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Metal-free reduction of unsaturated carbonyls, quinones, and pyridinium salts with tetrahydroxydiboron/water†

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A series of unsaturated carbonyls, quinones, and pyridinium salts have been effectively reduced to the corresponding saturated carbonyls, dihydroxybenzenes, and hydropyridines in moderate to high yields with tetrahydroxydiboron/water as a mild, convenient, and metal-free reduction system. Deuterium-labeling experiments have revealed this protocol to be an exclusive transfer hydrogenation process from water.

Introduction

The reduction of unsaturated carbon–carbon bonds belongs to one of the most fundamental transformations in organic synthesis and the chemical industry. Common reduction methods of converting carbon–carbon double or triple bonds to saturated carbon–carbon bonds include catalytic hydrogenation,[1] transfer hydrogenation,[2] reduction with a metal hydride reagent,[3] electrochemical reduction,[4] and others.[5] While all methods have their own merits, they also suffer from inconveniencies under various settings. For example, catalytic hydrogenation is the most atom-economical but requires a sophisticated hydrogenation apparatus to run under high pressure and handle hydrogen safely; metal hydride reagents are convenient to operate, but storage of reactive reagents and cost are factors to be considered in industry for scale-up activities. Therefore, there is a continuous effort in the search for a safe, mild, versatile, convenient, and selective reduction method for unsaturated carbon–carbon bonds. In this regard, the use of stable, nontoxic, noncorrosive, and nonflammable reagents with good chemo-selectivity under metal-free and aqueous conditions will be an appealing reduction method.[6] Herein we report tetrahydroxydiboron/water as a mild, safe, and versatile metal-free reduction system of unsaturated carbon–carbon bonds.

Diboron derivatives are a class of versatile compounds which can serve as borylation reagents, reducing agents and electron donors in organic synthesis.[7] Their high stability, ready availability and environmentally benign features have enabled wide applications in both academia and industry.[8] Tetrahydroxydiboron as the smallest diboron has been frequently applied to Miyaura borylation for the synthesis of arylboronic acid. However, only a limited number of protocols have been developed for reducing agents. Stokes and coworkers realized a Pd-catalyzed reduction of alkenes using $B_2(OH)_4/H_2O$ as a reducing agent (Scheme 1a).[9] Song, Zhou, and Uozumi independently developed Pd or Cu-catalyzed transfer hydrogenation for N-heteroaromatic compounds in the presence of tetrahydroxydiboron or diboron esters.[10] Alternatively, metal-free diboron-mediated transfer hydrogenation processes were reported by Jiao, Wu, and Zhou independently for the reduction of N-heterocycles (Scheme 1b).[11] We have established a chiral diboron-mediated reductive imine coupling reaction for the synthesis of chiral diamines.[12] During our continued studies on diboron-facilitated reductive transformations, we discovered that several types of electron-deficient carbon–carbon double or triple bonds were reduced by $B_2(OH)_4/H_2O$ under basic conditions. Herein, we report the reduction of unsaturated carbonyls, quinones, and pyridinium salts to the corresponding carbonyls, dihydroxybenzenes, and hydropyridines using $B_2(OH)_4/H_2O$ as the reducing system under metal-free conditions (Scheme 1c).

Results and discussion

The reduction of α,β-unsaturated carbonyl compounds represents one of the most important transformations in natural product synthesis, fine chemical production, and process chemistry. Herein, we chose the reduction of methyl (*E*)-4-oxo-

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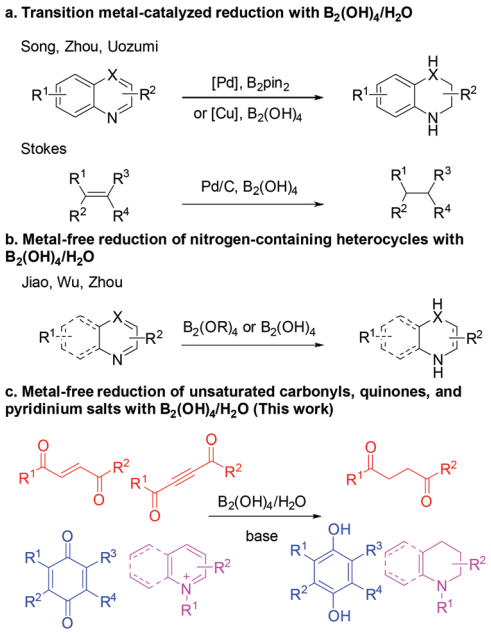
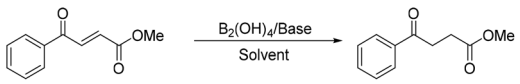


Scheme 1 Transition-metal-free reduction of unsaturated compounds with the $B_2(OH)_4/H_2O$ system.

4-phenylbut-2-enoate (**1a**) for a study using the $B_2(OH)_4/H_2O$ system. As shown in Table 1, when the reaction was conducted in the presence of 8 equiv. of $B_2(OH)_4$ in H_2O at 20 °C, the influence of the base (1 equiv.) was crucial to the yield of the reaction. With the increasing strength of the base, decreased yields were obtained due to the partial hydrolysis of methyl 4-oxo-4-phenylbutanoate (entries 1–5, Table 1). Therefore, $NaHCO_3$ was employed as the base for further optimization. Because of the poor solubility of **1a** in pure H_2O, the use of an organic or mixed solvent was examined. It was observed that the yield was higher in H_2O/THF than in H_2O/MeOH and the highest yield was obtained when the ratio of H_2O/THF was 2 : 1 (entries 6–9, Table 1). It was noteworthy that only a trace amount of the product was obtained when sole THF was used, demonstrating the important role of H_2O as a hydrogen source (entry 10, Table 1). A higher reaction temperature was helpful for the yield. When the reaction proceeded at 60 °C, 90% yield was achieved (entries 11 and 12, Table 1). Further increase of the reaction temperature proved to be ineffective (entry 13). Further optimization of the loadings of $B_2(OH)_4$ and $NaHCO_3$ led to 92% yield of **2a** by using 5 equiv. of $B_2(OH)_4$ and 0.2 equiv. of $NaHCO_3$ (entries 14–19, Table 1).

Having established the optimized reduction conditions, the substrate scope was evaluated (Table 2). A series of (*E*)-4-oxo-4-arylbut-2-enoates were reduced to the corresponding 4-oxo-4-arylbutanoates (**2a–2f**) in moderate to high yields using the $B_2(OH)_4/H_2O/NaHCO_3$ system. Substrates with both electron-donating (Me) and electron-withdrawing groups (Cl, F) on the aromatic rings were tolerated. No reaction, however, was observed on a MeO-substituted substrate. The current protocol was also applicable to the reduction of γ-ketoester, fumaric acid diester, and *N*-phenylmaleimide, affording **2g**, **2h**, and **2k** in high yields, respectively. In addition, α,β-unsaturated esters were also suitable substrates, which were converted to saturated esters **2j** and **2l**. It was noted that substrates containing the propiolate moiety were successfully reduced to the corresponding saturated carbonyls **4a** and **4b** in high yields by simply switching the base from $NaHCO_3$ to Na_2CO_3, demonstrating the generality of $B_2(OH)_4/H_2O$ as the reducing system.

Table 1 Reaction optimization for the reduction of unsaturated carbonyls[a]



1a **2a**

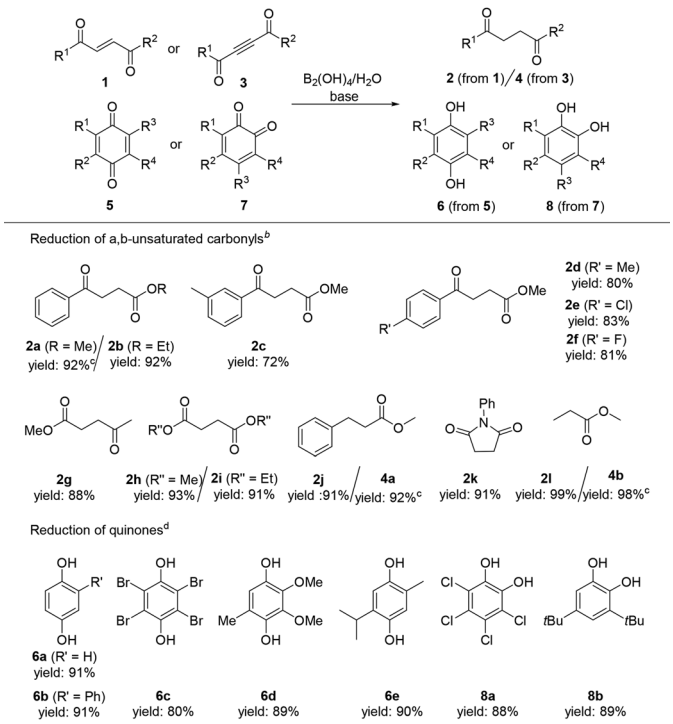
Entry	Solvent	Base (equiv.)	$B_2(OH)_4$ (equiv.)	Temp. (°C)	Yield[b] (%)
1	H_2O	$NaHCO_3$ (1)	8	20	57
2	H_2O	Na_2CO_3 (1)	8	20	55
3	H_2O	K_2CO_3 (1)	8	20	40
4	H_2O	NaOH (1)	8	20	32
5	H_2O	KO^{t}Bu (1)	8	20	18
6	H_2O/MeOH (2 : 1)	$NaHCO_3$ (1)	8	20	61
7	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	8	20	76
8	H_2O/THF (3 : 1)	$NaHCO_3$ (1)	8	20	73
9	H_2O/THF (1 : 1)	$NaHCO_3$ (1)	8	20	70
10	THF	$NaHCO_3$ (1)	8	20	Trace
11	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	8	40	84
12	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	8	60	90
13	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	8	80	90
14	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	6	60	90
15	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	5	60	90
16	H_2O/THF (2 : 1)	$NaHCO_3$ (1)	4	60	81
17	H_2O/THF (2 : 1)	$NaHCO_3$ (0.5)	5	60	92
18	H_2O/THF (2 : 1)	$NaHCO_3$ (0.2)	5	60	92
19	H_2O/THF (2 : 1)	$NaHCO_3$ (0.1)	5	60	86

[a] The reaction was conducted at the specified reaction temperature in the solvent (3 mL) with **1a** (0.3 mmol). [b] Yields determined by NMR with the internal standard (mandelic acid).

Hydroquinones (1,4-dihydroxybenzenes and 1,2-dihydroxybenzenes) are important chemical intermediates for the preparation of pesticides, flavoring agents, and medicines. Their derivatives have also been extensively used as preservatives, stabilizers, antioxidants, polymerization inhibitors, and photography chemicals. A straightforward approach to synthesize hydroquinones is the reduction of quinones which possess unsaturated carbonyl units. To our delight, treatment of 1,4-benzoquinones with $B_2(OH)_4/H_2O$ and $NaHCO_3$ led to hydroquinone products in high yields (Table 2). A series of partially or fully substituted 1,4-hydroquinones were synthesized (**6a–6e**). Under similar conditions, 1,2-benzoquinones were also reduced smoothly to the corresponding 1,2-hydroquinones (**8a** and **8b**).

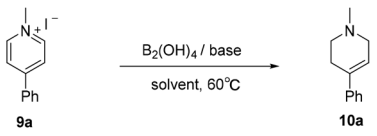
Pyridinium salts are a class of compounds with electron-deficient C–N and C–C double bonds, and serve as important precursors of hydropyridines. The reduction of pyridinium salts has been previously achieved by metal-catalyzed (transfer) hydrogenation and reduction with hydride reagents, alkaline metals, or other reducing agents.[13] To our knowledge, metal-

Table 2 $B_2(OH)_4/H_2O$-mediated reduction of unsaturated carbonyls and quinones[a]



[a] The reaction was conducted with the substrate (1 mmol), $B_2(OH)_4$ (5 mmol), and the base in the mixed solvent and isolated yields are given. [b] $NaHCO_3$ (0.2 mmol), H_2O/THF (3 mL/1.5 mL), 60 °C, 8 h. [c] Na_2CO_3 (0.2 mmol), H_2O/MeOH (3 mL/1.5 mL), 80 °C, 12 h. [d] $NaHCO_3$ (0.2 mmol), H_2O/THF (3 mL/1.5 mL), 60 °C, 6 h.

Table 3 Reduction of pyridinium salt **9a** with $B_2(OH)_4/H_2O$: optimization of reaction conditions[a]



Entries	Solvent	Base	$B_2(OH)_4$ (equiv.)	Yield[b] (%)
1	H_2O/THF (2 : 1)	$NaHCO_3$ (0.2 equiv.)	10	20
2	H_2O/THF (2 : 1)	KOH (0.2 equiv.)	10	52
3	H_2O/THF (2 : 1)	KO^{t}Bu (0.2 equiv.)	10	70
4	H_2O/MeOH (2 : 1)	KO^{t}Bu (0.2 equiv.)	10	81
5	H_2O/MeOH (2 : 1)	KO^{t}Bu (0.2 equiv.)	14	91
6	H_2O/MeOH (2 : 1)	KO^{t}Bu (0.2 equiv.)	20	92

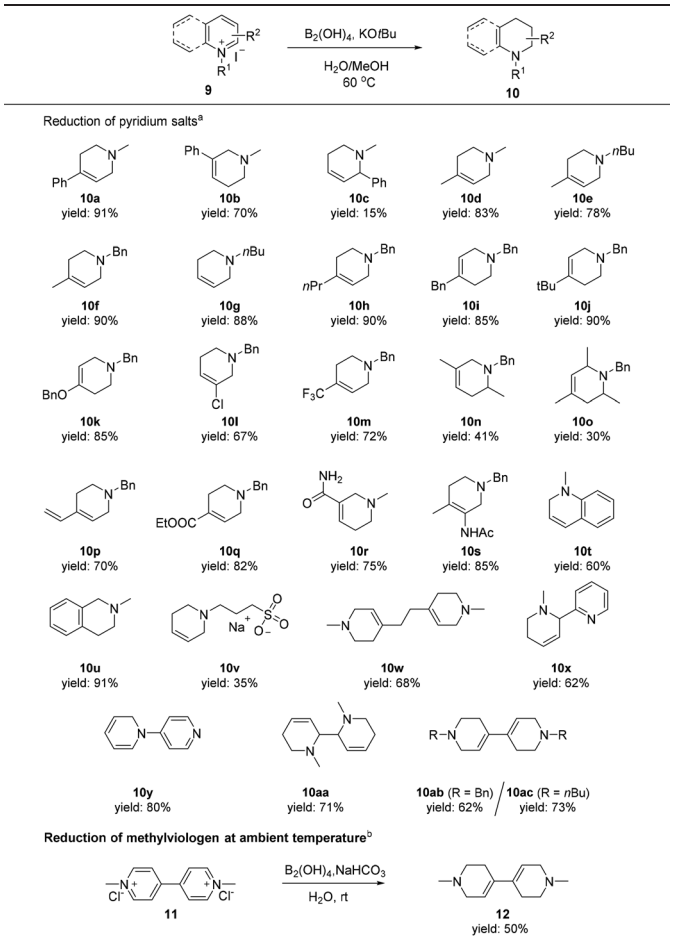
[a] Reaction conditions: **9a** (0.3 mmol), base, $B_2(OH)_4$ in solvent (3 mL), 60 °C, 8 h. [b] NMR assay yields with mandelic acid as the internal standard.

free tetrahydroxydiboron/water-mediated reduction of pyridinium salts has not been reported. We investigated the applicability of the $B_2(OH)_4/H_2O$-mediated reduction protocol to the synthesis of hydropyridines from pyridinium salts. As shown in Table 3, under the reaction conditions for the reduction of α,β-unsaturated carbonyls, the reduction of **9** provided **10** in 20% yield (entry 1, Table 3). Increasing the strength of the base was beneficial for the reduction efficiency, as the use of KOH provided 52% yield (entry 2, Table 3). The yield of the reaction was further increased to 70% with KO*t*Bu as the base (entry 3, Table 3). Subsequent change of the solvent system from H_2O/THF to H_2O/MeOH and increase of the $B_2(OH)_4$ stoichiometry (14 equiv.) led to 91% yield of **10a** (entries 4 and 5, Table 3). Further increase of the $B_2(OH)_4$ loading (20 equiv.) provided a comparable yield (entry 6). Thus, the optimal conditions with KO*t*Bu (0.2 equiv.) and $B_2(OH)_4$ (14 equiv.) in H_2O/THF at 60 °C for 6 h were used for further studies.

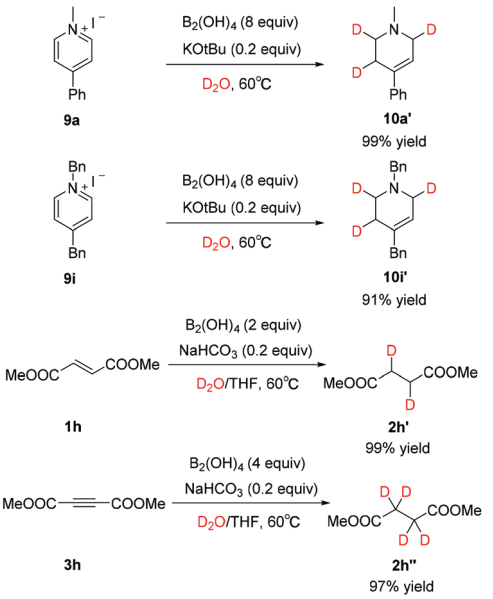
The substrate scope of this reduction method is presented in Table 4. The position of the substituent on the pyridine ring affected the reaction efficiency significantly. The reduction of the *para*-phenyl-substituted pyridinium salt **9a** provided tetrahydropyridine **10a** in 91% yield. This was in sharp contrast to the reduction of *meta*- and *ortho*-substituted substrates (**9b**, **9c**, **9n**, and **9o**), which led to a mixture of dihydro- and tetrahydropyridines (**10b**, **10c**, **10n**, and **10o**). Various substrates with different *N*-substituents, including *N*-Me (**9d**), *N*-*n*Bu (**9e** and **9g**), and *N*-Bn (**9f**), were all applicable to the $B_2(OH)_4/H_2O$-mediated reduction, forming smoothly the corresponding tetrahydropyridine products. A variety of different substituents including electron-donating groups such as alkyl (**10h–j**) and alkoxy (**10k**) and electron-withdrawing groups such as halogen (**10l**) and CF_3 (**10m**) were well tolerated. In addition, the current conditions were also applicable to form tetrahydropyridines with vinyl (**10p**), ester (**10q**), amide (**10r**), amido (**10s**), pyridinyl (**10x**), and *N*-pyridin-4-yl functionalities (**14y**), as well as 1-methyl-1λ^4-quinoline (**9t**) and 2-methyl-2λ^4-isoquinoline (**9u**). When a zwitterionic substrate was also employed, a mixture of tetrahydropyridine (**10v**) and dihydropyridine (**10v′**) products were obtained. Interestingly, bis-pyridinium and bipyridinium salts were also reduced to bis-tetrahydropyridine **10w** and **10aa–ac** in good yields, respectively. The utility of the $B_2(OH)_4/H_2O$ system was also exemplified by efficient reduction of methylviologen (**11**), an extremely deadly herbicide with 99% mortality in oral poisoning cases.[14] Upon treatment with $B_2(OH)_4$ and $NaHCO_3$ in H_2O at ambient temperature, methylviologen was completely reduced to form product **12** in 50% isolated yield.

To shed light on the mechanism of the $B_2(OH)_4/H_2O$ system in reducing pyridinium salts and unsaturated esters, reduction of pyridine salts **9a** and **9i**, alkene **1h**, and alkyne **3h** with $B_2(OH)_4/D_2O$ was studied (Scheme 2). Interestingly, 100% incorporation of deuterium atoms was observed in the structures of **10a′**, **10i′**, **2h′**, and **2h″**, demonstrating that D_2O was the sole provider of the addition source and the hydrogen from $B_2(OH)_4$ was not interfered. The observation further demonstrated that the proton exchange between D_2O and $B_2(OH)_4$ was a slow process and could be neglected under the reaction conditions. Thus, $B_2(OH)_4/H_2O$-mediated reduction is an exclusive transfer hydrogenation process from water, and

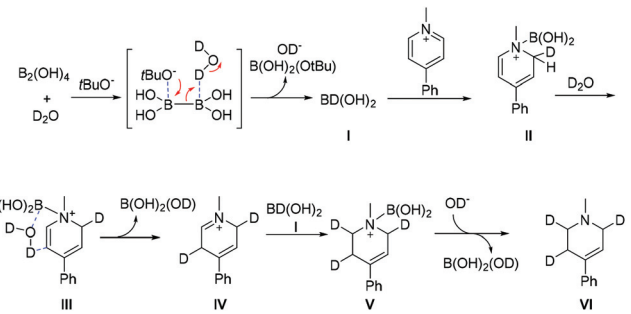
Table 4 Reduction of pyridinium salts with $B_2(OH)_4/H_2O$



[a] Reaction conditions: **9** (1 mmol), $B_2(OH)_4$ (14 mmol), KO*t*Bu (0.2 mmol), H_2O/MeOH (3 mL/1.5 mL), 60 °C, 8 h, isolated yield. [b] Methylviologen (1 mmol), $B_2(OH)_4$ (14 mmol), $NaHCO_3$ (0.2 mmol), H_2O (3 mL), 8 h.



Scheme 2 Deuterium-labeling experiments.



Scheme 3 A proposed reduction pathway of pyridinium salt **9a**.

$B_2(OH)_4/D_2O$ can be applied as a convenient and useful system for deuterium-labeling experiments.

Although several proposed mechanisms have been reported for metal-free diboron-mediated reduction of neutral compounds,[11,15] the current protocol applicable for reducing various types of electron-deficient carbon–carbon bonds, in particular pyridinium salts, is unprecedented and noteworthy. A plausible reduction pathway of pyridinium salt **9a** is proposed as shown in Scheme 3. Since H_2 is generated from the reaction between $B_2(OH)_4$ and H_2O under basic conditions,[16] $BD(OH)_2$ (**I**) could be formed initially in the presence of a base (Scheme 3). The reduction of the pyridinium salt by species **I** proceeds to provide intermediate **II**, which is transformed to **IV** through **III** upon hydrolysis. Further reduction of dihydropyridinium **IV** with $BD(OH)_2$ (**I**) proceeds through **V** and finally provides D_3-tetrahydropyridine product **VI**.

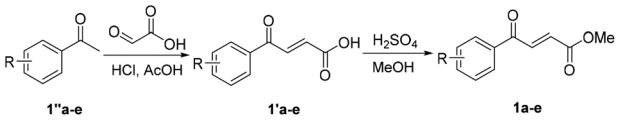
In conclusion, tetrahydroxydiboron/water has been demonstrated as a mild, versatile, safe, convenient, and metal-free reduction system and a series of unsaturated carbonyls, quinones, and pyridinium salts have been effectively reduced to the corresponding saturated carbonyls, dihydroxybenzenes, and hydropyridines in moderate to high yields. Deuterium-labeling experiments have revealed this protocol to be an exclusive transfer hydrogenation process from water and $B_2(OH)_4/D_2O$ can be applied as a convenient and useful system for deuterium-labeling experiments.

Experimental

General

All reactions were carried out under the designated conditions. Unless otherwise noted, commercial reagents were used without further purification. Methanol and tetrahydrofuran were purchased from J&K Scientific Ltd. All other solvents were purified and dried according to standard methods prior to use. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR data were recorded on a Bruker-Ultrashield PLUS400 NMR spectrometer or a 500 NMR Agilent spectrometer with $CDCl_3$, CD_3OD, $(CD_3)_2SO$ and D_2O

as the solvents. ^{1}H chemical shifts were referenced to $CDCl_3$ at 7.26 ppm. ^{1}H chemical shifts were referenced to CD_3OD at 3.31 ppm. ^{1}H chemical shifts were referenced to D_2O at 4.79 ppm. ^{1}H chemical shifts were referenced to $(CD_3)_2SO$ at 2.50 ppm. ^{13}C chemical shifts were referenced to $CDCl_3$ at 77.16 ppm and obtained with 1H decoupling. ^{13}C chemical shifts were referenced to CD_3OD at 49.00 ppm and obtained with ^{1}H decoupling. ^{13}C chemical shifts were referenced to $(CD_3)_2SO$ at 39.52 ppm and obtained with ^{1}H decoupling. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet-doublet (dd), quintet (quint), sextet (sextet), septet (septet), multiplet (m), and broad (br). MS was performed on a Waters Premier GC-TOF MS system, a Thermo Scientific Q Exactive HF Orbitrap-FTMS system and a Shimadzu LCMS-2010EV mass spectrometer.



General procedures for unsaturated carbonyls 1a, 1c–e. To a solution of aryl ketone **1″a**, **1″c–e** (10.0 mmol, 1.0 equiv.) in a solution of AcOH (20 mL) and HCl (2 mL) was added glyoxylic acid monohydrate (10.0 mmol, 1.0 equiv.). The mixture was heated at reflux for 18 h and then concentrated. The residue was washed with ice-cold water by decantation or on a filter. The crude product was dried under air at 40 °C and recrystallized from ethyl acetate or purified by column chromatography over silica gel with elution using a mixture of petroleum ether/ethyl acetate (2/1) to give the corresponding carboxylic acid **1′a**, **1′c–e**.[17]

To a solution of carboxylic acid **1′a**, **1′c–e** in MeOH (4 mL) was added H_2SO_4 (10.0 mmol, 1.0 equiv.) and the mixture was stirred at reflux until the complete consumption of the starting material. Saturated $NaHCO_3$ solution was added to neutralize the mixture. The reaction mixture was extracted with dichloromethane. The organic phase was separated, dried over anhydrous sodium sulfate, and purified by column chromatography over silica gel with elution using a mixture of petroleum ether/ethyl acetate (20/1) to give the corresponding ester **1a**, **1c–e**.

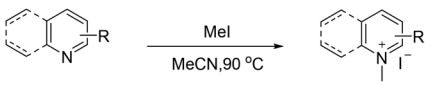
Methyl (*E*)-4-oxo-4-phenylbut-2-enoate (1a). Yellow oil, 88% yield. Eluent: petroleum ether/ethyl acetate = 20 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 15.6 Hz, 1H), 7.53 (t, J = 8.7 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 6.80 (d, J = 15.6 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.1, 165.8, 136.5 136.4, 133.8, 131.9, 128.8 128.7, 52.2. HRMS (FI) m/z calculated for $C_{11}H_{10}O_3$ $[M]^+$: 190.0624, found: 190.0628.

Methyl (*E*)-4-oxo-4-(*m*-tolyl)but-2-enoate (1c). Yellow oil, 71% yield. Eluent: petroleum ether/ethyl acetate = 20 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 15.5 Hz, 1H), 7.76–7.89 (m, 2H), 7.42–7.35 (m, 2H), 6.87 (d, J = 15.6 Hz, 1H), 3.83 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.5, 166.0, 138.8, 136.7, 134.7, 131.8, 129.3, 128.7, 126.3, 126.1, 52.3, 21.3. HRMS (ESI) m/z calculated for $C_{12}H_{13}O_3$ $[M + H]^+$: 205.0634, found: 205.0636.

Methyl (*E*)-4-oxo-4-(*p*-tolyl)but-2-enoate (1d). Yellow oil, 80% yield. Eluent: petroleum ether/ethyl acetate = 20 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.92 (m, 3H), 7.25–7.29 (m, 2H), 6.86 (d, J = 8.1 Hz, 1H), 3.82 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.8, 166.1, 145.0, 136.7, 134.1, 131.6, 129.6, 129.0, 52.3, 21.8. HRMS (ESI) m/z calculated for $C_{12}H_{13}O_3$ $[M + H]^+$: 205.0634, found: 205.0635.

Methyl (*E*)-4-(4-chlorophenyl)-4-oxobut-2-enoate (1e). Yellow solid, 75% yield. Eluent: petroleum ether/ethyl acetate = 20 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 2H), 7.87 (d, J = 15.5 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 15.5 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.1, 165.8, 140.5, 135.9, 134.9, 132.5, 130.2, 129.3, 52.4. HRMS (ESI) m/z calculated for $C_{11}H_{10}ClO_3$ $[M + H]^+$: 225.0352, found: 225.0356.

Methyl (*E*)-4-(4-fluorophenyl)-4-oxobut-2-enoate (1f). Yellow powder, 70% yield. Eluent: petroleum ether/ethyl acetate = 20 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06–8.02 (m, 2H), 7.90 (d, J = 15.5 Hz, 1H), 7.16–7.21 (m, 2H), 6.89 (d, J = 15.6 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.7, 166.3 (d, J = 257.3 Hz), 166.1, 136.3, 133.1 (d, J = 2.9 Hz), 132.4, 131.7 (d, J = 9.6 Hz), 116.3 (d, J = 22.1 Hz), 52.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.5. HRMS (ESI) m/z calculated for $C_{11}H_{10}O_3F$ $[M + H]^+$: 209.0608, found: 209.0607.



General procedures for methyl pyridium salts 9a–d, 9r, 9t, 9u, 9w and 9aa. To a solution of substituted pyridine **9′** (5.0 mmol, 1.0 equiv.) in acetone (2 mL) was added MeI (20.0 mmol, 4.0 equiv.) under nitrogen in a two-necked flask. The mixture was heated at 90 °C for 12 h, and then cooled to room temperature. Removal of the solvent under reduced pressure afforded the crude product, which was filtered, washed with dichloromethane (10 mL × 3), and dried under vacuum to afford the methyl pyridinium salt.[18]

1-Methyl-4-phenylpyridin-1-ium iodide (9a). Yellow solid, 91% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.51 (d, J = 5.2 Hz, 2H), 7.96 (d, J = 5.3 Hz, 2H), 7.64 (d, J = 6.9 Hz, 2H), 7.48 (m, 3H), 4.23 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 154.9, 144.6, 132.8, 132.0, 129.5, 127.6, 124.2, 47.3. HRMS (ESI) m/z calculated for $C_{12}H_{12}N$ $[M - I]^+$: 170.0964, found: 170.0967.

1-Methyl-3-phenylpyridin-1-ium iodide (9b). Yellow solid, 90% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.99 (s, 1H), 8.71 (d, J = 6.1 Hz, 1H), 8.66 (d, J = 8.3 Hz, 1H), 8.05 (dd, J = 8.1, 6.2 Hz, 1H), 7.72–7.70 (m, 2H), 7.59–7.54 (m, 3H), 4.42 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 143.0, 142.9, 142.7, 140.6, 132.9, 130.2, 129.5, 127.8, 127.2, 48.3. HRMS (ESI) m/z calculated for $C_{12}H_{12}N$ $[M - I]^+$: 170.0964, found: 170.0963.

1-Methyl-2-phenylpyridin-1-ium iodide (9c). Yellow solid, 88% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.88 (d, J = 6.2 Hz, 1H), 8.57 (td, J = 7.9, 1.1 Hz, 1H), 8.06 (m, 1H), 7.98 (dd, J = 8.0, 1.2 Hz, 1H), 7.72–7.62 (m, 5H), 4.18 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 155.7, 146.1, 145.5, 131.4, 131.4, 130.1, 129.2, 129.0,

126.7, 47.3. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{12}N$ [M − I]$^+$: 170.0964, found: 170.0966.

1,4-Dimethylpyridin-1-ium iodide (9d). White solid, 97% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.58 (d, J = 5.1 Hz, 1H), 7.85 (d, J = 5.1 Hz, 1H), 4.31 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 159.5, 143.9, 128.4, 47.4, 21.3. HRMS (ESI) *m*/*z* calculated for $C_7H_{10}N$ [M − I]$^+$: 108.0808, found: 108.0810.

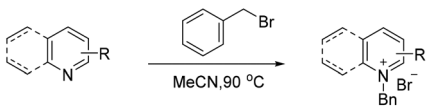
3-Carbamoyl-1-methylpyridin-1-ium iodide (9r). White solid, 91% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.33 (s, 1H), 9.02 (d, J = 6.1 Hz, 1H), 8.93 (d, J = 8.2 Hz, 1H), 8.25–8.22 (m, 1H), 4.53 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 165.8, 147.4, 145.2, 143.7, 133.5, 128.1, 48.8. HRMS (ESI) *m*/*z* calculated for $C_7H_9N_2O$ [M − I]$^+$: 137.0715, found: 137.0712.

1-Methylquinolin-1-ium iodide (9t). Yellow solid, 92% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.17 (d, J = 5.7 Hz, 1H), 9.06 (d, J = 8.5 Hz, 1H), 8.33 (d, J = 9.0 Hz, 1H), 8.29 (d, J = 8.2 Hz, 1H), 8.21–8.18 (m, 1H), 7.98–7.95 (m, 2H), 4.61 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 149.0, 147.4, 135.7, 130.3, 129.9, 129.5, 121.3, 118.1, 45.2. HRMS (ESI) *m*/*z* calculated for $C_{10}H_{10}N$ [M − I]$^+$: 144.0808, found: 144.0810.

2-Methylisoquinolin-2-ium iodide (9u). Yellow solid, 88% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.52 (d, J = 6.4 Hz, 1H), 8.36–8.30 (m, 1H), 8.26–8.18 (m, 2H), 8.09–8.00 (m, 2H), 7.92–7.83 (m, 1H), 4.45 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 149.5, 136.8 136.7, 134.8, 131.1, 129.7, 127.2, 126.9, 126.0, 48.0. HRMS (ESI) *m*/*z* calculated for $C_{10}H_{10}N$ [M − I]$^+$: 144.0808, found: 144.0810.

4,4′-(Ethane-1,2-diyl)bis(1-methylpyridin-1-ium) iodide (9w). White solid, 75% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.65 (d, J = 6.6 Hz, 4H), 7.91 (d, J = 6.6 Hz, 4H), 4.32 (s, 6H), 3.43 (s, 4H). ^{13}C NMR (126 MHz, D_2O) δ 159.8, 144.6, 127.9, 47.7, 34.0. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{17}N_2$ [M − 2I − H]$^+$: 213.1470, found: 213.1478.

1,1′-Dimethyl-[2,2′-bipyridine]-1,1′-diium iodide (9aa). Yellow solid, 81% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.27 (d, J = 6.1 Hz, 2H), 8.90–8.84 (m, 2H), 8.48–8.38 (m, 4H), 4.233 (s, 6H). ^{13}C NMR (126 MHz, D_2O) δ 149.2, 147.5, 142.7, 131.1, 130.9, 47.6. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{13}N_2$ [M − 2I − H]$^+$: 185.1073, found: 185.1075.



9′ 9

General procedures for benzyl pyridium salts 9f, 9h–j, 9l–q, 9s and 9ab. To a solution of substituted pyridine **9′** (5.0 mmol, 1.0 equiv.) in acetone (2 mL) was added benzyl bromide (5.5 mmol, 1.1 equiv.) under nitrogen in a two-necked flask at 90 °C for 12 h, and then cooled to room temperature. Removal of the solvent under reduced pressure afforded the crude product, which was filtered, washed with dichloromethane (10 mL × 3), and dried under vacuum to afford the benzyl pyridium salt.[19]

1-Benzyl-4-methylpyridin-1-ium bromide (9f). White solid, 98% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.67 (d, J = 6.6 Hz, 2H), 7.84 (d, J = 6.4 Hz, 2H), 7.60–7.36 (m, 5H), 5.70 (s, 2H), 2.61 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 160.4, 143.0, 132.9, 129.7, 129.4, 128.8, 128.7, 63.5, 21.3. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{14}N$ [M − Br]$^+$: 184.1126, found: 184.1121.

1-Benzyl-4-propylpyridin-1-ium bromide (9h). White solid, 88% yield. ^{1}H NMR (500 MHz, CD_3OD) δ 8.93 (d, J = 6.8 Hz, 2H), 7.98 (d, J = 6.6 Hz, 2H), 7.54–7.43 (m, 5H), 5.81 (s, 2H), 2.93 (t, J = 7.6 Hz, 2H), 1.83–1.74 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 165.5, 145.1, 134.9, 130.9, 130.7, 130.1, 129.4, 64.9, 38.5, 24.1, 13.9. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{18}N$ [M − Br]$^+$: 212.1439, found: 212.1434.

1,4-Dibenzylpyridin-1-ium bromide (9i). White solid, 95% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.59 (d, J = 6.4 Hz, 2H), 7.70 (d, J = 6.2 Hz, 2H), 7.44–7.13 (m, 10H), 5.61 (s, 2H), 4.15 (s, 2H). ^{13}C NMR (126 MHz, D_2O) δ 162.1, 143.4, 136.7, 132.7, 129.7, 129.4, 129.2, 129.1, 128.8, 127.9, 127.4, 63.6, 40.6. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{18}N$ [M − Br]$^+$: 260.1434, found: 260.1436.

1-Benzyl-4-(*tert*-butyl)pyridin-1-ium bromide (9j). White solid, 92% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.72 (d, J = 6.2 Hz, 2H), 7.97 (d, J = 6.2 Hz, 2H), 7.44–7.32 (m, 5H), 5.67 (s, 2H), 1.27 (s, 9H). ^{13}C NMR (126 MHz, D_2O) δ 171.8, 143.2, 133.0, 129.7, 129.4, 128.8, 125.4, 63.4, 35.9, 29.0. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{20}N$ [M − Br]$^+$: 226.1590, found: 226.1592.

1-Benzyl-3-chloropyridin-1-ium bromide (9l). Yellow solid, 83% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.05 (s, 1H), 8.88 (d, J = 6.1 Hz, 1H), 8.53 (d, J = 8.5 Hz, 1H), 8.04–7.98 (m, 1H), 7.51–7.39 (m, 5H), 5.78 (s, 2H). ^{13}C NMR (126 MHz, D_2O) δ 145.7, 143.4, 142.8, 135.8, 131.9, 130.1, 129.5, 129.3, 128.8, 64.9. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{11}ClN$ [M − Br]$^+$: 204.0575, found: 204.0577.

1-Benzyl-4-(trifluoromethyl)pyridin-1-ium bromide (9m). White solid, 91% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.19 (d, J = 5.8 Hz, 2H), 8.41 (d, J = 4.6 Hz, 2H), 7.48 (s, 5H), 5.92 (s, 2H). ^{13}C NMR (126 MHz, D_2O) δ 146.2 (t, J = 8.9 Hz), 131.7, 130.1, 129.6, 129.3, 129.16–127.95 (m), 125.2 (dd, J = 6.6, 3.1 Hz), 121.9, 65.3. ^{19}F NMR (471 MHz, D_2O) δ −65.5. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{11}F_3N$ [M − Br]$^+$: 238.0838, found: 238.0837.

1-Benzyl-2,5-dimethylpyridin-1-ium bromide (9n). White solid, 89% yield. ^{1}H NMR (500 MHz, CD_3OD) δ 8.91 (s, 1H), 8.37 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.50–7.43 (m, 3H), 7.27 (d, J = 7.5 Hz, 2H), 5.86 (s, 2H), 2.76 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 147.9, 146.6, 138.7, 134.0, 131.1, 130.6, 130.3, 128.5, 62.3, 20.1, 18.0. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{16}N$ [M − Br]$^+$: 198.1283, found: 198.1287.

1-Benzyl-2,4,6-trimethylpyridin-1-ium bromide (9o). White solid, 87% yield. ^{1}H NMR (500 MHz, D_2O) δ 7.61 (s, 1H), 7.37–7.29 (m, 3H), 6.92 (d, J = 7.3 Hz, 2H), 5.68 (s, 2H), 2.57 (s, 6H), 2.51 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 159.1, 154.6, 131.9, 129.4, 128.5, 128.4, 125.2, 54.7, 20.9, 20.5. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{18}N$ [M − Br]$^+$: 212.1434, found: 212.1437.

1-Benzyl-4-vinylpyridin-1-ium bromide (9p). White solid, 78% yield. ^{1}H NMR (500 MHz, D_2O) δ 8.67 (d, J = 6.3 Hz, 2H), 7.90 (d, J = 6.1 Hz, 2H), 7.40 (s, 5H), 6.84 (dd, J = 17.6, 10.9 Hz, 1H), 6.36 (d, J = 17.6 Hz, 1H), 5.89 (d, J = 10.9 Hz, 1H), 5.64 (s,

2H). ^{13}C NMR (126 MHz, D_2O) δ 153.7, 143.8, 132.8, 131.8, 129.7, 129.4, 128.9, 127.3, 124.5, 63.6. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{14}N$ $[M - Br]^+$: 196.1121, found: 196.1122.

1-Benzyl-4-(ethoxycarbonyl)pyridin-1-ium bromide (9q). Yellow solid, 88% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.07 (d, J = 6.7 Hz, 2H), 8.47 (d, J = 6.4 Hz, 2H), 7.51–7.43 (m, 5H), 5.85 (s, 2H), 4.46 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H).^{13}C NMR (126 MHz, D_2O) δ 163.0, 145.5, 145.2, 132.0, 130.0, 129.5, 129.2, 127.6, 64.9, 64.1, 13.1. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{16}NO_2$ $[M - Br]^+$: 242.1176, found: 242.1177.

3-Acetamido-1-benzyl-4-methylpyridin-1-ium bromide (9s). White solid, 91% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.07 (s, 1H), 8.52 (d, J = 6.3 Hz, 1H), 7.85 (d, J = 6.3 Hz, 1H), 7.44–7.39 (m, 5H), 5.66 (s, 2H), 2.48 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, D_2O) δ 173.3, 152.6, 139.5, 139.0, 136.0, 132.6, 129.8, 129.5, 129.4, 128.9, 63.9, 22.4, 17.8. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{17}N_2O$ $[M - Br]^+$: 241.1335, found: 241.1337.

1,1′-Dibenzyl-[4,4′-bipyridine]-1,1′-diium bromide (9ab). White solid, 78% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.12 (d, J = 7.0 Hz, 4H), 8.50 (d, J = 7.0 Hz, 4H), 7.52–7.46 (m, 10H), 5.89 (s, 4H). ^{13}C NMR (126 MHz, D_2O) δ 150.1, 145.4, 132.1, 130.0, 129.5, 129.2, 127.0, 64.7. HRMS (ESI) *m*/*z* calculated for $C_{24}H_{21}N_2$ $[M - 2Br - H]^+$: 337.1699, found: 337.1705.

Synthesis of 9ac. To a solution of 4,4′-bipyridine (5.0 mmol, 1.0 equiv.) in acetone (2 mL) was added 1-iodobutane (5.5 mmol, 1.1 equiv.) under nitrogen in a two-necked flask at 90 °C for 24 h, and then cooled to room temperature. Removal of the solvent under reduced pressure afforded the crude product, which was filtered, washed with dichloromethane (10 mL × 3), and dried under vacuum to afford the desired product **9ac**.[20]

1,1′-Dibutyl-[4,4′-bipyridine]-1,1′-diium bromide (9ac). Yellow solid, 70% yield. ^{1}H NMR (500 MHz, D_2O) δ 9.11 (d, J = 6.8 Hz, 4H), 8.54 (d, J = 6.5 Hz, 4H), 4.72 (t, J = 7.5 Hz, 4H), 2.10–2.01 (m, 4H), 1.45–1.35 (m, 4H), 0.95 (t, J = 7.4 Hz, 6H). ^{13}C NMR (126 MHz, D_2O) δ 149.9, 145.3, 126.9, 61.9, 32.5, 18.7, 12.6. HRMS (ESI) *m*/*z* calculated for $C_{18}H_{25}N_2$ $[M - 2Br - H]^+$: 269.2012, found: 269.2016.

General procedure for reduction of unsaturated carbonyls and quinones. To a solution of unsaturated carbonyl or quinone (1 equiv.) in THF (1.5 mL) was added a solution of $B_2(OH)_4$ (5 equiv.) and $NaHCO_3$ (0.2 equiv.) in H_2O (3 mL) under a nitrogen atmosphere. The mixture was heated at 60 °C for 6–8 h. After cooling to room temperature, the mixture was extracted with ethyl acetate three times. The ethyl acetate phase was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (10 : 1) as the eluent.

Methyl 4-oxo-4-phenylbutanoate (2a). Yellow oil, 92% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.94 (m, 2H), 7.48–7.51 (m, 1H), 7.36–7.42 (m, 2H), 3.65 (s, 3H), 3.22–3.28 (m, 2H), 2.68–2.73 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 173.3, 136.4, 133.2, 128.6, 128.0, 51.7, 33.3, 27.9. HRMS (EI) *m*/*z* calculated for $C_{11}H_{12}O_3$ (M): 192.0781, found: 192.0783.

Ethyl 4-oxo-4-phenylbutanoate (2b). Yellow oil, 92% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.94 (m, 2H), 7.50–7.52 (m, 1H), 7.41 (t, J = 8.0 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.26 (t, J = 6.6 Hz, 2H), 2.70 (t, J = 6.6 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 172.8, 136.5, 133.1, 128.5, 128.0, 60.6, 33.3, 28.2, 14.1. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{14}NaO_3$ $[M + Na]^+$: 229.0835, found: 229.0839.

Methyl 4-oxo-4-(*m*-tolyl)butanoate (2c). Colorless oil, 72% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.78 (m, 2H), 7.31–7.37 (m, 2H), 3.69 (s, 3H), 3.29 (t, J = 6.7 Hz, 2H), 2.75 (t, J = 6.7 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 173.5, 138.5, 136.6, 134.1, 128.6, 128.5, 125.3, 51.9, 33.5, 28.1, 21.4. HRMS (FI) *m*/*z* calculated for $C_{12}H_{14}O_3$ $[M]^+$: 206.0937, found: 206.0943.

Methyl 4-oxo-4-(*p*-tolyl)butanoate (2d). White solid, 80% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 3.70 (s, 3H), 3.29 (t, J = 6.7 Hz, 2H), 2.75 (t, J = 6.7 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 173.4, 144.0, 134.0, 129.3, 128.1, 51.8, 33.3, 28.1, 21.6. HRMS (EI) *m*/*z* calculated for $C_{12}H_{14}O_3$ (M): 206.0937, found: 206.0938.

Methyl 4-(4-chlorophenyl)-4-oxobutanoate (2e). White solid, 83% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 3.69 (s, 3H), 3.27 (t, J = 6.6 Hz, 2H), 2.75 (t, J = 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.8, 173.2, 139.7, 134.8, 129.4, 128.9, 51.9, 33.3, 27.9. HRMS (FI) *m*/*z* calculated for $C_{11}H_{11}O_3Cl$ $[M]^+$: 226.0391, found: 226.0389.

Methyl 4-(4-fluorophenyl)-4-oxobutanoate (2f). White solid, 81% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98–7.02 (m, 2H), 7.10–7.14 (m, 2H), 3.69 (s, 3H), 3.25–3.29 (m, 2H), 2.73–2.77 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.4, 173.3, 165.8 (d, J = 255.5 Hz), 132.9 (d, J = 3.0 Hz), 130.6 (d, J = 9.4 Hz), 115.7 (d, J = 21.9 Hz), 51.8, 33.2, 27.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ −105.0 (m). HRMS (FI) *m*/*z* calculated for $C_{11}H_{11}O_3F$ $[M]^+$: 210.0687, found: 210.0690.

Methyl 4-oxopentanoate (2g). Yellow oil, 88% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3H), 2.78 (t, J = 8.1 Hz, 2H), 2.57 (t, J = 8.3 Hz, 2H), 2.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.6, 173.1, 51.6, 37.7, 29.7, 27.6. HRMS (EI) *m*/*z* calculated for $C_6H_{10}O_3$ (M): 130.0624, found: 130.0623.

Dimethyl succinate (2h). Yellow oil, 93% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (s, 6H), 2.61 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 51.8, 28.8. HRMS (ESI) *m*/*z* calculated for $C_6H_{10}NaO_4$ $[M + Na]^+$: 169.0471, found: 169.0470.

Diethyl succinate (2i). Colorless oil, 91% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1, ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99–4.05 (m, 4H), 2.48–2.50 (m, 4H), 1.11–1.16 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 172.1, 60.5, 60.4, 29.0, 28.9, 14.0. HRMS (FI) *m*/*z* calculated for $C_8H_{14}O_4$ $[M]^+$: 174.0887, found: 174.0884.

Methyl 3-phenylpropanoate (2j/4a). Yellow oil, 91% yield (**2j**)/92% yield (**4a**). Eluent: petroleum ether/ethyl acetate =

10 : 1, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.33 (m, 2H), 7.21–7.24 (m, 3H), 3.68 (s, 3H), 2.98 (t, J = 7.9 Hz, 2H), 2.66 (t, J = 8.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 140.5, 128.6, 128.4, 128.3, 126.3, 51.6, 35.7, 31.0 HRMS (FI) m/z calculated for $C_{10}H_{12}O_2$ $[M]^+$: 164.0832, found: 164.0829.

1-Phenylpyrrolidine-2,5-dione (2k). White solid, 91% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.27 (d, J = 7.9 Hz, 2H), 2.87 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 131.9, 129.2, 128.7, 126.5, 28.4. HRMS (FI) m/z calculated for $C_{10}H_9O_2N$ $[M]^+$: 175.0628, found: 175.0626.

Methyl propionate (2l/4b). Yellow oil, 99% yield (**2l**)/98% yield (**4b**). Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.48 (s, 3H), 2.11–2.17 (m, 2H), 0.92–0.97 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 51.1, 27.0, 8.7. HRMS (FI) m/z calculated for $C_4H_8O_2$ $[M]^+$: 88.0519, found: 88.0517.

Hydroquinone (6a). White solid, 91% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 6.63 (s, 4H). ^{13}C NMR (126 MHz, CD_3OD) δ 149.8, 115.5. HRMS (FI) m/z calculated for $C_6H_6O_2$ $[M]^+$: 110.0362, found: 110.0361.

[1,1′-Biphenyl]-2,5-diol (6b). White solid, 91% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.51 (dd, J = 7.9, 1.15 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.19–7.23 (m, 2H), 6.75–6.78 (m, 2H), 6.64–6.67 (m, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 150.0, 146.8, 138.8, 129.5, 129.0, 127.8, 126.5, 116.8, 116.7, 114.8. HRMS (EI) m/z calculated for $C_{12}H_{10}O_2$ (M): 186.0675, found: 186.0679.

2,3,5,6-Tetrabromobenzene-1,4-diol (6c). Brown solid, 80% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, d_6-DMSO) δ 9.92 (s, 2H). ^{13}C NMR (126 MHz, d_6-DMSO) δ 146.9, 115.9. HRMS (FI) m/z calculated for $C_6H_2O_2Br_4$ $[M]^+$: 421.6783, found: 421.6780.

2,3-Dimethoxy-5-methylbenzene-1,4-diol (6d). Colorless oil, 89% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (s, 1H), 5.48 (s, 1H), 5.40 (s, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 140.4, 139.1, 137.2, 119.4, 111.4, 60.8, 60.7, 15.4. HRMS (FI) m/z calculated for $C_9H_{12}O_4$ $[M]^+$: 184.0730, found: 184.0733.

2-Isopropyl-5-methylbenzene-1,4-diol (6e). White solid, 90% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (400 MHz, CD_3OD) δ 6.58 (s, 1H), 6.49 (s, 1H), 3.14–3.22 (m, 1H), 2.09 (s, 3H), 1.16 (d, J = 8.7 Hz, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 147.8, 146.5, 132.9, 121.6, 117.0, 112.2, 26.3, 21.9, 14.5. HRMS (FI) m/z calculated for $C_{10}H_{14}O_2$ $[M]^+$: 166.0988, found: 166.0987.

3,4,5,6-Tetrachlorobenzene-1,2-diol (8a). Yellow solid, 88% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.0, 123.7, 118.8. HRMS (FI) m/z calculated for $C_6H_2O_2Cl_4$ $[M]^+$: 245.8803, found: 245.8807.

3,5-Di-*tert*-butylbenzene-1,2-diol (8b). Yellow solid, 89% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.81 (s, 1H), 1.49 (s, 9H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 142.3, 140.9, 135.8, 115.9, 110.6, 34.9, 34.4, 31.6, 29.7. HRMS (FI) m/z calculated for $C_{14}H_{22}O_2$ $[M]^+$: 222.1614, found: 222.1621

General procedure for reduction of pyridinium salts. To a mixture of pyridinium salts (1 equiv.), $B_2(OH)_4$ (14 equiv.) and KO^{t}Bu (0.2 equiv.) was added a mixed solvent of MeOH (1.5 mL) and H_2O (3 mL) under a nitrogen atmosphere. The mixture was heated at 60 °C for 6 h. After cooling to room temperature, the mixture was extracted with ethyl acetate (10 mL × 3) three times. The ethyl acetate layer was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography with petroleum ether/ethyl acetate (5/1) as the eluent.

1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (10a). White solid, 91% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.48 (d, J = 7.5 Hz, 2H), 7.40–7.35 (m, 2H), 7.34–7.30 (m, 1H), 6.16–6.12 (m, 1H), 3.89 (s, 2H), 3.51 (t, J = 6.0 Hz, 2H), 2.98 (s, 3H), 2.91–2.86 (m, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 139.9, 136.7, 129.7, 129.4, 126.2, 117.0, 53.8, 52.2, 43.2, 26.0. HRMS (ESI) m/z calculated for $C_{12}H_{16}N$ $[M + H]^+$: 174.1277, found: 174.1278.

1-Methyl-5-phenyl-1,2,3,6-tetrahydropyridine (10b). White solid, 70% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.34 (d, J = 7.2 Hz, 2H), 7.31–7.27 (m, 2H), 7.24–7.18 (m, 1H), 6.12–6.08 (m, 1H), 3.26 (dd, J = 4.5, 2.5 Hz, 2H), 2.54 (t, J = 6.0 Hz, 2H), 2.39 (s, 3H), 2.36–2.31 (m, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 140.8, 136.0, 129.4, 128.2, 125.9, 122.8, 56.9, 52.2, 45.8, 26.9. HRMS (ESI) m/z calculated for $C_{12}H_{16}N$ $[M + H]^+$: 174.1277, found: 174.1276.

1-Methyl-6-phenyl-1,2,3,6-tetrahydropyridine (10c). White solid, 15% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.36–7.30 (m, 4H), 7.29–7.24 (m, 1H), 5.86–5.81 (m, 1H), 5.78–5.73 (m, 1H), 3.38–3.32 (m, 1H), 3.26 (dd, J = 10.0, 4.3 Hz, 1H), 2.97–2.90 (m, 1H), 2.47–2.38 (m, 1H), 2.26–2.18 (m, 1H), 2.02 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 143.4, 129.7, 129.0, 128.7, 126.4, 125.7, 67.2, 56.5, 42.3, 36.1. HRMS (ESI) m/z calculated for $C_{12}H_{16}N$ $[M + H]^+$: 174.1277, found: 174.1280.

1,4-Dimethyl-1,2,3,6-tetrahydropyridine (10d). Yellow oil, 83% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.48–5.44 (m, 1H), 3.69 (s, 2H), 3.38 (t, J = 6.0 Hz, 2H), 2.93 (s, 3H), 2.41 (s, 2H), 1.80 (m, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 134.8, 115.1, 53.3, 52.0, 43.0, 28.2, 22.6. HRMS (ESI) m/z calculated for $C_7H_{14}N$ $[M + H]^+$: 112.1121, found: 112.1121.

1-Butyl-4-methyl-1,2,3,6-tetrahydropyridine (10e). Yellow oil, 78% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.50–5.46 (m, 1H), 2.89 (s, 2H), 2.58 (t, J = 5.9 Hz, 2H), 2.47 (t, J = 8 Hz, 2H), 2.20–2.14 (m, 2H), 1.66 (s, 3H), 1.50–1.51 (m, 2H), 1.36 (dd, J = 15.1, 7.5 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 132.6, 120.5, 59.3, 57.5, 50.7, 29.6, 26.2, 21.9, 21.0, 14.4. HRMS (ESI) m/z calculated for $C_{10}H_{20}N$ $[M + H]^+$: 154.1590, found: 154.1593.

1-Benzyl-4-methyl-1,2,3,6-tetrahydropyridine (10f). Colorless oil, 90% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.72–6.98 (m, 5H), 5.38 (s, 1H), 3.58 (s, 2H), 2.95 (s, 2H), 2.57 (t, J = 5.4 Hz, 2H), 2.08 (d, J = 0.6 Hz, 2H), 1.70 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 132.7, 129.3, 128.2, 127.0, 119.4, 62.9, 53.0, 50.0, 30.9, 23.0. HRMS (ESI) m/z calculated for $C_{13}H_{18}N$ $[M + H]^+$: 188.1434, found: 188.1435.

1-Butyl-1,2,3,6-tetrahydropyridine (10g). Colorless oil, 88% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.88–5.82 (m, 1H), 5.72–5.67 (m, 1H), 3.33 (s, 2H), 2.94 (t, J = 6.0 Hz, 2H), 2.74 (t, J = 8.1 Hz, 2H), 2.34–2.29 (m, 2H), 1.66–1.58 (m, 2H), 1.38 (dd, J = 15.0, 7.5 Hz, 2H), 0.97 (d, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 126.4, 123.7, 58.5, 52.6, 50.7, 28.6, 25.3, 21.5, 14.2. HRMS (ESI) m/z calculated for $C_9H_{18}N$ $[M + H]^+$: 140.1434, found: 140.1435.

1-Benzyl-4-propyl-1,2,3,6-tetrahydropyridine (10h). Yellow oil, 90% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.35–7.23 (m, 5H), 5.36–5.33 (m, 1H), 3.56 (s, 2H), 2.94–2.91 (m, 2H), 2.57 (t, J = 5.9 Hz, 2H), 2.10–2.05 (m, 2H), 1.95 (t, J = 7.6 Hz, 2H), 1.43 (dq, J = 14.9, 7.5 Hz, 2H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 138.2, 137.6, 130.8, 129.3, 128.4, 119.4, 63.6, 53.6, 50.8, 40.0, 29.4, 21.6, 14.2. HRMS (ESI) m/z calculated for $C_{15}H_{22}N$ $[M + H]^+$: 216.1747, found: 216.1750.

1,4-Dibenzyl-1,2,3,6-tetrahydropyridine (10i). Yellow oil, 85% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.26 (m, 10H), 5.49 (s, 1H), 3.67 (s, 2H), 3.40 (s, 2H), 3.09 (s, 2H), 2.64 (t, J = 5.8 Hz, 2H), 2.16 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.5, 138.3, 135.8, 129.1, 129.0, 128.2, 128.2, 127.0, 126.0, 120.8, 62.7, 52.9, 49.9, 43.5, 28.9. HRMS (ESI) m/z calculated for: $C_{19}H_{22}N$ $[M + H]^+$: 264.1747, found: 264.1748.

1-Benzyl-4-(*tert*-butyl)-1,2,3,6-tetrahydropyridine (10j). Yellow oil, 90% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.30 (m, 4H), 7.27–7.25 (m, 1H), 5.43–5.40 (m, 1H), 3.58 (s, 2H), 3.02 (dd, J = 5.7, 2.6 Hz, 2H), 2.53 (t, J = 5.7 Hz, 2H), 2.19–2.15 (m, 2H), 1.03 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1, 138.3, 129.2, 128.1, 127.0, 115.7, 62.8, 53.4, 50.1, 34.8, 28.8, 25.4. HRMS (ESI) m/z calculated for: $C_{16}H_{24}N$ $[M + H]^+$: 230.1903, found: 230.1906.

1-Benzyl-4-(benzyloxy)-1,2,3,6-tetrahydropyridine (10k). Yellow oil, 85% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.37–7.23 (m, 10H), 4.73 (s, 2H), 4.71 (t, J = 3.4 Hz, 1H), 3.59 (s, 2H), 3.01 (dd, J = 5.4, 2.1 Hz, 2H), 2.64 (t, J = 6.0 Hz, 2H), 2.25 (t, J = 6.0 Hz, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 154.1, 138.8, 138.4, 130.7, 129.3, 128.7, 128.5, 128.5, 93.5, 69.8, 63.1, 52.2, 50.7, 29.0. HRMS (ESI) m/z calculated for $C_{19}H_{22}NO$ $[M + H]^+$: 280.1696, found: 280.1698.

1-Benzyl-5-chloro-1,2,3,6-tetrahydropyridine (10l). Yellow oil, 67% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.27 (m, 1H), 5.91–5.88 (m, 1H), 3.66 (s, 2H), 3.15 (dd, J = 4.5, 2.6 Hz, 2H), 2.61 (t, J = 5.7 Hz, 2H), 2.27–2.23 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.8, 129.0, 128.8, 128.4, 127.3, 122.6, 61.7, 57.4, 48.4, 26.3. HRMS (ESI) m/z calculated for: $C_{12}H_{15}ClN$ $[M + H]^+$: 208.0888, found: 208.0888.

1-Benzyl-4-(trifluoromethyl)-1,2,3,6-tetrahydropyridine (10m). Yellow oil, 72% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.36 (m, 5H), 6.39–6.35 (m, 1H), 3.71 (s, 2H), 3.17 (dt, J = 5.9, 2.9 Hz, 2H), 2.73 (t, J = 5.7 Hz, 2H), 2.44–2.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9, 129.0, 128.4, 127.3, 126.8 (q, J = 31.0 Hz), 124.8, 122.6, 62.2, 51.5, 48.5, 23.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ −69.4. HRMS (ESI) m/z calculated for $C_{13}H_{15}F_3N$ $[M + H]^+$: 242.1151, found: 242.1154.

1-Benzyl-2,5-dimethyl-1,2,3,6-tetrahydropyridine (10n). Colorless oil, 41% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.39–7.25 (m, 5H), 5.45–5.41 (m, 1H), 3.69 (dd, J = 181.7, 12.6 Hz, 2H), 2.97–2.81 (m, 3H), 2.33–2.25 (m, 1H), 1.96–1.88 (m, 1H), 1.59 (s, 3H), 1.15 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 138.5, 131.7, 130.9, 129.4, 128.6, 119.6, 58.3, 53.7, 52.6, 32.8, 20.9, 15.4. HRMS (ESI) m/z calculated for $C_{14}H_{20}N$ $[M + H]^+$: 202.1590, found: 202.1591.

1-Benzyl-2,4,6-trimethyl-1,2,3,6-tetrahydropyridine (10o). Yellow oil, 30% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.38–7.18 (m, 5H), 5.27 (s, 1H), 3.69 (d, J = 13.4 Hz, 1H), 3.56 (d, J = 12.3 Hz, 1H), 3.11 (d, J = 28.1 Hz, 2H), 2.06 (d, J = 17.4 Hz, 1H), 1.76 (d, J = 18.0 Hz, 1H), 1.68 (s, 3H), 1.16–1.07 (m, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 132.2, 130.2, 129.2, 127.9, 125.3, 53.0, 36.3, 32.2, 30.1, 23.4, 19.9, 14.7. HRMS (ESI) m/z calculated for $C_{15}H_{22}N$ $[M + H]^+$: 216.1747, found: 216.1749.

1-Benzyl-4-vinyl-1,2,3,6-tetrahydropyridine (10p). Yellow oil, 70% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.42–7.24 (m, 5H), 6.45–6.33 (m, 1H), 5.70 (s, 1H), 5.11 (dd, J = 17.5, 7.2 Hz, 1H), 5.00–4.93 (m, 1H), 3.62 (d, J = 7.7 Hz, 2H), 3.08 (s, 2H), 2.72–2.60 (m, 2H), 2.30 (s, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 139.6, 138.1, 135.8, 130.8, 129.4, 128.5, 126.7, 111.7, 63.5, 53.7, 50.4, 25.3. HRMS (ESI) m/z calculated for $C_{14}H_{18}N$ $[M + H]^+$: 200.1434, found: 200.1436.

Ethyl 1-benzyl-1,2,3,6-tetrahydropyridine-4-carboxylate (10q). Yellow oil, 82% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.28 (m, 5H), 6.95–6.91 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.65 (s, 2H), 3.17 (dd, J = 6.3, 3.0 Hz, 2H), 2.66 (t, J = 5.8 Hz, 2H), 2.50–2.46 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 137.9, 136.4, 128.8, 128.7, 128.2, 127.0, 62.2, 60.1, 52.5, 49.2, 25.2, 14.2. HRMS (ESI) m/z calculated for $C_{15}H_{20}NO_2$ $[M + H]^+$: 246.1489, found: 246.1491.

1-Methyl-1,2,5,6-tetrahydropyridine-3-carboxamide (10r). Yellow oil, 75% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 6.74 (s, 1H), 3.63 (d, J = 17.4 Hz, 1H), 3.47 (d, J = 17.1 Hz, 1H), 2.96–2.89 (m, 2H), 2.56 (s, 3H), 2.96–2.89 (m, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 170.8, 131.7, 129.8, 58.3, 56.0, 48.9, 23.1. HRMS (ESI) m/z calculated for $C_7H_{13}N_2O$ $[M + H]^+$: 141.1022, found: 141.1022.

***N*-(1-Benzyl-4-methyl-1,2,5,6-tetrahydropyridin-3-yl) acetamide (10s).** Yellow oil, 85% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.40–7.20 (m, 5H), 3.58 (s, 2H), 3.00–2.89 (m, 2H), 2.60 (t, J = 5.9 Hz, 2H), 2.17 (t, J = 5.4 Hz, 2H), 1.96 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 170.3, 138.2, 130.8, 129.4, 128.5, 127.2, 125.4, 63.1,

55.3, 50.6, 31.2, 22.5, 17.7. HRMS (ESI) *m/z* calculated for $C_{15}H_{21}N_2O$ $[M + H]^+$: 245.1648, found: 245.1651.

1-Methyl-1,2,3,4-tetrahydroquinoline (10t). Yellow oil, 60% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 6.99 (t, J = 7.8 Hz, 1H), 6.78 (d, J = 7.3 Hz, 1H), 6.55 (t, J = 7.3 Hz, 1H), 6.48 (d, J = 8.1 Hz, 1H), 6.28 (d, J = 9.8 Hz, 1H), 5.72–5.66 (m, 1H), 3.92–3.89 (m, 2H), 2.69 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 147.6, 129.9, 127.7, 127.5, 124.2, 123.6, 118.4, 111.1, 53.7, 37.7. HRMS (ESI) *m/z* calculated for $C_{10}H_{12}N$ $[M + H]^+$: 146.0720, found: 146.0723.

2-Methyl-1,2,3,4-tetrahydroisoquinoline (10u). Yellow oil, 91% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16–7.00 (m, 4H), 3.62–3.57 (m, 2H), 2.93 (t, J = 5.8 Hz, 2H), 2.70–2.46 (m, 2H), 2.52–2.30 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.7, 133.8, 128.6, 126.4, 126.1, 125.6, 58.0, 52.9, 46.1, 29.2. HRMS (ESI) *m/z* calculated for $C_{10}H_{14}N$ $[M + H]^+$: 148.1121, found: 148.1118.

Sodium(ı) 3-(3,6-dihydropyridin-1(2*H*)-yl)propane-1-sulfonate (10v). White solid, 35% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 6.02–5.97 (m, 1H), 5.78–5.72 (m, 1H), 3.78 (s, 2H), 3.42 (brs, 2H), 3.37 (t, J = 7.4 Hz, 2H), 2.95 (t, J = 6.7 Hz, 2H), 2.49 (s, 2H), 2.28–2.18 (m, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 126.6, 121.0, 56.7, 51.7, 50.2, 23.6, 21.1. HRMS (ESI) *m/z* calculated for $C_8H_{15}NO_3S$ $[M + H]^+$: 205.0710, found: 205.0716.

1,2-Bis(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)ethane (10w). Yellow oil, 68% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.40 (s, 2H), 2.94 (d, J = 2.2 Hz, 4H), 2.58 (t, J = 5.8 Hz, 4H), 2.33 (s, 6H), 2.20–2.13 (m, 4H), 2.12 (s, 4H). ^{13}C NMR (126 MHz, CD_3OD) δ 135.7, 117.9, 53.7, 51.6, 44.1, 34.4, 28.0. HRMS (ESI) *m/z* calculated for $C_{14}H_{25}N_2$ $[M + H]^+$: 221.2012, found: 221.2010.

1-Methyl-1,2,5,6-tetrahydro-2,2′-bipyridine (10x). Yellow oil, 62% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 8.50 (dd, J = 4.3, 0.6 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.35–7.32 (m, 1H), 5.91–5.75 (m, 2H), 3.47 (dd, J = 10.0, 4.3 Hz, 1H), 3.38 (dd, J = 16.9, 1.3 Hz, 1H), 2.53–2.44 (m, 1H), 2.32–2.24 (m, 1H), 2.06 (s, 4H). ^{13}C NMR (126 MHz, CD_3OD) δ 162.9, 149.8, 138.8, 125.8, 125.7, 124.2, 123.9, 68.1, 56.2, 43.3, 34.5. HRMS (ESI) *m/z* calculated for $C_{11}H_{15}N_2$ $[M + H]^+$: 175.1230, found: 175.1231.

2*H*-1,4′-Bipyridine (10y). Yellow oil, 71% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 8.22 (dd, J = 5.1, 1.6 Hz, 2H), 6.83 (dd, J = 5.1, 1.6 Hz, 2H), 6.66 (d, J = 7.7 Hz, 1H), 5.98–5.89 (m, 1H), 5.57–5.51 (m, 1H), 5.27–5.21 (m, 1H), 4.30 (dd, J = 4.0, 2.0 Hz, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 152.1, 150.2, 128.1, 123.7, 119.1, 109.6, 105.3, 46.7. HRMS (ESI) *m/z* calculated for $C_{10}H_{11}N_2$ $[M + H]^+$: 159.0917, found: 159.0919.

1,1′-Dimethyl-1,1′,2,2′,3,3′,6,6′-octahydro-2,2′-bipyridine (10aa). Yellow oil, 71% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.82–5.76 (m, 2H), 5.62–5.56 (m, 2H), 3.26–3.09 (m, 4H), 2.82–2.76 (m, 2H), 2.33 (s, 6H), 2.18–2.13 (m, 4H). ^{13}C NMR (126 MHz, CD_3OD) δ 126.0, 124.6, 59.6, 54.0, 38.0, 23.5. HRMS (ESI) *m/z* calculated for $C_{12}H_{21}N_2$ $[M + H]^+$: 193.1696, found: 193.1699.

1,1′-Dibenzyl-1,1′,2,2′,3,3′,6,6′-octahydro-4,4′-bipyridine (10ab). Yellow oil, 62% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.26 (m, 10H), 5.67 (s, 2H), 3.60 (d, J = 10.9 Hz, 4H), 3.11 (s, 4H), 2.66–2.59 (m, 4H), 2.32 (s, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.3, 129.4, 128.4, 127.3, 119.5, 110.1, 62.5, 53.2, 49.9, 25.9. HRMS (ESI) *m/z* calculated for $C_{24}H_{29}N_2$ $[M + H]^+$: 345.2325, found: 345.2327.

1,1′-Dibutyl-1,1′,2,2′,3,3′,6,6′-octahydro-4,4′-bipyridine (10ac). Yellow oil, 73% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.83 (s, 2H), 3.53 (s, 4H), 3.08 (t, J = 6.0 Hz, 4H), 2.87–2.81 (m, 4H), 2.53 (t, J = 5.1 Hz, 4H), 1.70–1.61 (m, 4H), 1.40 (dd, J = 15.0, 7.5 Hz, 4H), 0.98 (t, J = 7.4 Hz, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 134.9, 119.0, 58.0, 52.6, 50.6, 28.4, 25.0, 21.4, 14.1. HRMS (ESI) *m/z* calculated for $C_{18}H_{33}N_2$ $[M + H]^+$: 276.2475, found: 276.2478.

1,1′-Dimethyl-1,1′,2,2′,3,3′,6,6′-octahydro-4,4′-bipyridine (12). Yellow oil, 50% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 5.76 (s, 1H), 3.08 (d, J = 2.4 Hz, 2H), 2.63 (t, J = 6.0 Hz, 4H), 2.41–2.37 (m, 4H), 2.35 (s, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 135.0, 120.3, 55.5, 53.0, 45.5, 26.6. HRMS (ESI) *m/z* calculated for $C_{12}H_{21}N_2$ $[M + H]^+$: 193.1699, found: 193.1701.

Deuterium-labeling experiments for 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-2,3,6-D$_3$ (2h′). To a solution of dimethyl fumarate (**1h**) (1 equiv.) in THF (1.5 mL) was added a solution of $B_2(OH)_4$ (2 equiv.) and $NaHCO_3$ (0.2 equiv.) in D_2O (2 mL) under a nitrogen atmosphere. The mixture was heated to 60 °C for 1 h. After cooling to room temperature, the mixture was extracted with ethyl acetate three times. Then, the ethyl acetate phase was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography with petroleum ether/ethyl acetate (10/1) as the eluent.

Dimethyl succinate-2,3-D$_2$ (2h′). Yellow oil, 99% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 (s, 6H), 2.55 (d, J = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 51.7, 28.2–28.7 (m). HRMS (EI) *m/z* calculated for $C_6H_8D_2O_4$ (M): 148.0705, found: 148.0709.

Deuterium-labeling experiments for dimethyl succinate-D$_4$ (2h″). To a solution of dimethyl but-2-ynedioate (**3h**) (1 equiv.) in THF (1.5 mL) was added a solution of $B_2(OH)_4$ (4 equiv.) and $NaHCO_3$ (0.2 equiv.) in D_2O (2 mL) under a nitrogen atmosphere. The mixture was heated to 60 °C for 4 h. After cooling to room temperature, the mixture was extracted with ethyl acetate three times. Then, the ethyl acetate phase was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography with petroleum ether/ethyl acetate (10/1) as the eluent.

Dimethyl succinate-D$_4$ (2h″). Yellow oil, 97% yield. Eluent: petroleum ether/ethyl acetate = 10 : 1 ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 51.7, 28.1–28.6 (m). HRMS (FI) *m/z* calculated for $C_6H_6D_4O_4$ $[M]^+$: 150.0825, found: 150.0827.

Deuterium-labeling experiments for dimethyl succinate-2,3-D$_2$ (10a′). To a solution of 1-methyl-4-phenylpyridin-1-ium iodide (**9a**, 1 equiv.) in D_2O (2 mL) at rt was charged $B_2(OH)_4$ (8 equiv.) and KO^{t}Bu (0.2 equiv.) under a nitrogen atmosphere.

The mixture was heated to 60 °C for 3 h. After cooling to room temperature, the mixture was extracted with ethyl acetate (10 mL × 3) three times. Then, the ethyl acetate phase was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography with petroleum ether/ethyl acetate (5/1) as the eluent.

1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine-2,3,6-D_3 (10a′). White solid, 96% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.49 (d, J = 7.5 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 6.17–6.12 (m, 1H), 3.92 (s, 1H), 3.54 (s, 1H), 3.01 (s, 3H), 2.88 (s, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 139.8, 136.7, 129.7, 129.4, 126.2, 116.7, 51.7–52.2 (m), 50.1–50.6 (m), 41.6, 23.8–24.4 (m). HRMS (EI) m/z calculated for $C_{12}H_{12}D_3N$ (M): 176.1387, found: 176.1389.

Deuterium-labeling experiments for 1,4-dibenzyl-1,2,3,6-tetrahydropyridine-2,3,6-D_3 (10i′). To a solution of 1,4-dibenzylpyridin-1-ium bromide (**9i**, 1 equiv.) in D_2O (2 mL) at rt was charged $B_2(OH)_4$ (8 equiv.) and KO^{t}Bu (0.2 equiv.) under a nitrogen atmosphere. The mixture was heated to 60 °C for 3 h. After cooling to room temperature, the mixture was extracted with ethyl acetate (10 mL × 3) three times. Then, the ethyl acetate phase was separated, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography with petroleum ether/ethyl acetate (5/1) as the eluent.

1,4-Dibenzyl-1,2,3,6-tetrahydropyridine-2,3,6-D_3 (10i′). Yellow oil, 91% yield. Eluent: petroleum ether/ethyl acetate = 5 : 1 ^{1}H NMR (500 MHz, CD_3OD) δ 7.41–6.91 (m, 10H), 5.42 (s, 1H), 3.57 (s, 2H), 3.29 (d, J = 9.1 Hz, 2H), 3.03–2.88 (m, 1H), 2.63–2.40 (m, 1H), 2.01 (s, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 139.3, 136.6, 136.1, 129.5, 128.6, 128.0, 127.9, 127.2, 125.8, 119.6, 62.0, 51.5–52.1 (m), 48.6–49.2 (m), 43.0, 27.6–26.5 (m). HRMS (EI) m/z calculated for $C_{19}H_{18}D_3N$ (M): 266.1857, found: 266.1855.

Conflicts of interest

There are no conflicts to declare.

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