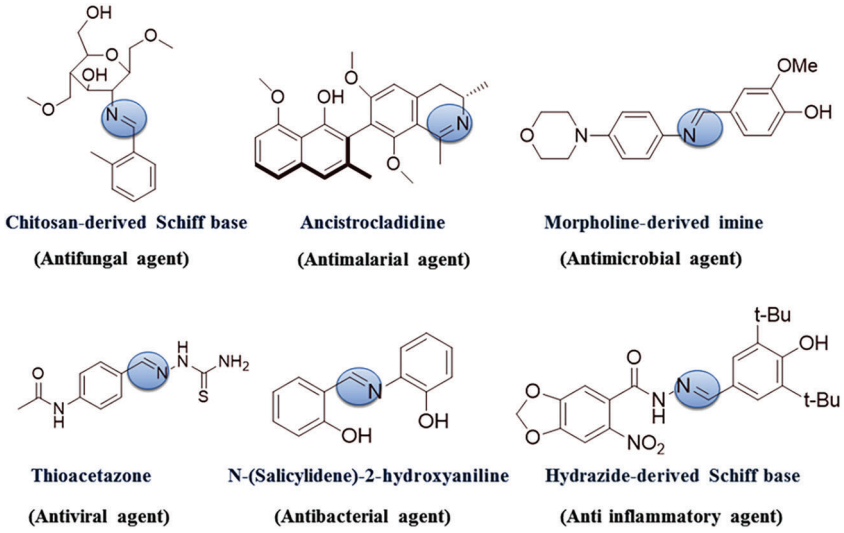
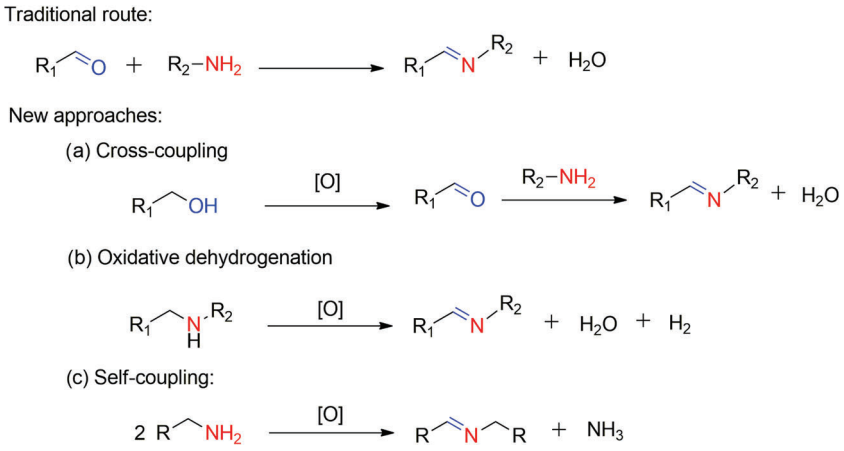


FIGURE 1 Examples for bioactive imine analogues

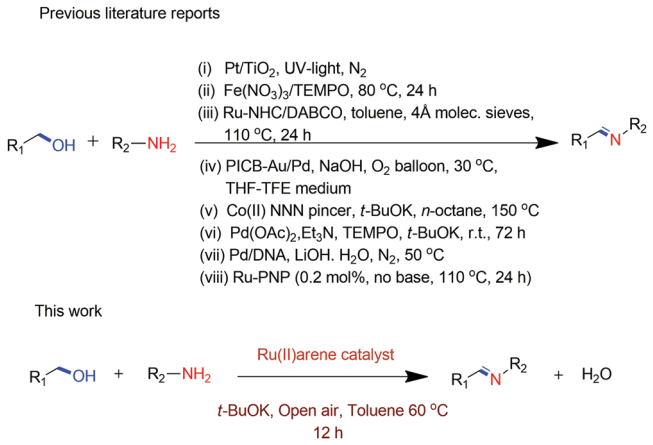


SCHEME 1 Imine formation via traditional method and new approaches by aerobic oxidation of alcohols and amines (a, b and c)

for the coupling of alcohol and amine to desired imine with the water as the by-product.

Milstein and co-workers reported Ru–PNP-type pincer complex that promoted synthesis of imines from alcohols and amines under nitrogen atmosphere.[9] This significant breakthrough methodology has garnered much attention from the researchers towards imine synthesis. Several wide transition metal complexes such as Ru, Os, Pd, Pt and Au have been reported as catalysts for imine synthesis under high temperature, inert atmosphere, special condition and long reaction time.[10–14] Shiraishi and co-workers employed a Pt/TiO_2 heterogeneous catalyst for the imine synthesis with UV radiation and used nitrogen atmosphere protection.[13] Soule and co-workers have reported synthesis of imines by gold/palladium alloy nanoparticles (1.5 mol%) in the presence of oxidant.[15] Donthiri et al. have described synthesis of imines by using NaOH (10 mol%) as a catalyst at high temperature.[16] The Tian research group explored imine formation by employing CuI/bipyridine/TEMPO under neat conditions.[17] Later, the Zhang group reported mild one-pot synthesis of imines using as $Fe(NO_3)_3$/TEMPO system used as a catalyst in the presence of additives.[18] Maggi et al. demonstrated the catalytic performance of Ru–NHC complex (5 mol%) in imine synthesis using DABCO ligand in the presence of molecular sieves for 24 h.[10b] The catalytic activity of Co(II)–NNN pincer complex has been explored for imine synthesis, and the reaction was carried out with *n*-octane as a solvent at high temperature[19] (Scheme 2).

Overall, a large number of metal complexes with different ligand systems have been explored as catalysts for this reaction. In particular, metal-based catalysts for the synthesis of imines with phosphine labile ligands have been well explored. However, the catalytic condition showed some drawbacks such as higher temperature, higher catalyst load and inert atmosphere. To overcome the above issues, we are interested to execute the imine synthesize protocol using metal complexes with phosphine-free ligands. Generally, metal complex containing phosphorus-free ligands has salient features like ease of synthesis and air stability, to avoid tedious separation and catalyst recovery. In the present art of research, we have described the synthesis and characterization of



SCHEME 2 Synthetic strategies of imine reaction

new binuclear Ru(II) complex of thiourea ligand and used as a catalyst for imine synthesis under the aerobic catalytic condition. A catalyst featuring two closely associated metal active sites is one of the emerging areas in homogeneous catalysis. This bimetallic catalytic system complements the traditional focus on parameters in order to optimize catalytic behaviour in a better way. Change of the steric and electronic properties of the ligands can fine-tune the performance of the bimetallic system. Such catalysts introduce new optimization parameters such as catalyst nuclearity and synergistic cooperation between the two metal active sites and the bridging ligands.[20] Hence, controlling selectivity and activity of the catalytic transformations will be offered by the suitable design of bimetallic catalysts. Exquisite levels of activities of these catalysts could be achieved by careful design of two metal active sites (Figure 2).

2 | RESULTS AND DISCUSSION

1-(5-Methylthiazole-2-yl)-3-phenylthiourea ligand (HL) was prepared from phenyl isothiocyanate with 5-methylthiazole-2-amine in the equimolar ratio in the presence of dimethylformamide (DMF) medium.[21] The synthesis cationic arene Ru(II) thiourea complex can be accomplished in good yield from complexation of ruthenium starting precursor $[(\eta^6\text{-}p\text{-cymene})RuCl_2]_2$ (1.0 mmol) with thiourea ligand in 1:2 molar respectively in benzene under the open-air condition. The complex was yellow in colour and air stable. It was easily soluble in solvents like CH_2Cl_2, $CHCl_3$, CH_3CN, dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF). The resulting complex was crystallized from the mixture of solvents dichloromethane and methanol (1:1) (Scheme 3).

In the IR spectrum, thiazole N–H and phenyl group N–H in the ligand showed bands in the regions 3,366 and 3,162 cm^{-1}, respectively. Also, free ligand displayed the thiocarbonyl ($\nu_{C=S}$) stretching frequencies at 1,254 cm^{-1}. On complexation, thiazole-attached N–H stretching vibration was not observed in the complex, indicating that the ligand underwent enolization and decrease in $\nu_{C=S}$ (1,150 cm^{-1}). The shift in these bands revealed the coordination of ligand to the metal via thiazole nitrogen and thiocarbonyl sulfur.

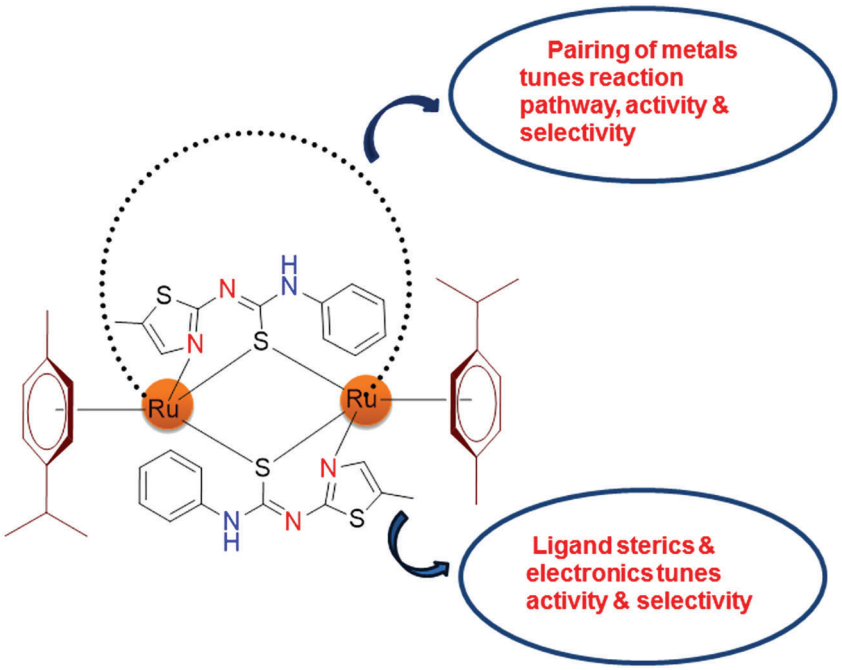
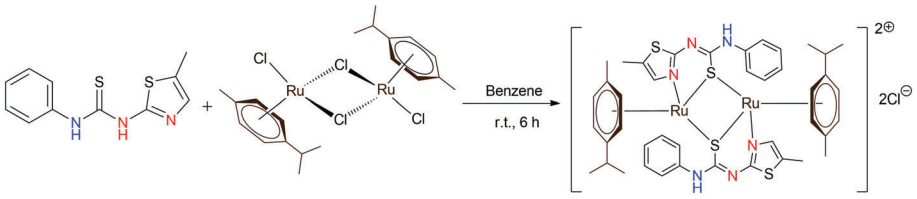


FIGURE 2 Structure–function relationship available in bimetallic catalysis



SCHEME 3 Synthetic route to [Ru(η^6-*p*-cymene)(HL)]$_2$Cl$_2$ complex

In the ^{1}H NMR spectrum, the free ligand showed signals at 12.30 and 10.23 ppm due to N–H protons. Upon complexation, the thiazole-connected –NH proton disappeared from the complex, further supporting enolization and coordination through thiocarbonyl sulfur to the Ru(II) ion. All aromatic protons of the complex appeared as multiplet in the region of 7.30–7.60 ppm. The arene protons of the complex were observed at 5.30–5.56 ppm. The methyl protons of isopropyl group in *p*-cymene moiety exhibited as singlet in the region 1.21–1.26 ppm. A septet appeared in the range of 2.80 ppm due to a methine proton of the isopropyl group. Further, signals due to the methyl protons of the *p*-cymene were observed at 2.43 ppm as singlet (Figures S1, S2).

The solid state structure of the complex [Ru(η^6-*p*-cymene)(HL)]$_2$Cl$_2$ has been studied by X-ray crystallographic technique. Crystals of suitable size were obtained from mixed solvents of dichloromethane and methanol (1:1). The Oak Ridge thermal ellipsoid plot (ORTEP) view of the complex is shown in Figure 3, and the crystallographic data and selected bond distances and bond angles are shown in the supporting information (Table S1, S2). The crystal belongs to the monoclinic space group '*C* 2/*c*' with $Z = 4$. The thiourea chelates to Ru(II) ion through the two thiolato sulfur ions and thiazole nitrogen, and the remaining position is occupied by arene moiety forming a pseudo octahedral geometry. A four-membered Ru–S–Ru–S ring system is formed owing to the bridging position of sulfur atoms between the two Ru ions. The unprecedented formation of bridging system is due to pushing of electron density by the thiazole group through the amino nitrogen atom. This enabled the sulfur atom to make the new Ru–S bond, resulting in dimer formation. The observed dimeric structure is similar to the related compound containing a [Rh–N–C–S]$_2$ sulfur-bridged dinuclear unit.[22] The Ru_2S_2 core is essentially planar, which indicated that the cymene ligands adopted *cis* arrangement in the complex, similar to the arrangement observed in [(η^6-$C_6H_3Me_3$)Ru{$SCMe_2CH$–(CO_2H)NH_2}$_2$]$_2$.[23] All of the Ru–S distances of complex are basically of equal length [range 2.3765(15)–2.4204(16) Å], indicating symmetrical sulfur atoms. It has been observed that the Ru–S–Ru bond angle [99.25 (6)°] is slightly larger than the corresponding chloride bridging Ru–Cl–Ru [98.22°] bond angle.[24] Hence, the single-crystal X-ray diffraction studies confirmed the structure proposed with the aid of other spectroscopic techniques.

With the novel dinuclear arene Ru(II) thiourea complex in hand, we wish to study the catalytic utility in the synthesis of imines from coupling of alcohols and amines at open atmospheric conditions. For that, we initiated with test reaction between the equimolar amounts of 4-methylbenzyl alcohol and aniline with complex (1 mol%) as a catalyst with various solvents and KOH as a base to optimize the reaction condition (Table 1). When toluene was used as solvent, the corresponding imine product **3a** was obtained 83% yield in 12 h (Table 1, entry 1). Switching the solvent to xylene and benzene is also effective, furnishing imines up to 80% and 72% yield, respectively (Table 1, entries 2 and 3). Moderate yields of imines were obtained when the reaction was performed in various polar solvents like dioxane, THF, acetonitrile, DMF

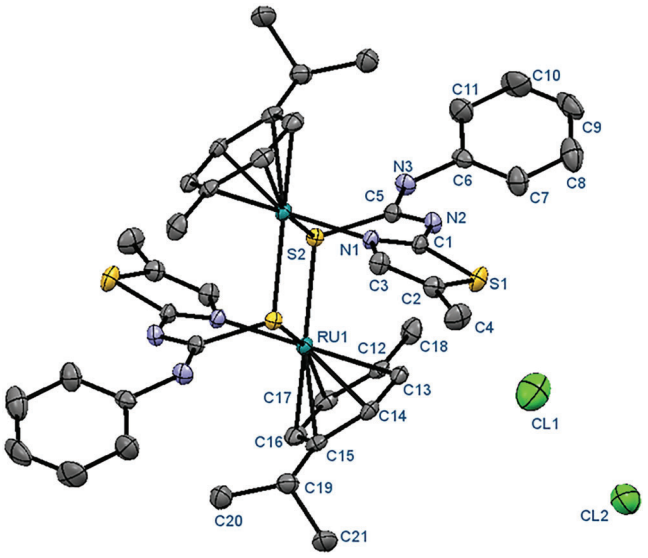
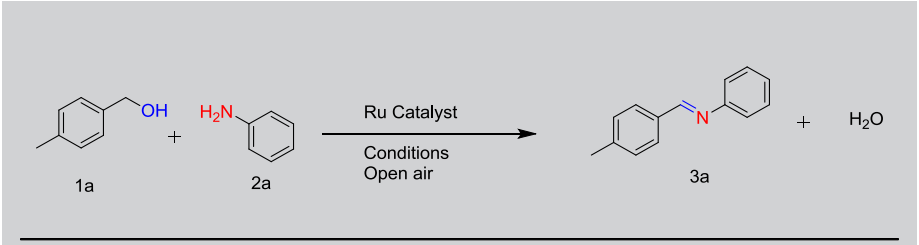


FIGURE 3 Oak Ridge thermal ellipsoid plot (ORTEP) representation of complex [Ru(η^6-*p*-cymene)(HL)]$_2$Cl$_2$ with 50% probability level. All hydrogen atoms were omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru(1)–S [2] = 2.3765 [15], Ru(2)–S [2] = 2.4204 [16], Ru(1)–N [1] = 2.120 [5], Ru(1)–C [12] = 2.261 [6], Ru(1)–C [13] = 2.189 [6]; Ru(1)–S(2)–Ru [2] = 99.25 [6], S(2)–Ru(1)–S [1] = 80.75 [6], N(1)–Ru(1)–S [2] = 86.99 [14], N(1)–Ru(1)–C [12] = 122.3 [2], N(1)–C(1)–S [1] = 112.2 [5], C(5)–S(2)–Ru [1] = 103.4 [2], C(12)–Ru(1)–S [2] = 97.35 [17]

TABLE 1 Screening of solvents, bases and temperatures[a]



Entry	Solvent	Base	Temp. (°C)	Yield(%)[b]
1	Toluene	KOH	110	83
2	Xylene	KOH	140	80
3	Benzene	KOH	80	72
4	1,4-Dioxane	KOH	100	65
5	THF	KOH	66	78
6	Acetonitrile	KOH	82	60
7	DMF	KOH	150	52
8	Methanol	KOH	65	70
9[c]	Toluene	—	r.t	NR
10[c]	Toluene	—	80	NR
11[d]	Toluene	*t*-BuOK	110	10
12	Toluene	NaOH	110	82
13	Toluene	NaOMe	110	85
14	Toluene	K_2CO_3	110	79
15	Toluene	CS_2CO_3	110	80
16	Toluene	*t*-BuOK	110	88
17	Toluene	*t*-BuOK	80	90
18	**Toluene**	***t*-BuOK**	**60**	**98**
19[e]	Toluene	*t*-BuOK	r.t	70

Abbreviations: DMF, dimethylformamide; THF, tetrahydrofuran.
The bold data in the table 1 indicates the best optimized reaction condition.
[a]Conditions: 4-methyl benzyl alcohol (1 mmol), aniline (1 mmol), catalyst, (1.0 mol%) and base (0.5 mmol) in the presence of solvent (5 ml) at 60°C for 12 h.
[b]Isolated yield.
[c]Absence of base.
[d]Absence of catalyst.
[e]Time for 24 h.

and methanol (Table 1, entries 4–8). These results indicated that nonpolar solvents outperformed polar solvents in the test reaction. No further reaction proceeded in the absence of a base or a catalyst (Table 1, entries 9–11). Furthermore, good product yields are observed in the presence of NaOH and NaOMe (Table 1, entries 12 and 13). In addition, up to 80% of imines were noted when K_2CO_3 and Cs_2CO_3 are present (Table 1, entries 14 and 15). Further, it has been observed that *t*-BuOK outperformed other bases, which afforded **3a** in 90% yield of imine (Table 1, entries 16 and 17). Notably, the cationic dinuclear ruthenium complex catalyzed effectively the coupling of alcohol and amine and yielded 98% of selective imine under the optimized condition of toluene/*t*-BuOK at 60°C (Table 1, entry 18).

Further, the effectiveness of our catalyst was examined with different catalyst loadings for the test reaction (Table 2). Upon reducing the catalyst loading from 1 mol % to 0.25 mol%, there was a substantial decrease in yields (Table 2, entries 1–4). Therefore, 1 mol% catalyst loading is the best choice for optimization.

The substrate scope of the reaction with respect to various types of alcohols and amines under the optimized catalytic conditions is displayed in Table 3. Fabulously, electron-rich functionalities of benzyl alcohols (–CH_3, –OCH_3) are efficiently reacted with aniline to yield the respective imines **3a**–**3c** in 83–95% of isolated yields

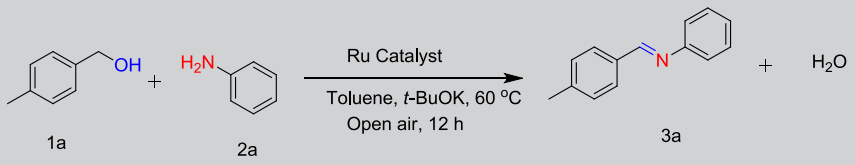


TABLE 2 The screening of the catalyst loadings[a]

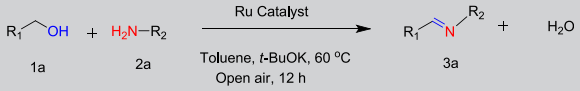
Entry	Catalyst (mol %)	Yield (%)
1	**1.0**	**97**
2	0.5	80
3	0.3	61
4	0.1	39

The bold data in the table 2 indicates the best optimized condition.
[a]Conditions: 4-methylbenzyl alcohol (1 mmol), aniline (1 mmol) and base (0.5 mmol) in the presence of solvent (5 ml) at 60°C for 12 h.

(Figures S3–S8). Further, electron-withdrawing substituents (–Cl, –F) on benzyl alcohols were tolerated well with aniline that acquired desired imines **3d** and **3e** in the yields of 88–78% (Figures S9–S12). In addition, the coupling reactions between different benzyl alcohols and 4-ethoxy and 4-methoxy anilines afforded the corresponding imines **3f** and **3g** in 80–83% of isolated yields (Figures S13–S16). More interestingly, the complex catalysed well in the coupling of sterically hindered 2-bromobenzyl alcohol with 4-methoxy aniline to afford the respective imine **3h** in 75% of yield (Figures S17, S18). However, the electron-withdrawing substituent of 4-chlorobenzyl alcohol with 4-methoxy aniline showed a better result in the formation of respective imine **3i** in 79% of yield (Figures S19, S20). The high yield of 82% for **3j** was obtained by the reaction of 4-methoxybenzyl alcohol and 4-methoxy aniline (Figures S21, S22). Coupling of benzyl alcohol-bearing electron-donating and withdrawing substituents (4-methyl and 4-chloro) with 4-bromoaniline gave respective imines **3k** and **3l** in 98% and 90% of yields (Figures S23–S26). Importantly, piperonyl-based imine moieties were found to be effective in pharmaceutically active ingredients. But the synthesis of piperonyl-derived imines is less covered in previous literature.[25] Hence, we are interested in coupling the piperonyl alcohol with various amines. More significantly, we attained the piperonyl-derived imines **3m**–**3o** up to 94% of yields (Figures S27–S32). Gratifyingly, the catalytic efficiency of the present complex proved the synthesis of bis-imine product **3p** with the appreciable yield of 75% under the optimized condition (Figures S33, S34). Deliberately, a chiral imine **3q** was achieved from the coupling of 4-methylbenzyl alcohol with (*R*)-(+)-α-methylbenzylamine gave an 84% yield (Figures S35, S36). Notably, the complex efficiently promoted the synthesis of imines from heterocyclic alcohols, and amines resulted in good yields of imine products **3r** and **3s** (Figures S37–S40). The attempt taken for coupling of alcohol and aliphatic amine to provide the expected product **3t** was successful (Figures S41, S42). Further, the catalytic condition was found to be ineffective for the coupling of aliphatic alcohols with amines.

It is crucial at this point to compare the catalytic efficiency and scope of our catalytic system with other reported ruthenium(II) catalysts. Maggi et al. demonstrated the catalytic performance of Ru–NHC complex (5 mol%) in imine synthesis using DABCO ligand in the presence of molecular sieves for 24 h.[10b] Musa et al. have reported the catalytic activity of bifunctional Ru(II) PCP pincer complexes towards synthesis of imine from alcohols and amines in *p*-xylene medium with 2 mol% catalyst loading for 24 h under argon atmosphere.[26] The binuclear Ru catalyst was documented to catalyze an imine formation reaction with 5 mol% DABCO ligand, and molecular sieves for 24 h were reported.[27] In addition, Higuchi and co-workers reported the ruthenium complex catalyzed imination reaction with Zn $(OCOCF_3)_2$ (1 mol%) and KO^{t}Bu (20 mol%) as a base in dioxane medium.[28] The arene Ru(II) complex has considerable benefits over other reported catalysts. In contrast, the salient features of titled catalysts are insensitive towards air and simple, convenient catalytic method for the synthesis of imines. Further, the bimetallic catalytic system, with a cooperative effect between the two metal centres, enhances the strong metal–metal interaction, which interact with the substrates, increasing the rate of the reaction than the monometallic system. We speculated that the

TABLE 3 Synthesis of imines from alcohols and amine[a]



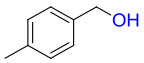
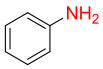
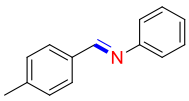
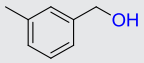
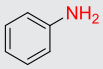
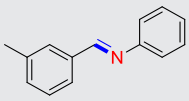
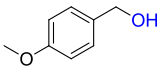
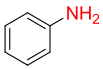
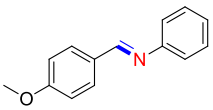
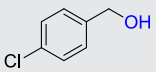
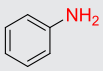
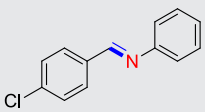
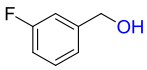
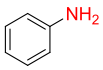
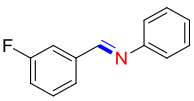
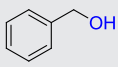
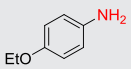
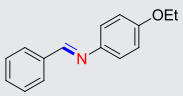
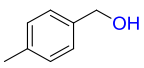
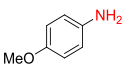
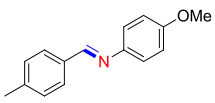
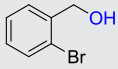
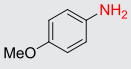
Entry	1	2	3		Yield[b] %
1				(**3a**)	95
2				(**3b**)	80
3				(**3c**)	83
4				(**3d**)	88
5				(**3e**)	78
6				(**3f**)	80
7				(**3g**)	83
8				(**3h**)	75

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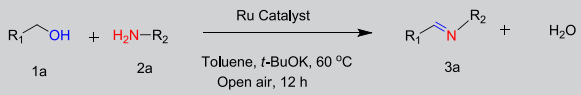
TABLE 3 (Continued)



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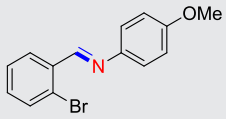
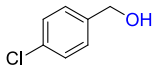
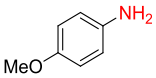
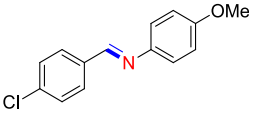
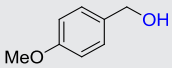
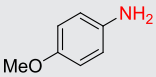
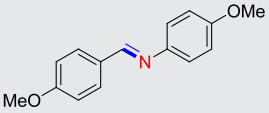
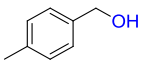
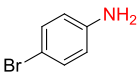
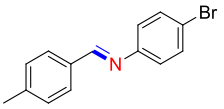
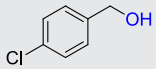
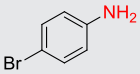
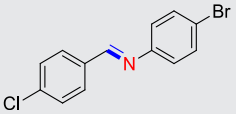
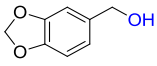
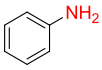
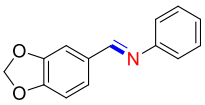
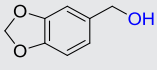
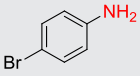
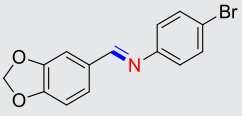
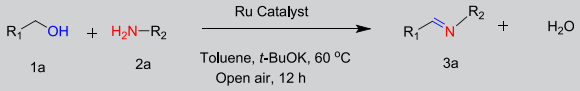
					
9				(**3i**)	79
10				(**3j**)	82
11				(**3 k**)	98
12				(**3 l**)	90
13				(**3m**)	70
14				(**3n**)	94
15				(**3o**)	82

TABLE 3 (Continued)



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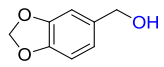
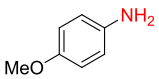
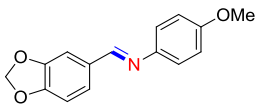
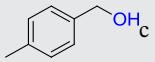
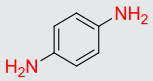
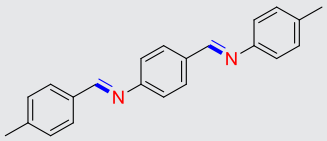
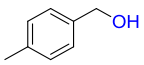
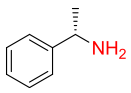
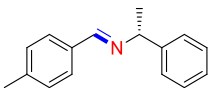
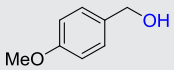
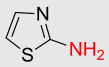
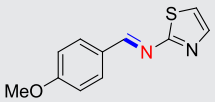
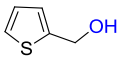
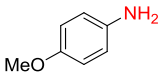
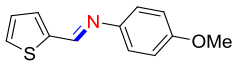
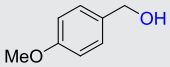
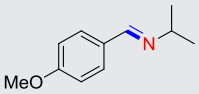
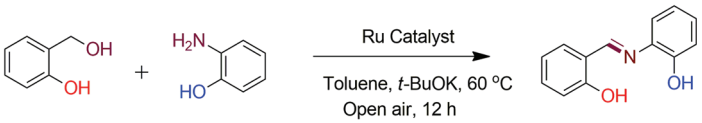
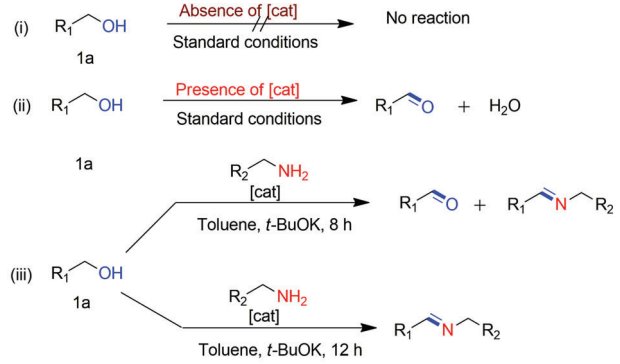
					
16[c]				(**3p**)	75
17				(**3q**)	84
18				(**3r**)	70
19				(**3s**)	87
20				(**3t**)	60

[a]Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), catalyst (1 mol%), *t*-BuOK (0.5 mmol) and toluene (5 ml) stirred for 12 h in open air.
[b]Isolated yields.
[c]Reaction for 24 h.

SCHEME 4 Preparation of *N*-(salicylidene)-2-hydroxyaniline using our protocol





[a] Reaction conditions: alcohol 1a (1 mmol), amine (1 mmol) catalyst (1 mol %), *t*-BuOK (0.5 mmol), Toluene (5 mL) stirred for 12 h in open air.

SCHEME 5 Control experiments

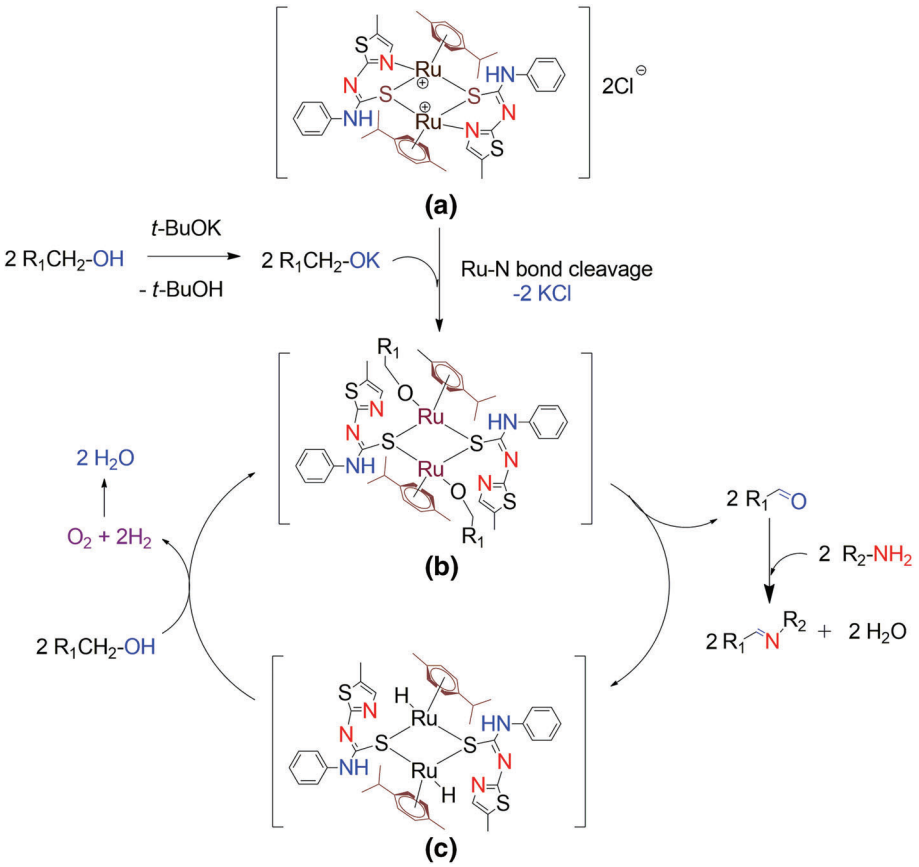
catalytic performance may be from two active metal centres of the complex working independently, or only an active metal centre under the electronic influence of the second one. Hence, the catalyst loading is 1 mol% sufficient to catalyse the reaction with good-to-excellent yields.[29]

It is worth to note that one of the antibacterial drugs, namely, *N*-(salicylidene)-2-hydroxyaniline, was synthesized from 2-hydroxybenzyl alcohol and 2-amino phenol using our present protocol (Scheme 4), and an excellent yield of 95% was obtained (Figures S43, S44).

3 | CONTROL EXPERIMENTS FOR THE MECHANISTIC INVESTIGATIONS[A]

Control experiments were performed under standard conditions in order to examine the mechanism of the imination (Scheme 5). Initially, oxidation of alcohol leads to the formation of aldehyde. Further, a mixture of products aldehyde and imine was obtained when the reaction was conducted in the presence of amine for 8 h. Complete imine product was obtained only after 12 h of the reaction. Hence, the formation of aldehyde clearly indicates that the reaction proceeds via oxidation of alcohol as an initial step (Figures S45–S50).

A plausible mechanism has been proposed based on the results from the control experiments and on the previously reported literature (Scheme 6). The reaction involves the formation of ruthenium alkoxide species from the catalyst through deprotonation of the alcohol followed by β-hydride elimination to form aldehyde. This aldehyde intermediate further reacts with amines to produce imines, and water is eliminated as a by-product. Further, the ruthenium hydride[10b,30] complex reacts with alcohol to form the next catalytic cycle with the release of two molecules of water. The detailed studies on the mechanism for imine synthesis are under investigation.



SCHEME 6 Plausible mechanism for imine formation

4 | CONCLUSIONS

Summing up, we have presented the first example of thiolato-bridged dinuclear arene Ru(II) arene complex that promoted green synthesis of highly desirable imines obtained from readily available alcohols and amines in open air as an eco-friendly oxidant. To our knowledge, this is a convenient and straightforward method for one-pot synthesis of imines from alcohols and amines. The catalyst system provides selective imination reactions of substituted alcohols with various amines with good tolerance to reducible functional groups. The complex was demonstrated as an efficient catalyst with 1 mol% loading under optimized conditions to afford up to 98% yield.

5 | EXPERIMENTAL SECTION

5.1 | General method for the synthesis of binuclear *p*-cymene ruthenium(II) complex

$[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$ (1 equiv) and 1-(5-methylthiazole-2-yl)-3-phenylthiourea(HL) (2 equiv) were dissolved in 25 ml of benzene and stirred for 6 h. The solution was reduced to 2 ml, and addition of petroleum ether (60–80°C) in excess gave a clear yellow solid.

5.1.1 | $[Ru(\eta^6\text{-}p\text{-cymene})(HL)]_2Cl_2$

Yellow solid. Yield: 92%: Anal. Calcd. For $C_{42}H_{48}Cl_2N_6Ru_2S_4$: C, 48.59; H, 4.66; N, 8.09. Found: C, 48.62; H, 4.60; N, 8.01. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 11.55 (*s*, 2H, $N\text{–}H_{(phenyl)}$), 7.58–7.60 (*m*, 4H, $ArH_{(ligand)}$), 7.43–7.47 (*m*, 4H, $ArH_{(ligand)}$), 7.36–7.38 (*m*, 4H, $ArH_{(ligand)}$), 5.43–5.57 (*m*, 2H, $CH_{(p\text{-cymene})}$), 5.30–5.38 (*m*, 6H, $CH_{(p\text{-cymene})}$), 2.80 (*sept*, 2H, CH $(CH_3)_{2\ (p\text{-cymene})}$), 2.43 (*s*, 6H, $CH_{3(p\text{-cymene})}$), 2.08 (*s*, 6H, $CH_{3\ (ligand)}$), 1.21–1.26 (*m*, 12H, CH $(CH_3)_{2(p\text{-cymene})}$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) = 175.35 (C–S), 158.22 (C═N), 140.52, 136.32, 129.19, 128.95, 127.89, 125.28 (Ar carbons of ligand), 106.66 and 100.06 (quaternary carbons of *p*-cymene), 86.29, 84.89, 84.73, 84.24 (Ar carbons of *p*-cymene), 30.78 (CH of *p*-cymene), 22.52, 22.17 ($2CH_3$, *p*-cymene), 18.54 (CH_3, *p*-cymene), 12.53 (CH_3 of ligand). Fourier transform infrared (FT-IR) (cm^{-1}): 2,925 (N–H), 1,642 (C═N), 1,594 (C═C), 1,261 (N–C═S), 1,149 and 910 (C═S). UV–vis ($CHCl_3$): λ_{max} (nm) 280, 340, 463.

5.2 | Typical procedure for imine formation reaction

The alcohol (1 mmol), an amine (1 mmol), *t*-BuOK (0.5 mmol), and a catalyst (1 mol%) were stirred at 60°C for 12 h under open-air atmosphere in 5 ml of toluene, and the reaction was monitored by thin-layer chromatography (TLC) until completion. Then, the reaction mixture was cooled and diluted with ethyl acetate (10 ml). For calculation of isolated yield, the layers were formed upon addition of water (5 ml), and organic layer was separated. The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was purified by column chromatography using EtOAc:hexane to afford imine products.

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AUTHOR CONTRIBUTIONS

Veerappan Tamilthendral: Investigation; methodology; writing-original draft. **Rengan Ramesh:** Conceptualization; supervision; validation; writing-review and editing. **Jan Grzegorz Malecki:** Software.

CONFLICT OF INTEREST

The authors declare no competing financial interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

ORCID

Rengan Ramesh https://orcid.org/0000-0001-8358-9583

REFERENCES

[1] a)W. R. Layer, *Chem. Rev.* **1963**, *63*, 489. b)R. Bloch, *Chem. Rev.* **1998**, *98*, 1407. c)S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069. d)J. P. Adams, *J. Chem. Soc. Perkin Trans.* **2000**, *1*, 125. e)A. Erkkila, I. Majander, P. M. Pihko, *Chem. Rev.* **2007**, *107*, 5416.

[2] a)J. Gawronski, N. Wascinska, J. J. Gajewy, *Chem. Rev.* **2008**, *108*, 5227. b)J. Adrio, J. C. Carretero, *Chem. Commun.* **2011**, *47*, 6784. c)S. Kobayashi, Y. Mori, J. S. Fossey, M. M. Salter, *Chem. Rev.* **2011**, *111*, 2626. d)J. H. Xie, S. F. Zhu, Q. L. Zhou, *Chem. Rev.* **2011**, *111*, 1713.

[3] a)S. Patai, *The Chemistry of the Carbon Nitrogen Double Bond (Chemistry of Functional Goups)*, New York, Wiley Interscience **1970**. b)S. F. Martin, *Pure Appl. Chem.* **2009**, *81*, 195. c) Z. Guo, R. Xing, S. Liu, Z. Zhong, X. Ji, L. Wang, *Carbohydr. Res.* **2007**, *342*, 1329.

[4] a)E. M. Hodnett, P. D. Mooney, *J. Med. Chem.* **1970**, *13*, 786. b) C. M. Silva, D. L. Silva, *J. Adv. Res.* **2011**, *2*, 1.

[5] a)R. D. Patil, S. Adimurthy, *Asian J. Org. Chem.* **2013**, *2*, 726. b)W. Qin, S. Long, S. M. Panunzio, S. Biondi, *Molecules* **2013**, *18*, 12264.
[6] a)P. T. Lansbury, J. G. Colson, *J. Am. Chem. Soc.* **1962**, *84*, 4167. b)F. Palacios, C. Alonso, D. Aparicio, G. Rubiales, *Tetrahedron* **2007**, *63*, 523.
[7] a)M. Ochiai, D. Kajishima, T. Sueda, *Heterocycles* **1997**, *46*, 71. b)K. Orito, T. Hatakeyama, M. Takeo, S. Uchiito, M. Tokuda, H. Suginome, *Tetrahedron* **1998**, *54*, 8403.
[8] a)F. Westheimer, K. J. Taguchi, *Org. Chem.* **1971**, *36*, 1570. b) R. S. Varma, R. Dahiya, S. Kumar, *Tetrahedron Lett.* **1997**, *38*, 2039. c)H. Naeimi, F. Salimi, K. Rabiei, *J. Mol. Catal. A: Chem.* **2006**, *260*, 100. d)J. T. Reeves, M. D. Visco, M. A. Marsini, N. Grinberg, C. A. Busacca, A. E. Mattson, C. H. Senanayake, *Org. Lett.* **2015**, *17*, 2442.
[9] B. Gnanaprakasam, J. Zhang, D. Milstein, *Angew. Chem., Int. Ed.* **2010**, *49*, 1468.
[10] a)R. Cano, D. J. Ramon, M. J. Yus, *Org. Chem.* **2011**, *76*, 5547. b)A. Maggi, R. Madsen, *Organometallics* **2012**, *31*, 451. c)X. N. Fan, H. D. Ou, W. Deng, Z. J. Yao, *Inorg. Chem.* **2020**, *59*, 4800. d)G. Vinoth, S. Indira, M. Bharathi, A. Durgadevi, R. Abinaya, L. G. Alves, A. M. Martin, K. S. Bharathi, *Appl. Organomet. Chem.* **2019**, *33*, e5200.
[11] a)M. A. Esteruelas, N. Honczek, M. Oliván, E. Onate, M. Valencia, *Organometallics* **2011**, *30*, 2468. b)Y. H. Li, X. L. Liu, Z. T. Yu, Z. S. Li, S. C. Yan, G. H. Chen, Z. G. Zou, *Dalton Trans.* **2016**, *45*, 12400.
[12] a)M. S. Kwon, S. Kim, S. Park, W. Bosco, R. K. Chidrala, J. Park, *J. Org. Chem.* **2009**, *74*, 2877. b)L. Jiang, L. Jin, H. Tian, X. Yuan, X. Yu, Q. Xu, *Chem. Commun.* **2011**, *47*, 10833.
[13] Y. Shiraishi, M. Ikeda, D. Tsukamoto, S. Tanaka, T. Hiraia, *Chem. Commun.* **2011**, *47*, 4811.
[14] a)S. Kegnæs, J. Mielby, U. V. Mentzel, C. H. Christensen, A. Riisager, *Green Chem.* **2010**, *12*, 1437. b)H. Sun, F. Z. Su, J. Ni, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem., Int. Ed.* **2009**, *48*, 4390.
[15] J. Soule, H. Miyamura, S. Kobayashi, *Chem. Commun.* **2013**, *49*, 355.
[16] R. R. Donthiri, R. D. Patil, S. Adimurthy, *Eur. J. Org. Chem.* **2012**, *24*, 4457.
[17] H. Tian, X. Yu, Q. Li, J. Wang, Q. Xua, *Adv. Synth. Catal.* **2012**, *354*, 2671.
[18] E. Zhang, H. Tian, S. Xu, X. Yu, Q. Xu, *Org. Lett.* **2013**, *15*, 2704.
[19] S. P. Midya, J. Pitchaimani, E. Balaraman, *Catal. Sci. Technol.* **2018**, *8*, 3469.
[20] a)A. Furstner, H. Krause, C. W. Lehmann, *Chem. Commun.* **2001**, *1*, 2372. b)J. Buijtenen, J. Meuldijk, J. A. Vekemans, L. A. Hulshof, H. Kooijman, A. L. Spek, *Organometallics* **2006**, *25*, 873. c)B. Punji, J. T. Mague, M. S. Balakrishna, *Inorg. Chem.* **2007**, *46*, 11316. d)S. Priyarega, D. S. Raja, S. Ganesh Babu, R. Karvembu, T. Hashimoto, A. Endo, K. Natarajan, *Polyhedron* **2012**, *34*, 143. e)K. C. Cheung, L. Wong, M. H. So, Z. Y. Zhou, S. C. Yan, K. Y. Wong, *Chem. Commun.* **2013**, *49*, 710. f)N. P. Mankad, *Chem. – Eur. J.* **2016**, *22*, 5822. g)D. R. Pye, N. P. Mankad, *Chem. Sci.* **2017**, *8*, 1705. h)T. S. Manikandan, R. Ramesh, D. Semeril, *Organometallics* **2019**, *38*, 319.
[21] K. A. Alfallous, M. Aburzeza, *Int. J. Sci. Res.* **2015**, *4*, 350.
[22] K. Yamanari, I. Fukuda, S. Yamamoto, Y. Kushi, A. Fuyuhiro, N. Kubota, T. Fukuo, R. J. Arakawa, *J. Chem. Soc. Dalton Trans.* **2000**, (13), 2131.
[23] G. Capper, D. L. Davies, J. Fawcett, D. R. Russell, *Acta Crystallogr.* **1995**, *51*, 578.
[24] J. Canivet, B. Therrien, G. S. Fink, *Acta Crystallogr. Sect. E* **2005**, *61*, 1090.
[25] a)R. Kholiya, S. I. Khan, A. Bahuguna, M. Tripathi, D. S. Rawat, *Eur. J. Med. Chem.* **2017**, *131*, 126. b)M. Arshad, A. R. Bhat, S. Pokharel, J. E. Kim, E. J. Lee, F. Athar, I. Choi, *Eur. J. Med. Chem.* **2014**, *71*, 229.
[26] S. Musa, S. Fronton, L. Vaccaro, D. Gelman, *Organometallics* **2013**, *32*, 3069.
[27] B. Saha, S. M. W. Rahaman, P. Daw, G. Sengupta, J. K. Bera, *Chem. – Eur. J.* **2014**, *20*, 6542.
[28] T. Higuchi, R. Tagawa, A. Iimuro, S. Akiyama, H. Nagae, K. Mashima, *Chem. – Eur. J.* **2017**, *23*, 12795.
[29] S. Huang, X. Hong, H. Z. Cui, B. Zhan, Z. M. Li, X. F. Hou, *Organometallics* **2020**, *39*, 3514.
[30] S. Saranya, R. Ramesh, J. G. Małecki, *Eur. J. Org. Chem.* **2017**, *45*, 6726.

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