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Mn-Catalyzed Ligand-Free One-Pot Synthesis of (*E*)-6,7-Dihydrodibenzo[*b*,*j*][1,7]phenanthrolines and (*E*)-1,2,3,4-Tetrahydrobenzo[*b*][1,6]naphthyridines through Dehydrogenative Friedlander Annulation/C(sp^3)−H Functionalization

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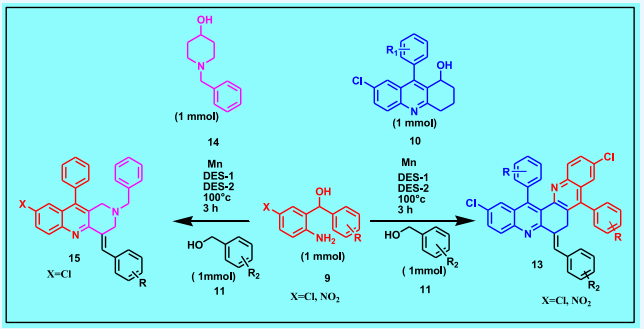
ABSTRACT: An efficient, MnO_2-catalyzed ligand-free synthesis of (*E*)-6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthrolines, **13,** and (*E*)-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines, **15,** utilizing, 2-amino-5-chloro-benzhydrol, **9,** acridinol, **10,** or 1-benzyl-4-piperidinol, **14,** and benzyl alcohols, **11,** is reported. The MnO_2-catalyzed dehydrogenative Friedlander annulation utilizing ChCl/p-TSA (DES-1) and subsequent C(sp^3)−H functionalization with TBAB/p-TSA (DES-2) was effected at 100 °C. The optimized reaction conditions gave excellent product yields, and the products were evaluated for their by UV absorption and fluorescence emission studies.



INTRODUCTION

Quinoline is a N-heterocyclic compound with a variety of applications such as agrochemicals, dye chemistry, and medicines.[1] Likewise, the phenanthrolines and naphthyridines are significant nitrogen-containing heterocyclic compounds.[2] As shown in Figure 1, phenanthrolines possess a variety of biological significance, including antibacterial,[3,4] antiparasitic,[4,5] anticancer (A_1, A_2, and A_3),[6−8] antitumor (A_4),[9] and antiviral (A_5)[10] effects. Likewise, naphthyridines have demonstrated anti-inflammatory,[11] antitumor,[12,13] anti-HSV,[14] marine alkaloids (A_6 and A_7),[15] and anti-HIV (A_8)[16] activities.

However, very few synthetic routes (Scheme 1) were reported for 6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthrolines and 1,6 naphthyridine. Rajawinslin and co-workers have reported **3,** involving iron/acetic acid medium via aldol addition, followed by intramolecular reductive cyclization (eq 1).[17] Kumaraswamy and co-workers have reported dihydrodibenzo phenanthrolines, **3,** via Friedlander annulation through self-catalyzed reaction (eq 2).[18] Likewise, Kulikova, et al. have synthesized **6,** via cyclization of anthranilic acid (eq 3).[19] Alvarez-Pérezand co-workers have reported **8,** under reflux conditions (eq 4).[20]

There are many methods for the synthesis of quinoline, like Friedlander,[21] Dobner-von miller,[22] Skraup,[23] and Conrad-Limpach.[24] Among them, the Friedlander annulation is a condensation reaction between ortho amino arylaldehydes/ketones with carbonyl compounds.[25−28] The dehydrogenative Friedlander annulation was utilized for the Ru-,[29] Pd-,[30] Co-,[31] and Rh-catalyzed[32] quinolones synthesis from alcohols or ketones. In addition, alkenylation C(sp^3)−H functionalization (C−C bonds formation) was effected utilizing alcohols and transition metal catalysts.[33] Cui et al. have reported alkenylation of C(sp^3)−H functionalization of N-heterocycles involving acrylic acid and alcohols through copper decarboxylative coupling.[34] Das and co-workers have reported Fe- and Ni-catalyzed dehydrogenative C−H functionalization of methyl heteroarenes utilizing alcohols.[35,36] The aforementioned literature has some limitations such as harsh reaction conditions, expensive catalysts, and hazardous solvents. To overcome these drawbacks, researchers have searched for environmentally friendly strategies and solvents. For example, in the deep eutectic solvent system (DES), a combination of hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) plays an important role in organic synthesis[37] as an environmentally friendly solvent. The HBA includes quaternary ammonium salts like TBAB, ChCl, TBAI, etc., whereas HBD includes alcohols, amide, and acids. The resulting melting point should be lower than those two components and DES is also an alternative to the ionic liquid.[38−42] DES has several advantages, including nontoxicity, biodegradability, low cost, easy synthesis, and good thermal stability; it acts as a catalyst as well as a solvent.[43,44]

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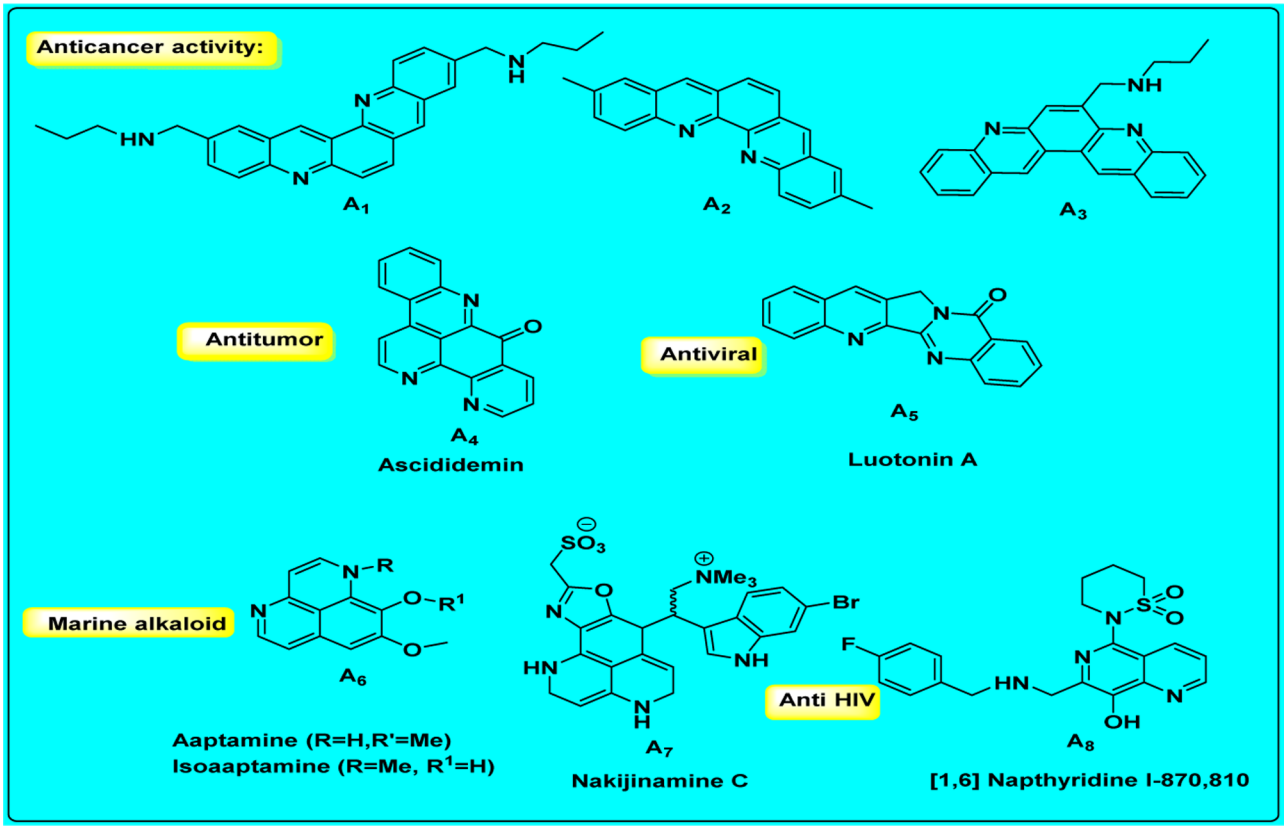
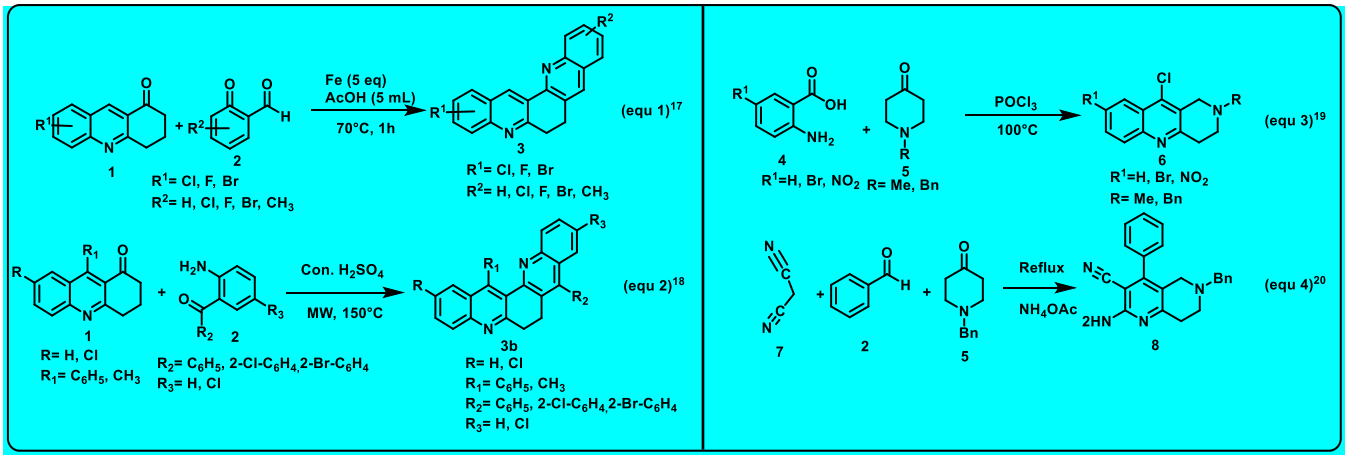


Figure 1. Biologically active 6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthrolines and 1,6 naphthyridines.

Scheme 1. Literature Reports



Our research team has recently focused on deep eutectic solvents, for example, Ir-,[45] Cu-,[46] and Ru-catalyzed[47] synthesis of quinolones, dehydrogenative Friedlander annulation, and C(sp^3)−H functionalizations. In our continued research, Mn-catalyzed dehydrogenative Friedlander annulation/alkenylation or C(sp^3)−H functionalization is reported here in this article.

The 2-amino-5-choloro-benzhydrols, **9**, acridinols **10**, or 1-benzyl-4-piperidinols, **14**, and benzyl alcohols, **11**, were dehydrogenated initially to the respective carbonyl derivatives with ChCl/p-PTSA (1:1) (as DES-1) and then to the Friedlander annulation products, **13** and **15**, while TBAB/p-TSA (1:1) (as DES-2) for the alkenylation [C(sp^3)−H functionalization] of the above products, as depicted in Scheme 2.

RESULTS AND DISCUSSIONS

Synthesis of 2,10-dichloro-8,14-diphenyl-6,7-dihyrodibenzo-[*b*,*j*][1,7]phenanthroline (**13f**) was carried out by paths I and II. By path I, initially, the reaction was performed in the presence of 1,4 dioxane or acetonitrile, utilizing 1 mmol of **9a**, and 1 mmol of **10a**, MnO_2 (10 mol %), and KO^{t}Bu (1.5 equiv) at 100 °C for 90 min to form an intermediate 2,10-dichloro-8,14-diphenyl-6,7-dihydrodibenzo [*b*,*j*][1,7]phenanthroline, **16**, at a 10% yield. Then, with the sequential addition of benzyl alcohol, **11a**, at the same temperature and condition, there is no desired product formation (see entry 1, Table 1). When changed to solvent toluene, the same condition provided 70% intermediate, **16** (see entry 2, Table 1). Further

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Scheme 2. Synthesis of (*E*)-2,10-Dichloro-8,14-diphenyl-6,7-dihyrodibenzo[*b*,*j*][1,7]Phenanthrolines, 13 and (*E*)-1,2,3,4-Tetrahydrobenzo[*b*][1,6]naphthyridines, 15 through Dehydrogenative Friedlander Annulation/sp^3 C−H Functionalization Using DES

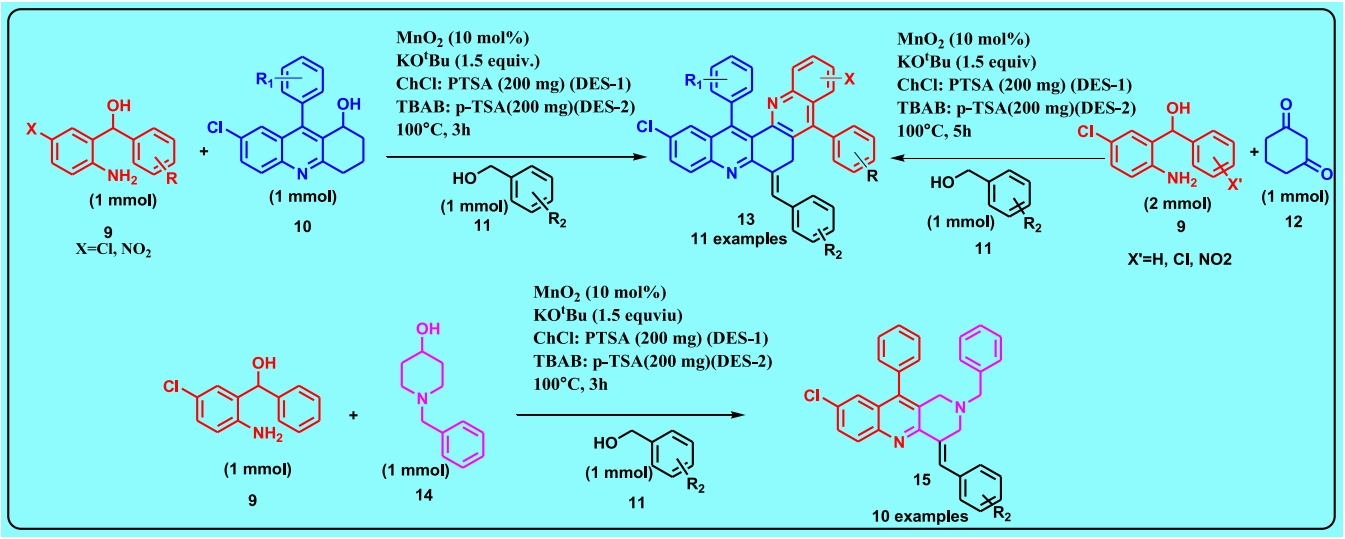
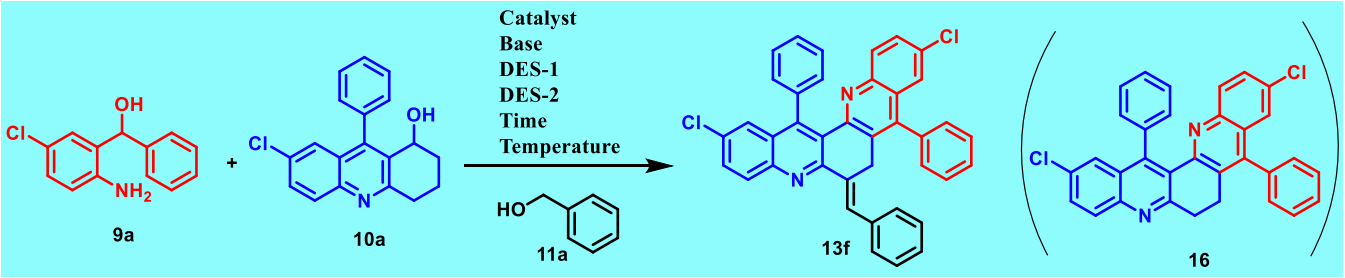


Table 1. Optimization of the Reaction Condition[a]



entry	catalyst (10 mol %)	base (1.5 equiv)	DES-1 (W/W)	solvent/additive/DES-2 (200 mg W/W)	temp. °C	time h	yield (%) **16**	yield (%) **13f**
1	MnO_2	KO^{t}Bu		1,4 dioxane or acetonitrile	100	4	10	
2	MnO_2	KO^{t}Bu		toluene	100	4	70	
3	MnO_2	KO^{t}Bu		toluene with tartaric acid/oxalic acid/ malonic acid/succinic acid/p-TSA	100	4	5[b], 10[c], 20[d], 30, 70[f]	
4	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB with tartaric acid/oxalic acid/malonic acid/succinic acid	100	4		40[b], 40[c], 10[d], 5[e]
5	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	2−4		50[f], 75[f], 70[f]
6	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	90	4		50
7	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	110	4		50
8	$CuSO_4$/$ZnSO_4$/$NiSO_4$/ $MnCl_2$/$FeSO_4$	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		10[g], 10[h], 5[i], 20[j], 5[k]
9	MnO_2	NaOH, Na_2CO_3, KOH, K_2CO_3, DBU	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		10[l], 20[m], 20[n], 40[o], 5[p]
10	MnO_2		ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		
11		KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		

[a]Reaction conditions for compound (**13f**): **9a** (1 mmol) and **10a** (1 mmol) were added to the reaction medium (100 mg) in DES 1 (ChCl/p-TSA (1:1) (100 mg/100 mg)) in the presence of a catalyst (10 mol %) and base (1.5 equiv) at 100 °C for completion of dehydrogenation, and then TBAB/p-TSA (1:1) (100 mg/100 mg) DES 2 was heated at 100 °C for reaction completion to provide intermediate, **16**. Then, **11a** (1 mmol) was added into the reaction medium, and heating was continued for 3h at 100 °C to provide the product **13f**. [b]Tartaric acid. [c]Oxalic acid. [d]Malonic acid. [e]Succinic acid. [f]p-TSA. [g]$CuSO_4$. [h]$ZnSO_4$. [i]$NiSO_4$. [j]$MnCl_2$. [k]$FeSO_4$. [l]NaOH. [m]Na_2CO_3. [n]KOH. [o]K_2CO_3. [p]DBU.

investigation utilizing toluene in the presence of additives tartaric acid/oxalic acid/malonic acid/succinic acid/p-TSA gave 5−75% of the desired intermediate, **16;** however, there was no desired product **13f** formation (Table 1, entry 3). Based on these results, we tried to optimize the deep eutectic solvent ChCl/p-TSA (DES-1) (1:1) (100 mg/100 mg) for the

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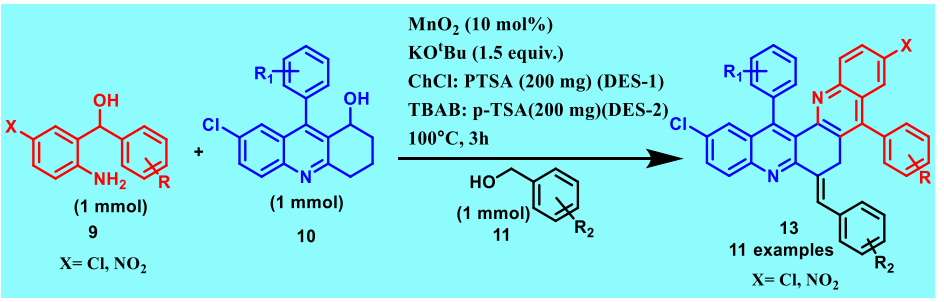
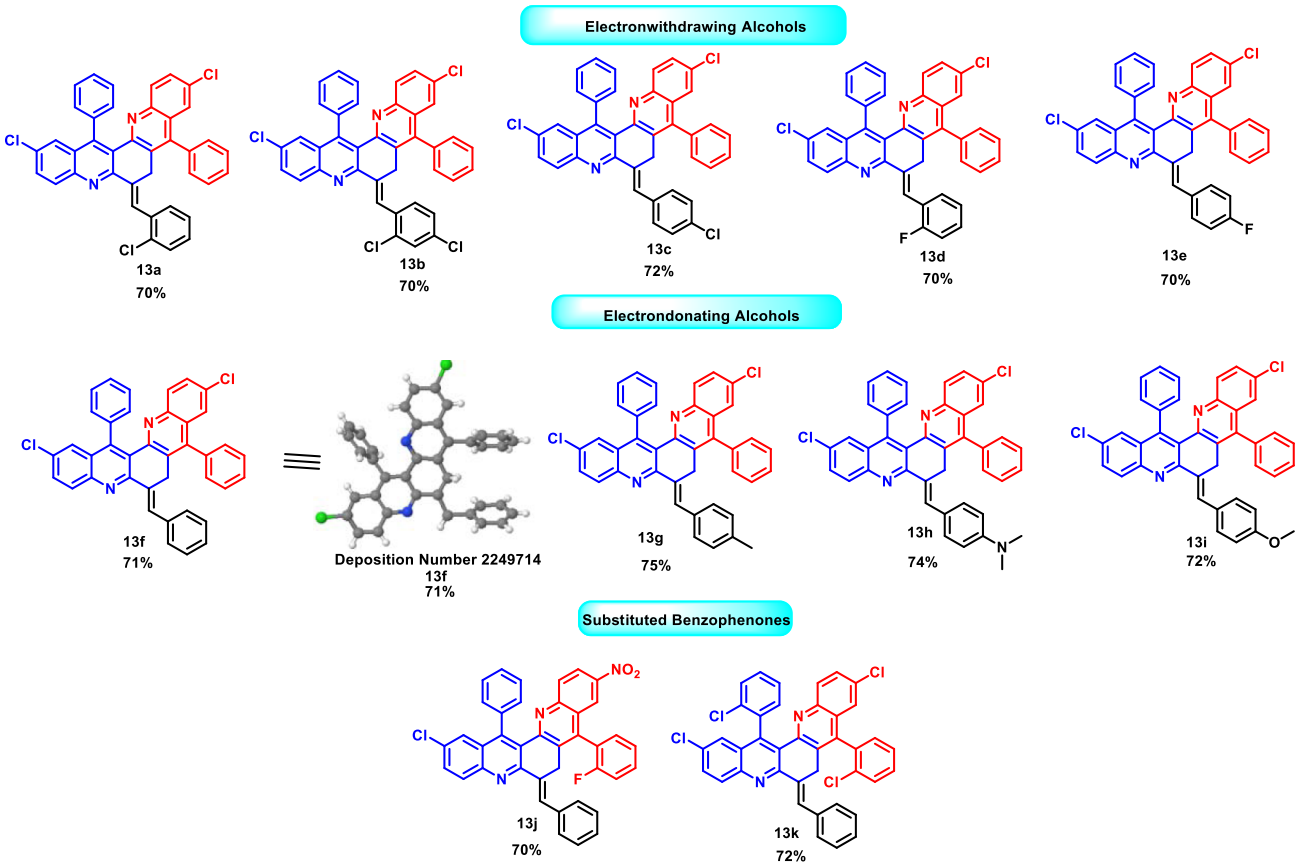
Table 2. Synthesis of 13[a]





[a]Standard reaction conditions for product, 13: 9 (1 mmol) and **10** (1 mmol) ChCl/p-TSA (1:1) (100 mg/100 mg), MnO_2 (10 mol %), and KO^{t}Bu (1.5 equiv) were heated at 100 °C, and then TBAB/p-TSA (1:1) (100 mg/100 mg) was added and heating was continued. Then, **11** (1 mmol) was added into the reaction medium, and heating was continued at 100 °C for 3h to provide the targeted product, **13**.

dehydrogenation process and TBAB-based DES-2 (1:1) (100 mg/100 mg) for the desired product to provide **16** and **13f** formation. For instance, with ChCl/p-TSA (DES-1) (100 mg/100 mg), MnO_2 (10 mol %), KO^{t}Bu (1.5 equiv), and TBAB with tartaric acid/oxalic acid/malonic acid/succinic acid (1:1) (100 mg/100 mg) at 100 °C, 5−40% of the desired product yield was observed (see Table 1, entry 4). To our surprise, an increased yield of 50−75% of the desired product **13f** was observed with TBAB/p-TSA (Table 1, Entry 5). With increasing and decreasing the temperature at 90 and 110 °C, the yield was drastically decreased to 50% (Table 1, entries 6 and 7). When the reactions proceeded with different catalysts ($CuSO_4$/$NiSO_4$/$ZnSO_4$/$MnCl_2$), 5−20% of the product (**13f**) yield was observed (Table 1, entry 8). Further, with different bases (NaOH, K_2CO_3, KOH, Na_2CO_3, and DBU), only 10−40% of the product **13f** was formed (Table 1, entry 9). The reaction is futile in the absence of a base or the catalyst (Table 1, entries 10, 11). Path II is described in the Supporting Information (see Supporting Information page no. S11−S13).

Under the optimal conditions (Table 1, entry 5), the substrate scope for the construction of (*E*)-2,10-dichloro-8,14-diphenyl-6,7-dihyrodibenzo[*b*,*j*][1,7]phenanthrolines **13** was explored with different benzyl alcohols, **11** (Table 2). The electron-withdrawing group (EWG) containing aromatic alcohols yielded 70−72% of the desired products **13a, 13d, 13b, 13c, and 13e** (Table 2). Likewise, electron-donating groups (EDG) [H, −CH_3, N, N−$(CH_3)_2$, and OMe] containing alcohols provide a good yield (71−75%) of the desired products **3f, 13g, 13h, and 13i**. However, the reaction proceeds to fail when the methoxy group is at the meta-position. The substrate scope utilizing different benzhydrol-containing fluoro, nitro, and dichloro substituents gave the

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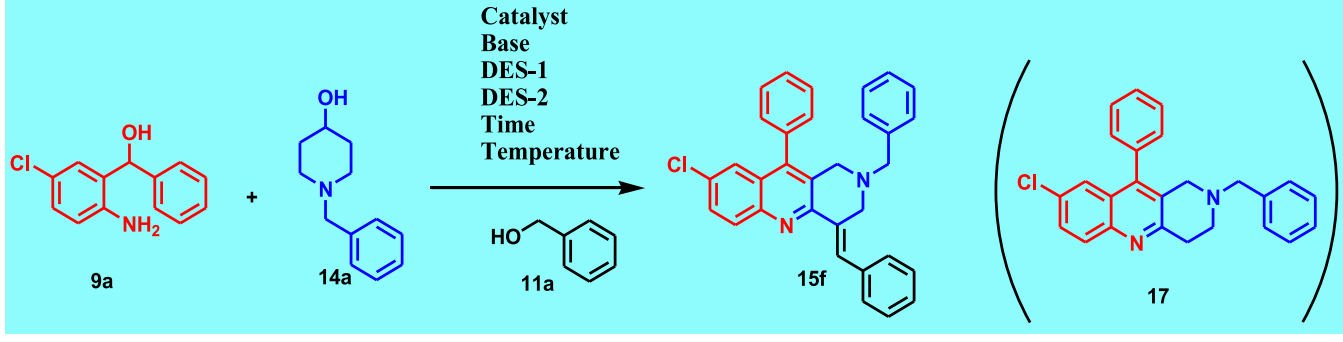
Table 3. Optimization of the Reaction Condition[a]



entry	catalyst (10 mol %)	base (1.5 equiv)	DES-1 (W/W)	solvent/additive (mol %) DES-2 (200 mg W/W)	temp. °C	time h	yield (%) **17**	yield (%) **15f**
1	MnO_2	KO^{t}Bu		1,4 dioxane, ACN	100	4	20	
2	MnO_2	KO^{t}Bu		toluene	100	4	60	
3	MnO_2	KO^{t}Bu		toluene with tartaric acid/oxalic acid/malonic acid/succinic acid/p-TSA	100	4	10[b], 10[c], 20[d], 30[e], 70[f]	
4	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB: tartaric acid/oxalic acid/malonic acid/succinic acid (1:1)	100	4		60[b], 60[c], 20[d], 10[e]
5	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	2−4		70[f], 85[f], 80[f]
6	MnO_2	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	90/110	4		60
7	$CuSO_4$/$ZnSO_4$/$NiSO_4$/$MnCl_2$/$FeSO_4$	KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		20[g], 20[h], 10[i], 30[j], 10[k]
8	MnO_2	NaOH, Na_2CO_3, KOH, K_2CO_3, DBU	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		20[l], 10[m], 10[n], 40[o], 10[p]
9	MnO_2		ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		
10		KO^{t}Bu	ChCl/p-TSA (1:1)	TBAB/p-TSA (1:1)	100	4		

[a]Standard reaction condition for product (**15f**): **9a** (1 mmol) and **14a** (1 mmol) were added to the reaction medium (100 mg) in DES-1 (1:1) (100 mg/100 mg) in the presence of MnO_2 (10 mol %), KO^{t}Bu (1.5 equiv), and DES-2 (1:1) (100 mg/100 mg) and heated at 100 °C for 1.5 h to provide intermediate (**17**). Then, **11a** (1 mmol) was added into reaction medium, and heating was continued for 3 h at 100 °C to provide the product (15f). [b]Tartaric acid. [c]Oxalic acid. [d]Malonic acid. [e]Succinic acid. [f]p-TSA. [g]$CuSO_4$. [h]$ZnSO_4$. [i]$NiSO_4$. [j]$MnCl_2$. [k]$FeSO_4$. [l]NaoH. [m]Na_2CO_3. [n]KOH. [o]K_2CO_3. [p]DBU.

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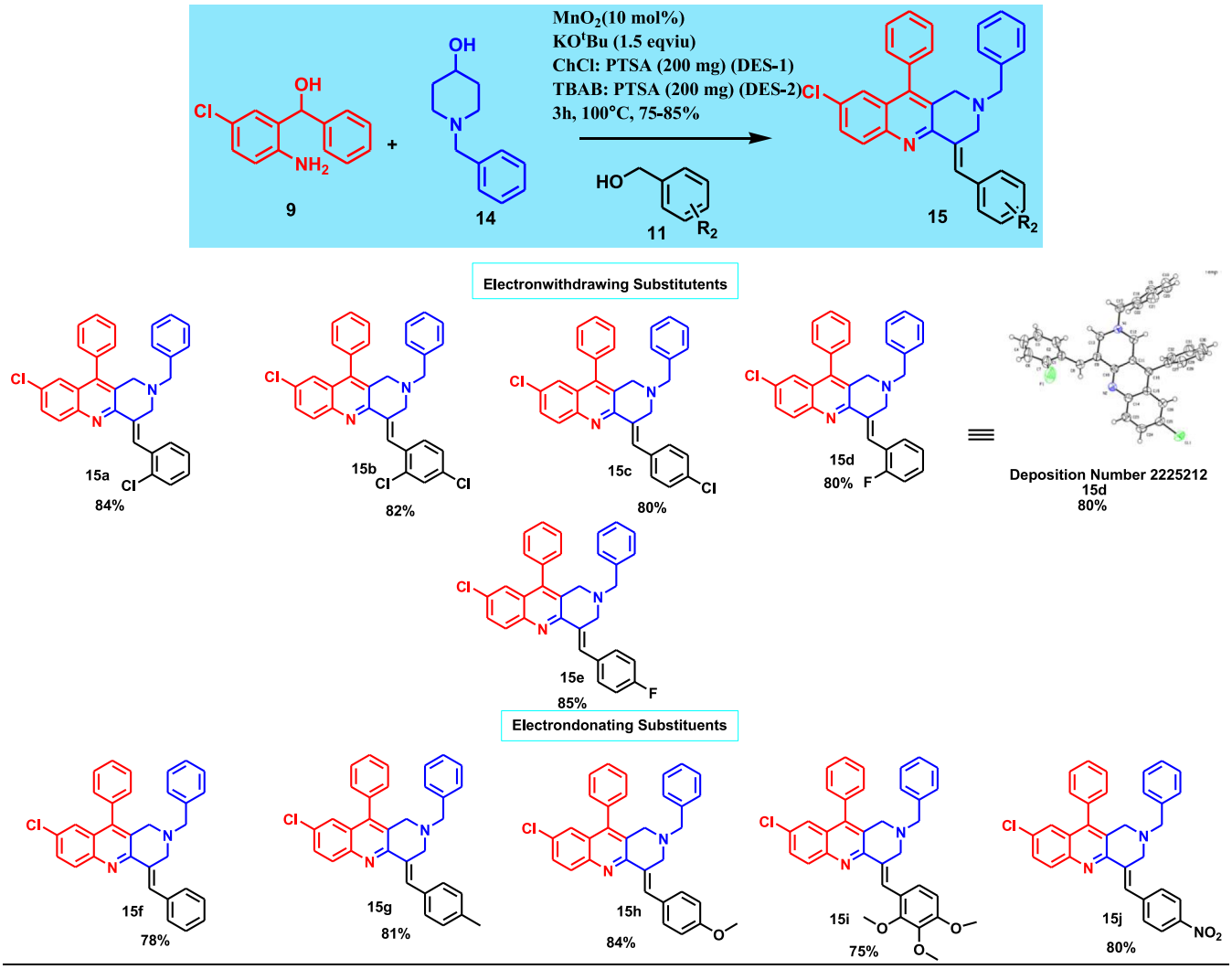
Table 4. Synthesis of (*E*)-1,2,3,4-Tetrahydrobenzo[*b*][1,6]naphthyridines, 15[a]



[a]Standard reaction conditions for product (**15**): **9** (1 mmol) and **14** (1 mmol) were added to the reaction medium ChCl/p-TSA (1:1) (100 mg/100 mg), MnO_2 (10 mol %), KO^{t}Bu (1.5 equiv), and TBAB/p-TSA (1:1) (100 mg/100 mg) and heated at 100 °C. Then, **11** (1 mmol) was added into reaction medium, heating was continued at 100 °C for 3h to provide the product **15**.

desired products **13j and 13k** in 70% yield. The crystal structure of 13f was analyzed, and the desired product formation was confirmed; data are given in the Supporting Information (see Supporting Information page no. S71−S85).

Likewise, an optimization condition was established for the synthesis of (*E*)-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridines, **15f** (Table 3). The 2-amino-5-chloro-benzhydrol, **9**, 1-benzyl-4-piperidinol, **14,** along with (ChCl/p-TSA) (DES-1) (1:1) (100 mg/100 mg), MnO_2 (10 mol %), and KO^{t}Bu (1.5 equiv) were heated at 100 °C for 45 min, and then TBAB/p-TSA (DES-2) (1:1) (100 mg/100 mg) was added and heated at 100 °C for 1.5 h to provide an intermediate 2-benzyl-8-chloro-10-phenyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridine, **17**. Further, with the sequential addition of benzyl alcohol, **11,** heating was continued at 100 °C for 3 h to provide the desired product **15f** with a good yield (85%).

The scope of the reaction was explored with the optimized conditions for the synthesis of (*E*)-1,2,3,4-tetrahydrobenzo-[*b*][1,6]naphthyridines, **15** (Table 4). The electron-withdrawing groups (EWG) containing aromatic alcohols (Cl, F) yielded 82 and 84%, respectively, of the desired product (Table 4, **15a and 15d**). It had no effect on the product yield (82, 80, and 86%) with the EDG at the para position, such as Cl and F (Table 4, 15b, 15c, and 15e). Likewise, electron-donating groups such as H, $-CH_3$, N-$(CH_3)_2$, OMe, and NO_2 provided products (15f, 15g, 15h, 15i, and 15j) in good yield (78, 81, 84, 84, 75, and 80%, respectively).

Control experiments were carried out to better understand the reaction pathways and the significance of the DES (Figure 2). The ^{1}H NMR spectrum (I) of the reaction mixture of 2-amino-5-chloro-benzhydrol, **9,** and acridinol, **10,** revealed OH protons and benzyl CH protons (a and b), which disappeared when heated at 100 °C in the presence of MnO_2 (10 mol %), KO^{t}Bu (1.5 equiv), and ChCl/p-TSA (DES-1) (100 mg/100 mg) due to the formation of dehydrogenation products, 2-amino-5-chloro benzophenone **9′**, and acridione, **10′**, as seen in the spectrum after 45 min (II). The reaction was continued at the same temperature after adding TBAB/p-TSA (DES-2) (100 mg/100 mg) into the reaction mixture for the Friedlander annulation, as revealed by the disappearance of the CH_2 (C) proton of acridone to provide an intermediate (III) at 1.30 h. Further, the sequential addition of

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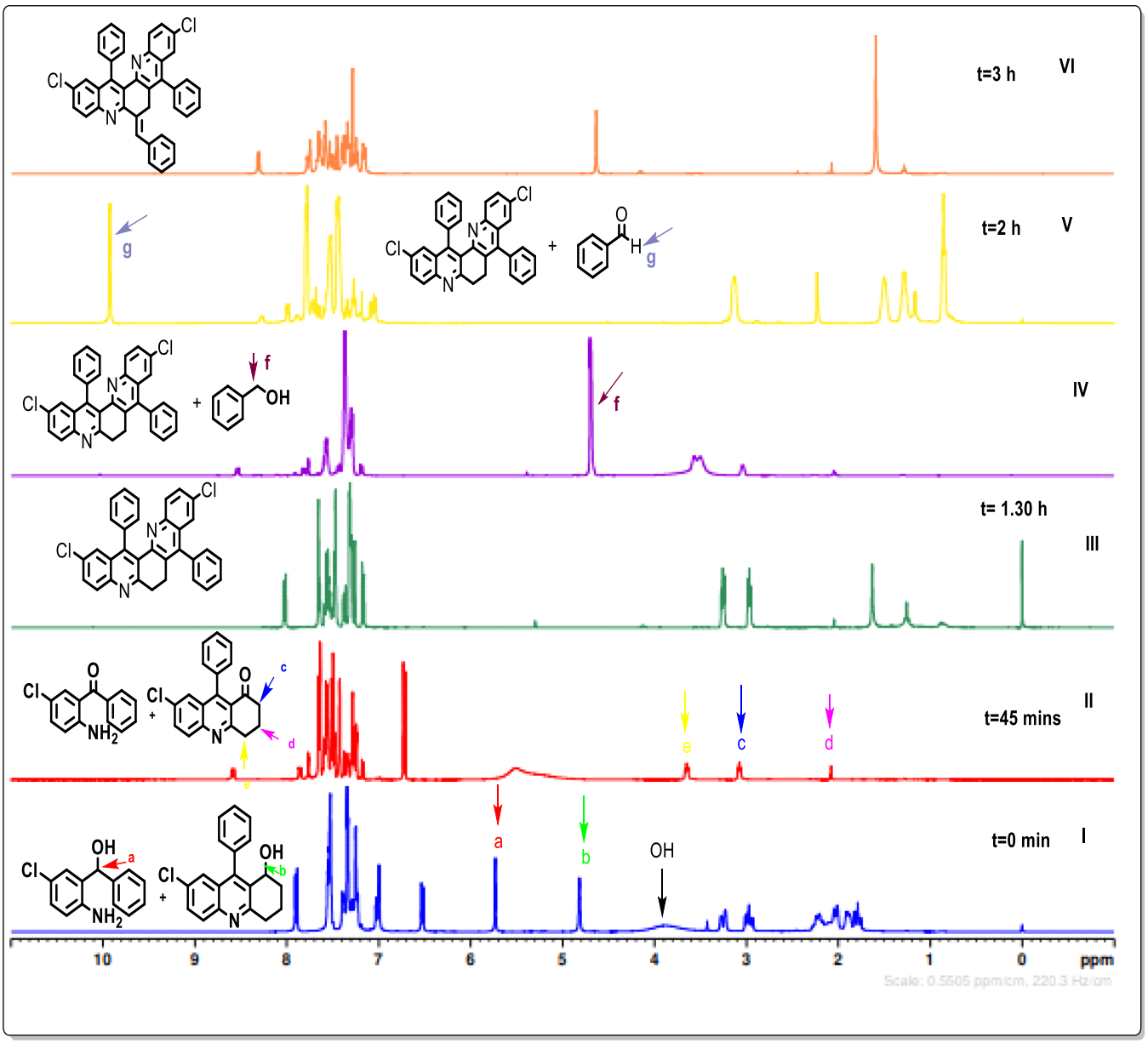

Figure 2. Control experiment for the path-1 synthesis of (*E*)-2,10-dichloro-8,14-diphenyl-6,7-dihyrodibenzo[*b*,*j*][1,7]phenanthroline, **13**.

benzylalcohol, **11**, to the reaction mixture indicated benzylic CH_2 (f) protons in the spectrum (IV), and heating was continued. Then, the spectrum (V) revealed the disappearance of aliphatic CH_2 (f) due to the dehydrogenative benzaldehyde formation. The continued heating at 100 °C for 3 h provided the desired product **13**, as seen in the spectrum (VI). Similar control experiments were done for the synthesis of (*E*)-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine **15** (see Supporting Information page no. S14, S15).

Based on the previous reports[48−50] and control experiment results, a plausible mechanism (Figure 3) is proposed for the synthesis of **13**. Initially, **9** (1 mmol), and **10** (1 mmol) were used. The CH−OH group gets activated by the ChCl/p-TSA (100 mg/100 mg) based (DES-1) and further activated by MnO_2 and the base KO^{t}Bu to provide the corresponding dehydrogenated (with the liberation of hydrogen) intermediates 2-amino-5-chloro-benzophenone, **9′**, and **10′**. Further, on heating with TBAB/p-TSA (100 mg/100 mg)-based DES-2, an acidic medium, which activates the oxygen atom of **9′**, and **10′**, through H bonds, and on dehydration, provided an imine product, **18**. Then, enamine condensation provided **19**, which on sequential cyclization and annulation offered intermediate **16**. Then, sequential addition of benzyl alcohol, **11** (1 mmol), and continued heating provided a dehydrogenated product benzaldehyde, **11′**. The TBAB/p-TSA DES-2 then activated the benzaldehyde, **11′**, and enamine intermediate, **21**, to undergo dehydration and to provide the desired product, **13**. A similar reaction mechanism for the synthesis of compound **15** is given in Supporting Information page no. S16.

UV and Fluorescent Absorption Studies. The synthesized compounds **13a−l** and **15a−k** exhibited high and low levels of energy absorption peak due to the ($\pi-\pi^*$) and ($n-\pi^*$) electronic transitions and the light-induced intramolecular charge transfer behavior due to their expanded delocalized electron system. The charge transfer occurred due to the electron-donating and -withdrawing substituents in

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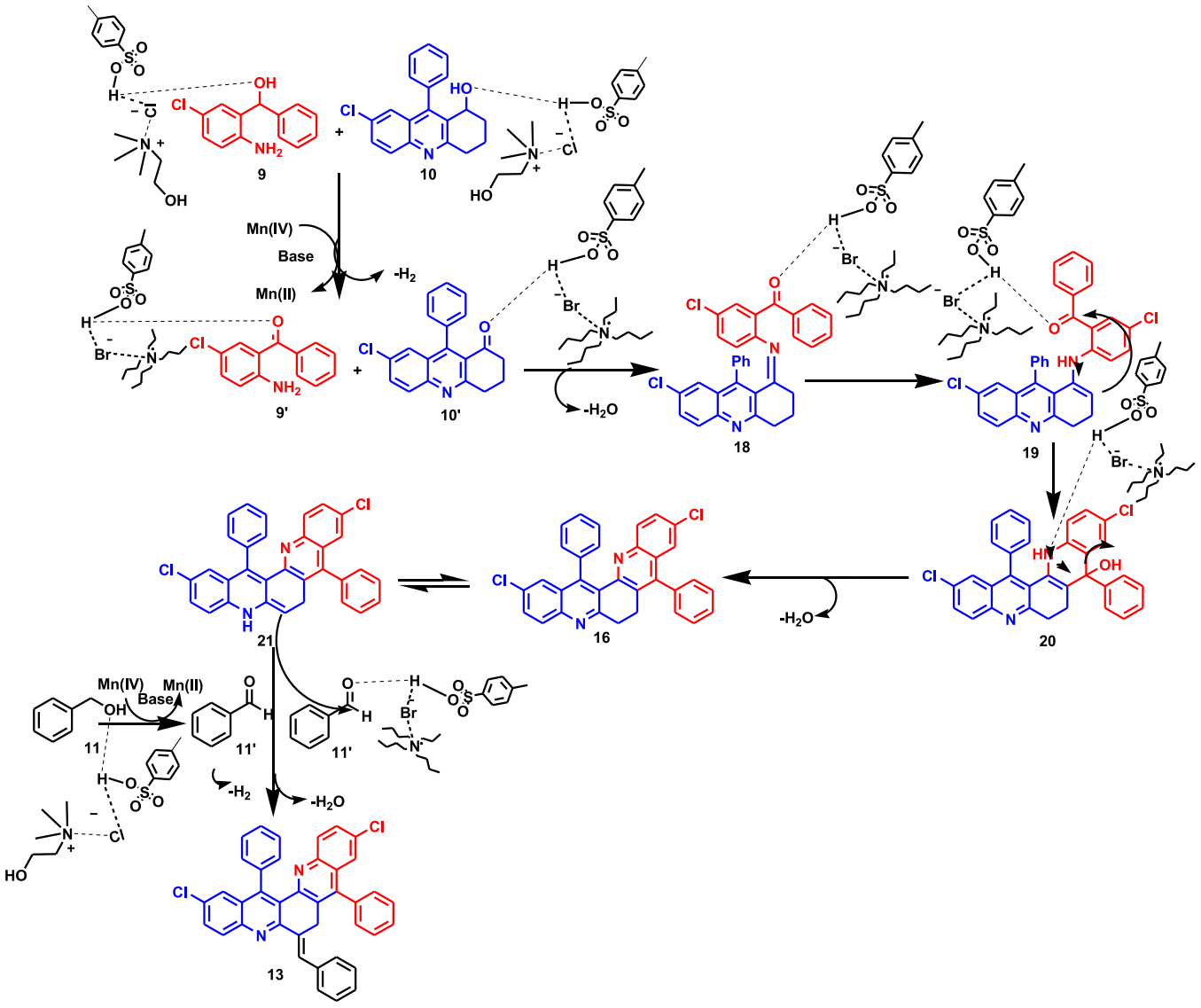

Figure 3. Plausible reaction mechanism for the formation of compound 13.

various positions. The electronic properties of compounds **13a−l** and **15a−k** were investigated utilizing UV−visible (A, B and E, F) and fluorescence spectroscopy (C, D and G, H) (Figure 4) in a dichloromethane solvent. The absorption, emission wavelengths, and Stokes shift values are tabled in the Supporting Information (Supporting Information, page no. S17). The absorption wavelength of **13a−l** ranged from 277 to 337 nm, while that of **15a−15l** ranged from 354 to 373 nm. Compounds (**13a−f**, **13h**, and **13j−l**), exhibited lower energy (n−π^*) absorption due to EWG/EDG on the phenyl ring, while **13g** and **13i** exhibited higher energy absorption ($\pi-\pi^*$) due to the methoxy group on the phenyl ring. Similarly, all compounds **15a−k** exhibited lower energy absorption (n−π^*). The emission wavelengths of compounds **13a−l** and **15a−k** ranged from 433 to 459 nm, with a stoke shift range of 99−165 nm, whereas the emission wavelengths of compounds **15a−k** ranged from 468−551 nm, with a stoke shift ranges of 86−178 nm.

The solvatochromism using different solvents of synthesized compounds is investigated by absorption and emission spectra. The absorption solvatochromism (323−360 nm) and emission solvatochromism (353−459 nm) of compounds **13a, 13c, 13d, and 13e and 15a, 15c, 15d, and 15e** were measured in different solvents of increased polarity from MeOH to DMF and are explained in the Supporting Information (see Supporting Information, page no. S17 and S18). Compared with absorption, the solvent effect was greater in emission. Furthermore, quantum yield (Φ) was calculated for compounds **13a−l** and **15a−k** and tabulated in the Supporting Information (Supporting Information, page no. S18−S20).

The synthetic utility was further explored with a heterocyclic alcohol, **18**. A mixture of **9** (1 mmol), **10** (1 mmol), and (1,3-diphenyl-1*H*-pyrazol-4-yl)methanol (**18**) (1 mmol) in the presence of MnO_2, KO^{t}Bu, DES-1, and DES-2 was heated at 100 °C for 3 h to get the desired product (*E*)-2,10-dichloro-6-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-8,14-diphenyl-6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthroline (**13l**) (Scheme 3, equiv 3.1). The same reaction condition was followed for compound **15k**. Instead of **10**, 1-benzyl-4-piperdinol (**14**) (1 mmol) was added into the reaction mixture to get the desired product (*E*)-2-benzyl-8-chloro-4-((1,3-diphenyl-1*H*-pyrazol-4-yl) methylene)-10-phenyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]-naphthyridine, **15k** (Scheme 3 equiv 3.2).

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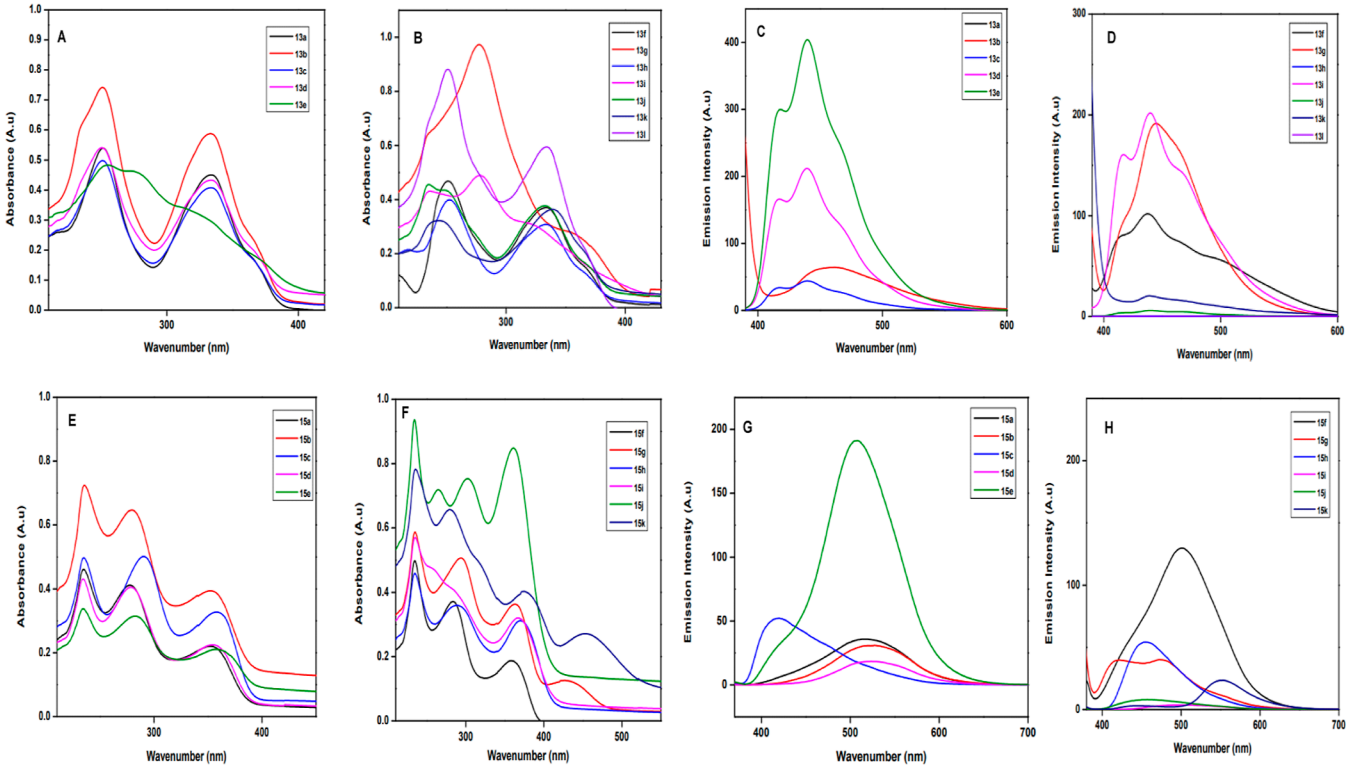

Figure 4. Absorption (A,B and E,F) and emission (C,D and G,H) spectrum for electron-withdrawing and -donating group containing alcohols of (*E*)-2,10-dichloro-8,14-diphenyl-6,7-dihyrodibenzo[*b,j*][1,7]phenanthroline (**13a-13l**) and (*E*)-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine (**15a-15k**) in DCM solvent.

The gram scale utility was explored for the synthesized compounds (**13f** and **15f**) with a good yield (71 and 78%) (Scheme 3, equiv 3.3 and 3.4).

CONCLUSIONS

A dehydrogenative Friedlander annulation/C(sp^3)−H functionalization is utilized for the synthesis of (*E*)-6,7-dihydrodibenzo[*b,j*][1,7] phenanthrolines, **13,** and (*E*)-1,2,3,4-tetrahydrobenzo[*b,j*][1,6]naphthyridines, **15**. The strategy involved easily available starting materials MnO_2, KO^{t}Bu, ChCl/p-TSA (DES-1), and TBAB/p-TSA (DES-2)-based deep eutectic solvent systems to provide a good yield of desired products. A plausible reaction mechanism for the product formation has been proposed utilizing control experiments. The photophysical studies and synthetic and gram scale utility were established for the reported synthetic methodology.

EXPERIMENTAL PROCEDURE

Materials and Methods. All of the compounds utilized in our study were obtained from Sigma-Aldrich and TCI Chemicals Ltd. and were used without additional purification. Reaction vials were used throughout the entire process of the reactions and were carried out on the Aptech Lab Mate Manual Parallel Synthesizer. Thin-layer chromatography (TLC) was tested using precoated metal TLC sheets (silica gel 60 F254, Merck). The reaction mixture was allowed to cool at room temperature before being extracted with water and CH_2Cl_2 as a solvent, the organic extracts were dried over anhydrous Na_2SO_4, and the crude reaction mixtures were processed by manual column chromatography to get pure products. Column chromatography on silica gel (100−200 mesh, Merck Ltd.) was used to get pure products with petroleum ether and ethyl acetate (petroleum ether/EtOAc 8:2 v/v). Nuclear magnetic resonance (NMR) spectra were acquired using a Bruker AVANCE-III (400 MHz) with $CDCl_3$ as the solvent solution. The Fourier transform infrared (FT-IR) spectra were recorded using a Shimadzu IR Tracer-100 spectrometer. A XEVO G2-XS-QToF high-resolution mass spectrometer (HRMS) was utilized for mass analysis. The single crystal X-ray diffraction facility was obtained using the Bruker D8 Quest. The absorption spectra (UV) were obtained using a JASCO V-670 PC, and the emission (fluorescence spectrometer) spectra were obtained using a Hitachi.

General Procedure for the Synthesis of (*E*)-6,7-Dihydrodibenzo[*b,j*][1,7]phenanthroline, 13: Path-I from Acridinol. A mixture of ChCl/p-TSA (100 mg/100 mg) (1:1) (DES-1) was stirred at 100 °C to offer DES-1 Then, 2-amino-5-chloro-benzhydrol (**9**) (1 mmol) and acridinol (**10**) (1 mmol) were added in the presence of MnO_2 (10 mol %) as a catalyst and KO^{t}Bu (1.5 equiv) as a base, and heating was continued at 100 °C for 45 min to complete the dehydrogenation step. Further, TBAB/p-TSA (100 mg/100 mg) (1:1) (DES-2) continued the reaction at the same temperature for 45 min to provide the Friedlander quinoline product (16). Then, sequential addition of benzyl alcohol (**11**) (1 mmol) into the reaction mixture and continued heating at 100 °C achieved the desired product (*E*)-6,7-dihydrodibenzo [*b,j*]-[1,7]phenanthrolines (**13a−13k**) with a good yield (75%) in 1.30 h. The reaction progress was monitored and manual column chromatography was done as above to get the pure products (**13a-13k**).

General Procedure for the Synthesis of (*E*)-6,7-Dihydrodibenzo[*b,j*][1,7]phenanthroline, 13f: Path-II. A

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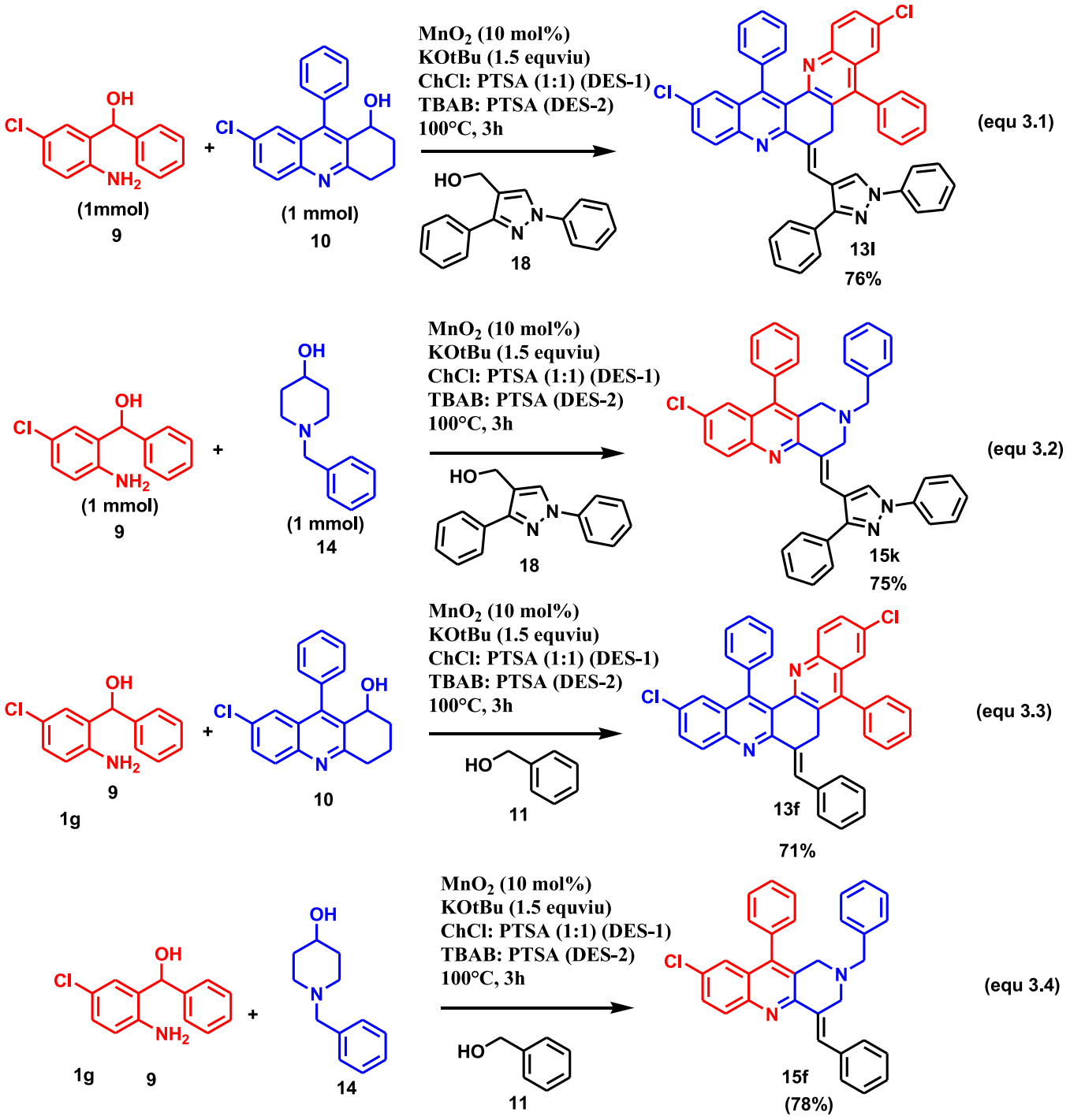
Scheme 3. Synthetic Utility and Gram Scale Synthesis



mixture of (ChCl/p-TSA) (100 mg/100 mg) (1:1) (DES-1) was stirred at 100 °C to offer DES-1 Then, 2-amino-5-chloro-benzhydrol (**9**) (2 mmol) and 1,3 cyclohexanedione (**12**) were added in the presence of MnO_2 (10 mol %) as a catalyst and KO^{t}Bu (1.5 equiv) as a base and heating was continued at 100 °C for 30 min to complete the dehydrogenation step. Further addition of TBAB/p-TSA (100 mg/100 mg) (1:1) (DES-2) to continue the reaction at the same temperature for 2 h provided the Friedlander annulation product (**16**). Then sequential addition of benzyl alcohol (**11**) (1 mmol) into the reaction mixture was done, and heating was continued at 100 °C to achieve the desired product (*E*)-6,7-dihydrodibenzo[*b*,*j*][1,7]-phenanthrolines (**13f**) with a good yield (50%) in 2.30 h. The pure product was obtained as above (**13f**).

General Procedure for the Synthesis of (*E*)-1,2,3,4-Tetrahydrobenzo[*b*][1,6]naphthyridine (15) from Piperidinol. A mixture of (ChCl/p-TSA) (100 mg/100 mg) (1:1) (DES-1) was stirred at 100 °C to offer DES-1. Then 2-amino-5-cl-benzhydrol (**9**) (1 mmol) and 1-benzyl-4-piperidinol (**14**) (1 mmol) were added in the presence of MnO_2 (10 mol %) as a catalyst and KO^{t}Bu (1.5 equiv) as a base and heating was continued at 100 °C for 45 min to complete the dehydrogenation step. Further addition of TBAB/p-TSA (100 mg/100 mg) (1:1) (DES-2) to continue the reaction at the same

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temperature for 45 min provided the Friedlander quinoline product (17). Then sequential addition of benzyl alcohol (**11**) (1 mmol) into the reaction mixture was done, heating was continued at 100 °C to achieve the desired product (*E*)-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridines (**15a−15j**) in good yield (85%) for 1.30 h. The pure products were obtained as above **15a−15j**.

Synthetic Application of (*E*)-2,10-Dichloro-6-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-8,14-diphenyl-6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthroline (13l) and Product (*E*)-2-Benzyl-8-chloro-4-((1,3-diphenyl-1*H*-pyrazol-4-yl) Methylene)-10-phenyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine (15k). A mixture of ChCl/p-TSA (100 mg/100 mg) (1:1) (DES-1) was stirred at 100 °C to offer DES-1. Then, 2-amino-5-chloro-benzhydrol (**9**) (1 mmol) and acridinol (10) (1 mmol) were added in the presence of MnO_2 (10 mol %) as a catalyst and KO^{t}Bu (1.5 equiv) as a base and heating was continued at 100 °C for 45 min to complete the dehydrogenation step. Further, TBAB/p-TSA (100 mg/100 mg) (1:1) (DES-2) continued the reaction at the same temperature for 45 min to provide Friedlander quinoline product (**16**). Then sequential addition of (1,3-diphenyl-1*H*-pyrazol-4-yl)methanol (**18**) (1 mmol) was added into the reaction mixture, and heating was continued at 100 °C to achieve the desired product (*E*)-2,10-dichloro-6-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-8,14-diphenyl-6,7-dihydrodibenzo[*b*,*j*][1,7]phenanthroline (**13l**) with good yield (76%) for 1.30 h. The same reaction condition was followed for the synthesis of (*E*)-2-benzyl-8-chloro-4-((1,3-diphenyl-1*H*-pyrazol-4-yl) methylene)-10-phenyl-1,2,3,4-tetrahydrobenzo[*b*][1,6]naphthyridine (**15k**). Instead of acridinol, 1-benzyl-4-piperidone (14) (1 mmol) was added to provide the desired product (**15k**) with good yield (75%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c00188.

Copies of ^{1}H NMR, ^{13}C NMR, HRMS, FT-IR, and SC-XRD of the synthesized targeted compounds, control experiments, plausible mechanism, and additional data (PDF)

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

DES, deep eutectic solvent system; ChCl, choline chloride; p-TSA, para-toluene sulfonic acid; TBAB, tetra butyl ammonium bromide; KO^{t}Bu, potassium tertiary butoxide; MnO_2, manganese(IV) oxide; NMR, nuclear magnetic resonance spectroscopy; HRMS, high resolution mass spectroscopy; FT-IR, Fourier-transform infrared spectroscopy; SC-XRD, single crystal X-ray diffraction; UV&FL, ultraviolet absorption and fluorescence emission spectroscopy

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