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H_2O_2/DMSO-Promoted Regioselective Synthesis of 3,3′-Bisimidazopyridinylmethanes via Intermolecular Oxidative C(sp^2)−H Bond Activation of Imidazoheterocycles

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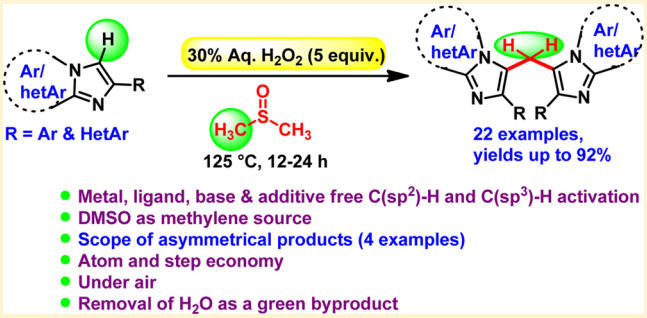
Supporting Information

ABSTRACT: In the past decade, metal-free approaches for C−C bond formation have attracted a great deal of attention due to their ease of use and low cost. This report represents a novel and metal-free synthesis of 3,3′-bisimidazopyridinylmethanes via intermolecular oxidative C(sp^2)−H bond functionalization of imidazo[1,2-*a*]pyridines with dimethyl sulfoxide as the carbon synthon (CH_2) using H_2O_2 as a mild oxidant under air. A library of 3,3′-bis(2-arylimidazo[1,2-*a*]pyridin-3-yl)methanes has been achieved in good to excellent yields. The present methodology has been successfully applied to imidazo[2,1-*b*]thiazoles and imidazo[2,1-*b*]benzothiazoles. Furthermore, the current approach was also extended for the synthesis of unsymmetrical 3,3′-bisimidazopyridinylmethanes under optimized reaction conditions. A mechanistic pathway is proposed on the basis of experiments with radical scavengers and DMSO-d_6 and ESI-MS observations.



INTRODUCTION

Dimethyl sulfoxide has been extensively employed as a solvent in organic synthesis due to its rather low cost, relative stability, and low toxicity. Besides being an effective polar medium, DMSO is also used as a substrate and synthon in organic transformations.[1] An abundance of recent reports have shown that it has been used as a source of −O, −SMe, $-CH_2SMe$, $-SO_2Me$, −Me, −CN, −CHO, and CH_2 as a functional unit inserted into target molecules.[1] Currently, our interest is focused on the functionalization of heteroarenes (imidazoheterocycles) by using DMSO as a carbon synthon. Imidazo[1,2-*a*]pyridines and their derivatives are important structural units found in various natural products and pharmaceuticals such as zolpidem, alpidem, zolimidine, olprinone, saripidem, and necopidem (Figure 1).[2] Therefore, several methodologies have been developed for the preparation and post-transformation of imidazo[1,2-*a*]pyridines and related imidazo[1,2-*a*]heterocycles.[2,3] Due to the electron-rich nature of the C-3 position of imidazo[1,2-*a*]pyridine, several synthetic methods have emerged for regioselective oxidative C−H bond functionalization at the C-3 position.[3] Very recently, three similar reports were developed for the synthesis of 3,3′-bisimidazopyridinylmethanes.[4] (i) The Sun group successfully realized a H_3PO_4-promoted synthesis of bis(imidazo[1,2-*a*]pyridin-3-yl)methanes using DMSO as the methylene source (Scheme 1a).[4a] The reaction proceeds through an ionic mechanistic pathway via in situ formation of formaldehyde. (ii) Patel et al. reported a copper-catalyzed approach to synthesize similar target compounds using dimethylacetamide (DMA) as the carbon synthon (Scheme 1b).[4b] (iii) Kumar and co-workers also developed a vanadyl acetylacetonate-catalyzed methylenation of imidazo[1,2-*a*]pyridines by using DMA as a methylene source (Scheme 1c).[4c] A similar strategy was developed by Cui et al. to synthesize 3,3′-diindolylmethane via a palladium-catalyzed postfunctionalization strategy using DMSO as the methylene source.[5] Despite having a few valuable advantages, these reactions suffer from certain limitations such as the use of metal catalysts,[4b,c,5] inorganic acid,[4a] base, and inert atmosphere[5] to catalyze the reaction via an ionic mechanistic pathway.

In continuation of our research program for the development of mild and efficient approaches for C−H bond functionalization,[6] herein we report a unique approach for the synthesis of bis(2-arylimidazo[1,2-*a*]pyridin-3-yl)methanes via C(sp^2)−H bond activation by using H_2O_2 as a mild oxidant and DMSO as the carbon source. The present protocol represents a facile transformation for the construction of 3,3′-bisimidazopyridinylmethanes under metal-free and aerobic conditions and provided a practical yield.

RESULTS AND DISCUSSION

The oxidative coupling reaction condition was optimized using 2-phenylimidazo[1,2-*a*]pyridine (**1a**) as the model substrate. The reaction was initially performed in DMSO at 125 °C under

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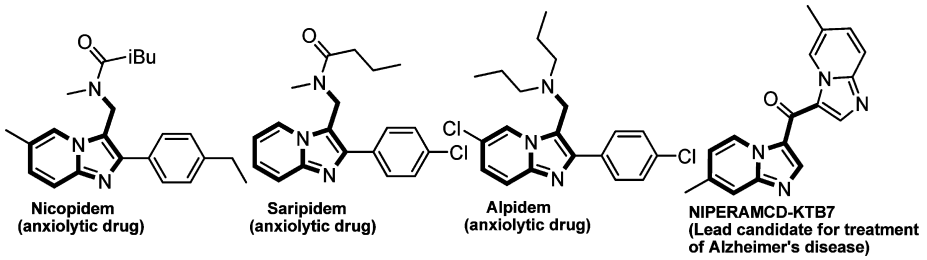
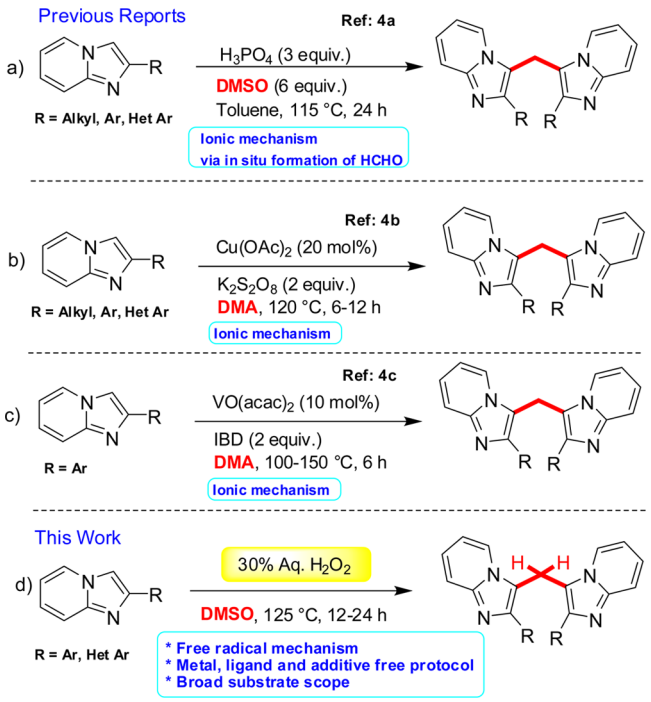


Figure 1. Representative examples of anxiolytic drugs and bioactive agents.[2]

Scheme 1. Recent Reports for C-3 Functionalization of Imidazo[1,2-*a*]pyridines



air without the use of any external oxidant. The respective product **2a** was formed in 37% yield in 24 h (Table 1, entry 1), and the structure was unambiguously confirmed by 1D and 2D NMR spectroscopy and HRMS analysis (Supporting Information). The initial result prompted us to optimize the reaction conditions to enhance the yield of desired product **2a**. In this regard, a series of external oxidants, namely TBHP, DTBP, TBPB, H_2O_2, and Oxone (3 equiv each), were employed under identical reaction conditions (Table 1, entries 2−6). Pleasingly, only H_2O_2 (3 equiv) provided the product **2a** with 68% yield in 24 h (Table 1, entry 5), whereas other oxidants were found to diminish the yield of **2a**. It was noticed that in the case of TBHP, DTBP, and TBPB the reaction produced a complex mixture of products. From this complex mixture, the C-3-formylated product, 2-phenylimidazo[1,2-*a*]pyridine-3-carbaldehyde (**4a**), was isolated in 13%, 30%, and <5% yields, respectively. By increasing the equiv of TBHP and DTBP (5 equiv each) in the reaction, **4a** was formed in enhanced yields of 22% and 50%, respectively, without formation of the desired product **2a** (Table 1, entries 7 and 8). The difference in the course of reaction of peroxide oxidants (H_2O_2 vs TBHP/DTBP) may be due to the in situ formation of *tert*-butoxy and *tert*-butylperoxy radicals in the case of TBHP/DTBP,[7] which leads to C-3 formylation instead of coupling with another mol of 2-phenylimidazo[1,2-*a*]pyridine (**1a**). However, in the case of H_2O_2 ($^{\bullet}OH$) the methylated intermediate undergoes a sequence of hydrogen atom abstraction followed by radical coupling of **1a** to afford the desired final product **2a**. Further, an increase in the amount of H_2O_2 concentration to 5 equiv facilitated the product **2a** with 82% yield in 18 h (Table 1, entry 10). On decreasing the reaction temperature to 80 °C from 125 °C, the corresponding product **2a** was formed in 11% yield with 80% recovery of **1a** (Table 1, entry 11). No significant enhancement in the yield of **2a** was observed by increasing the H_2O_2 loading to 6 equiv in the reaction (Table 1, entry 12).

Having optimized reaction conditions in hand (Table 1, entry 10), the utility of the present approach was systematically investigated by introducing substrates bearing a wide variety of functional groups (electron-withdrawing and electron-donating groups) on the C-2 aryl ring and pyridine ring of imidazo[1,2-*a*]pyridine (Scheme 2). At first, the effect of electron-withdrawing substituents (4-Cl, F, Br, and CN) on the C-2 aryl ring of imidazo[1,2-*a*]pyridine was examined. All the corresponding products (**2a−e**) were formed in good to excellent yields (75%−82%). In the case of CF_3 present on the *meta* position of the aryl ring, only 51% yield of **2f** was obtained, perhaps due to the deactivation of the C-3 position by the strong electron-withdrawing nature of CF_3 group. Next, the effect of electron-donating groups (*p*-CH_3 and *p*-OCH_3) present on the aryl ring of imidazo[1,2-*a*]pyridine was studied. The respective products **2g** and **2h** were obtained in excellent yields (84% and 92%, respectively), representing a relatively better yield compared to the electron-neutral 2-phenylimidazo-[1,2-*a*]pyridine under identical reaction conditions.

Next, the electronic effects of substituents (R^2= EWGs and EDGs) on the pyridine ring of imidazo[1,2-*a*]pyridine at different positions were studied. Interestingly, substrates bearing electron-withdrawing substituents such as 5-Br, 5-I, and 5,7-diCl on the pyridine ring of imidazo[1,2-*a*]pyridine smoothly underwent in the reaction and yielded the corresponding products (**2i**, **2j**, and **2k**, respectively) in moderate to good yields (55−67%). It is worth noting that halogens (F, Cl, Br, and I) and −CN groups are tolerated under optimized conditions and may serve as crucial substituents for postfunctionalization reactions. Further, employing the substrate bearing 5-Cl and *p*-Br on the pyridine ring and aryl ring of imidazo[1,2-*a*]pyridine, respectively, furnished the desired product **2l** in 65% yield. On the other hand, substrates containing electron-donating groups (6-CH_3 and 5-CH_3) present on the pyridine ring of imidazo[1,2-*a*]pyridine smoothly participated in the reaction and provided the corresponding products **2m** and **2n** in high yields under optimized reaction conditions. The substrates bearing electron-donating groups such as 6-Et and *p*-OCH_3 present on pyridine and the aryl ring of imidazo[1,2-*a*]pyridine, respectively,

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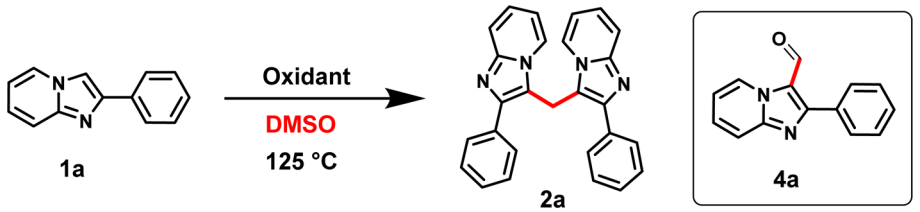
Table 1. Optimization of the Reaction Conditions[a]



entry	oxidant (equiv)	solvent (10 mL)	time (h)	yield[b] (%)
1		DMSO	24	37
2	TBHP (3)	DMSO	24	0[c]
3	DTBP (3)	DMSO	24	0[d]
4	TBPB (3)	DMSO	24	0[e]
5	H_2O_2 (3)	DMSO	24	68
6	Oxone (3)	DMSO	24	0
7	TBHP (5)	DMSO	18	0[f]
8	DTBP (5)	DMSO	18	0[g]
9	H_2O_2 (5)	DMSO	12	71
10	**H_2O_2 (5)**	**DMSO**	**18**	**82**
11	H_2O_2 (5)	DMSO	20	11[h]
12	H_2O_2 (6)	DMSO	18	81

[a]Reaction conditions: **1a** (1 equiv), oxidant (3−5 equiv) in 10 mL of DMSO at 125 °C. [b]Isolated yield. [c]2-Phenylimidazo[1,2-*a*]pyridine-3-carbaldehyde (**4a**) was formed in 13% yield. [d]**4a** was formed in 30% yield. [e]**4a** was formed in <5% yield. [f]**4a** was formed in 22% yield. [g]**4a** was formed in 50% yield. [h]Reaction performed at 80 °C. TBHP = *tert*-butyl hydroperoxide (70% aq solution), DTBP = di-*tert*-butyl peroxide, TBPB = *tert*-butyl peroxybenzoate, DMSO = dimethyl sulfoxide.

facilitated the desired product **2o** in about 86% yield. The reaction of heteroarene (thiophene) at the C-2 position of imidazo[1,2-*a*]pyridine was also carried out. To our delight, the respective product bis(2-(thiophene-2-yl)imidazo[1,2-*a*]-pyridin-3-yl)methane (**2p**) was obtained in 60% yield. However, substrates bearing CF_3, *tert*-butyl, and H at the C-2 position of imidazo[1,2-*a*]pyridine failed to deliver the corresponding products **2q−s** under identical reaction conditions, indicating that aryl substitution at the C-2 position is necessary for the reaction to proceed.[8]

The scope of the present protocol was further elaborated with other imidazoheterocycles like imidazo[2,1-*b*]thiazole and imidazo[2,1-*b*]benzothiazole under the reaction conditions (Scheme 3). Gratifyingly, substrates bearing electron-withdrawing (*p*-Cl and *p*-F) and electron-donating groups (*p*-CH_3) present on the aryl ring of imidazo[2,1-*b*]thiazole and imidazo[2,1-*b*]benzothiazole were well-tolerated in the reaction and furnished the corresponding products in good to excellent yields (Scheme 3, entries **2t−y**). We also attempted the reaction of 1-methyl-2-phenyl-1*H*-indole (**1z**) under optimal reaction conditions. However, the reaction failed to furnish the respective product **2z**.

Furthermore, the scope of present method was extended for the synthesis of unsymmetrical 3,3′-bisimidazopyridinyl compounds under optimized reaction conditions. The cross-coupling reaction of various substituents present on the C-2 aryl ring (−Cl, −Br, and −OCH_3) and pyridine ring (−Cl, −dichloro, and −Br) of imidazoheterocycles were amenable to the reaction conditions and afforded the respective unsymmetrical products (**3al**, **3hk**, **3hi**, and **3hu**) in good yields compared to the corresponding symmetrical products (Scheme 4).

To gain insight into the mechanism of the oxidative coupling reaction, a series of control experiments were performed. The isotopic labeling experiment was carried out using **1a** in the presence of DMSO-d_6 under the optimized reaction conditions. The deuterated product **2aA** was formed in 78% yield with more than 99% incorporation of deuterium (Scheme 5, eq 1). This study clearly indicated that DMSO is a source of one-carbon synthon. Mass spectrometric analysis of the crude reaction mixture after 18 h revealed the presence of methylated intermediate (**B′**), which showed a $[M + H]^+$ peak at 212 Da (Scheme 5, eq I). To detect the kind of mechanism involved in this transformation, well-known radical scavengers such as TEMPO (2,2,6,6-tetramethylpiperidine 1-oxy) and BHT (butylated hydroxytoluene) were added to the reaction (Scheme 5, eqs II and III). The product formation was completely inhibited, suggesting an involvement of radical-mediated pathway. To further confirm the mechanistic pathway, the reaction of the 3-methyl-2-phenylimidazo[1,2-*a*]pyridine (**B**) with **1a** was carried out in DMF under standard reaction conditions. The respective product **2a** was formed in 61% yield (Scheme 5, eq IV). These experiments together with ESI-MS observations confirm that the reaction may proceed via formation of methylated intermediate **B**.

In accordance with the preliminary mechanistic studies and literature precedents,[9] a proposed mechanistic pathway is depicted as shown in Scheme 6. Initially, the hydroxyl radical generated through homolytic cleavage of H_2O_2 and subsequently reacts with DMSO to produce methyl radical species.[9a−c] The methyl radical reacts with **1a** to afford the radical intermediate **A**, which could be stabilized by the adjacent phenyl ring. The radical intermediate **A** leads to methylated intermediate **B** via $^{\bullet}H$ abstraction by hydroxyl radical with subsequent loss of H_2O. The hydroxyl radical subsequently abstracts $^{\bullet}H$ from **B** to form the radical intermediate **C** with the removal of H_2O. The intermediate **C** reacts with another mole of **1a** to afford the radical intermediate **D**, which upon subsequent loss of H_2O in the presence of hydroxyl radical delivers the corresponding final product **2a**.

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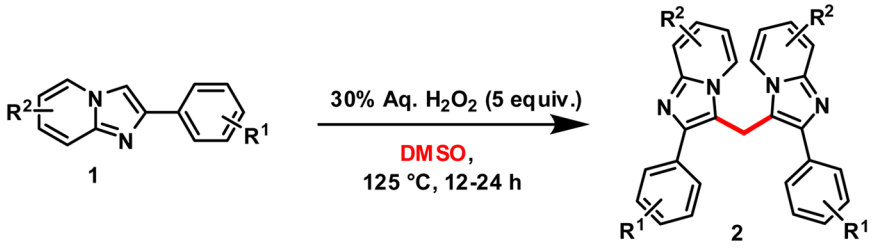
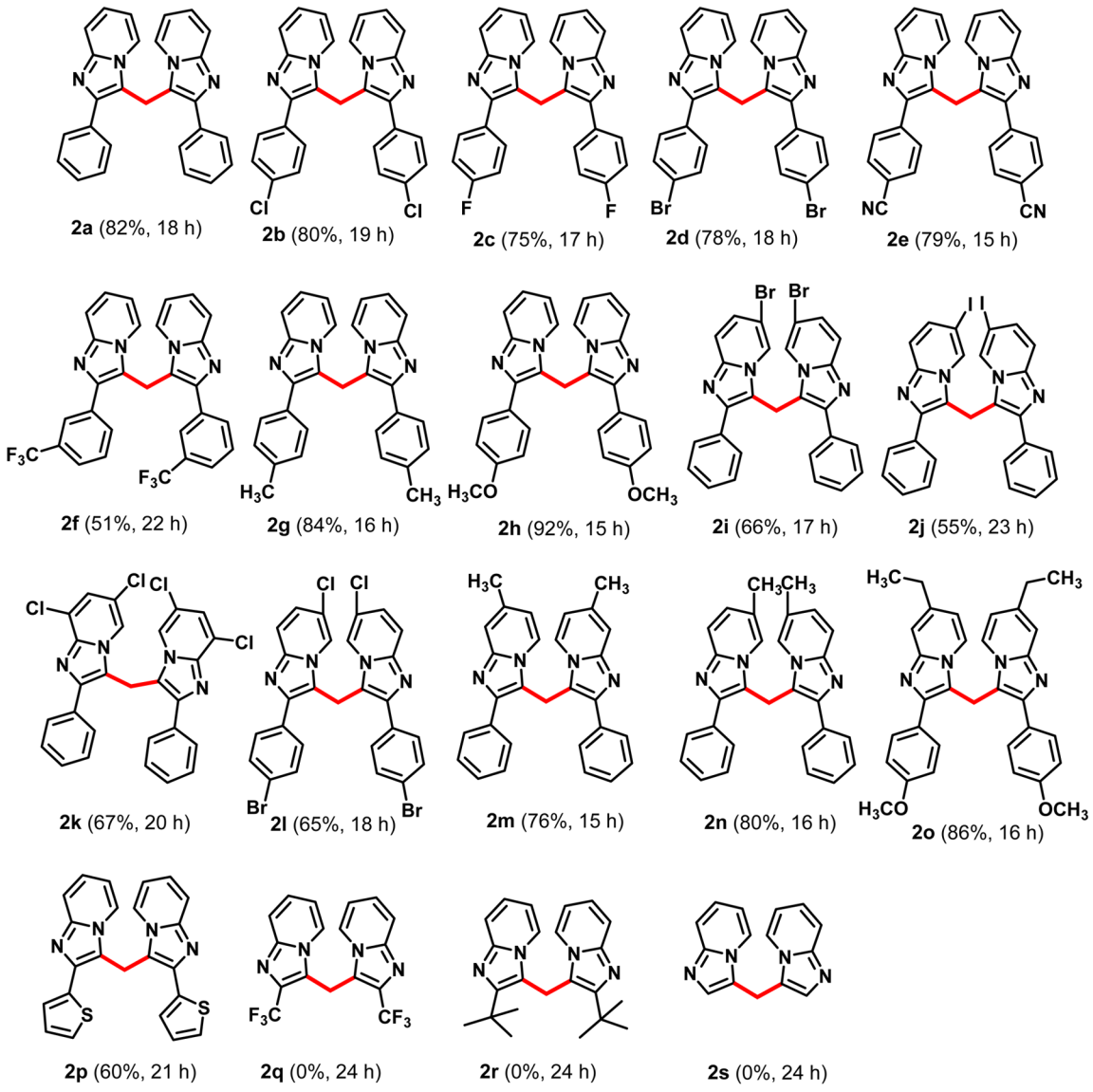
Scheme 2. Substrate Scope of Imidazo[1,2-*a*]pyridine[a,b]





[a]All reactions were performed by using **1** (1 equiv, 300 mg) and 30% aq H_2O_2 (5 equiv) in 10 mL of DMSO at 125 °C for 12−24 h. [b]Isolated yields.

CONCLUSION

In summary, we have developed a facile, transition-metal-free, and regioselective approach for the synthesis of 3,3′-bisimidazopyridinylmethanes using DMSO as the methylene source. The radical mechanism was established by experiments with radical scavengers (TEMPO and BHT), DMSO-d_6, and ESI-MS analysis. The use of mild oxidant H_2O_2 to activate $C(sp^2)$−H/$C(sp^3)$−H in a cascade manner under aerobic conditions to furnish symmetrical and unsymmetrical products in good to excellent yields is an attractive feature of this approach. Moreover, further applications of this approach are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information. Melting points were determined on a capillary melting point apparatus and are uncorrected. All the compounds were fully characterized by ^{1}H, ^{13}C, and IR and further confirmed through ESI-MS and HRMS analysis. ^{1}H NMR spectra were recorded on 400 and 500 MHz in $CDCl_3$, DMSO-d_6, and ^{13}C NMR spectra recorded on 100 and 125 MHz in $CDCl_3$, DMSO-d_6, CD_3OD, and TFA using TMS as an internal standard. Multiplicities

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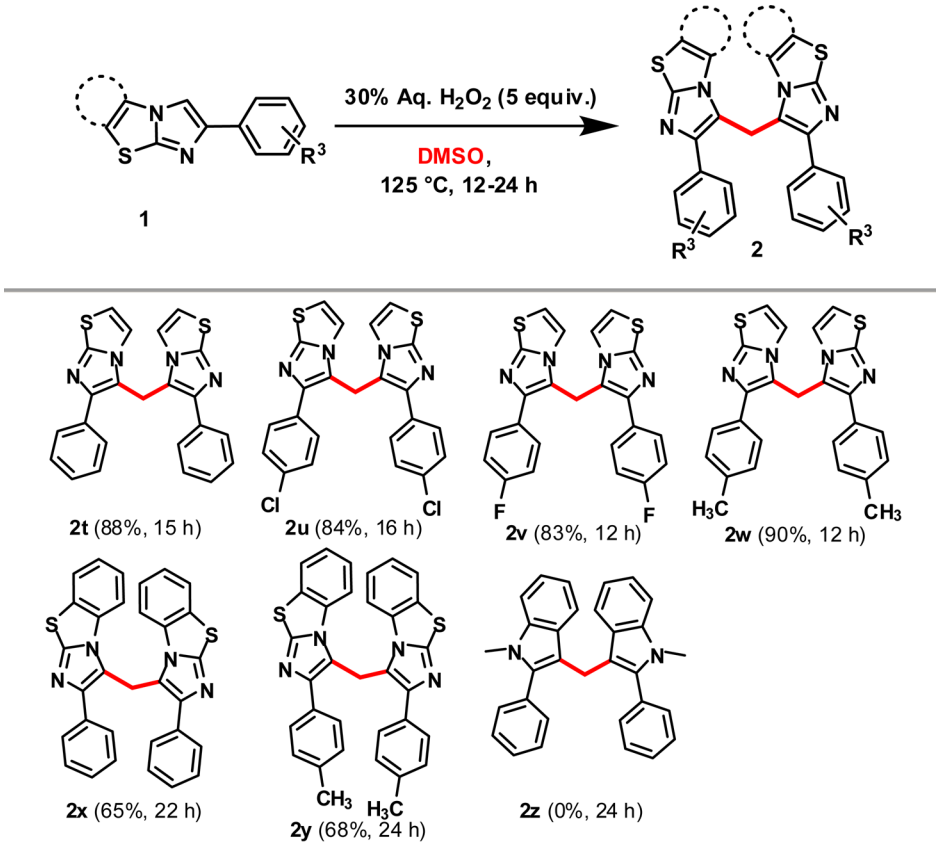
Scheme 3. Substrate Scope of Other Heterocycles[a,b]



[a]Reaction conditions similar to those of Scheme 2. [b]Isolated yields.

are reported as follows: singlet (s), doublet (d), broad singlet (br s), doublet of doublets (dd), triplet (t), doublet of doublet of doublet (ddd), doublet of triplet (dt), and multiplet (m). Chemical shifts (δ) and coupling constants (J) are reported in parts per million (ppm) relative to the residual signal of TMS in deuterated solvents and hertz, respectively. IR spectra were recorded using an FT-IR spectrophotometer, and values are reported in cm^{-1}. HRMS were recorded using a Q-TOF mass spectrometer. Column chromatography was performed over silica gel (60−120 mesh) using EtOAc-*n*-hexane as an eluent. All chemicals and reagents were purchased from commercial sources and used without further purification.

General Experimental Procedure for the Preparation of Starting Materials 1. The starting materials 2-arylimidazo[1,2-*a*]pyridines **1a−y** (known compounds)[10,11] and **1o** (unknown) were prepared by a known literature procedure.[11]

Experimental Procedure for the Synthesis of Symmetrical Compounds 2a−z. To a well-stirred solution of substrate **1** (300 mg, 1 equiv) in DMSO (10 mL) placed into a 50 mL round-bottom flask was added 30% aq H_2O_2 (5 equiv) at room temperature. The resulting mixture was heated at 125 °C for 12−24 h. After completion of the reaction monitored by TLC, the reaction mixture was allowed to stand at room temperature for 30 min. Then 20 mL of H_2O was added to the mixture followed by extraction with EtOAc (3 × 50 mL), washing with brine (10 mL), and drying over Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by silica gel (60−120 mesh) column chromatography and eluted with EtOAc and *n*-hexane (8:2 to 1:9) to afford the respective products (**2**).

Experimental Procedure for the Synthesis of Unsymmetrical Compounds 3. To a well-stirred solution of substrate **1** (300 mg, 1 equiv) and **1′** (1 equiv) in DMSO (10 mL) placed in a 50 mL, round-bottom flask was added 30% aq H_2O_2 (5 equiv) at room temperature. The resulting mixture was heated at 125 °C for 17−23 h. After completion of the reaction as monitored by TLC, the reaction mixture was allowed to stand at room temperature for 30 min. Then the mixture was mixed with 20 mL of H_2O and extracted with EtOAc (3 × 50 mL) followed by washing with brine (10 mL) and drying over Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by silica gel (60−120 mesh) column chromatography and eluted with EtOAc and *n*-hexane (8:2 to 1:9) to afford respective products **2**, **3**, and **2′**.

*Bis(2-phenylimidazo[1,2-a]pyridin-3-yl)methane (**2a**):* white solid (255 mg, 82%); mp 216−218 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3684, 3019, 1602, 1520, 1476, 1334, 1072, 928, 848, 627, 493; δ_H (400 MHz; $CDCl_3$) = 7.78 (4H, dd, J = 8.4, 1.4 Hz), 7.53−7.49 (6H, m), 7.44−7.40 (2H, m), 7.33 (2H, d, J = 6.9 Hz), 7.04 (2H, m), 6.46 (2H, td, J = 6.8, 1.2 Hz), 4.99 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.1 (2 × C), 144.3 (2 × C), 134.4 (2 × C), 129.01 (4 × CH), 128.9 (4 × CH), 128.3 (2 × CH), 124.3 (2 × CH), 123.8 (2 × CH), 117.5 (2 × CH), 114.3 (2 × C), 112.3 (2 × CH) 19.8 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{21}N_4$ $[M + H]^+$ 401.1766, found 401.1755.

*Bis(2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methane (**2b**):* white solid (195 mg, 80%); mp 270−272 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3019, 1636, 1522, 1476, 1404, 1022, 928, 669, 626; δ_H (400 MHz; $CDCl_3$) = 7.64 (4H, dt, J = 9, 2.4 Hz), 7.54 (2H, dt, J = 9.0, 1.0 Hz), 7.43 (4H, dt, J = 9.0, 2.4 Hz), 7.38 (2H, dt, J = 6.9, 1.0 Hz), 7.10 (2H, ddd, J = 9, 6.8, 1.2 Hz), 6.55 (2H, td, J = 6.8, 1.2 Hz), 4.90 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.1 (2 × C), 143.2 (2 × C), 134.3 (2 × C), 132.7 (2 × C), 130.0 (4 × CH), 129.0 (4 × CH), 124.7 (2 × CH), 123.5 (2 × CH), 117.7 (2 × CH), 114.1 (2 × C), 112.7 (2 × CH), 20.1 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{19}Cl_2N_4$ $[M + H]^+$ 469.0987, found 469.0976.

*Bis(2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl)methane (**2c**):* white solid (231 mg, 75%); mp 190−192 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3745, 3391, 3019, 1637, 1517, 1403, 1047, 928, 669; δ_H (400 MHz; $CDCl_3$) = 7.69−7.66 (4H, m), 7.52 (2H, dd, J = 9.0, 0.1 Hz), 7.38−7.36 (2H, m), 7.17−7.06 (6H, m), 6.54 (2H, t, J = 6.8 Hz), 4.88 (2H, s) ppm; δ_C (125 MHz; $CDCl_3$) = 162.8 (J_{C-F} = 246.2, 2 × C),

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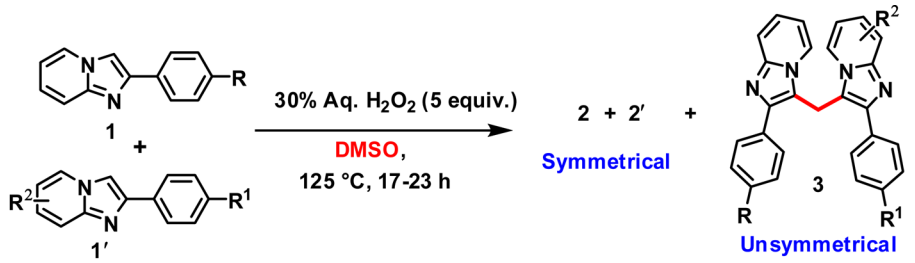
Scheme 4. Substrate Scope of Unsymmetrical Imidazoheterocycles[a,b]



Entry (Product)	Time	Yields (%)[b]
2a + 2l → 3al	23 h	16, **31**, 13
2h + 2k → 3hk	20 h	19, **29**, 14
2h + 2i → 3hi	19 h	20, **27**, 11
2h + 2u → 3hu	17 h	21, **35**, 18

[a]Reaction was performed by using **1** (1 equiv), **1′** (1 equiv), and 30% aq H_2O_2 (5 equiv) in 10 mL of DMSO at 125 °C for 17−23 h. [b]Isolated yields of each products.

145.0 (2 × C), 143.4 (2 × C), 130.5 (J_{C-F} = 8.7 Hz, 4 × CH), 130.3 (J_{C-F} = 2.5 Hz, 2 × C), 124.5 (2 × CH), 123.5 (2 × CH), 117.6 (2 × CH), 115.8 (J_{C-F} = 21.2, 4 × CH), 113.9 (2 × C), 112.6 (2 × CH), 20.0 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{19}F_2N_4$ $[M + H]^+$ 437.1578, found 437.1566.

*Bis(2-(4-bromophenyl)imidazo[1,2-a]pyridin-3-yl)methane (**2d**):* white solid (239 mg, 78%); mp 274−276 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3390, 3019, 1638, 1402, 1215, 1070, 768, 668; δ_H (400 MHz; $CDCl_3$) = 7.58 (8H, s), 7.54 (2H, dt, *J* = 9.1, 1 Hz), 7.37 (2H, dd, *J* = 5.9, 1 Hz), 7.10 (2H, ddd, *J* = 9.0, 6.8, 1.2 Hz), 6.56 (2H, td, *J* = 6.8, 1.2 Hz), 4.88 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.1 (2 × C), 143.2 (2 × C), 133.1 (2 × C), 131.9 (4 × CH), 130.2 (4 × CH), 124.7 (2 × CH), 123.5 (2 × CH), 122.5 (2 × C), 117.7 (2 × CH), 114.1 (2 × C), 112.8 (2 × CH), 20.1 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{19}Br_2N_4$ $[M + H]^+$ 558.9956, found 558.9955.

*Bis(2-(4-cyanophenyl)imidazo[1,2-a]pyridin-3-yl)methane (**2e**):* white solid (243 mg, 79%); mp 295−297 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3401, 3019, 1635, 1385, 1216, 1070, 669; δ_H (400 MHz; $CDCl_3$) = 7.69 (4H, d, *J* = 8.2 Hz), 7.63 (4H, d, *J* = 8.2 Hz), 7.57 (2H, d, *J* = 9.1 Hz), 7.47 (2H, d, *J* = 6.9 Hz), 7.19 (2H, t, *J* = 6.9 Hz), 6.68 (2H, t, *J* = 6.8 Hz), 4.89 (s, 2H) ppm; δ_C (100 MHz; $CDCl_3$ + CD_3OD) = 145.2 (2 × C), 142.3 (2 × C), 138.5 (2 × C), 132.1 (4 × CH), 128.9 (4 × CH), 125.5 (2 × CH), 123.1 (2 × CH), 118.5 (2 × C), 117.8 (2 × CH), 114.5 (2 × C), 113.4 (2 × CH), 111.7 (2 × C), 20.4 (CH_2) ppm; HRMS (ESI) calcd for $C_{29}H_{19}N_6$ $[M + H]^+$ 451.1671, found 451.1663.

*Bis(2-(3-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridin-3-yl)-methane (**2f**):* white solid (157 mg, 51%); mp 186−188 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3853, 3745, 3392, 3019, 1638, 1403, 1050, 929, 669; δ_H (400 MHz; $CDCl_3$) = 7.94 (2H, s), 7.75 (2H, d, *J* = 7.6 Hz), 7.61 (2H, d, *J* = 7.6 Hz), 7.56−7.49 (4H, m), 7.43 (2H, d, *J* = 6.9 Hz), 7.14

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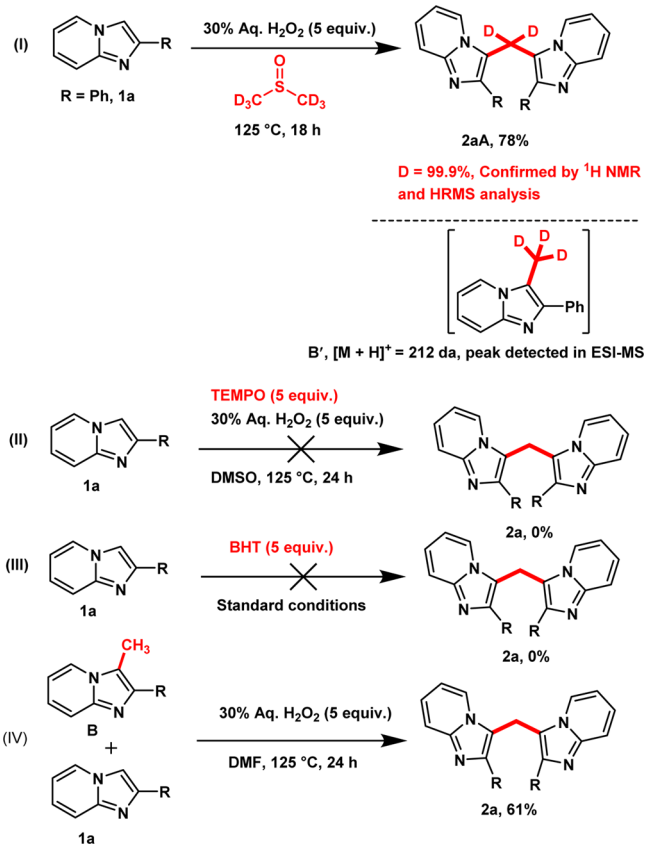
J. Org. Chem. 2016, 81, 7626−7634

Scheme 5. Preliminary Mechanistic Studies



(2H, td, J = 7.9, 0.1 Hz), 6.64−6.61 (2H, m), 4.89 (2H, s) ppm; δ_C (125 MHz; $CDCl_3$) = 145.1 (2 × C), 143.0 (2 × C), 135.0 (2 × C), 131.7 (2 × CH), 131.2 (2 × C, q, J_{C-F} = 32.5 Hz), 129.0 (2 × CH), 125.6 (2 × CH, br q, J_{C-F} = 3.7 Hz), 125.0 (2 × CH), 124.9 (2 × CH, br q, J_{C-F} = 3.7 Hz), 123.3 (2 × CH), 117.8 (2 × CH), 114.2 (2 × C), 113.0 (2 × CH), 20.2 (CH_2) ppm; HRMS (ESI) calcd for $C_{29}H_{19}F_6N_4$ $[M + H]^+$ 537.1514, found 537.1509.

Bis(2-p-tolylimidazo[1,2-a]pyridin-3-yl)methane (***2g***): yellow solid (259 mg, 84%); mp 255−257 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3400, 3019, 1634, 1385, 1215, 1070, 769, 669; δ_H (400 MHz; $CDCl_3$) = 7.69 (4H, d, J = 8.0 Hz), 7.51 (2H, d, J = 9.0 Hz), 7.33 (6H, br t, J = 7.6 Hz), 7.03 (2H, t, J = 7.8 Hz), 6.45 (2H, t, J = 6.8 Hz), 4.98 (2H, s), 2.44 (s, 6H) ppm; δ_C (100 MHz; $CDCl_3$) = 145.0 (2 × C), 144.3 (2 × C), 138.1 (2 × C), 131.5 (2 × C), 129.6 (4 × CH), 128.9 (4 × CH), 124.2 (2 × CH), 123.9 (2 × CH), 117.4 (2 × CH), 114.2 (2 × C), 112.2 (2 × CH), 21.4 (2 × CH_3), 19.9 (CH_2) ppm; HRMS (ESI) calcd for $C_{29}H_{25}N_4$ $[M + H]^+$ 429.2079, found 429.2069.

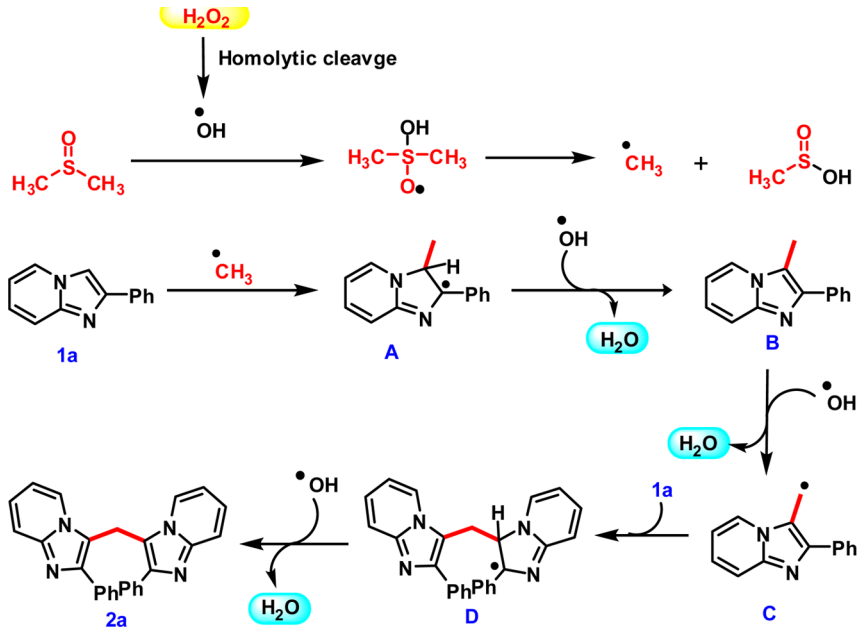
Bis(2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)methane (***2h***): white solid (296 mg, 92%); mp 214−216 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3682, 3391, 3019, 1614, 1474, 1032, 928, 669, 627; δ_H (400 MHz; $CDCl_3$) = 7.74−7.70 (4H, m), 7.50 (2H, d, J = 9.0 Hz), 7.35 (2H, d, J = 6.9 Hz), 7.06−7.0 (6H, m), 6.45 (2H, td, J = 6.8, 1.1 Hz), 4.94 (2H, s), 3.88 (6H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 159.8 (2 × C), 145.0 (2 × C), 144.1 (2 × C), 130.27 (4 × CH), 126.9 (2 × C), 124.2 (2 × CH), 123.9 (2 × CH), 117.3 (2 × CH), 114.4 (4 × CH), 113.9 (2 × C), 112.3 (2 × CH), 55.5, 19.9 (CH_2) ppm; HRMS (ESI) calcd for $C_{29}H_{25}N_4O_2$ $[M + H]^+$ 461.1978, found 461.1967.

Bis(6-bromo-2-phenylimidazo[1,2-a]pyridin-3-yl)methane (***2i***): orange solid (202 mg, 66%); mp 286−288 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3019, 1602, 1522, 1475, 1023, 928, 669, 626; δ_H (400 MHz; $CDCl_3$) = 7.75 (4H, br d, J = 7.7 Hz), 7.57 (4H, t, J = 7.2 Hz), 7.50−7.46 (2H, m), 7.43−7.39 (4H, m), 7.11 (2H, dd, J = 9.4, 1.8 Hz), 4.92 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.2 (2 × C), 143.6 (2 × C), 133.7 (2 × C), 129.3 (4 × CH), 129.2 (4 × CH), 128.8 (2 × CH), 128.0 (2 × CH), 124.2 (2 × CH), 118.1 (2 × CH), 114.6 (2 × C), 107.1 (2 × C), 19.2 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{18}Br_2N_4$ $[M + H]^+$ 558.9956, found 558.9955.

Bis(6-iodo-2-phenylimidazo[1,2-a]pyridin-3-yl)methane (***2j***): white solid (147 mg, 55%); mp 282−284 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3684, 3399, 3019, 1635, 1523, 1419, 1069, 928, 669; δ_H (400 MHz; $CDCl_3$) = 7.81−7.79 (4H, m), 7.60−7.56 (6H, m), 7.48 (2H, t, J = 7.4 Hz), 7.31 (2H, d, J = 9.4 Hz), 7.22 (2H, dd, J = 9.4, 1.5 Hz), 4.93 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$ + DMSO-d_6 + TFA) = 138.8 (2 × C), 138.4 (2 × C), 135.7 (2 × C), 129.5 (2 × CH), 128.0 (10 × CH), 126.7 (2 × C), 115.3 (2 × CH), 113.7 (2 × CH), 79.8 (2 × C), 19.1 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{19}I_2N_4$ $[M + H]^+$ 652.9699, found 652.9677.

Bis(6,8-dichloro-2-phenylimidazo[1,2-a]pyridin-3-yl)methane (***2k***): white solid (206 mg, 67%); mp 268−270 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3390, 3019, 1637, 1402, 1068, 669; δ_H (400 MHz; $CDCl_3$) =

Scheme 6. Plausible Mechanistic Pathway



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J. Org. Chem. 2016, 81, 7626−7634

7.77−7.75 (4H, m), 7.58−7.54 (4H, m), 7.51−7.47 (2H, m), 7.24 (2H, d, J = 1.7 Hz), 7.15 (2H, d, J = 1.7 Hz), 4.89 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 146.0 (2 × C), 141.1 (2 × C), 133.2 (2 × C), 129.3 (8 × CH), 129.1 (2 × CH), 124.9 (2 × CH), 123.7 (2 × C), 120.8 (2 × CH), 119.9 (2 × C), 116.3 (2 × C), 19.5 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{17}Cl_4N_4$ $[M + H]^+$ 537.0207, found 537.0200.

*Bis(2-(4-bromophenyl)-6-chloroimidazo[1,2-a]pyridin-3-yl)-methane (**2l**):* white solid (199 mg, 65%); mp 273−275 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3390, 3019, 1645, 1522, 1403, 1069, 928, 831, 669, 626; δ_H (400 MHz; $CDCl_3$) = 7.65−7.62 (4H, m), 7.57−7.54 (4H, m), 7.47 (2H, dd, J = 9.5, 0.1 Hz), 7.32 (2H, br d, J = 1.2 Hz), 7.07 (2H, dd, J = 9.5, 1.9 Hz), 4.80 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 144.4 (2 × C), 143.5 (2 × C), 132.6 (2 × C), 132.3 (4 × CH), 130.4 (4 × CH), 126.3 (2 × CH), 123.2 (2 × C), 121.7 (2 × CH), 121.0 (2 × C), 118.0 (2 × CH), 114.5 (2 × C), 19.5 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{17}Br_2Cl_2N_4$ $[M + H]^+$ 626.9177, found 626.9145.

*Bis(7-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methane (**2m**):* white solid (234 mg, 76%); mp 215−217 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3684, 3019, 1647, 1522, 1475, 1023, 928, 669; δ_H (400 MHz; DMSO-d_6) = 7.61 (2H, d, J = 6.9 Hz), 7.55 (4H, d, J = 6.9 Hz), 7.31−7.25 (8H, m), 6.57 (2H, d, J = 6.9 Hz), 4.97 (2H, s), 2.27 (6H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.5 (2 × C), 143.8 (2 × C), 135.3 (2 × C), 134.7 (2 × C), 129.0 (4 × CH), 128.9 (4 × CH), 128.1 (2 × CH), 123.1 (2 × CH), 115.8 (2 × CH), 114.9 (2 × CH), 114.0 (2 × C), 21.24 (2 × CH_3), 19.8 (CH_2) ppm; HRMS (ESI) calcd for $C_{29}H_{25}N_4$ $[M + H]^+$ 429.2079, found 429.2084.

*Bis(6-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methane (**2n**):* yellow solid (246 mg, 80%); mp 273−275 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3673, 3391, 3019, 1637, 1402, 1216, 1068, 771, 669; δ_H (400 MHz; $CDCl_3$) = 7.84 (4H, d, J = 7.1 Hz), 7.57 (4H, t, J = 7.4 Hz), 7.49−7.45 (2H, m), 7.38 (2H, d, J = 9.2 Hz), 7.05 (2H, s), 6.86 (2H, dd, J = 9.1, 1.5 Hz), 4.96 (2H, s), 1.89 (6H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 144.1 (2 × C), 143.7 (2 × C), 135.1 (2 × C), 129.1 (8 × CH), 128.3 (2 × CH), 127.6 (2 × CH), 122.1 (2 × CH), 121.8 (2 × C), 116.6 (2 × CH), 114.5 (2 × C), 19.1 (CH_2), 18.0 (2 × CH_3) ppm; HRMS (ESI) calcd for $C_{29}H_{25}N_4$ $[M + H]^+$ 429.2079, found 429.2072.

*Bis(7-ethyl-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-methane (**2o**):* white solid (264 mg, 86%); mp 217−219 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3364, 1640, 1400, 1248, 1067, 837, 769; δ_H (400 MHz; $CDCl_3$) = 7.74 (4H, dt, J = 9.6, 2.8 Hz), 7.27−7.24 (4H, m), 7.06 (4H, dt, J = 9.6, 2.8 Hz), 6.31 (2H, dd, J = 7.0, 1.7 Hz), 4.90 (2H, s), 3.89 (6H, s), 2.55 (4H, q, J = 7.5 Hz), 1.17 (6H, t, J = 7.5 Hz) ppm; δ_C (100 MHz; $CDCl_3$) = 159.6 (2 × C), 145.5 (2 × C), 143.6 (2 × C), 141.3 (2 × C), 130.1 (4 × CH), 127.1 (2 × C), 123.3 (2 × CH), 114.3 (4 × CH), 114.2 (2 × CH), 113.8 (2 × CH), 113.5 (2 × C), 55.4, 28.3 (2 × CH_2), 19.8 (CH_2), 14.4 (2 × CH_3) ppm; HRMS (ESI) calcd for $C_{33}H_{33}N_4O_2$ $[M + H]^+$ 517.2604, found 517.2592.

*Bis(2-(thiophene-2-yl)imidazo[1,2-a]pyridin-3-yl)methane (**2p**):* off-white solid (185 mg, 60%); mp 259−261 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3392, 3019, 1636, 1403, 1215, 1051, 928, 669; δ_H (400 MHz; $CDCl_3$) = 7.59 (2H, d, J = 3.4 Hz), 7.53 (4H, br t, J = 8.0 Hz), 7.48 (2H, d, J = 4.8 Hz), 7.22−7.20 (2H, m), 7.09−7.05 (2H, m), 6.51 (2H, t, J = 6.3 Hz) 5.15 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.3 (2 × C), 138.6 (2 × C), 137.0 (2 × C), 128.0 (2 × CH), 126.6 (2 × CH), 125.9 (2 × CH), 125.0 (2 × CH), 123.9 (2 × CH), 117.5 (2 × CH), 113.6 (2 × C), 112.9 (2 × CH), 20.4 (CH_2) ppm; HRMS (ESI) calcd for $C_{23}H_{17}N_4S_2$ $[M + H]^+$ 413.0895, found 413.0887.

*Bis(6-phenylimidazo[2,1-b]thiazol-5-yl)methane (**2t**):* white solid (271 mg, 88%); mp 262−264 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3682, 3019, 1635, 1522, 1404, 1070, 928, 830, 669; δ_H (500 MHz; $CDCl_3$) = 7.75 (4H, br d, J = 7.7 Hz), 7.51−7.48 (4H, m), 7.41−7.37 (2H, m), 6.56 (2H, d, J = 3.6 Hz), 6.55 (2H, d, J = 3.6 Hz), 4.83 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$ + CD_3OD) = 149.4 (2 × C), 144.4 (2 × C), 133.9 (2 × C), 128.9 (4 × CH), 128.1 (4 × CH), 128.0 (2 × CH), 117.2 (2 × CH and 2 × C, overlapped), 113.1 (2 × CH), 21.0 (CH_2) ppm; HRMS (ESI) calcd for $C_{23}H_{17}N_4S_2$ $[M + H]^+$ 413.0895, found 413.0888.

*Bis(6-(4-chlorophenyl)imidazo[2,1-b]thiazol-5-yl)methane (**2u**):* white solid (259 mg, 84%); mp 261−263 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3392, 3019, 1644, 1402, 1215, 1048, 928, 669; δ_H (400 MHz; $CDCl_3$) = 7.68−7.64 (4H, m), 7.46−7.43 (4H, m), 6.62 (2H, d, J = 4.5 Hz), 6.57 (2H, d, J = 4.5 Hz), 4.76 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 149.6 (2 × C), 143.7 (2 × C), 133.8 (2 × C), 132.8 (2 × C), 129.2 (8 × CH), 117.0 (2 × CH), 113.4 (2 × CH), 21.6 (CH_2) ppm; HRMS (ESI) calcd for $C_{23}H_{15}Cl_2N_4S_2$ $[M + H]^+$ 481.0115, found 481.0110.

*Bis(6-(4-fluorophenyl)imidazo[2,1-b]thiazol-5-yl)methane (**2v**):* white solid (256 mg, 83%); mp 253−255 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3390, 3019, 1645, 1403, 1215, 1156, 1068, 929, 669; δ_H (400 MHz; $CDCl_3$) = 7.69 (4H, dd, J = 8.3, 5.4 Hz), 7.18 (4H, br t, J = 8.5 Hz), 6.61 (2H, dd, J = 4.5, 0.6 Hz), 6.56 (2H, dd, J = 4.6, 0.6 Hz), 4.75 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 162.5 (J = 246 Hz, 2 × C), 149.4 (2 × C), 143.9 (2 × C), 130.4 (J = 3 Hz, 2 × C), 129.7 (J = 8 Hz, 4 × CH), 117.0 (2 × CH), 116.8 (2 × C), 115.9 (J = 22 Hz, 4 × CH), 113.1 (2 × CH), 21.4 (CH_2) ppm; HRMS (ESI) calcd for $C_{23}H_{15}F_2N_4S_2$ $[M + H]^+$ 449.0706, found 449.0696.

*Bis(6-p-tolylimidazo[2,1-b]thiazol-5-yl)methane (**2w**):* white solid (277 mg, 90%); mp 254−256 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3369, 3019, 1637, 1403, 1215, 1069, 831, 769, 668; δ_H (400 MHz; $CDCl_3$) 7.64 (4H, d, J = 8.0 Hz), 7.30 (4H, d, J = 7.9 Hz), 6.56 (2H, d, J = 4.6 Hz), 6.54 (2H, d, J = 4.5 Hz), 4.80 (2H, s), 2.42 (6H, s) ppm; δ_C (100 MHz; $CDCl_3$) 149.3 (2 × C), 144.7 (2 × C), 137.6 (2 × C), 131.5 (2 × C), 129.7 (4 × CH), 127.9 (4 × CH), 117.3 (2 × CH), 117.0 (2 × C), 112.6 (2 × CH), 21.4 (CH_2 and 2 × CH_3, overlapped) ppm; HRMS (ESI) calcd for $C_{25}H_{21}N_4S_2$ $[M + H]^+$ 441.1208, found 441.1184.

*Bis(2-phenylbenzo[d]imidazo[2,1-b]thiazol-3-yl)methane (**2x**):* white solid (191 mg, 65%); mp 277−279 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3684, 3019, 1604, 1497, 1404, 1215, 1025, 928, 669, 627; δ_H (400 MHz; $CDCl_3$) = 7.68−7.64 (2H, m), 7.45−7.41 (2H, m), 7.32−7.28 (4H, m), 7.26−7.23 (4H, m), 7.18−7.12 (6H, m), 5.18 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 147.3 (2 × C), 145.9 (2 × C), 133.6 (2 × C), 133.2 (2 × C), 130.6 (2 × C), 128.1 (4 × CH), 127.8 (4 × CH), 127.6 (2 × CH), 126.0 (2 × CH), 124.5 (2 × CH), 124.3 (2 × CH), 118.9 (2 × C), 113.0 (2 × CH), 24.0 (CH_2) ppm; HRMS (ESI) calcd for $C_{31}H_{21}N_4S_2$ $[M + H]^+$ 513.1208, found 513.1195.

*Bis(2-(p-tolyl)phenylbenzo[d]imidazo[2,1-b]thiazol-3-yl)methane (**2y**):* white solid (208 mg, 68%); mp 314−316 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3392, 3019, 1645, 1522, 1403, 1069, 928, 831, 669, 626; δ_H (400 MHz; $CDCl_3$) 7.66−7.64 (2H, m), 7.43−7.39 (2H, m), 7.30−7.25 (4H, m), 7.12 (4H, d, J = 7.9 Hz), 6.93 (4H, d, J = 7.8 Hz), 5.13 (2H, s), 2.28 (6H, s) ppm; δ_C (100 MHz; $CDCl_3$) 147.2 (2 × C), 145.9 (2 × C), 137.2 (2 × C), 133.2 (2 × C), 130.7 (2 × C), 130.5 (2 × C), 128.5 (4 × CH), 128.0 (4 × CH), 125.9 (2 × CH), 124.4 (2 × CH), 124.2 (2 × CH), 118.8 (2 × C), 113.0 (2 × CH), 24.0 (CH_2), 21.2 (2 × CH_3) ppm; HRMS (ESI) calcd for $C_{33}H_{25}N_4S_2$ $[M + H]^+$ 541.1521, found 541.1506.

*2-(4-Bromophenyl)-6-chloro-3-((2-phenylimidazo[1,2-a]pyridin-3-yl)methyl)imidazo[1,2-a]pyridine (**3al**):* orange solid (244 mg, 31%); mp 214−216 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3019, 1602, 1522, 1476, 1070, 830, 669, 626; δ_H (400 MHz; $CDCl_3$) = 7.72 (2H, d, J = 7.3 Hz), 7.65−7.60 (4H, m), 7.57−7.49 (3H, m), 7.45−7.40 (3H, m), 7.30 (1H, d, J = 6.8 Hz), 7.11−7.08 (1H, m), 7.03 (1H, dd, J = 9.5, 1.8 Hz), 6.53 (1H, t, J = 6.8 Hz), 4.90 (2H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 145.2 (C), 144.7 (C), 143.9 (C), 143.4 (C), 134.0 (C), 132.9 (C), 132.1 (2 × CH), 130.3 (2 × CH), 129.1 (2 × CH), 129.0 (2 × CH), 128.5 (CH), 126.1 (CH), 124.6 (CH), 123.5 (CH), 122.9 (C), 122.0 (CH), 120.8 (C), 117.8 (2 × CH), 115.3 (C), 113.5 (C), 112.6 (CH), 19.7 (CH_2) ppm; HRMS (ESI) calcd for $C_{27}H_{19}BrClN_4$ $[M + H]^+$ 513.0482, found 513.0476.

*6,8-Dichloro-3-((2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)methyl)-2-phenylimidazo[1,2-a]pyridine (**3kh**):* white solid (192 mg, 29%); mp 174−176 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3019, 1602, 1522, 1420, 1022, 928, 668, 626; δ_H (400 MHz; $CDCl_3$) = 7.80 (2H, d, J = 7.1 Hz), 7.65 (2H, d, J = 8.6 Hz), 7.56−7.52 (3H, m), 7.47 (1H, br t, J = 7.2 Hz), 7.33 (1H, d, J = 1.6 Hz), 7.27 (1H, d, J = 6.9 Hz), 7.13 (1H, d, J = 1.6 Hz), 7.09−7.04 (3H, m), 6.49 (1H, t, J = 6.8

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J. Org. Chem. 2016, 81, 7626−7634

Hz), 4.90 (2H, s), 3.88 (3H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 160.0 (C), 145.6 (C), 145.1 (C), 144.5 (C), 141.0 (C), 133.6 (C), 130.3 (2 × CH), 129.2 (2 × CH), 129.1 (2 × CH), 128.8 (CH), 126.4 (C), 124.6 (CH), 124.5 (CH), 123.6 (CH), 123.4 (C), 121.1 (CH), 119.6 (C), 117.6 (CH), 117.2 (C), 114.5 (2 × CH), 113.1 (C), 112.4 (CH), 55.5, 19.7 (CH_2) ppm; HRMS (ESI) calcd for $C_{28}H_{21}Cl_2N_4O$ $[M + H]^+$ 499.1092, found 499.1080.

6-Bromo-3-((2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)-methyl)-2-phenylimidazo[1,2-a]pyridine (**3hi**): white solid (182 mg, 27%); mp 194−196 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3683, 3389, 3019, 1634, 1522, 1403, 1069, 928, 831, 627; δ_H (400 MHz; $CDCl_3$) = 7.78 (2H, d, J = 7.2 Hz), 7.69 (2H, d, J = 8.7 Hz), 7.56−7.44 (5H, m), 7.38 (1H, d, J = 9.5 Hz), 7.28 (1H, d, J = 6.9 Hz), 7.11−7.03 (4H, m), 6.45 (1H, td, J = 6.8, 0.9 Hz), 4.92 (2H, s), 3.88 (3H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 159.9 (C), 145.0 (C), 144.9 (C), 144.4 (C), 143.4 (C), 134.1 (C), 130.4 (2 × CH), 129.08 (2 × CH), 129.0 (2 × CH), 128.6 (CH), 127.8 (CH), 126.5 (C), 124.4 (CH), 124.3 (CH), 123.7 (CH), 118.0 (CH), 117.5 (CH), 115.3 (C), 114.6 (2 × CH), 113.5 (C), 112.2 (CH), 107.0 (C), 55.5, 19.5 (CH_2) ppm; HRMS (ESI) calcd for $C_{28}H_{22}BrN_4O$ $[M + H]^+$ 509.0977, found 509.0977.

6-(4-Chlorophenyl)-5-((2-(4-methoxyphenyl)imidazo[1,2-a]-pyridin-3-yl)methyl)imidazo[2,1-b]thiazole (**3hu**): brown solid (219 mg, 35%); mp 234−236 °C; FT-IR (KBr, ν_{max}/cm^{-1}) 3387, 3019, 1636, 1403, 1215, 1069, 929, 831, 668; δ_H (400 MHz; $CDCl_3$) = 7.74 (2H, d, J = 8.7 Hz), 7.69 (2H, d, J = 8.4 Hz), 7.57 (1H, d, J = 9.0 Hz), 7.46 (2H, d, J = 8.4 Hz), 7.34 (1H, d, J = 6.9 Hz), 7.13−7.09 (1H, m), 7.04 (2H, d, J = 8.7 Hz), 6.56 (1H, td, J = 6.8, 0.7 Hz), 6.51 (1H, d, J = 4.6 Hz), 6.45 (1H, d, J = 4.6 Hz), 4.86 (2H, s), 3.88 (3H, s) ppm; δ_C (100 MHz; $CDCl_3$) = 159.8 (C), 149.5 (C), 145.0 (C), 143.9 (C), 143.7 (C), 133.7 (C), 133.0 (C), 129.9 (2 × CH), 129.4 (2 × CH), 129.1 (2 × CH), 126.6 (C), 124.6 (CH), 123.3 (CH), 117.5 (CH), 117.4 (CH), 116.8 (C), 114.6 (2 × CH), 114.0 (C), 112.9 (CH), 112.6 (CH), 55.5, 20.9 (CH_2) ppm; HRMS (ESI) calcd for $C_{26}H_{20}ClN_4OS$ $[M + H]^+$ 471.1046, found 471.1076.

2-Phenylimidazo[1,2-a]pyridine-3-carbaldehyde (**4a**):[6a] white solid (172 mg, 50%); mp 129−131 °C (lit.[6a] mp 128−130 °C); FT-IR (KBr, ν_{max}/cm^{-1}) 3401, 3019, 1630, 1328, 1211, 831, 758, 669; δ_H (400 MHz; $CDCl_3$) 10.06 (1H, s), 9.66 (1H, dt, J = 6.8, 1.1 Hz), 7.84−7.79 (3H, m), 7.60−7.50 (4H, m), 7.12 (1H, td, J = 6.9, 1.2 Hz); δ_C (100 MHz; $CDCl_3$) 179.6, 158.4 (C), 147.8 (C), 132.4 (C), 130.5 (CH), 129.9 (3 × CH), 128.98 (2 × CH), 128.91 (CH), 120.8 (C), 117.5 (CH), 115.3 (CH); HRMS (ESI) calcd for $C_{14}H_{11}N_2O$ $[M + H]^+$ 223.0871, found 223.0870.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01355.

^1H and ^{13}C NMR and HRMS spectra of all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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