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Ru-Catalyzed Selective Catalytic Methylation and Methylenation Reaction Employing Methanol as the C1 Source

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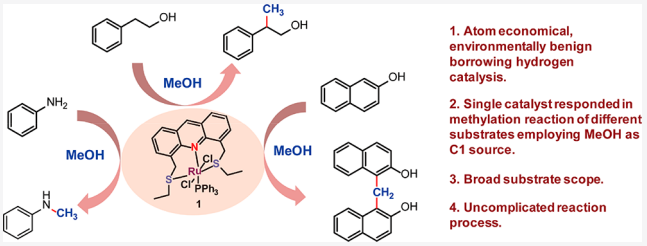
ABSTRACT: Methanol can be employed as a green and sustainable methylating agent to form C−C and C−N bonds via borrowing hydrogen (BH) methodology. Herein we explored the activity of the acridine-derived SNS-Ru pincer for the activation of methanol to apply it as a C1 building block in different reactions. Our catalytic system shows great success toward the β-C(sp^3)-methylation reaction of 2-phenylethanols to provide good to excellent yields of the methylated products. We investigated the mechanistic details, kinetic progress, and temperature-dependent product distribution, which revealed the slow and steady generation of in situ formed aldehyde, is the key factor to get the higher yield of the β-methylated product. To establish the environmental benefit of this reaction, green chemistry metrics are calculated. Furthermore, dimerization of 2-naphthol via methylene linkage and formation of *N*-methylation of amine are also described in this study, which offers a wide range of substrate scope with a good to excellent yield.



INTRODUCTION

The methyl group is an important functionality found in many biologically active molecules[1] and plays a significant role in regulating the pharmaceutical properties[2] of a molecule. A report says that around 67% of the top-selling drugs of 2011 contain at least one methyl group that is bound to a carbon, nitrogen, or oxygen atom.[3] In particular, the installation of methyl groups can dramatically improve IC_{50} values of a specific drug.[3,4] Therefore, the direct introduction of a methyl group to such moiety in a single step and in a greener way is an important area of scientific research. Methanol can be renewably obtained from lignocellulosic biorefinery.[5] Thus, the applicability of methanol as a methylating agent relative to commonly employed methylating reagents such as diazomethane, dimethyl sulfate, and iodomethane[6] is highly desirable as methanol is considered as a sustainable and atom economical C1 source.[7] Recently, (de)hydrogenative[8] construction of C−C, C−N, and C−S bonds using renewable alcohols has attracted enormous attention due to its atom-efficient and environmentally benign nature. However, methylation reactions are quite challenging over alkylation[8c,9] as a large enthalpy (ΔH for methanol is +84 kJ mol^{-1})[10] is required to convert methanol to formaldehyde via dehydrogenation. Therefore, the development of new catalytic protocols for selective methylation is highly demanding.

The β-methylation of aliphatic alcohols plays an important role in the synthesis of higher or branched alcohols, in particular for alcohol biofuels.[10b,11] The coupling of methanol and primary alcohol[12] or secondary alcohol[12f,13] is highly challenging compare to α-methylation of ketone[14] as it involves multiple reaction steps[12a] including dehydrogenation, aldol condensation, and hydrogenation.[12a] In 2014, Beller and co-workers[12a] first demonstrated β-methylation of 2-arylethanols. The cooperative reactivity of Ru-MACHO and Shvo's diruthenium complex is highly essential to afford the desired β-methylated product in good yield. In 2019, Leitner and his group demonstrated the selective β-methylation of 2-arylethanols in the presence of a single Ru(II) catalyst [RuH(CO)(BH_4)(HN($C_2H_4PPh_2$)$_2$)]. Two equivalents of NaOMe is essential to promote the reaction at 150 °C.[12b] Very recently, Fe-catalyzed β-methylation of 2-arylethanols was reported by Renaud[12c] and Morrill,[12d] utilizing either a mixture of bases or applying of trimethylamine N-oxide additive and base (2 equiv). In 2020, Leitner demonstrated Mn-catalyzed β-methylation of 2-arylethanols at higher temperatures and high base loading.[12e] Heterogeneous catalysts such as Iridium nanocluster[12f] and platinum on carbon[12g] are utilized for this reaction. Thus, the development of a more general sustainable protocol for methylation reaction is an area of importance. Recently, we explored the applicability of air-stable Ru complexes (Figure 1) in the de(hy)drogenative reactions.[15] Engrossed by the salient benefit of methylation reaction using methanol and motivated our recent work on multistep de(hydrogenative) transformation,[16] herein we demonstrated

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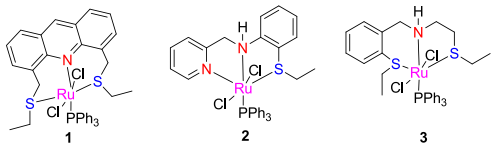
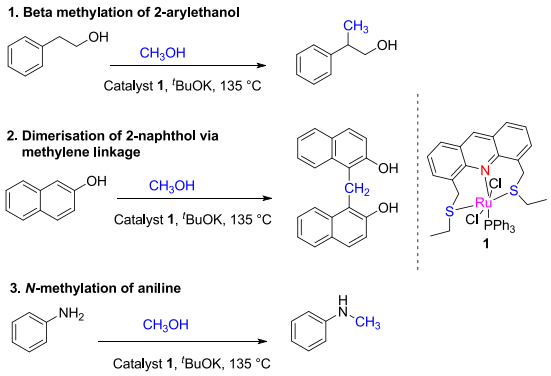


Figure 1. Ruthenium pincer complexes.

the β-methylation of alcohols. Furthermore, the protocol expanded toward selective mono *N*-methylation reaction of amine and dimerization of 2-naphthol via methylene linkage to present the versatility of the developed catalyst (Scheme 1).

Scheme 1. C-Methylation and *N*-Methylation Reactions Using Methanol as the Methylating Agent

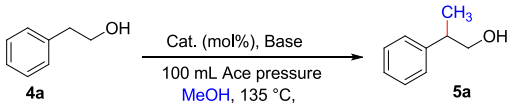


RESULT AND DISCUSSION

In our initial experiments, the methylation of 2-phenylethanol (**4a**) was selected as a model system to find out the optimum reaction conditions. When 2-phenylethanol (1 mmol), MeOH (3 mL), KOH (1 mmol) was heated at 135 °C for 48 h in a100 mL Ace pressure tube in the presence of 2 mol % catalyst **1**, 68% 2-phenylpropan-1-ol (**5a**) was obtained (Table 1, entry 1). Interestingly, a lower amount of MeOH (1 mL) under similar conditions improved the yield of **5a** to 98% (Table 1, entry 2). However, a lower reaction time (36 h) resulted in a decrease of the yield of **5a** (Table 1, entry 3). On the other hand, within 36 h, quantitative conversion was observed when ^{t}BuOK was used as a base (Table 1, entry 5). Decreasing the amount of ^{t}BuOK (0.5 mmol) led to lower conversions of the product even after 48 h. (Table 1, entry 8). Bases like ^{t}BuONa and NaOH gave a moderate yield (Table 1, entries 9 and 10) under similar reaction conditions, whereas K_2CO_3 failed to give the desired product (Table 1, entry 11). Without the presence of any base, catalyst **1** failed to activate the alcohols; similarly, in the absence of catalyst **1**, 1 mmol ^{t}BuOK did not give any desired 2-phenylpropan-1-ol (**5a**) (Table 1, entries 13 and 14). Cat. **2** and cat. **3** are incompetent toward this β-C(sp^3)-methylation reaction (Table 1, entries 16 and 17).

With optimized reaction conditions in hand (Table 1, entry 5), the scope of the Ru-catalyzed β-C(sp^3)-methylation of alcohols was explored (Scheme 2). Gratifyingly, high conversions and good yields were observed for substituted 2-arylethanols (Scheme 2, **5a**−**5m**). Electron-donating substituents such as 2-(*p*-tolyl)ethanol (**4b**) and 2-(4-methoxyphenyl)-ethanol (**4c**) afforded excellent yields of the corresponding methylated products (87%, **5b**; 81%, **5c**). 2-(2,4,6-Trimethoxyphenyl)propan-1-ol afforded 92% yield (**5d**), indicating that the increased steric effect provided by aryl

Table 1. Optimization of the Reaction Conditions for the β-Methylation of 2-Phenylethanol[a]



entry	cat. (mol %)	base (mmol)	MeOH (mL)	time (h)	yield (%)[b]
1	**1** (2 mol %)	KOH (1)	3	48	68
2	**1** (2 mol %)	KOH (1)	1	48	98
3	**1** (2 mol %)	KOH (1)	1	36	70
4	**1** (2 mol %)	^{t}BuOK (1)	1	48	99
5	**1** (2 mol %)	^{t}BuOK (1)	1	36	99
6	**1** (2 mol %)	^{t}BuOK (1)	1	24	70
7	**1** (2 mol %)	^{t}BuOK (0.5)	1	36	66
8	**1** (2 mol %)	^{t}BuOK (0.5)	1	48	70
9	**1** (2 mol %)	^{t}BuONa (1)	1	36	75
10	**1** (2 mol %)	NaOH (1)	1	36	50
11	**1** (2 mol %)	K_2CO_3 (1)	1	36	
12	**1** (1 mol %)	^{t}BuOK (1)	1	48	70
13	**1** (2 mol %)		1	36	
14		^{t}BuOK (1)	1	36	
15[c]	**1** (2 mol %)	^{t}BuOK (1)	1	48	75
16	**2** (2 mol %)	^{t}BuOK (1)	1	36	
17	**3** (2 mol %)	^{t}BuOK (1)	1	36	
18[d]	**1** (2 mol %)	^{t}BuOK (1)	1	36	56

[a]Reaction conditions: alcohol (1 mmol), cat. **1** (2 mol %), base (1 mmol), MeOH (1 mL), 135 °C, 100 mL Ace pressure tube. [b]NMR yield using acetonitrile as an internal standard. [c]110 °C. [d]30 mL Ace pressure tube.

substitution at the 2- and 6-positions does not hinder β-C(sp^3)-methylation. Fluoro- and chloro-substituted compounds were well tolerated. However, 2-(4-bromophenyl)-ethanol gave the corresponding product in a moderate yield 60% (**5g**) along with 20% (**5a**) dehalogenated product. Heterocyclic alcohol such as thiophene-substituted ethanol was smoothly converted to the corresponding methylated product (**5h**) with a high yield, 90%. The extended aromatic system, 2-naphthylethanol, responded well under the reaction conditions. Unfortunately, 2-phenoxyethan-1-ol (**4k**) failed to give any product. When 2-(4-aminophenyl)ethanol was used as a substrate, both β-C(sp^3)-methylation and *N*-methylation occurred, providing **5l** in 60% isolated yield together with some *N*-methylated product (**5m**), indicating that *N*-methylation is much faster than the β-C(sp^3)-methylation reaction. 2-Phenylethanol having a −CN or $-NO_2$ group in the aromatic nucleus failed to give the desired product. Methylation of 3-(4-methoxyphenyl)propan-1-ol (Scheme 2) afforded **5p** in 55% isolated yield. It is important to note that the starting material 3-(4-methoxyphenyl)propan-1-ol was also prepared by reacting 4-methoxybenzyl alcohol with ethanol via BH reaction,[17] employing our developed catalyst.

For the preparative scale synthesis of **5a**, we were able to lower the catalyst loading (1 mol %) as well as the **4a**/MeOH ratio, and 100% conversion of **4a** with a high isolated yield (86%) of **5a** was obtained. The green chemistry metrics[18] of this reaction with an E-factor of 1.34, 88% atom economy, 76% atom efficiency, 100% carbon efficiency, and 76% reaction mass efficiency clearly exposed the technical and environmental benefits of this methodology (Scheme 3).

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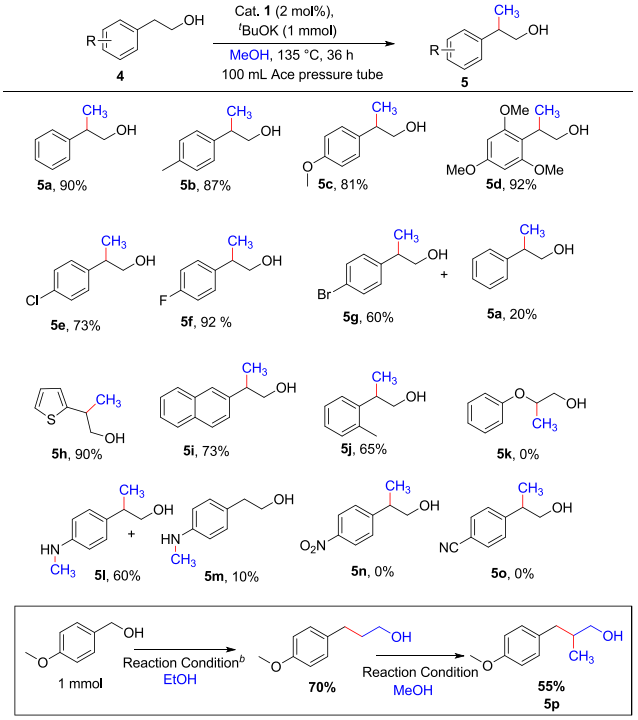
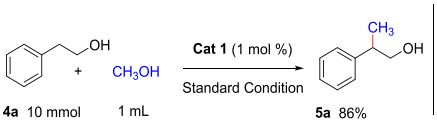
Scheme 2. Substrate Scope for β-Methylation of 2-Phenylethanols[a]



[a]Reaction condition: alcohol (1 mmol), cat. **1** (2 mol %), ^{t}BuOK (1 mmol), MeOH (1 mL), 135 °C, 100 mL Ace pressure tube. [b]Reaction condition: alcohol (2 mmol), cat. **1** (1 mol %), ^{t}BuOK (1 mmol), EtOH (1 mL), 135 °C, 100 mL Ace pressure tube.

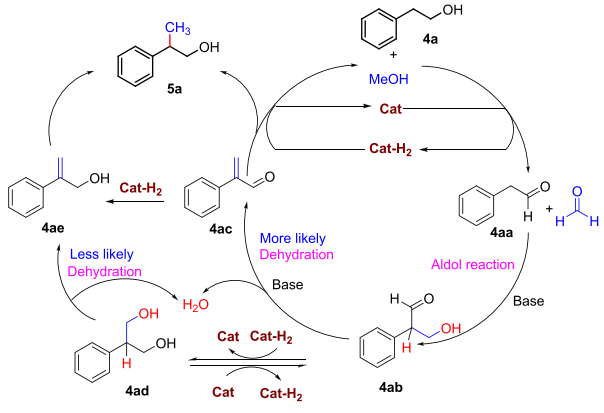
Scheme 3. Green Chemistry Metrics



E-factor:	1.34
Atom Economy:	88%
Atom efficiency:	76%
Carbon efficiency:	100%
Reaction mass efficiency:	76%

The β-C(sp^3)-methylation method may likely follow a borrowing-hydrogen mechanism[12a,g] (Scheme 4). First, dehydrogenation of 2-phenylethanol and methanol leads to the formation of **4aa** and formaldehyde, which can form condensation product **4ab**. Compound **4ab** will eventually transform to **4ae** either via dehydration followed by hydrogenation of **4ac** or first hydrogenation followed by dehydration

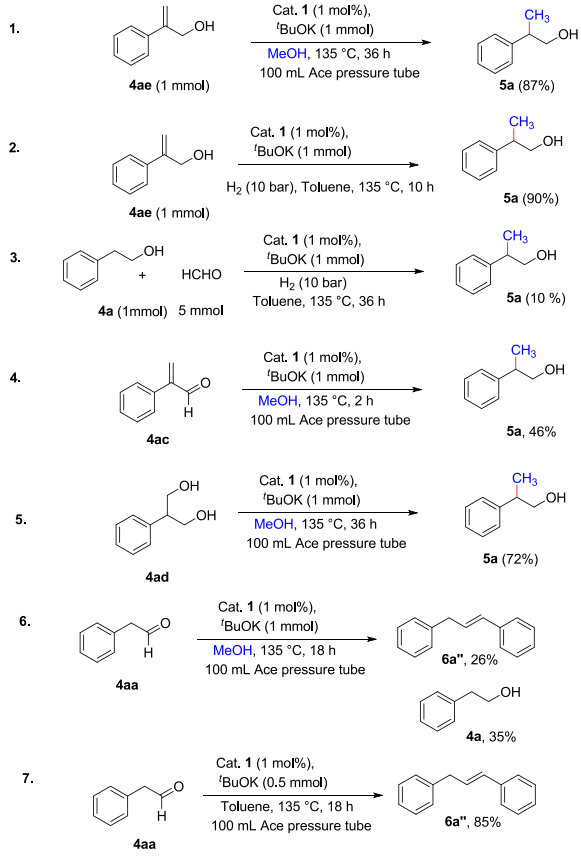
Scheme 4. Proposed Reaction Mechanism



of **4ad**. Next, **4ae** will lead to the formation of **5a** via the hydrogen-autotransfer process.

We carried out some control experiments (Scheme 5) to shed light on the proposed mechanism. When preformed 2-

Scheme 5. Controlled Experiments



phenylprop-2-en-1-ol **4ae** was subjected to the "standard" reaction conditions, β-C(sp^3)-methylated product **5a** was formed in 87% yield. The compound **4ae** was also converted to **5a** (90%) in the presence of cat. **1** and molecular H_2. This clearly indicates the involvement of compound **4ae** as an intermediate in the β-C(sp^3)-methylation reaction. Intermediate **4ad** under the standard reaction conditions smoothly converted to **5a** (72%), which underpins **4ad** and might be another possible intermediate. The reaction with 2-phenylethanol **4a** and formaldehyde in a hydrogen atmosphere (10 bar) in toluene keeping other conditions unaltered gives β-C(sp^3)-methylated product **5a** with 10% yield, supporting that formaldehyde is another plausible intermediate. The low yield of this experiment was possibly because of the low solubility of formaldehyde in toluene[12e] and the hydrogenation reaction of formaldehyde in the presence of a hydrogen atmosphere. When the intermediate **4ac** was subjected to the standard reaction conditions, **5a** was formed with 46% yield after 2 h. Under standard reaction conditions, phenylacetaldehyde (**4aa**) gave deoxygenative coupling[19] product (**6a**) with 26% yield and 2-phenylethanol **4a** (35%). Thus, slow generation of phenylacetaldehye from **4a** is important to form the desired product **5a** in a high yield.

To gain further mechanistic insight, a deuterium-labeling experiment with CD_3OD was carried out (Scheme 6). The β-CD_3 group incorporation within alcohol yielded 76% β-CD_3-

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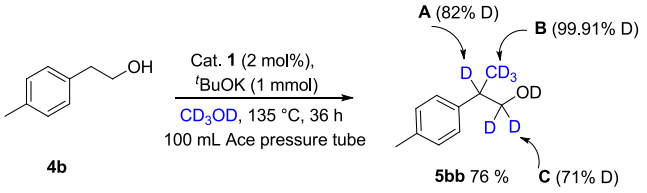
Scheme 6. Labeling Experiments with Deuterated Methanol



labeled 2-phenylethanol with 99.91% deuterium incorporation, in addition to significant deuterium incorporation at the α-(71% D) and β-(82% D) positions. This experiment confirmed methanol acting as the methylating agent and provided the support for the borrowing hydrogen mechanism (Scheme 6).

Next, we have studied the time-dependent product distribution of the catalytic reaction of β-methylation of 2-phenylethanol (Figure 2). The concentrations of the substrate

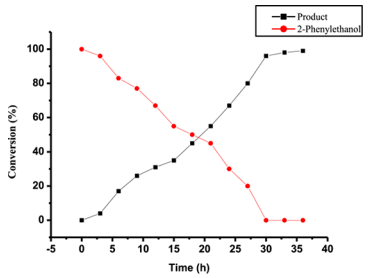


Figure 2. Time-dependent product distribution in β-methylation of 2-phenylethanol with methanol at 135 °C catalyzed by complex **1**.

(2-phenylethanol **4a**) gradually decreased with time, and concurrently, the concentration of product **5a** increased at 135 °C. From the curve, it is clear that very slow conversion of 2-phenylethanol happened with the optimum reaction conditions, and it takes 30 h to complete the reaction. Subsequently, we have checked the temperature-dependent product distribution of β-methylation of 2-phenylethanol (Figure 3). At temperatures 90, 110, and 135 °C, the reaction

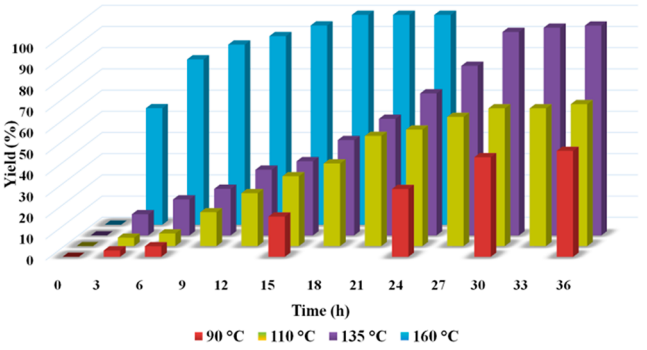
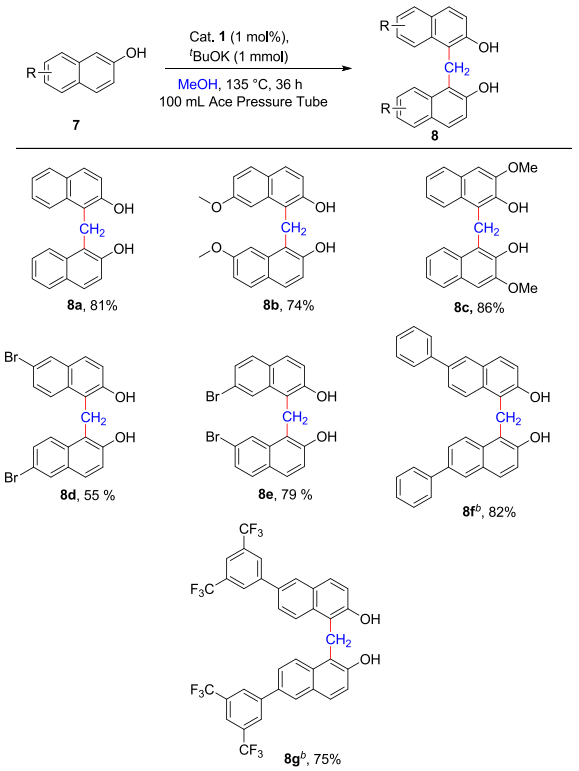


Figure 3. Temperature-dependent product distribution in β-methylation of 2-phenylethanol with methanol catalyzed by complex **1**.

proceeded slowly and steadily, whereas, at a higher temperature (160 °C), a sharp rise in product formation was observed. Within 3 h, 55% conversion was noticed, and it took only 15 h to complete the reaction. Therefore, the high temperature has some salient effect on product distribution over time.

To expand the scope of methanol activation, next, we are interested in investigating the reactivity of methanol with β-naphthol to synthesize 1,1′-methylene-bis(2-naphthol). These compounds frequently occur in various biologically active compounds[20] and are used as versatile synthetic intermediates and anion receptors.[20a] 1,1′-Methylene-di(2-naphthol) radiolabeled with carbon-11 (ST1859) also used as a drug for the treatment of Alzheimer's disease.[21] Kirchner's group showed the possibility (one example) of the formation of 1,1′-methylene-bis(2-naphthol) in their work on three-component aminomethylation reaction of 2-naphthol.[22] Herein, we applied our protocol to synthesize several important 1,1′-methylene-bis(2-naphthol) derivatives. When 2-naphthol (1 mmol), tBuOK (1 mmol), MeOH (1 mL), and Cat. **1** (1 mol %) were refluxed in Ace pressure tube at 135 °C for 36 h, 1,1′-methylenebis(naphthalen-2-ol) **8a** was isolated in 81% yield (Scheme 7). 2-Naphthol with an electron-donating group like

Scheme 7. Substrate Scope for Methylation of 2-Naphthol[a]



[a]Reaction conditions: 2-naphthol (1 mmol), cat. **1** (1 mol %), tBuOK (1 mmol), MeOH (1 mL), 36 h, 135 °C, 100 mL Ace pressure tube. [b]0.5 mmol scale.

7-methoxynaphthalen-2-ol and 3-methoxynaphthalen-2-ol also participated well in the reaction and produced 1,1′-methylenebis(7-methoxynaphthalen-2-ol) **8b** and 1,1′-methylenebis(3-methoxynaphthalen-2-ol) **8c** in good yields. Electron-withdrawing groups like 6-bromo and 7-bromo napthalen-2-ol gave moderate to good yields (**8d**, 55%; **8e**, 79%).

Gram-scale synthesis of 1,1′-methylenebis(naphthalen-2-ol) with catalyst loading 0.5 mol %, using MeOH 2 mL, giving 69% isolated yield. The green chemistry metrics for this reaction with an E-factor of 2.24, 94% atom economy, 65% atom efficiency, 100% carbon efficiency, and 65% reaction

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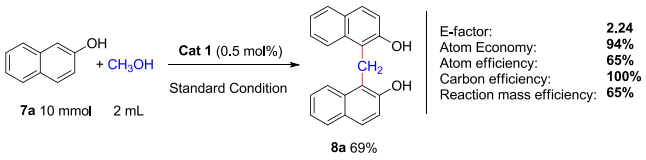
mass efficiency clearly exposed the synthetic utility of this methodology (Scheme 8).

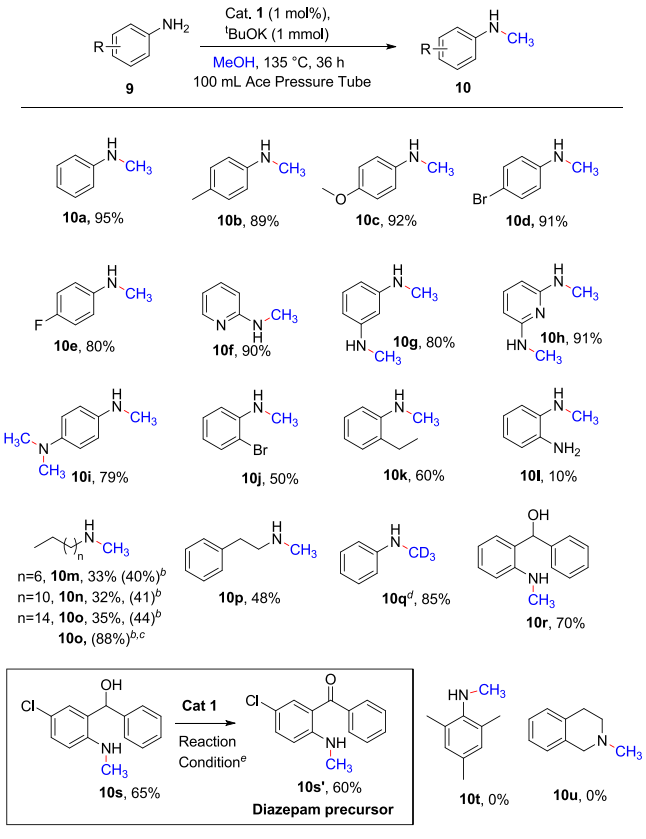
Scheme 8. Green Chemistry Metrics



Next, to check the versatility of our catalyst, the direct *N*-methylation of amines[17e,23,24] was investigated as this is considered as one of the most important transformations in the synthesis of natural products, fine chemicals, and pharmaceuticals.[25] Thus, when a mixture of aniline (1 mmol), KOH (0.5 mmol), cat. **1** (1 mol %), and MeOH was refluxed at 135 °C in a 100 mL Ace pressure tube for 48 h, 50% *N*-methylaniline (**10a**) (Table S1) was formed. The reaction is selective toward monomethylation as no *N*,*N*-dimethyl aniline was not detected. The yield of **10a** was further improved to 95% when the base amount increased to 2 mmol (Table S1, entry 3). A quick screening of different bases (Table S1, entries 4, 5, and 8−10) revealed that ^{t}BuOK is a better choice over KOH.

After having the optimized reaction condition, we explored the substrate scope of the *N*-methylation reaction (Scheme 9).

Scheme 9. Substrate Scope for Methylation of Amine[a]

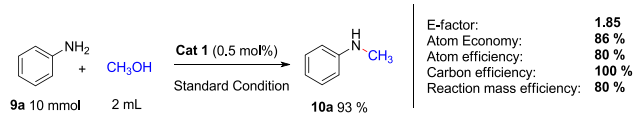


[a]Reaction conditions: aniline (1 mmol), cat. **1** (1 mol %), ^{t}BuOK (1 mmol), MeOH (1 mL), 135 °C, 36 h, 100 mL Ace pressure tube. [b]Yield in the parentheses is the NMR yield. [c]5 mol % catalyst. [d]48 h. [e]**10p** (0.5 mmol), cat. **1** (1 mol %), ^{t}BuOK (5 mol %), toluene (1 mL), 135 °C, 24 h, argon.

Aniline with electron-donating and electron-withdrawing groups responded well, giving excellent yields (80−92%) of the corresponding products (**10b**−**10e**). 2-Aminopyridine was also well-tolerated and afforded 90% yield **10f**. Benzene-1,3-diamine and pyridine-2,6-diamine were also converted to corresponding methylated products N^1,N^3-dimethylbenzene-1,3-diamine (**10g**, 80%) and N^2,N^6-dimethylpyridine-2,6-diamine (**10h**, 91%) in good yields. Furthermore, when two $-NH_2$ groups are para to each other in an aromatic ring, then double methylation occurs in one amine group, and mono methylation occurs on the other amine group, giving N^1,N^1,N^4-trimethylbenzene-1,4-diamine **10i** (79%). Substituents at the *ortho* position suppressed the product yield (**10j**−**10l**) due to the steric effect. More sterically demanding 2,4,6-trimethylaniline did not respond toward this reaction. Only moderate yields of the monomethylated products were isolated (32−35%) when aliphatic amines such as octylamine, dodecylamine, and hexadecylamine were used as substrates. Under the optimized reaction conditions in the presence of 1 mol % cat. **1**, hexadecylamine converted to the corresponding monomethylated product **10o** in 44% yield (35% isolated), whereas no dimethylated product was detected. Interestingly, when 5 mol % of cat. **1** was used, 88% conversion (NMR) to the monomethylated product was observed with a small amount (8%) of dimethylated product. Furthermore, when monomethylated product **10o** was separately treated with MeOH under the optimized reaction condition in the presence of 2 mol % cat. **1** only 10% dimethylated product was formed. When secondary amines such as 1,2,3,4-tetrahydroisoquinoline were subjected to the methylation reaction, no methylated tertiary amine (**10u**) was observed. When (2-aminophenyl)-(phenyl)methanone and (5-chloro-2-(methylamino)phenyl)-(phenyl)methanol were used as substrates, **10r** and **10s** were obtained in 70% and 65% yields, respectively. Here, the carbonyl group was also hydrogenated due to the presence of excess H_2 in the reaction medium. Nevertheless, when dehydrogenative reaction conditions were employed, using cat. **1**, **10s** can be easily converted to the biologically important[26] diazepam precursor (**10s′**) with 60% isolated yield.

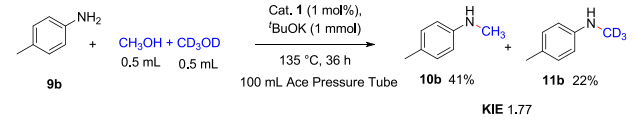
For the preparative scale synthesis of *N*-methylaniline, the green chemistry metrics with an E-factor of 1.85, 86% atom economy, 80% atom efficiency, 100% carbon efficiency, and 80% reaction mass efficiency clearly exposed the technical and environmental benefits of this methodology (Scheme 10).

Scheme 10. Green Chemistry Metrics



In order to gain insight, kinetic isotope experiments (KIE) were carried out (Scheme 11). First, a mixture of CD_3OD/

Scheme 11. Labeling Experiments with Deuterated Methanol



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CH_3OH (1:1, v/v) was used in a competitive experiment. In a 100 mL Ace pressure tube, a mixture of CD_3OD (0.5 mL) and CH_3OH (0.5 mL) was reacted with *p*-toluidine under standard conditions. The observed product ratio of the deuterated and nondeuterated products was determined by ^1H NMR, which indicates the KIE value ~1.77.

CONCLUSION

In summary, we have developed an acridine-derived air-stable ruthenium pincer complex catalyzed *β*-methylation of 2-arylethanol and *N*-methylation of amines using methanol as a C1 building block via the borrowing hydrogen approach. In addition, dehydrogenative dimerization of 2-naphthol via methylene linkage was also illustrated. This straightforward protocol applies to a wide range of substrates giving well to excellent isolated yields. Kinetics and mechanistic investigations help to know the reaction pathway. A temperature-dependent kinetic profile *β*-methylation of 2-phenylethanol is also demonstrated. The technical and environmental benefit of this methodology was revealed, which clearly shows high atom economy and atom efficiency and 100% carbon efficiency. This work expands the scope and builds on our previous successful protocols on borrowing hydrogen catalysis.[16]

EXPERIMENTAL SECTION

General Information. Unless otherwise mentioned, all chemicals were purchase from common commercial sources and used as received. $RuCl_2(PPh_3)_3$ was purchased from Sigma-Aldrich. All solvents were dried by standard procedures.[27] Solvents such as MeOH are typically dried by heating over iodine-activated magnesium and storage of the methanol over 20% m/v 3 Å molecular sieves. The catalyst preparation was carried out under an argon atmosphere with freshly distilled dry THF or dichloromethane. All catalytic reactions were carried out under an argon atmosphere using dry glassware and standard syringe/septa techniques. DRX-400 Varian and Bruker Avance III 600 and 400 spectrometers were used to record ^1H and $^{13}C\{^1H\}$ NMR, respectively. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane; spin−spin coupling constants (J) are expressed in hertz (Hz), and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, and br s = broad singlet. Column chromatography was done with SRL silica gel 100−200 mesh. Analytical thin-layer chromatography (TLC) was carried out on silica gel plates (silica gel 60 F_{254}) that were visualized by exposure to ultraviolet light and an aqueous solution of *p*-anisaldehyde. Compound **4a** is commercially available. Compounds **4a**, **7a**, **7c**, **7d**, **7e**, and **9a−9q** were commercially available. Compounds **4b−4n**[28a] were known compounds synthesized from the corresponding phenyl acetic acid derivatives according to the literature procedure. Compounds **4ae**,[28b] **4ac**,[28c] **4ad**,[28d] **7b**,[28e] and **7f−7g**[28f] were also synthesized following the literature procedure.

General Procedure for the *β*-C(sp^3)-Methylation of 2-Phenylethanol Derivatives. 2-Phenylethanol (1 mmol, 1 equiv), MeOH (1 mL), ^{t}BuOK (1 mmol, 1 equiv), and complex **1** (15.2 mg, 0.02 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere. The tube was sealed with a screw cap, then it was immersed in an oil bath at 135 °C, and the mixture was stirred at this temperature for 36 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane, and filtered over a plug of Celite. The solvent was evaporated under reduced pressure, and the residue obtained was purified by column chromatography (hexane/ethyl acetate 50:1) on silica gel to afford the desired product.

General Procedure for the Methylation of 2-Naphthol. 2-Naphthol (1 mmol, 1 equiv), MeOH (1 mL), ^{t}BuOK (1 mmol, 1 equiv), and complex **1** (7.6 mg, 0.01 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere. The tube was sealed with a screw cap, then it was immersed in an oil bath at 135 °C, and the mixture was stirred at this temperature for 36 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane, and filtered over a plug of Celite. The solvent was evaporated under reduced pressure, and the residue obtained was purified by column chromatography (hexane/ethyl acetate) on silica gel to afford the desired product.

General Procedure for the Methylation of Amines. Aniline (1 mmol, 1 equiv), MeOH (1 mL), ^{t}BuOK (1 mmol, 1 equiv), and complex **1** (7.6 mg, 0.01 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere. The tube was sealed with a screw cap, then it was immersed in an oil bath at 135 °C, and the mixture was stirred at this temperature for 36 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane, and filtered over a plug of Celite. The solvent was evaporated under reduced pressure, and the residue obtained was purified by column chromatography (hexane/ethyl acetate/triethylamine 50:1:1) on silica gel to afford the desired product.

Isotopic Labeling Experiments for the *N*-Methylation Reaction. *Competition Reaction.* Aniline (1 mmol, 1 equiv), MeOH (0.5 mL), CD_3OD (0.5 mL), ^{t}BuOK (1 mmol, 1 equiv), and complex **1** (7.6 mg, 0.01 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere. The tube was sealed with a screw cap, then it was immersed in an oil bath at 135 °C, and the mixture was stirred at this temperature for 36 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane, and filtered over a plug of Celite. The solvent was evaporated under reduced pressure, and the residue obtained was purified by column chromatography (hexane/ethyl acetate/triethylamine 50:1:1) on silica gel to afford the mixture of **10b** and **11b** in 63% yield.

*Gram-Scale Synthesis of **5a**.* 2-Phenylethanol (10 mmol), MeOH (1 mL), ^{t}BuOK (10 mmol), and complex **1** (2 mol %, 0.20 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere, and the general procedure for the *β*-C(sp^3)-methylation of 2-phenylethanol derivatives was used. Yield: 86%, 1.04 g.

*Gram-Scale Synthesis of **8a**.* 2-Naphthol (10 mmol), MeOH (2 mL), ^{t}BuOK (10 mmol), and complex **1** (0.5 mol %, 0.05 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere, and the general procedure for the methylation of 2-naphthol was used. Yield: 69%, 1.03 g.

*Gram-Scale Synthesis of **10a**.* Aniline (10 mmol), MeOH (1 mL), ^{t}BuOK (10 mmol), and complex **1** (0.5 mol %, 0.05 mmol) were placed in a 100 mL Ace pressure tube under an argon atmosphere and the general procedure for the methylation of amines was used. Yield: 93%, 0.99 g.

*2-Phenylpropan-1-ol (**5a**).*[12a] Pale yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 90%, 122.4 mg. ^1H NMR (600 MHz, $CDCl_3$): δ 7.32−7.29 (m, 2H), 7.22−7.19 (m, 3H), 3.64 (d, J = 7.3 Hz, 2H), 2.94−2.86 (m, 1H), 1.95 (br s, 1H), 1.25 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 143.9, 128.5 (2C), 127.5 (2C), 126.5, 68.5, 42.4, 17.6.

*2-(p-Tolyl)propan-1-ol (**5b**).*[12d] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 87%, 130.5 mg. ^1H NMR (600 MHz, $CDCl_3$): δ 7.16−7.13 (m, 4H), 3.69−3.67 (m, 2H), 2.94−2.90 (m, 2H), 2.34 (s, 3H), 1.39 (br s, 1H), 1.26 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 140.6, 136.3, 129.4 (2C), 127.4 (2C), 68.8, 42.1, 21.1, 17.7.

*2-(4-Methoxyphenyl)propan-1-ol (**5c**).*[12a] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 81%, 134.5 mg. ^1H NMR (600 MHz, $CDCl_3$): δ 7.16 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 3.66−3.64 (m, 2H), 2.92−2.88(m, 1H), 1.71 (br s, 1H), 1.24 (d, J = 7.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 158.4, 135.7, 128.5 (2C), 114.1 (2C), 68.9, 55.3, 41.6, 17.8.

*2-(2,4,6-Trimethoxyphenyl)propan-1-ol (**5d**).* Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 92%, 208.0 mg. ^1H NMR (600 MHz, $CDCl_3$): δ 6.43 (s, 2H), 3.85 (s, 6H), 3.85 (s, 3H), 3.67−3.65 (m, 2H), 2.90−2.84 (m, 1H), 1.82 (br s, 1H), 1.24 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 153.3, 139.5, 136.6, 104.2, 68.7, 60.9, 56.1, 42.9, 17.7. HRMS (ESI+): m/z calcd. for $C_{12}H_{19}O_4$: 227.1283 [M + H]+; Found: 227.1288.

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2-(4-Chlorophenyl)propan-1-ol (**5e**).[12a] Pale yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 73%, 124.1 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 3.87−3.39 (m, 2H), 2.96−2.90 (m, 1H), 1.46 (br s, 1H), 1.25 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 142.3, 132.4, 128.9 (2C), 128.8 (2C), 68.6, 41.9, 17.6.

2-(4-Fluorophenyl)propan-1-ol (**5f**).[12a] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 92%, 141.6 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.20−7.16 (m, 2H), 3.64−3.61 (m, 2H), 2.95−2.86 (m, 1H), 1.85 (br s, 1H), 1.24 (d, J = 7.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 161.6 (d, J = 244.3 Hz), 139.5 (d, J = 3.2 Hz), 128.9 (d, J = 7.8 Hz), 115.3 (d, J = 21.0 Hz), 68.6, 41.7, 17.7.

2-(4-Bromophenyl)propan-1-ol (**5g**).[12d] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 60%, 129.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 3.72−3.67 (m, 2H), 2.97−2.92 (m, 1H), 1.36 (br s, 1H), 1.28 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 142.9, 131.8, 129.3 (2C), 126.8 (2C), 68.6, 42.6, 17.6.

2-(Thiophen-2-yl)propan-1-ol (**5h**).[12d] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 90%, 127.8 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16 (d, J = 4.7 Hz, 1H), 6.97−6.93 (m, 1H), 6.87 (d, J = 3.1 Hz, 2H), 3.64 (d, J = 6.3 Hz, 2H), 3.23−3.19 (m, 1H), 1.33 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 147.5, 126.9, 124.0, 123.6, 69.1, 38.2, 18.7.

2-(Naphthalen-2-yl)propan-1-ol (**5i**).[12a] Off-white solid. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 73%, 135.8 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 1.5 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.59−7.48 (m, 3H), 7.45 (d, J = 7.0 Hz, 1H), 3.98−3.84 (m, 3H), 1.58 (br s, 1H), 1.47 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 139.6, 134.1, 132.0, 129.1, 127.2, 126.1, 125.6 (2C), 123.1, 123.1, 68.2, 36.4, 17.9.

2-(o-Tolyl)propan-1-ol (**5j**).[12a] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 65%, 97.5 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.22−7.11 (m, 4H), 3.76−3.67 (m, 2H), 3.29−3.24 (m, 1H), 2.37 (s, 3H), 1.62 (br s, 1H), 1.25 (d, J = 7.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 141.8, 136.5, 130.6, 126.4, 126.3, 125.5, 68.1, 37.3, 19.7, 17.6.

2-(4-(Methylamino)phenyl)propan-1-ol (**5l**).[12d] Pale yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 60%, 99.0 mg. ^{1}H NMR (600 MHz $CDCl_3$): δ 7.05 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 8.5 Hz, 2H), 3.64−3.62 (m, 2H), 2.82 (s, 3H), 1.23 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 148.2, 132.1, 128.3 (2C), 112.82 (2C), 68.9, 41.6, 30.9, 17.8.

2-(4-(Methylamino)phenyl)ethanol (**5m**).[29] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 10%, 15.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.06 (d, J = 8.4 Hz, 2H), 6.59 (d, J = 8.4 Hz, 2H), 3.80 (t, J = 6.5 Hz, 2H), 2.83 (s, 3H), 2.77 (t, J = 6.5 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 148.1, 129.9 (2C), 126.8, 112.8 (2C), 64.1, 38.3, 31.0.

3-(4-Methoxyphenyl)-2-methylpropan-1-ol (**5p**).[30] Colorless oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 55%, 99.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 3.79 (s, 3H), 3.54−3.45 (m, 2H), 2.68 (dd, J = 13.6, 6.4 Hz, 1H), 2.38 (dd, J = 13.6, 8.0 Hz, 1H), 1.97−1.85 (m, 1H), 0.90 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 157.9, 132.7, 130.1, 113.8, 67.8, 55.3, 38.9, 38.0, 16.5.

2-Phenylprop-2-en-1-ol (**4ae**).[31] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 85%, 113.9 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 5.48 (d, J = 1.1 Hz, 1H), 5.36 (d, J = 1.4 Hz, 1H), 4.55 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 147.3, 138.5, 128.6, 128.0, 126.1, 112.7, 65.1.

2-Phenylacrylaldehyde (**4ac**).[32] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 50%, 66.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.47−7.38 (m, 1H), 6.67 (s, 1H), 6.22 (s, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 193.2, 148.6, 135.8, 133.8, 128.9, 128.5, 128.2.

2-Phenylpropane-1,3-diol (**4ad**).[33] Column chromatography (hexane/ethyl acetate = 50:1). Yield: 59%, 89.6 mg. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.31 (m, 2H), 7.28−7.17 (m, 3H), 4.05−3.86 (m, 4H), 3.07 (m, 1H), 1.94 (brs, 2H).

(E)-Prop-1-ene-1,3-diyldibenzene (**6a″**).[34] Yellow oil. Column chromatography (hexane/ethyl acetate = 50:1). Yield: 85%, 165.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.79−7.04 (m, 10H), 6.55 (d, J = 15.8 Hz, 1H), 6.45 (dt, J = 15.8, 6.8 Hz, 1H), 3.64 (d, J = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 140.3, 137.6, 131.2, 129.4, 128.8, 128.6 (2C),127.23, 126.31, 126.27, 39.48.

1,1′-Methylenebis(naphthalen-2-ol) (**8a**).[35] White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 81%, 121.5 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.22 (d, J = 8.6 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.45 (t, J = 8.1 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 6.60 (br s, 2H), 4.81 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 151.6 (2C), 133.5 (2C), 129.8 (2C), 129.0 (2C), 129.0 (2C), 127.0 (2C), 123.4 (2C), 123.2 (2C), 118.1 (2C), 117.3 (2C), 21.8.

1,1′-Methylenebis(7-methoxynaphthalen-2-ol) (**8b**). White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 74%, 133.2 mg. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.22 (s, 2H), 7.66−7.33 (m, 6H), 7.11 (d, J = 8.7 Hz, 2H), 6.73 (d, J = 8.8 Hz, 2H), 4.64 (s, 2H), 3.69 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 157.1 (2C), 152.5 (2C), 135.0 (2C), 129.5 (2C), 127.2 (2C), 123.7 (2C), 118.1 (2C), 114.9 (2C), 114.5 (2C), 102.8 (2C), 54.9 (2C), 20.4. HRMS (ESI+): m/z calcd. for $C_{23}H_{21}O_4$: 361.1440 [M + H]$^+$; Found: 361.1441.

1,1′-Methylenebis(3-methoxynaphthalen-2-ol) (**8c**). White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 86%, 154.8 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 (dd, J = 6.3, 3.4 Hz, 2H), 7.63 (dd, J = 6.2, 3.3 Hz, 2H), 7.24 (dd, J = 6.3, 3.3 Hz, 4H), 7.04 (s, 2H), 6.61 (s, 2H), 4.88 (s, 2H), 4.04 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 146.9 (2C), 143.3 (2C), 129.3 (2C), 129.1 (2C), 127.2 (2C), 124.2 (2C), 123.9 (2C), 123.6 (2C), 119.1 (2C), 104.7 (2C), 56.0 (2C), 21.8. HRMS (ESI-): m/z calcd. for $C_{23}H_{20}O_4$: 359.1283 [M-H]; Found: 359.1290

1,1′-Methylenebis(6-bromonaphthalen-2-ol) (**8d**).[36] White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 55%, 126.0 mg. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.47 (s, 2H), 8.08 (d, J = 9.2 Hz, 2H), 7.93 (d, J = 2.1 Hz, 2H), 7.62 (d, J = 8.9 Hz, 2H), 7.44−7.22 (m, 4H), 4.64 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 152.4 (2C), 132.3 (2C), 130.0 (2C), 129.9 (2C), 128.4 (2C), 127.2 (2C), 126.1 (2.C), 119.6 (2C), 119.4 (2C), 115.31 (2C), 20.3.

1,1′-Methylenebis(7-bromonaphthalen-2-ol) (**8e**). White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 79%, 180.9 mg. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.62 (s, 2H), 8.43 (s, 2H), 7.66−7.63 (m, 4H), 7.34 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.6 Hz, 2H), 4.59 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 152.8 (2C), 134.9 (2C), 130.36 (2C), 127.9 (2C), 126.8 (2C), 125.9 (2C), 125.1 (2C), 119.6 (2C), 118.4 (2C), 118.2 (2C), 20.0. HRMS (ESI-): m/z calcd. for $C_{21}H_{14}Br_2O_2$: 456.9262 [M-H]$^-$; Found: 456.9268.

1,1′-Methylenebis(6-phenylnaphthalen-2-ol) (**8f**). White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 82%, 92.6 mg. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.30 (s, 2H), 8.38−8.21 (m, 2H), 7.96 (s, 2H), 7.71 (d, J = 11.0 Hz, 2H), 7.67 (d, J = 7.9 Hz, 6H), 7.51 (d, J = 8.9 Hz, 4H), 7.41 (t, J = 7.6 Hz, 6H), 7.35−7.28 (m, 4H), 4.74 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 152.1 (2C), 140.0 (2C), 133.75 (2C), 133.0 (2C), 128.9 (4C), 128.8 (2C), 128.1 (2C), 128.1 (2C), 127.0 (2C), 126.5 (4C), 125.6 (2C), 124.5 (2C), 119.38 (2C), 118.6 (2C), 20.5. HRMS (ESI-): m/z calcd. for $C_{33}H_{24}O_2$: 451.1698 [M-H]$^-$, Found: 451.1705.

1,1′-Methylenebis(6-(3,5-bis(trifluoromethyl)phenyl)-naphthalen-2-ol) (**8g**). White solid. Column chromatography (hexane/ethyl acetate = 50:5). Yield: 75%, 135.7 mg. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.48 (s, 2H), 8.35 (s, 4H), 8.31−8.23 (m, 4H), 8.00 (s, 2H), 7.80 (d, J = 8.9 Hz, 2H), 7.71 (d, J = 9.1 Hz, 2H), 7.37 (d, J = 8.9 Hz, 2H), 4.77 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 153.3 (2C), 143.0 (2C), 134.2 (2C), 131.3 (q, J = 32.8 Hz) (4C), 129.0 (d, J = 9.3 Hz) (4C), 127.5 (2C), 127.4 (2C), 126.5 (2C), 125.2 (2C), 124.7 (d, J = 6.5 Hz) (2C), 122.9 (2C), 121.1 (2C), 120.7 (2C), 119.8 (2C), 119.3 (2C), 20.9. Several peaks are

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eclipsed. HRMS (ESI-): m/z calcd. for $C_{37}H_{20}F_{12}O_2$: 723.1193 $[M-H]^-$; Found: 723.1200.

*N-Methylaniline (**10a**).*[23j] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 95%, 101.6 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23 (t, J = 8.4 Hz, 2H), 6.75 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 7.7 Hz, 2H), 3.72 (br s, 1H), 2.86 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 149.4, 129.3 (2C), 117.3, 112.5 (2C), 30.8.

*N,4-Dimethylaniline (**10b**).*[17e] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 89%, 107.7 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.06 (d, J = 8.6 Hz, 2H), 6.59 (d, J = 8.4 Hz, 2H), 3.59 (br s, 1H), 2.85 (s, 3H), 2.30 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 147.2, 129.7 (2C), 126.5, 112.68 (2C), 31.1, 20.4.

*4-Methoxy-N-methylaniline (**10c**).*[17e] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 92%, 126.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.81 (d, J = 8.9 Hz, 2H), 6.60 (d, J = 8.9 Hz, 2H), 3.76 (s, 3H), 3.17 (br s, 1H), 2.81 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 152.2, 143.72, 115.0 (2C), 113.8 (2C), 55.9, 31.7.

*4-Bromo-N-methylaniline (**10d**).*[17e] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 91%, 169.2 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24 (d, J = 8.9 Hz, 2H), 6.46 (d, J = 8.8 Hz, 2H), 3.71 (br s, 1H), 2.78 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 148.3, 131.9 (2C), 114.0 (2C), 108.8, 30.7.

*4-Fluoro-N-methylaniline (**10e**).*[17d] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 80%, 100.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.93−6.90 (m, 2H), 6.56−6.54 (m, 1H), 2.81 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 155.8 (d, J = 234.4 Hz), 145.8 (d, J = 1.8 Hz), 115.7 (d, J = 22.5 Hz, 2C), 113.2 (d, J = 7.6 Hz, 2C), 31.4.

*N-Methylpyridin-2-amine (**10f**).*[37] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 90%, 97.2 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, J = 4.8 Hz, 1H), 7.50−7.34 (m, 1H), 6.63−6.49 (m, 1H), 6.36 (d, J = 8.4 Hz, 1H), 4.70 (br s, 1H), 2.88 (d, J = 5.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 159.7, 148.2, 137.5, 112.7, 106.2, 29.1.

*N^1,N^3-Dimethylbenzene-1,3-diamine (**10g**).*[38] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 80%, 108.8 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.05−7.00 (m, 1H), 6.08−6.01 (m, 2H), 5.89 (d, J = 2.3 Hz, 1H), 3.61 (br s, 2H), 2.83 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 150.6 (2C), 129.9, 102.6 (2C), 96.4, 30.9 (2C).

*N^2,N^6-Dimethylpyridine-2,6-diamine (**10h**).*[38] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 91%, 124.6 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 (t, J = 7.9 Hz, 1H), 5.73 (d, J = 7.9 Hz, 2H), 2.84 (d, J = 5.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 159.2 (2C), 139.2, 94.1 (2C), 29.3 (2C).

*N^1,N^1,N^4-Trimethylbenzene-1,4-diamine (**10i**).*[39] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 79%, 118.5 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.78 (d, J = 8.8 Hz, 2H), 6.63 (d, J = 8.8 Hz, 2H), 3.38 (br s, 1H), 2.83 (s, 6H), 2.81 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.2, 142.2, 116.1 (2C), 114.0 (2C), 42.5 (2C), 31.8.

*2-Bromo-N-methylaniline (**10j**).*[40] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 50%, 93.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 (d, J = 7.9 Hz, 1H), 7.25 (t, J = 7.7 Hz, 2H), 6.66 (d, J = 9.1 Hz, 1H), 6.61 (t, J = 8.3 Hz, 1H), 4.39 (br s, 1H), 2.93 (d, J = 5.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 146.0, 132.3, 128.6, 117.7, 110.8, 109.7, 30.7.

*2-Ethyl-N-methylaniline (**10k**).*[17e] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 60%, 81.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18 (t, J = 7.7 Hz, 1H), 7.09 (m, 1H), 6.73 (t, J = 7.4 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 3.68 (br s, 1H), 2.90 (s, 3H), 2.49 (q, J = 7.5 Hz, 2H), 1.26 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 146.7, 127.7, 127.6, 127.1, 117.1, 109.5, 30.9, 23.8, 12.9.

*N^1-Methylbenzene-1,2-diamine (**10l**).*[41] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield:10%, 12.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ6.86−6.85 (m, 1H), 6.73−6.65 (m, 1H), 3.33 (s, 2H), 2.87 (s, 3H). $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$): δ 139.1, 134.1, 120.9, 118.5, 116.4, 111.0, 31.1.

*N-Methyloctan-1-amine (**10m**).*[42] Pale yellow oil. Column chromatography (DCM/MeOH/triethylamine 50:1:1). Yield: 33%, 47.2 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.57 (t, J = 7.4 Hz, 2H), 2.43 (s, 3H), 1.53−1.45 (m, 1H), 1.30−1.2 (m, 10H), 0.85 (t, J = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 51.5, 35.6, 31.9, 29.5, 29.3, 28.9, 27.3, 22.7, 14.2.

*N-Methyldodecan-1-amine (**10n**).*[43] White solid. Column chromatography (DCM/MeOH/triethylamine 50:1:1). Yield: 32%,63.7 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.74 (t, J = 7.9 Hz, 2H), 2.54 (s, 3H), 1.67−1.65 (m, 2H), 1.41−1.09 (m, 18H), 0.84 (t, J = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 50.4, 34.2, 32.0, 29.7, 29.6, 29.6, 29.4, 29.3, 27.4, 27.3, 27.0, 22.7, 14.2.

*N-Methylhexadecan-1-amine (**10o**).*[44] White solid. Column chromatography (DCM/MeOH/triethylamine 50:1:1). Yield: 35%,89.2 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.54 (t, J = 7.3 Hz, 2H), 2.41 (s, 3H), 1.84 (brs, 1H), 1.48−1.42 (m, 2H), 1.33−1.13 (m, 26H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 52.2, 36.5, 32.1, 30.0, 29.8, 29.8, 29.7, 29.7, 29.5, 27.4, 22.8, 14.3.

*N-Methyl-2-phenylethanamine (**10p**).*[45] White solid. Column chromatography (DCM/MeOH/triethylamine 50:1:1). Yield: 48%, 64.8 mg. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31−7.24 (m, 2H), 7.22−7.16 (m, 3H), 2.97−2.95 (m, 4H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 128.8, 128.7, 126.7, 52.0, 34.7, 34.42.

*N-(Trideuteromethyl)aniline (**10q**).*[46] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 85%, 93.5 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23 (t, J = 7.9 Hz, 2H), 6.75 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 7.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 149.4, 129.2 (2C), 117.3, 112.5 (2C), 30.3−29.8 (m).

*(2-(Methylamino)phenyl)(phenyl)methanol (**10r**).*[47] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 70%, 149.1 mg. ^{1}H NMR (600 MHz, $CDCl_3$) 7.42−7.28 (m, 6H), 6.97 (d, J = 7.6 Hz, 1H), 6.72 (d, J = 7.3 Hz, 2H), 5.84 (s, 1H), 2.80 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 147.7, 141.9, 129.3, 128.6, 128.5 (2C), 127.6, 126.9, 126.6 (2C), 116.6, 110.9, 75.1, 30.6.

*(5-Chloro-2-(methylamino)phenyl)(phenyl)methanol (**10s**).*[48] Pale yellow oil. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 65%, 160.5 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45−7.30 (m, 5H), 7.18 (dd, J = 8.6, 2.6 Hz, 1H), 6.95 (d, J = 2.6 Hz, 1H), 6.57 (d, J = 8.6 Hz, 1H), 5.75 (s, 1H), 4.53 (brs, 1H), 2.74 (d, J = 4.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 146.2, 141.2, 128.8, 128.7 (2C), 128.3, 128.2, 128.1, 126.7 (2C), 121.4, 112.0, 74.6, 30.7.

*(5-Chloro-2-(methylamino)phenyl)(phenyl)methanone (**10s′**).*[49] Yellow solid. Column chromatography (hexane/ethyl acetate/triethylamine 50:1:1). Yield: 60%, 147.0 mg. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.61 (d, J = 7.3 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.49−7.42 (m, 3H), 7.37 (dd, J = 9.0, 2.5 Hz, 1H), 6.73 (d, J = 9.0 Hz, 1H), 2.98 (d, J = 5.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 198.4, 151.3, 139.9, 135.0, 134.1, 131.2, 129.1 (2C), 128.3 (2C), 118.3, 118.0, 112.85, 29.74.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01185.

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

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Notes

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