Electrochemical ammonium-cation-assisted pyridylation of inert N-heterocycles via dual-proton-coupled electron transfer

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Highlights

Electrochemical NH4+-assisted dual PCET followed by the radical cross-coupling

Straightforward and practical synthetic route for N-fused heterocycles

Fluorescence recognition of Fe2+ and Pd2+ with high-sensitivity

Inert N-heterocycle

Metal-free

NH4+ dual-role

40 examples

up to 93% yields

Dual PCET chemistry

DFT calculation

Fluorescence recognition of Fe2+ and Pd2+

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Electrochemical ammonium-cation-assisted pyridylation of inert N-heterocycles via dual-proton-coupled electron transfer

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SUMMARY
A straightforward and practical strategy for pyridylation of inert N-heterocycles, enabled by ammonium cation and electrochemical, has been described. This protocol gives access to various N-fused heterocycles and bidentate nitrogen ligand compounds, through dual-proton-coupled electron transfer (PCET) and radical cross-coupling in the absence of exogenous metal and redox reagent. It features broad substrate scope, wide functional group tolerance, and easy gram-scale synthesis. Various experiments and density functional theory (DFT) calculation results show the mechanism of dual PCET followed by radical cross-coupling is the preferred pathway. Moreover, ammonium salt plays the dual role of protonation reagent and electrolyte in this conversion, and the resulting product 9-(pyridin-4-yl)acridine compound can be used for fluorescence recognition of Fe^{2+} and Pd^{2+} with high sensitivity.

INTRODUCTION
Pyridines are among the most representative heterocycles in pharmaceuticals, materials, natural product molecules, and organic functional materials (Yadav and Reddy, 2003, Chen et al., 2006; Moser et al., 2008; Misale et al., 2013; Afeli et al., 2013; Felding et al., 2014; Kouznetsov et al., 2017; Gil-Martins et al., 2020). As a result, new methods for the construction of functionalized pyridines from abundant precursors are an important synthetic goal (Nakao, 2011; Murakami et al., 2017; Wang et al., 2021, Zhou and Jiao, 2021). It is considered a straightforward and challenging protocol to access biologically active N-heterocyclic compounds from the inert N-heterocycles with cyanopyridine derivatives via the mechanism of radical cross-coupling reaction (Scheme 1A) (Proctor and Phipps, 2019; Bardi and Starr, 2017; Dong et al., 2021, Jin and MacMillan, 2015; Li, 2009; Ma et al., 2017, Wang et al., 2017). It is well known that electron-deficient pyridine derivatives are often modified into salts as radical acceptors for Minisci reactions due to their inherently negative electrode potential, which makes them difficult to activate (Scheme 1B) (Proctor and Phipps, 2019). The dual-proton-coupled electron transfer strategy may provide a promising roadmap for this transformation (Lehnerr et al., 2020; Murray et al., 2022; Tay et al., 2022). Although various elegant pyridylation strategies have been established in recent years by employing photocatalysis and metal or metal-free catalysis (Huang et al., 2021; Kim et al., 2019; Novaes et al., 2021; Shen et al., 2021; Tong et al., 2021; Xu et al., 2021; Zhang et al., 2017a, 2017b, 2020, 2021; Zhu et al., 2019). However, the pyridylation of inert N-heterocyclic derivatives via dual-proton-coupled electron transfer with radical cross-coupling in the absence of metals and external reducing agents under the conditions of electrochemical has not been reported (Wu et al., 2021; Zeng et al., 2021; Liu et al., 2018; Lu et al., 2022; Yuan et al., 2021; Chen et al., 2010; Zhao et al., 2006).

In recent years, multifarious important pyridine-containing functional molecules have been constructed based on the decyanation of cyanopyridines mediated by electrochemical reduction (Xu et al., 2021; Zhang et al., 2020, 2021; Lehnerr et al., 2020, Wen et al., 2021). Previously, we have delivered the C3 pyridylation of quinoxalin-2(1H)-ones with readily available cyanopyridines under the electrochemical conditions by employing HFIP as the protonation reagent (Scheme 1C) (Wen et al., 2021). However, we found that the pyridylation of electron-deficient quinolines cannot be achieved by adopting the previous protocol. Inspired by the mechanism of electrochemical ammonium cation-assisted ketone-activated alkene hydrogenation of pyridine to obtain β-pyridyl ketones (Yang et al., 2022), Herein, we developed the first straightforward and practical strategy for the pyridylation of electron-deficient quinolines aided by NH4⁺ in an...
undivided cell via the dual PCET followed by the radical cross-coupling (Scheme 1D). All the experimental and DFT calculation results have disclosed that the mechanism of dual PCET and radical cross-coupling pathway is more reasonable. Interestingly, 9-(pyridin-4-yl)acridine compounds can be applied to the fluorescence recognition of Fe$^{2+}$ and Pd$^{2+}$ with high sensitivity.

**RESULTS AND DISCUSSION**

**Optimization conditions**

The electrochemical pyridylation of electron-deficient quinolines was selected as a benchmark (Table 1). Initially, 4-methylquinoline 1e and 4-cyanopyridine 2a were selected as the template coupling substrate to optimize the reaction conditions. By optimizing various reaction parameters, it was found that the desired product 3ea was obtained in 88% isolated yield by performing the reaction under constant current electrolysis at 20 mA cm$^{-2}$ in an undivided cell using NH$_4$OAc as the electrolyte and protonation reagent and two carbon rods as the working electrode and anode in CH$_3$CN/DMSO at 60°C for 5 h (Table 1, entry 1). Undoubtedly, the control experiments demonstrate that both electricity and NH$_4^+$ play a key role in this

![Scheme 1. Pyridation of N-heterocycles](image-url)

(A) Radical cross-coupling strategy, (B) Minisci reaction, (C) Our previous work, (D) Pyridylation of N-heterocycles.
transformation (Table 1, entries 2–3). Moving the reaction to ambient temperature caused the yield to fall from 88% to 65%, suggesting that adequate heating is more conducive to this conversion (Table 1, entry 4). To our delight, the desired product 3ea can be delivered in 66% and 93% yields by employing NH4I and NH4Br as sources of ammonium cations (Table 1, entries 5–6). Besides, it was found that both increasing and decreasing the amount of NH4OAc or the total charge was detrimental to the output of the desired product (Table 1, entries 7–8). Varying the mixed solvent of CH3CN/DMSO also led to significantly lower yields (Table 1, entries 9–11). Finally, the effect of the electrode material was also investigated, and the reaction efficiency was lower when platinum plates were used in place of carbon rods as anode or cathode (Table 1, entries 12–13).

Mechanistic studies

Experimental studies

With the optimized conditions at hand, to better understand the mechanism of this reaction, various CV, 1H NMR, and control experiments were preferentially carried out. Firstly, several CV and 1H NMR experiments were performed to expound the role of NH4+ in the pyridylation of 4-methylquinoline (Figure 1). The reduction electrode potentials of 1e and 2a were preferentially recorded with Eonset = 1.86 V versus Ag/AgCl (Figure 1A, black line) and Eonset = 1.6 V versus Ag/AgCl (Figure 1B, black line), respectively. Based on the CV results, we speculate that the peaks of 0.98 V versus Ag/AgCl and 1.01 V versus Ag/AgCl should be attributed to the reduction electrode potentials of INT1 and INT4, respectively. Subsequently, we observed a significant positive shift in the reduction electrode potential of 1e or 2a with the increasing NH4OAc concentration. These results are consistent with the PCET process in this reaction. Besides, a series of 1H NMR experiments were designed and carried out to further verify the protonation of 1e or 2a with NH4OAc. As shown in Figure 2, the hydrogen of NH4+ (5.91 ppm) was completely consumed in the presence of 1e or 2a, a broad peak at 6.28 ppm or 6.7 ppm was

### Table 1. Optimization of the reaction conditions

| Entry | Deviation from standard conditions | The yield of 3ea (%) |
|-------|-----------------------------------|---------------------|
| 1     | none                              | 88                  |
| 2     | without current                   | n. d.               |
| 3     | without NH4OAc with n-Bu4NBF4 as electrolyte | 10                  |
| 4     | room temperature                  | 65                  |
| 5     | NH4I instead of NH4OAc            | 66                  |
| 6     | NH4Br instead of NH4OAc           | 93                  |
| 7     | entry 1, but 1.0 mmol or 2.0 mmol of NH4OAc | 65, 80             |
| 8     | entry 1, but 15 mA, or 25 mA      | 53, 84              |
| 9     | without DMSO                      | 4                   |
| 10    | DMF instead of DMSO               | 16                  |
| 11    | CH3ClI instead of CH3CN           | 51                  |
| 12    | Pt (−) instead of C (−)           | 14                  |
| 13    | Pt (+) instead of C (+)           | 27                  |

*Reaction conditions: carbon rods (Φ = 6 mm) as the anode, carbon rods (Φ = 6 mm) as the cathode, constant current 20 mA, 1d (0.25 mmol), 2a (0.75 mmol), NH4OAc (1.5 mmol, 115.5 mg), CH3CN/DMSO (1:1, v/v, 10.0 mL), 60 °C, N2, 5 h (14.9 Fmol−1). ’n. d.’ = not detected.

*Isolated yield.
highlighted, and all of the chemical shifts were shifted to higher filed. These results further demonstrate that both $1e$ and $2a$ are readily protonated with NH$_4^+$ to generate pyridinium, which leads to the electrode potential of $1e$ to drop from -1.86 V to -1.45 V versus Ag/AgCl and $2a$ to drop from -1.61 V to -1.27 V versus Ag/AgCl. Moreover, the reduction electrode potentials of $1e$ ($E_{onset} = -1.45$ V versus Ag/AgCl) and $2a$ ($E_{onset} = -1.27$ V versus Ag/AgCl) in the presence of NH$_4$OAc were compared, and the result confirms that the protonated $2a$ should be preferentially reduced on the surface of the cathode (Figure 3A).
Furthermore, the square-wave voltammetry (SWV) experiments of 1e and 2a were performed in the presence of NH₄OAc to further explore the electron transfer of the reaction mechanism (Figure 3B) (Yang et al., 2022; Peters et al., 2019; Liu et al., 2020). The peak splits significantly with the frequency change, which is consistent with the process of proton-coupled electron transfer. To our delight, the SWV results of the mixture of 1e and 2a indicate that this transformation should be performed by four-electron transfer (Figure 3B, black line, 5 Hz), which is consistent with the conclusion of the DFT calculation.

Next, various radical inhibition and potentiostatic electrolysis experiments were performed to gain insight into the details of the reaction mechanism (Scheme 2). First, the desired product 3ea was almost suppressed when CBr₄ and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) were employed as radical inhibitors, indicating that the mechanism of the radical process should be experienced in this transformation (Schemes 2A and 2B). Subsequently, a series of potentiostatic electrolysis experiments were carried out to verify our speculation on the reduction potential of INT1 (−0.98 V versus Ag/AgCl) and INT4 (−1.01V versus Ag/AgCl). To our delight, the desired product 3ea was not observed when the reaction was performed at −0.3 V ~ −0.9 V versus Ag/AgCl. Moreover, an isolated yield of 85% can be obtained when the reaction was performed at −1.2 V versus Ag/AgCl, and the increasing voltage has practically no effect on the yield of 3ea (Scheme 2C). The results of these potentiostatic electrolysis experiments further confirmed our speculation. Based on the aforementioned experimental results, we speculate the more reasonable mechanism of the reaction should be through the concerted PCET (vide infra) and free radical cross-coupling pathways.

**Computational investigations**

The density functional theory (DFT) calculation was employed to further verify our speculation on this conversion mechanism. All DFT calculations of both ground-state and transition-state structures were performed using M06-2X/6-31+G(d,p) with SMD = DMSO solvation and the Gaussian 09 software package (Frisch et al., 2009). Frequencies were calculated for all the stationary points to confirm if each optimized structure is a local minimum on the respective potential energy surface or a transition state structure with only one imaginary frequency. Scheme 3A outlines several potential reaction pathways to obtain the desired product 3ea from 4-cyanopyridine 2a and 4-methylquinoline 1e under cathodic electrolysis, via sequential reduction and convergence of diradical coupling process. Reduction of each coupling partner (4-cyanopyridine and 4-methylquinoline) can occur from either its neutral entity or protonated state. For example, the subsequent radical (e.g., radical INI2) could add to the radical anion intermediate 1e' (Scheme 3A, path a) or protonated state (INT4, Scheme 3A path b). Alternatively, the mechanism of biradical coupling (path c) could be smoothly operated, in which each coupling partner is singly reduced before a barrierless biradical coupling to afford INT7, which after the loss of two H⁺ and one HCN would produce the desired product 3ea. To discern between these pathways, we examined each pathway using DFT
calculations. The reduction of 4-methylquinoline 1e can occur from its neutral entity or protonated state. In contrast, the electrochemical reduction of the protonated state INT4 (E_red = -1.16 V versus SCE) is easier to generate the radical intermediates INT6. Similarly, the electroreduction of the protonated state INT1 of 4-cyanopyridine 2a is quite facile (E_red = -1.15 V versus SCE) to deliver the intermediate INT2, which can be demonstrated by various potentiostatic electrolysis experiments (Scheme 2C). In path a, the cross-coupling step is the reaction of radical anion intermediate 1e' (E_red = -2.06 V versus SCE) with INT2 via transition state TS1, forming complex INT3 absorbs protons to gain INT7. However, the determining step is that the formation of the radical anion intermediate 1e requires a more negative electrode potential in path a, and this conclusion can also be verified from the CV experiments of 1e (Figure 2A). To examine path b in Scheme 3A, we performed a relaxation energy scan to afford the Minisci-type complex INT5 between the radical intermediate INT2 and the protonated form of 1a by employing NH4+ as the acid. The energy increased monotonically without passing through a maximum as the C−C interatomic distance was decreased from 2.25 to 1.65 Å with 0.05 Å increments, suggesting this process is unfeasible. The aforementioned data suggest that path a and path b can be ruled out.

Alternatively, a biradical pathway could be invoked (Scheme 3A, path c). The intermediates INT2 (ΔG = 3.6 kcal/mol, E_red = -1.15 V versus SCE) and INT6 (ΔG = 2.7 kcal/mol, E_red = -1.16 V versus SCE) are simultaneously produced on the cathode surface from 2a and 1e with NH4+ via the mechanism of PCET. Subsequently, the intermediate INT7 can be obtained through a barrierless radical cross-coupling of the intermediate INT2 and INT6, with an energy release of 6.9 kcal/mol (calculated relative to the complexes [Int2 + Int6]). Next, the direct dissociation of HCN molecules from INT7 through transition state TS2 to provide INT8 was regarded as a routine process in the previous work. The corresponding transition state TS3 was obtained to be 37.6 kcal/mol lower than TS2 when the direct coordination of NH3 to INT7 affords INT9 with the release of NH4+, suggesting the reaction pathway via TS3 more favorable kinetically. The intermediate INT9 removes the cyano group to give INT10 from the transition state TS4, and then the

Scheme 2. Control experiments

| entry | Potential (V vs Ag/AgCl) | Isolated yield of 3ea (%) |
|-------|-------------------------|--------------------------|
| 1     | - 0.3 ~ - 0.9            | 0                        |
| 2     | - 1.0 for 6 h            | 42                       |
| 3     | -1.2                     | 85                       |
| 4     | -1.4 for 4.5 h           | 86                       |
| 5     | -1.6 for 3.75 h          | 85                       |

A

\[
\begin{align*}
1e & \quad + \quad 2a \\
\text{NH}_2\text{OAc} (1.5 \text{ mmol}), 60 ^\circ \text{C}, \text{N}_2 \quad & \quad \text{C (+)} + \text{C (-)}, I = 20 \text{ mA} \\
\text{CH}_3\text{CN/DMSO} (10.0 \text{ mL}, v = 1 : 1) \quad & \quad \text{undivided cell} \\
\text{CBrz} (3.0 \text{ equiv}), 5 \text{ h} (14.9 \text{ Fmol}^{-1}) \quad & \quad \text{3ea, n. d.}
\end{align*}
\]

B

\[
\begin{align*}
1e & \quad + \quad 2a \\
\text{NH}_2\text{OAc} (1.5 \text{ mmol}), 60 ^\circ \text{C}, \text{N}_2 \quad & \quad \text{C (+)} + \text{C (-)}, I = 20 \text{ mA} \\
\text{CH}_3\text{CN/DMSO} (10.0 \text{ mL}, v = 1 : 1) \quad & \quad \text{undivided cell} \\
\text{TEMPO (3.0 equiv), 5 h} (14.9 \text{ Fmol}^{-1}) \quad & \quad \text{3ea, 23%}
\end{align*}
\]

C

\[
\begin{align*}
1e & \quad + \quad 2a \\
\text{NH}_2\text{OAc} (1.5 \text{ mmol}), 60 ^\circ \text{C}, \text{N}_2 \quad & \quad \text{C (+)} + \text{C (-)}, I = 20 \text{ mA} \\
\text{CH}_3\text{CN/DMSO} (10.0 \text{ mL}, v = 1 : 1) \quad & \quad \text{undivided cell} \\
\text{Potentiostatic electrolysis} \quad & \quad \text{3ea}
\end{align*}
\]
β-hydrogen of INT10 is attacked by CN⁻ to deliver INT11 through TS5 with the release of HCN. Moreover, we noticed that INT13 was obtained from INT11 through coherent anodization and deprotonation with the help of NH₃ molecules via transition state TS6. Finally, the anodized intermediate INT13 would yield the desired product 3ea. The ΔG⁰ barrier associated with the loss of cyanide from INT9 via rate-determining transition state TS4 is smaller (+23.6 kcal/mol) and can be easily overcome at 60°C temperature. Furthermore, the models of key calculation intermediates have been arranged in Scheme 3B (Legault, 2009). Besides, we also checked the hydrogen generation pathways using DFT calculations and found that all pathways are infeasible starting from INT7 and INT10 in path c (Scheme S1).

**Substrate scope**

Guided by the proposed reaction mechanism, the substrate scope and limitations of the established protocol were examined under optimal reaction conditions as shown in Table 1, entry 1. Initially, the scope of the pyridylation of quinoline derivatives agreeable to this protocol was investigated based on 4-cyanopyridine 2a. As shown in Scheme 4, a variety of quinolines bearing electron-donating and electron-withdrawing substituents in different positions are viable partners under the current protocols (3aa-3na) and selective, affording the corresponding products in yields of 52%–93%. Specifically, the C4 pyridylation of quinoline derivatives is the main product when C4 has no substituent. Interestingly, the desired product 4aa can be obtained with a yield of 40% when 2a was carried out under the given conditions, whereas only trace amounts of 3oa and 3pa were observed under the present protocol. Moreover, the reaction proceeded smoothly, and the corresponding products were delivered with a yield of 58%–70% when quinazoline, phenanthridine, and acridine were executed under the established conditions (3qa-3sa). Subsequently, the scope of the cyanopyridines was investigated by employing acridine as a...
benchmark. To our delight, the desired products 3sc and 3sd can be delivered smoothly when 2-fluoroisonicotinonitrile and 3-chloroisonicotinonitrile were executed under current condition, which was difficult to achieve in previous reports (Xu et al., 2021; Zhang et al., 2020, 2021; Lehnherr et al., 2020; Wen et al., 2021). Besides, a variety of 2-cyanopyridine derivatives can also be compatible with the present protocol and deliver the corresponding products with good yields (3se–3sb). Unfortunately, benzonitrile and terephthalonitrile do not yield the desired product under established conditions. Finally, a series of important bidentate nitrogen ligand compounds (3ai–3eb) were synthesized by employing this simple and practical strategy to further enrich the types of bidentate nitrogen ligand library.

**Scheme 4. Substrate scope**

Reaction conditions: carbon rods (ϕ = 6 mm) as the anode, carbon rods (ϕ = 6 mm) as the cathode, constant current 20 mA, 1 (0.25 mmol), 2 (0.75 mmol), NH4Br (1.5 mmol), CH3CN/DMSO (1 : 1, v/v, 10.0 mL), 60°C, N2, 5 h (14.9 Fmol⁻¹). “n. d.” = not detected. "NH4OAc (1.5 mmol), DMSO (6.0 mL). All cited yields are isolated yields.

**Gram-scale synthesis**

The synthetic applicability of this protocol was investigated on a gram-scale reaction between 1e or 1s and 2a. As shown in Scheme 5, the reaction could afford 3sa and 3sa in 76% and 60% yields, respectively. The results demonstrate the present protocol can serve as a simple and practical strategy to obtain the desired products via pyridylation of inert N-heterocycles.

**Synthetic application**

To display the potential application prospects of these compounds, 3sa was selected as the benchmark for a series of fluorescence experiments (Figure 4) (Zou et al., 2008). At the outset, we found that 3sa has strong fluorescence absorption in neutral and alkaline aqueous solutions (7 times stronger than acridine, Figure S84), and the obvious redshift was imagined to be caused by the acidification of 3sa into salt in an acidic environment (Figure 4A). Subsequently, the fluorescence response of various metal ions was investigated in
a neutral aqueous solution, and it was found that Fe\(^{2+}\) had a significant redshift, whereas Pd\(^{2+}\) had no absorption (Figure 4B). These results indicate that 3sa could be served as a sensor for the fluorescence recognition of Fe\(^{2+}\) and Pd\(^{2+}\) in aqueous solutions. Moreover, the response of 3sa for the concentration of Fe\(^{2+}\) was investigated in a neutral aqueous solution, and the results showed that the recognizable Fe\(^{2+}\) concentration was as low as \(2.5 \times 10^{-5}\) mmol/L (Figure 4C). Furthermore, we also found that the fluorescence redshift response concentration of Fe\(^{2+}\) ranges from \(2.5 \times 10^{-5}\) mmol to \(2 \times 10^{-4}\) mmol/L (Figure 4D).

**Scheme 5. Gram-scale synthesis**

**Figure 4. Fluorescence experiments**

(A–C) Concentration of 3sa: \(5 \times 10^{-5}\) mmol/L.

(B) Concentration of metal ions: \(5 \times 10^{-5}\) mmol/L.

(C) Fluorescence response of different Fe\(^{2+}\) concentrations.

(D) The relationship between the concentration of Fe\(^{2+}\) and the wavelength.
**Conclusion**

In summary, the electrochemical NH4+ -assisted pyridylation of the inert N-heterocycles approach has been developed. A variety of important N-fused heterocycles and bidentate nitrogen ligand compounds has been obtained via the mechanism of dual PCET and radical cross-coupling mediated by sequentially paired electrolysis. The proposed mechanism has been confirmed from experiments and DFT calculations. Moreover, the resulting product 9-(pyridin-4-yl)acridine derivatives could be served as a sensor for fluorescence recognition of Fe2+ and Pd2+, and the recognizable Fe2+ concentration was as low as $2.5 \times 10^{-5}$ mmol/L. Finally, we anticipate the report of this work will provide theoretical support for the activation and functionalization of N-containing compounds under electrochemical conditions.

**Limitations of study**

Substrate scope of inert N-heterocycles is limited to the cyanopyridine and quinoline derivatives.

**STAR METHODS**

Detailed methods are provided in the online version of this paper and include the following:

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**SUPPLEMENTAL INFORMATION**

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2022.104253.

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**AUTHOR CONTRIBUTIONS**

N. C., Y. J., and W. J. conceived the project and designed the experiments. Y. J. and W. J. wrote the manuscript. N. C., J. W., and X. J. performed and analyzed experiments. L. B. performed theoretical calculations. All the authors discussed the results of the manuscript.

**DECLARATION OF INTERESTS**

The authors declare no competing interests.

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## STAR METHODS

### KEY RESOURCES TABLE

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---------------------|--------|------------|
| Quinoline           | Adamas | 91-22-5    |
| 2-Methylquinoline   | Adamas | 91-63-4    |
| 2-Phenylquinoline   | Aladdin| 612-96-4   |
| 3-Chloroquinoline   | Adamas | 612-59-9   |
| 4-Methylquinoline   | Adamas | 491-35-0   |
| 5-Chloroquinoline   | Aladdin| 635-27-8   |
| 5-Bromoquinoline    | Adamas | 4964-71-0  |
| 6-Fluoroquinoline   | Adamas | 396-30-5   |
| 7-Chloroquinoline   | Aladdin| 612-61-3   |
| 2,6-Dimethylquinoline| Macklin| 877-43-0  |
| 6-Bromo-2-methylquinoline| Macklin| 877-42-9 |
| 8-Methylquinoline   | Adamas | 611-32-5   |
| 8-Fluoroquinoline   | Adamas | 394-68-3   |
| 8-Chloroquinoline   | Aladdin| 611-33-6   |
| Pyridine            | Adamas | 110-86-1   |
| 4-Methylpyridine    | Adamas | 108-89-4   |
| Quinazoline         | Arkpharm| 253-82-7  |
| Phenanthridine      | MREDA  | 229-87-8   |
| Acridine            | Macklin| 260-94-6   |
| 4-Cyanopyridine     | Macklin| 100-48-1   |
| Isoquinoline-1-carbonitrile| Macklin| 1198-30-7 |
| 2-Fluoroisonicotinonitrile| Macklin| 3939-14-8 |
| 3-Chloro-4-cyanopyridine| Aladdin| 68325-15-5|
| 4-Methyl-2-pyridinecarbonitrile| Adamas| 1620-76-4 |
| Methyl 2-cyanoisonicotinate| Arkpharm| 94413-64-6|
| 4-tert-butylpyridine-2-carbonitrile| Bidei| 42205-73-2|
| 2-Cyano-6-methylpyridine| Aladdin| 1620-75-3|
| NH₄OAc              | Adamas | 631-61-8   |
| NH₄Br               | Aladdin| 12124-97-9 |
| NH₃                 | Adamas | 12027-06-4 |

### RESOURCE AVAILABILITY

#### Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Jiangwei Wen ([wenjy@qfnu.edu.cn](mailto:wenjy@qfnu.edu.cn)).

#### Materials availability

All materials generated in this study are available in the article and [supplemental information](#) or from the lead contact without restriction upon reasonable request.

#### Data and code availability

Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.
METHOD DETAILS

General information
All glassware was oven dried at 100 °C for hours and cooled down under vacuum. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. The instrument for electrolysis is dual display potentiostat (DJS-292B) (made in China), the carbon rod (d: 6 mm) was purchased from Xuzhou Xinke Instrument and Meter Co. LTD. Cyclic voltammetry was performed in a three-necked flask (25.0 mL) with CHI/760E as the electrochemical workstation, glassy carbon as the working electrode, Pt (1.5 × 1.5 cm⁻¹) as the counter electrode, and Ag/AgCl (KCl) as the reference electrode. Thin-layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200–300 mesh silica gel in petroleum (b. p. 60-90 °C). 1H, 13C NMR, and 19F NMR data were recorded with Bruker Advance III (500 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. All chemical shifts are reported relative to tetramethylsilane and d-solvent peaks (77.00 ppm, chloroform), respectively.

General procedure for electrochemical ammonium cation-assisted pyridylation of inert N-heterocycles
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, 1 (0.25 mmol), 2 (0.75 mmol), and NH4OAc (1.5 mmol, 115.5 mg) or NH4Br (1.5 mmol, 145.5 mg) were combined and added. The flask was equipped with carbon rods (φ = 6 mm) as the anode and carbon rods (φ = 6 mm) as the cathode (distance between electrodes (5 - 10 mm)) and was then charged with nitrogen. Under the protection of nitrogen, DMSO (6.0 mL) or DMSO/CH3CN (10.0 mL, v/v = 1 : 1) were slowly injected into the reaction flask. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA under 60 °C for 5 h. When the reaction was finished, the reaction mixture was washed with water and extracted with CH2Cl2 (10 mL x 3). The organic layers were combined, dried over Na2SO4, and concentrated. The pure product was obtained by flash column chromatography on silica gel (Scheme 4).

Procedure for gram-scale experiments
In an oven-dried undivided three-necked flask (150 mL) equipped with a stir bar, 1e or 1s (5.0 mmol), 2a (35.0 mmol), and NH4OAc (7.5 mmol, 577.5 mg) were combined and added. The flask was equipped with carbon rods (φ = 6 mm) as the anode and carbon rods (φ = 6 mm) as the cathode and was then charged with nitrogen. Under the protection of nitrogen, DMSO (50.0 mL) or CH3CN/DMSO (50.0 mL, v = 1/1) was slowly injected into the reaction flask. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA under 60 °C for 24 h (3.58 Fmol⁻¹). When the reaction was finished, the reaction mixture was washed with water and extracted with CH2Cl2 (10 mL x 3). The organic layers were combined, dried over Na2SO4, and concentrated. The pure products 3ea and 3sa were obtained with isolated yields of 76 and 60%, respectively (Scheme 5).

Procedure for radical trapping experiments
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, 2a (0.75 mmol, 78.0 mg), CBr4 or TEMPO (0.75 mmol), and NH4OAc (1.5 mmol, 115.5 mg) were combined and added. The flask was equipped with a carbon rod (φ = 6 mm) as the anode and carbon rods (φ = 6 mm) as the cathode and was then charged with nitrogen. Under the protection of nitrogen, CH3CN (5.0 mL), DMSO (5.0 mL), and 1e (0.25 mmol, 33.0 μL) were slowly injected into the reaction flask. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA under 60 °C for 5 h (14.9 Fmol⁻¹). After the reaction was completed, the solution was concentrated in a vacuum and not detected the desired product 3ea when CBr4 was added. Only 24% yield of the product can be obtained when TEMPO was added into the reaction (Schemes 2A and 2B).

Procedure for potentiostatic electrolysis
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, 1e (0.25 mmol), 2a (0.75 mmol), and NH4OAc (1.5 mmol, 115.5 mg) were combined and added. The flask was equipped with carbon rods (φ = 6 mm) as the anode and carbon rods (φ = 6 mm) as the cathode and was then charged with nitrogen. Under the protection of nitrogen, CH3CN/DMSO (10.0 mL, v = 1/1) was slowly injected into the reaction flask. The reaction mixture was stirred and potentiostatic electrolysis under 60 °C. When the reaction was finished, the reaction mixture was washed with water and extracted with CH2Cl2 (10 mL x 3). The
organic layers were combined, dried over Na₂SO₄, and concentrated. The pure products 3ea was obtained with isolated yields of 42–86%, respectively (Scheme 2C).

**Cartesian coordinates of DFT optimized structures (Scheme 3)**

Structure: 2a

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -340.405766087 hartree

SCF Energy + ZPVE: -340.317523087 hartree

Free Energy: -340.347767 hartree

| C    | -2.571884265 | 1.008116473 | 000077007 |
|------|--------------|-------------|-----------|
| C    | -1.175925754 | 1.010471325 | 000502393 |
| C    | -0.533527459 | 2.245577093 | 000013667 |
| C    | -2.519576754 | 3.392171115 | 001469848 |
| C    | -3.267667316 | 2.218197647 | 000937630 |
| H    | -0.609408387 | 0.086322260 | 001278108 |
| H    | 0.551840938  | 2.292079008 | 000017144 |
| H    | -3.022314843 | 4.355143705 | 002257963 |
| H    | -4.351332571 | 2.246710177 | 001289917 |
| C    | -3.293429947 | 0.240181311 | 000662913 |
| N    | -3.871729476 | 1.242053748 | 001118242 |
| N    | -1.182578166 | 3.414798258 | 001092178 |

Structure: NH₄⁺

Charge = 1 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -56.997554118 hartree

SCF Energy + ZPVE: -56.948082118 hartree

Free Energy: -56.967730 hartree

| N    | -3.902376867 | -1.296316683 | 0000861666 |
|------|--------------|-------------|-----------|
| H    | -3.106389072 | -0.750596627 | 0341988950 |
| H    | -3.828533098 | -2.258260512 | 0342612795 |
| H    | -4.772431434 | -0.878589496 | 0342376399 |
| H    | -3.902166819 | -1.296676883 | -1022342560 |

Structure: INT1

Charge = 1 Multiplicity = 1

Number of imaginary frequencies: 0
SCF Energy: -397.412869783 hartree

SCF Energy + ZPVE: -397.273779783 hartree

Free Energy: -397.309668 hartree

Structure: NH₃

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -56.535103739 hartree

SCF Energy + ZPVE: -56.500700739 hartree

Free Energy: -56.519774 hartree

Structure: INT2

Charge = 0 Multiplicity = 2

Number of imaginary frequencies: 0

SCF Energy: -340.984355474 hartree

SCF Energy + ZPVE: -340.885420474 hartree
Free Energy: -340.916771 hartree

|   |      |      |            |
|---|------|------|------------|
| C | -2.625614870 | 0.915486388 | 0.000117019 |
| C | -1.190496524 | 0.944926376 | 0.000538036 |
| C | -0.534952869 | 2.136576333 | -0.000067998 |
| C | -2.613074753 | 3.336464230 | -0.001493200 |
| C | -3.317554432 | 2.173163608 | -0.000928158 |
| H | -0.619407753 | 0.023642152 | 0.001334928 |
| H | 0.544290599  | 2.220436237 | 0.000207966 |
| H | -3.07964374  | 4.313115715 | -0.002257037 |
| H | -4.400993132 | 2.207334391 | -0.001258608 |
| C | -3.328365783  | -0.301726503 | 0.000703575 |
| N | -3.913051903  | -1.314732364 | 0.001188513 |
| N | -1.235910945  | 3.22170170 | -0.001084947 |
| H | -0.730234263  | 4.199111267 | -0.001537088 |

Structure: 1e

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -441.084039483 hartree

SCF Energy + ZPVE: -440.919256483 hartree

Free Energy: -440.952206 hartree

|   |      |      |            |
|---|------|------|------------|
| C | -6.052787032 | 0.198268067 | 0.004442261 |
| C | -4.679378011 | 0.234322053 | 0.00420657 |
| C | -3.990412913 | 1.476567647 | 0.004374773 |
| C | -4.737154211 | 2.688138076 | 0.004709541 |
| C | -6.156801963 | 2.618571489 | 0.004903976 |
| C | -6.799192167 | 1.402753683 | 0.004776347 |
| H | -6.572388904 | -0.755121859 | 0.004334742 |
| H | -4.086670151 | -0.677337313 | 0.003985549 |
| C | -4.021330757 | 3.927305617 | 0.004833892 |
| H | -6.735463755 | 3.537122220 | 0.005155339 |
| H | -7.884123641 | 1.361810148 | 0.004928006 |
| C | -2.647808027 | 3.864453918 | 0.004622763 |
| C | -1.996526890 | 2.606650612 | 0.004296614 |
| H | -2.050857765 | 4.771412918 | 0.004702891 |
| H | -0.908567346 | 2.572214846 | 0.004118963 |
| N | -2.622393020 | 1.451477026 | 0.004162886 |
| C | -4.748731360 | 5.240331314 | 0.005182644 |
| H | -5.391314758 | 5.331814259 | -0.876784405 |
| H | -5.391057754 | 5.331490908 | 0.887305452 |
| H | -4.040104575 | 6.070889372 | 0.005232019 |
Structure: 1e'

Charge = -1 Multiplicity = 2

Number of imaginary frequencies: 0

SCF Energy: -441.158308434 hartree

SCF Energy + ZPVE: -440.998059434 hartree

Free Energy: -441.031990 hartree

| C     | -6.087369789 | 0.195105912 | 0.004457004 |
|-------|--------------|-------------|-------------|
| C     | -4.682835599 | 0.237470034 | 0.004269133 |
| C     | -3.976751039 | 1.461728019 | 0.004382576 |
| C     | -4.736528928 | 2.694326508 | 0.004696802 |
| C     | -6.152499852 | 2.61567993  | 0.004881879 |
| C     | -6.818879512 | 1.378634621 | 0.004755561 |
| H     | -6.598048742 | -0.764711389| 0.004348504 |
| H     | -4.101619629 | -0.681741731| 0.004029013 |
| C     | -4.019799349 | 3.926615093 | 0.004819292 |
| H     | -6.732363245 | 3.534413117 | 0.005119557 |
| H     | -7.90572968  | 1.351889271 | 0.004891948 |
| C     | -2.609564466 | 3.86109219  | 0.004582019 |
| C     | -1.967370859 | 2.63504527  | 0.004823273 |
| H     | -2.021305247 | 4.777180741 | 0.004651253 |
| H     | -0.878984037 | 2.591305885 | 0.004111179 |
| N     | -2.608250485 | 1.43963975  | 0.004184028 |
| C     | -4.753895299 | 5.234925909 | 0.005204020 |
| H     | -5.405762658 | 5.34460074  | -0.874084158|
| H     | -5.405479494 | 5.344230311 | 0.884748441 |
| H     | -4.052104801 | 6.074331464 | 0.005270675 |

Structure: TS1

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -782.156567594 hartree

SCF Energy + ZPVE: -781.99427594 hartree

Free Energy: -781.934341 hartree

| C     | -2.322445394 | 7.635236839 | 1.511953960 |
|-------|--------------|-------------|-------------|
| C     | -3.188124982 | 6.656092180 | 1.060110682 |
| C     | -2.709140329 | 5.439986945 | 0.494140779 |
| C     | -1.281057537 | 5.254956055 | 0.443442355 |
| C     | -0.432573653 | 6.26642959  | 0.913087281 |
| C     | -0.928755279 | 7.453640971 | 1.437445988 |
| H     | -2.725173584 | 8.555977635 | 1.926852984 |
Structure: **INT3**

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -782.166007206 hartree

SCF Energy + ZPVE: -781.901971206 hartree

Free Energy: -781.945969 hartree

| Atom | X      | Y      | Z      | Atomic Number |
|------|--------|--------|--------|---------------|
| H    | -4.264673131 | 6.799913279 | 1.115088049 |
| C    | -0.803358098 | 3.984985820 | -0.069446134 |
| H    | 0.642869496 | 6.114503813 | 0.861924304 |
| H    | -0.252229318 | 8.226285170 | 1.789180131 |
| C    | -1.714833778 | 3.089401033 | -0.525283140 |
| C    | -3.128162811 | 3.425297612 | -0.597309245 |
| H    | -1.388797334 | 2.124381142 | -0.905670957 |
| N    | -3.607163741 | 4.511173367 | 0.075386782 |
| C    | 0.670297113 | 3.687348540 | -0.091526135 |
| H    | 1.116821171 | 3.768301860 | 0.905774205 |
| H    | 0.851644617 | 2.678599660 | -0.471131045 |
| H    | 1.200387167 | 4.395359921 | -0.74045291 |
| C    | -3.319730153 | 3.740144001 | -2.675829815 |
| C    | -2.882759428 | 2.501391115 | -3.366123034 |
| C    | -1.635919502 | 2.386731110 | -3.856215998 |
| C    | -1.207849424 | 4.709630570 | -3.476205108 |
| C    | -2.446060627 | 4.894908248 | -2.984761840 |
| H    | -3.563615813 | 1.659140078 | -3.44247236 |
| H    | -1.274045458 | 1.480081899 | -4.328524879 |
| H    | -0.523805602 | 5.530660007 | -3.66554115 |
| H    | -2.785458502 | 5.902553392 | -2.764409212 |
| N    | -0.705944135 | 3.431924624 | -3.76867101 |
| H    | -3.819498283 | 2.582058002 | -0.654850610 |
| C    | -4.716933535 | 3.982227683 | -2.670174461 |
| N    | -5.867752626 | 4.148334663 | -2.542310816 |
| H    | 0.067010313 | 3.395747806 | -4.420387031 |

**C**

-2.276059373   7.692487922   1.552609220
-3.133694011   6.693678891   1.128328866
-2.65538424    5.452439212   0.588291952
-1.218808081   5.283291431   0.584183724
-0.380749837   6.313022251   1.028558166
-0.879437516   7.527731010   1.498897100
-2.694374984   8.622352005   1.933123935
-4.211148872   6.839605161   1.174786637
-0.716627444   3.961619870   0.208956061
0.696085022    6.156254601   1.009150144
-0.209647977   8.316179549   1.826824900
Structure: INT7

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -782.675159941 hartree

SCF Energy + ZPVE: -782.396750941 hartree

Free Energy: -782.440196 hartree

| Atom | x          | y          | z          | Energy       |
|------|------------|------------|------------|--------------|
| C    | -1.584233352 | 3.050529624 | -0.274760490 |
| C    | -3.021276622 | 3.95350738  | -0.556088950 |
| H    | -1.244038091 | 2.040590927 | -0.497434618 |
| N    | -3.533176041 | 4.533786913 | 0.171575179  |
| C    | 0.736986443  | 3.62927418  | 0.421050107  |
| H    | 1.037019965  | 3.782532600 | 1.463915522  |
| H    | 0.938135828  | 2.589400491 | 0.150723108  |
| H    | 1.380138000  | 4.26976067  | -0.194281009 |
| C    | -3.220079639 | 3.602700093 | -2.134908458 |
| C    | -2.822737583 | 2.36406097  | -2.916152821 |
| C    | -1.743089771 | 2.337537184 | -3.71454928  |
| C    | -1.387815029 | 4.676870958 | -3.458271487 |
| C    | -2.452528326 | 4.80371404  | -2.65007988  |
| H    | -3.404540280 | 1.458891112 | -2.773180766 |
| H    | -1.430709654 | 1.436221406 | -4.230974212 |
| H    | -0.807020070 | 5.533221488 | -3.783644001 |
| H    | -2.749049154 | 5.789022270 | -2.306869464 |
| N    | -0.955691445 | 3.451191301 | -3.926218783 |
| H    | -3.648518007 | 2.514109595 | -0.34068798  |
| C    | -4.669051682 | 3.834763489 | -2.329509635 |
| N    | -5.806791217 | 3.982385568 | -2.493771101 |
| H    | -0.242454119 | 3.420549361 | -4.646486599 |

SCF Energy + ZPVE: -782.396750941 hartree

Free Energy: -782.440196 hartree
Structure: INT4

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -782.163198498 hartree

SCF Energy + ZPVE: -781.900079498 hartree

Free Energy: -781.943687 hartree
**Structure: INT6**

Charge = 0  Multiplicity = 2

Number of imaginary frequencies: 0

SCF Energy: -441.652756029 hartree

SCF Energy + ZPVE: -441.478331029 hartree

Free Energy: -441.512412 hartree

| Atom | X        | Y        | Z        | Energy  |
|------|----------|----------|----------|---------|
| H    | -5.812300986 | 4.915734167 | -1.175304088 |
| H    | -5.948184626 | 5.109627017 | 0.572173696 |
| H    | -4.675971841 | 5.972983556 | -0.318534979 |
| H    | -2.043720215 | 0.959296002 | 0.862044759 |
| C    | -1.312489842 | 2.590535999 | -1.242109956 |
| C    | -0.488189104 | 3.652306021 | -1.801221591 |
| C    | -0.271410741 | 3.725599036 | -3.156228309 |
| C    | -1.825426561 | 2.128800732 | -3.597943117 |
| C    | -2.131729012 | 1.962000174 | -2.68272924 |
| H    | 0.040623967  | 4.324062321 | -1.128926955 |
| H    | 0.421743641  | 4.475699862 | -3.537764074 |
| H    | -2.400164592 | 1.575764638 | -4.341271285 |
| H    | -2.916570840 | 1.267601849 | -1.980446261 |
| C    | -0.119416787 | 1.284269494 | -0.685466641 |
| N    | 0.759718706  | 0.521459055 | -0.793269689 |
| N    | -0.877031008 | 2.958730097 | -4.093226403 |

C -6.078091951  C -4.021818173  C -4.751314099  C -6.159342481  C -6.813673066  H -6.581840817  H -4.092764064  C -4.035762644  H -6.742850700  H -7.898802210  C -2.626636632  C -1.942287084  H -2.058193272  H -0.863566274  N -2.638657000  C -4.782170921  H -5.408876380  H -5.454350403  H -4.086897379  H -2.125345490
Structure: **TS2**

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -782.583335878 hartree

SCF Energy + ZPVE: -782.311381878 hartree

Free Energy: -782.354800 hartree

| Atom | X         | Y         | Z         |
|------|-----------|-----------|-----------|
| C    | -6.108954945 | 0.239240507 | -0.191950784 |
| C    | 0.154034572  | 0.686809032 |
| C    | 1.004758267  | -0.445778593 |
| C    | 2.087448882  | 0.279746934 |
| C    | 1.970950319  | 0.769508482 |
| C    | 0.823587799  | 0.540688852 |
| H    | -1.136030116 | 0.372971224 |
| H    | -0.98812052  | -1.254108563 |
| C    | 0.321586058  | 0.466816523 |
| C    | 2.791234745  | 1.332525865 |
| H    | 0.747449111  | 0.927245097 |
| C    | 3.259405239  | 0.010340437 |
| C    | 2.107860979  | -0.644557922 |
| H    | 4.118229121  | 0.158632425 |
| H    | 1.829805342  | 0.475663322 |
| N    | 1.110446596  | -0.944240489 |
| C    | 4.471278903  | 1.163684300 |
| H    | 4.826254541  | 0.654309533 |
| H    | 4.224464595  | 2.19323713 |
| H    | 5.282246205  | 1.190135850 |
| H    | 0.337821255  | -1.50659050 |
| C    | 0.248454484  | -1.526428167 |
| C    | 3.29780956   | -2.596518160 |
| C    | 3.003249385  | -3.910351214 |
| C    | 0.730716252  | -3.470699281 |
| C    | 0.928436137  | -2.130239915 |
| H    | 4.326854970  | -4.289206946 |
| H    | 0.889911732  | -4.677661331 |
| H    | -0.223298718 | -3.904191497 |
| H    | 0.114530702  | -1.472954043 |
| C    | 2.541800808  | -0.367695681 |
| N    | 1.294974207  | -0.020269914 |
| N    | 1.727086822  | -4.366810891 |
| H    | 1.553119139  | -5.359619202 |

Structure: **INT8**

Charge = 0 Multiplicity = 1
Number of imaginary frequencies: 0

SCF Energy: -689.266209167 hartree

SCF Energy + ZPVE: -689.009411167 hartree

Free Energy: -689.050254 hartree

Structure: TS3

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -839.198116000 hartree

SCF Energy + ZPVE: -838.887099000 hartree
Free Energy: -838.934380 hartree

Structure: INT9
Charge = -1 Multiplicity = 1
Number of imaginary frequencies: 0
SCF Energy: -782.175664824 hartree

| Atom | X     | Y     | Z     | Energy  | Force  |
|------|-------|-------|-------|---------|--------|
| C    | 1.02350600 | -2.02772200 | 1.71121000 |
| C    | 1.74833700 | -3.16121200 | 1.01358000 |
| C    | -0.33338400 | -2.52503800 | 2.16839300 |
| C    | 1.13223200 | -4.32707100 | 0.70943800 |
| H    | 2.77434200 | -2.99684700 | 0.70101300 |
| C    | -0.82300100 | -3.73027300 | 1.79158500 |
| H    | -0.94399990 | -1.85796000 | 2.77068800 |
| H    | 1.68139700 | -5.08320800 | 0.14804000 |
| H    | -1.82946400 | -4.01064600 | 2.10227000 |
| C    | -0.37341900 | -7.76117100 | 1.09667500 |
| N    | 1.80779500 | -1.59465900 | 2.89271000 |
| N    | 2.42157900 | -1.25145800 | 3.81397200 |
| N    | -0.15888000 | -4.66939900 | 1.04084600 |
| H    | -0.44828000 | -7.10207800 | 1.87176900 |
| H    | -1.36774400 | -7.21654600 | 2.29828300 |
| H    | -0.31466400 | -5.96291600 | 1.47395900 |
| N    | 0.25630200 | -7.34616000 | 2.56696200 |
| H    | -0.77084800 | -2.69172600 | -3.32230900 |
| C    | 0.48685600 | -2.58436200 | -3.91749800 |
| C    | -1.00532500 | -2.14701200 | -2.06108000 |
| C    | 1.51087100 | -1.92230900 | -3.23700500 |
| C    | 1.30134200 | -1.36148000 | -1.97284800 |
| C    | 0.02050600 | -1.47883000 | -1.38062500 |
| C    | 0.86016100 | -0.71447300 | 0.79757000 |
| C    | 2.12978700 | -0.35749800 | 0.07929700 |
| C    | 2.35145300 | -0.66869500 | -1.21042000 |
| H    | -1.98319700 | -2.23258500 | -1.59253100 |
| H    | 2.49263100 | -1.84144200 | -3.69591100 |
| H    | 2.90394600 | 0.14125100 | 0.65885500 |
| N    | -0.21180500 | -0.86018000 | -0.16143700 |
| H    | -1.12093200 | -1.05512700 | 0.24567400 |
| H    | 0.59049300 | 0.09694000 | 1.48441100 |
| C    | 3.65129600 | -0.34338600 | -1.89239000 |
| H    | 4.20647200 | -1.25748400 | -2.13287600 |
| H    | 3.48221400 | 0.18986200 | -2.83454000 |
| H    | 4.27876900 | 0.27823000 | -1.24979100 |
| H    | 0.67142500 | -3.01043000 | -4.89839800 |
| H    | -1.57597500 | -3.20815500 | -3.83758200 |
SCF Energy + ZPVE: -781.911354824 hartree
Free Energy: -781.955228 hartree

| Atom | X            | Y            | Z            | SCF Energy | ZPVE       | Total Energy |
|------|--------------|--------------|--------------|------------|------------|--------------|
| C    | -5.789514822 | -0.060858735 | 0.546789824  |
| C    | -4.446877813 | 0.203638616  | 0.803931994  |
| C    | -3.908770789 | 1.469756757  | 0.527666350  |
| C    | -4.743155405 | 2.483783219  | -0.002486608 |
| C    | -6.087987344 | 2.191741831  | -0.248385512 |
| C    | -6.619589760 | 0.928443334  | 0.015385419  |
| H    | -6.186748005 | -1.049188334 | 0.760926457  |
| H    | -3.799849781 | -0.566885010 | 1.215927239  |
| C    | -4.149244093 | 3.810741799  | -0.241787683 |
| H    | -6.731475073 | 2.96448348   | -0.655751012 |
| H    | -7.665056292 | 0.721320196  | -0.188934641 |
| C    | -2.819564262 | 3.970797332  | -0.129996546 |
| C    | -1.877976559 | 2.838109220  | 0.163962063  |
| H    | -2.374162129 | 4.946410113  | -0.305218598 |
| H    | -1.084210628 | 3.187900864  | 0.837906532  |
| N    | -2.595407669 | 1.764604804  | 0.831556594  |
| C    | -5.053548113 | 4.954872300  | -0.609049848 |
| H    | -5.555711025 | 4.763797760  | -1.56509367 |
| H    | -5.835981361 | 5.103163503  | 0.143442022  |
| H    | -4.481119443 | 5.880501916  | -0.704579055 |
| H    | -2.031972101 | 0.980404448  | 1.141215761  |
| C    | -1.141453104 | 2.365228459  | -1.16727681  |
| C    | -0.340912027 | 3.490819222  | -1.789918215 |
| C    | -0.748266295 | 4.085557948  | -2.948177369 |
| C    | -2.370297958 | 2.542582875  | -3.344002455 |
| C    | -2.088932131 | 1.826573972  | -2.218216336 |
| H    | 0.518068519  | 3.874692729  | -1.245774942 |
| H    | -0.180853808 | 4.950468873  | -3.298004963 |
| H    | -3.130498934 | 2.144485361  | -4.019255381 |
| H    | -2.607651124 | 0.892783014  | -2.018602131 |
| C    | -0.221392002 | 1.282258368  | -0.732496746 |
| N    | 0.492149042  | 0.436854699  | -0.385254399 |
| N    | -1.782687913 | 3.706101200  | -3.753101465 |

Structure: TS4
Charge = -1  Multiplicity = 1
Number of imaginary frequencies: 1

SCF Energy: -782.163198498 hartree
SCF Energy + ZPVE: -781.900079498 hartree
Free Energy: -781.943687 hartree
| Element | X-Position | Y-Position | Z-Position | Energy |
|---------|------------|------------|------------|--------|
| C       | -5.831076442 | -0.074705223 | 0.502742400 |
| C       | -4.475706458 | 0.187351210  | 0.679949856  |
| C       | -3.972652842 | 1.483068775  | 0.486056441  |
| C       | -4.853966523 | 2.525426051  | 0.111934318  |
| C       | -6.212057530 | 2.235205983  | -0.056394348 |
| C       | -6.709597498 | 0.945780466  | 0.130972133  |
| H       | -6.201053016 | -1.085000491 | 0.653554042  |
| H       | -3.791671994 | -0.606874088 | 0.968607070  |
| C       | -4.292584786 | 3.877132925  | -0.055269156 |
| H       | -6.891756696 | 3.033199130  | -0.341548141 |
| H       | -7.765937220 | 0.741071698  | -0.009987457 |
| C       | -2.960091880 | 4.045557961  | -0.032308380 |
| C       | -1.979520858 | 2.910129881  | 0.117885117  |
| H       | -2.534974215 | 5.037418639  | -0.165032026 |
| H       | -1.169922458 | 3.225667064  | 0.787654109  |
| N       | -2.642192444 | 1.766927632  | 0.723140631  |
| C       | -5.231797300 | 5.034737367  | -0.253418793 |
| H       | -5.812300986 | 4.915734167  | -1.175304088 |
| H       | -5.948184626 | 5.109627017  | 0.572173696  |
| H       | -4.675971841 | 5.972983556  | -0.318534979 |
| H       | -2.043720215 | 0.959296002  | 0.862044759  |
| C       | -1.312489842 | 2.590535999  | -1.242109956 |
| C       | -0.488189104 | 3.652306021  | -1.801221591 |
| C       | -0.271410741 | 3.725599363  | -3.156228309 |
| C       | -1.825426561 | 2.128800732  | -3.597943117 |
| C       | -2.131729012 | 1.962000174  | -2.268272924 |
| H       | 0.040623967  | 4.324062321  | -1.128926955 |
| H       | 0.421743641  | 4.475699862  | -3.537764074 |
| H       | -2.400164592 | 1.575764638  | -4.341271285 |
| H       | -2.916570840 | 1.267601849  | -1.980446261 |
| C       | -0.119416787 | 1.284269494  | -0.685466641 |
| N       | 0.759718706  | 0.521459055  | -0.793269689 |
| N       | -0.877031008 | 2.958730097  | -4.093226403 |

Structure: CN

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -92.928430526 hartree

SCF Energy + ZPVE: -92.923391526 hartree

Free Energy: -92.942428 hartree

Structure: INT10
Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -689.278393740 hartree

SCF Energy + ZPVE: -689.020606740 hartree

Free Energy: -689.061653 hartree

C  -5.803437139  -0.032528013  0.285181869
C  -4.447507585  0.235045287  0.449059074
C  -3.972130062  1.551970149  0.370769628
C  -4.877660695  2.611321142  0.129816590
C  -6.236388432  2.315115664  -0.028033026
C  -6.706956365  1.004822543  0.041932320
H  -6.154234484  -1.058880241  0.344871929
H  -3.742770974  -0.571270717  0.637017210
C  -4.347207514  3.986587484  0.104170329
H  -6.937266924  3.125199207  -0.208151121
H  -7.763796729  0.796049727  -0.088850611
C  -3.018364289  4.177686642  0.086331030
C  -2.035083589  3.029142245  0.013778862
H  -2.603164128  5.182011990  0.062515759
H  -1.151351725  3.281607255  0.609944116
N  -2.635389603  1.839863375  0.592612981
C  -5.312060381  5.13985954  0.103223525
H  -5.933619547  5.12943325  -0.799275118
H  -5.989081975  5.090470446  0.963018424
H  -4.774081694  6.097777307  0.136350414
C  -2.023589655  1.032074194  0.634895528
C  -1.565100988  2.858184074  -1.430190132
C  -0.732061888  3.822801687  -2.005119826
C  -0.331293223  3.671180652  -3.327501257
C  -1.493810839  1.718537565  -3.54368332
C  -1.947509361  1.778823605  -2.225712271
H  -0.393592194  4.680704353  -1.430235575
H  0.320276699  4.409373820  -3.788808702
H  -1.783467816  0.884437961  -4.178322874
H  -2.581389906  0.98364712  -1.840719845
N  -0.701074695  2.639614606  -4.099334095

Structure: TS5

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -782.168126497 hartree

SCF Energy + ZPVE: -781.910934497 hartree
Free Energy: -781.954818 hartree

|          |          |          |
|----------|----------|----------|
| C        | -6.056279974 | 0.235406910 | 1.228739461 |
| C        | -4.875421107  | 0.344057701  | 0.488901682  |
| C        | -4.467983252  | 1.578052496  | -0.028077532 |
| C        | -5.255777748  | 2.732180987  | 0.212240273  |
| C        | -6.433504338  | 2.596432372  | 0.950204392  |
| C        | -6.843950720  | 1.358316703  | 1.460971293  |
| H        | -6.351862066  | -0.733929630  | 1.620207264  |
| H        | -4.260773571  | -0.533682088  | 0.303159496  |
| C        | -4.787374935  | 4.025788375  | -0.320306969 |
| H        | -7.042657895  | 3.476091016  | 1.137860003  |
| H        | -7.763346854  | 1.282100285  | 2.032843318  |
| C        | -3.570220201  | 4.083772776  | -0.909422053 |
| C        | -2.682522507  | 2.943367853  | -1.04399710  |
| H        | -3.214447641  | 5.04491673  | -1.273884068 |
| H        | -1.816732527  | 2.992746107  | 0.178769359  |
| N        | -3.326606753  | 1.659501423  | -0.825865502 |
| C        | -5.662555257  | 5.237486247  | -0.167730175 |
| H        | -6.640632570  | 5.090917382  | -0.642863473 |
| H        | -5.854828160  | 5.467386238  | 0.887971421  |
| H        | -5.189555937  | 6.111381269  | -0.623407955 |
| H        | -2.676912521  | 0.900491292  | -0.640247456 |
| C        | -1.541886929  | 2.954178288  | -1.903828056 |
| C        | -0.841901593  | 4.151545300  | -2.233070815 |
| C        | 0.339705231   | 4.094283348  | -2.944435383 |
| C        | 0.283853485   | 1.826895174  | -3.057970649 |
| C        | -0.908571814  | 1.761442341  | -2.348709148 |
| H        | -1.216681301  | 5.122540096  | -1.925793814 |
| H        | 0.856066457   | 5.020614805  | -3.191538916 |
| H        | 0.745949568   | 0.901911612  | -3.399958562 |
| H        | -1.350763364  | 0.785490675  | -2.179213745 |
| N        | 0.929755616   | 2.958095525  | -3.372831513 |
| C        | -1.158521141  | 2.813163570  | 1.285718859  |
| N        | -0.619424191  | 2.768222269  | 2.314904803  |

Structure: HCN

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -93.391984157 hartree

SCF Energy + ZPVE: -93.378253157 hartree

Free Energy: -93.391906 hartree
Structure: INT11

Charge = -1 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -688.772093742 hartree

SCF Energy + ZPVE: -688.529452742 hartree

Free Energy: -688.570183 hartree

| C   | -6.058890797 | 0.233758464 | 1.225184058 |
| C   | -4.899175167 | 0.340110108 | 0.446368655 |
| C   | -4.506781596 | 1.573060118 | -0.085270196 |
| C   | -5.278600222 | 2.735900402 | 0.190453362 |
| C   | -6.428575855 | 2.600803822 | 0.972081867 |
| C   | -6.830671271 | 1.358283896 | 1.488400653 |
| H   | -6.346725429 | -0.736495793 | 1.620446542 |
| H   | -4.295654520 | -0.539935030 | 0.236489674 |
| C   | -4.808217513 | 4.021994213 | -0.338064387 |
| H   | -7.024421007 | 3.483057737 | 1.188484646 |
| H   | -7.731398562 | 1.284781254 | 2.089987605 |
| C   | -3.609645180 | 4.064002600 | -0.988814099 |
| C   | -2.802500932 | 2.920659709 | -1.262207435 |
| H   | -3.246032693 | 5.030089952 | -1.330126976 |
| N   | -3.399230216 | 1.661277223 | -0.912964055 |
| C   | -5.624232607 | 5.256752967 | -0.085060660 |
| H   | -6.637077868 | 5.170077948 | -0.500852422 |
| H   | -5.744041060 | 5.454870650 | 0.989043678 |
| H   | -5.147941059 | 6.131131488 | -0.537282314 |
| H   | -2.774866819 | 0.867578517 | -0.851731205 |
| C   | -1.577567539 | 2.943322213 | -1.918206194 |
| C   | -0.892774774 | 4.153980569 | -2.322906745 |
| C   | 0.321378850 | 4.099408999 | -2.960593556 |
| C   | 0.374648250 | 1.829367058 | -2.917346516 |
| C   | -0.843287630 | 1.747195553 | -2.274203544 |
| H   | -1.320528053 | 5.130425340 | -2.118436942 |
| H   | 0.804341658 | 5.035042165 | -3.243906122 |
| H   | 0.892482551 | 0.902836488 | -3.167891167 |
| H   | -1.231013124 | 0.756282157 | -2.059956669 |
| N   | 1.005299836 | 2.966899453 | -3.280831751 |

Structure: INT12

Charge = 0 Multiplicity = 2

Number of imaginary frequencies: 0

SCF Energy: -688.672674813 hartree
SCF Energy + ZPVE: -688.427444813 hartree

Free Energy: -688.468281 hartree

| C    | -6.048762514 | 0.233447467 | 1.199230319 |
| C    | -4.848990443 | 0.352816348 | 0.508137768 |
| C    | -4.448503203 | 1.604302134 | 0.018881503 |
| C    | -5.252420173 | 2.751571225 | 0.225572384 |
| C    | -6.460856734 | 2.596810271 | 0.925975619 |
| C    | -6.859634099 | 1.35400802 | 1.408927716 |
| H    | -6.353759245 | -0.738305411 | 1.575411779 |
| H    | -4.212736489 | -0.511673282 | 0.338255126 |
| C    | -4.785630444 | 4.025458121 | -0.294158546 |
| H    | -7.090424347 | 3.465370996 | 1.092353427 |
| H    | -7.796508246 | 1.256947603 | 1.947993532 |
| C    | -3.587825309 | 4.067586723 | -0.964446319 |
| C    | -2.785296933 | 2.923674443 | -1.178547629 |
| H    | -3.252610630 | 5.016423453 | -1.36890650 |
| N    | -3.260359021 | 1.728392368 | -0.670942996 |
| C    | -5.618265937 | 5.257117239 | -0.09966975 |
| H    | -6.608433014 | 5.143445145 | -0.557436495 |
| H    | -5.779836313 | 5.463295391 | 0.964908648 |
| H    | -5.130588317 | 6.125080816 | -0.54734109 |
| H    | -2.683383893 | 0.897862263 | -0.728963536 |
| C    | -1.545185607 | 2.931433298 | -1.910659970 |
| C    | -0.888824650 | 4.136564457 | -2.26535384 |
| C    | 0.304106512 | 4.092742531 | -2.96375928 |
| C    | 0.304144943 | 1.817009087 | -3.017746297 |
| C    | -0.892839491 | 1.742437695 | -2.320101094 |
| H    | -1.288386157 | 5.104157117 | -1.984356864 |
| H    | 0.802830594 | 5.023037331 | -3.226158915 |
| H    | 0.793556248 | 0.897712674 | -3.32267062 |
| H    | -1.307421485 | 0.757115761 | -2.133875480 |
| N    | 0.921153397 | 2.960093734 | -3.349767235 |

Structure: TS6

Charge = 0 Multiplicity = 2

Number of imaginary frequencies: 1

SCF Energy: -745.203464040 hartree

SCF Energy + ZPVE: -744.925073040 hartree

Free Energy: -744.969045 hartree
### Structure: INT13

**Charge = -1 Multiplicity = 2**

Number of imaginary frequencies: 0

SCF Energy: -688.187140108 hartree

SCF Energy + ZPVE: -687.955661108 hartree

Free Energy: -687.996217 hartree

| Atom | X            | Y            | Z            | Atomic Number | Charge | Atomic Weight |
|------|--------------|--------------|--------------|---------------|--------|---------------|
| C    | -5.30146200  | 2.82593600   | 0.21660800   | C             | -1     |               |
| C    | -6.53445700  | 2.67061900   | 0.87358300   | C             | -1     |               |
| C    | -6.93028600  | 1.43871800   | 1.38749900   | C             | -1     |               |
| H    | -6.40003900  | -0.64290500  | 1.61746500   | H             | 1      |               |
| H    | -4.23352100  | -0.41947600  | 0.43741600   | H             | 1      |               |
| C    | -4.84721500  | 4.08493500   | -0.34290900  | C             | -1     |               |
| H    | -7.18721100  | 3.53159000   | 0.98438800   | H             | 1      |               |
| H    | -7.88426000  | 1.34030900   | 1.89594700   | H             | 1      |               |
| C    | -3.65672800  | 4.09337300   | -1.02109700  | C             | -1     |               |
| C    | -2.84810000  | 2.93099300   | -1.14896300  | C             | -1     |               |
| H    | -3.34232600  | 5.00908900   | -1.51352100  | H             | 1      |               |
| N    | -3.20696300  | 1.78362800   | -0.50389100  | N             | 1      |               |
| C    | -5.68626500  | 5.32070600   | -0.19911400  | C             | -1     |               |
| H    | -6.70007300  | 5.16617500   | -0.58697900  | H             | 1      |               |
| H    | -5.78876000  | 5.60933000   | 0.85434200   | H             | 1      |               |
| H    | -5.23662500  | 6.15670600   | -0.74003600  | H             | 1      |               |
| H    | -2.27019300  | 0.98905300   | 0.04464800   | H             | 1      |               |
| C    | -1.59441600  | 2.94806600   | -1.85419800  | C             | -1     |               |
| C    | -0.91887200  | 4.14069600   | -2.22886100  | C             | -1     |               |
| C    | 0.26800000   | 4.07027400   | -2.93441300  | C             | -1     |               |
| C    | 0.22454400   | 1.79184100   | -2.98050900  | C             | -1     |               |
| C    | -0.96156300  | 1.74420800   | -2.26857500  | C             | -1     |               |
| H    | -1.29425000  | 5.11648300   | -1.93994800  | H             | 1      |               |
| H    | 0.78399600   | 4.99052300   | -3.20135100  | H             | 1      |               |
| H    | 0.69023800   | 0.86325300   | -3.30562600  | H             | 1      |               |
| H    | -1.42669900  | 0.78237800   | -2.07778500  | H             | 1      |               |
| N    | 0.86482500   | 2.92482500   | -3.32411100  | N             | 1      |               |
| N    | -1.42658700  | 0.28155800   | 0.61611800   | N             | 1      |               |
| H    | -1.09640000  | -0.49709500  | 0.04525300   | H             | 1      |               |
| H    | -1.84198700  | -0.11378000  | 1.46005200   | H             | 1      |               |
| H    | -0.61297000  | 0.83261800   | 0.89212100   | H             | 1      |               |
Structure: 3ea

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: -688.096726629 hartree
SCF Energy + ZPVE: -687.862336629 hartree
Free Energy: -687.902386 hartree

| Atom | X   | Y   | Z   | X   | Y   | Z   |
|------|-----|-----|-----|-----|-----|-----|
| C    | -6.867500176 | 1.348634626 | 1.371383725 |
| H    | -6.399578776  | -0.761773650 | 1.430255360 |
| H    | -4.278040922  | -0.526293266 | 0.174268744 |
| C    | -4.767733439  | 4.040873071  | -0.257762561 |
| H    | -7.052534993  | 3.474934960  | 1.145230657 |
| H    | -7.797280182  | 1.246309746  | 1.922357561 |
| C    | -3.584424105  | 4.072381009  | -0.939945698 |
| C    | -2.820670344  | 2.885400813  | -1.190799158 |
| H    | -3.221136958  | 5.030613361  | -1.300155916 |
| N    | -3.260979794  | 1.670983468  | -0.749924292 |
| C    | -5.566051333  | 5.286301010  | 0.002353782 |
| H    | -5.859167460  | 5.216487474  | -0.435560786 |
| H    | -5.69846335   | 5.458142501  | 1.077272038 |
| H    | -5.067038634  | 6.160094007  | -0.424101293 |
| C    | -1.576224625  | 2.932568075  | -1.090177278 |
| C    | -0.989287907  | 4.126068735  | -2.425689383 |
| C    | 0.210953245   | 4.076252049  | -3.106816667 |
| C    | 0.373606558   | 1.817711264  | -2.858619898 |
| C    | -0.818966525  | 1.749621543  | -2.164046589 |
| H    | -1.463010403  | 5.093603829  | -2.928490237 |
| H    | 0.640167208   | 4.999496678  | -3.492716106 |
| H    | 0.935142734   | 0.902658320  | -3.042423610 |
| H    | -1.179600359  | 0.790044185  | -1.812260644 |
| N    | 0.922171160   | 2.950803694  | -3.345769902 |

SCF Energy: -688.096726629 hartree
SCF Energy + ZPVE: -687.862336629 hartree
Free Energy: -687.902386 hartree
### Structure: TSS1

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -782.523330951 hartree

SCF Energy + ZPVE: -782.255123951 hartree

Free Energy: -782.298793 hartree

| Atom | Coordinates | SCF Energy | ZPVE Energy | Free Energy |
|------|-------------|------------|-------------|-------------|
| C    | -2.842843632 2.887021808 | -1.162152806 |
| H    | -3.302436002 4.990849865 | -1.485827159 |
| N    | -3.202023224 1.724297222 | -1.658823363 |
| C    | -5.684104106 5.247691454 | -2.113659998 |
| H    | -6.669817707 5.087613348 | -2.660595029 |
| H    | -5.842357284 5.491692274 | 0.844287448 |
| H    | -5.214687477 6.104139612 | -0.699003124 |
| C    | -1.551366127 2.923207275 | -1.906342525 |
| C    | -0.814708547 4.100913938 | -2.060632138 |
| C    | 0.387731863 4.058122626 | -2.762343589 |
| C    | 1.774366000 1.820403325 | -3.161812974 |
| C    | -1.030048485 1.756791430 | -2.474811773 |
| H    | -1.144877243 5.041148590 | -1.632380180 |
| H    | 0.975811443 4.964277796 | -0.789475020 |
| H    | 0.593279153 0.92109271 | -3.15036782 |
| H    | -1.562310212 0.81115426 | -2.388237918 |
| N    | 0.887104312 2.946051979 | -3.311468391 |

C: Carbon
H: Hydrogen
N: Nitrogen

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| Atom | Coordinates | SCF Energy | ZPVE Energy | Free Energy |
|------|-------------|------------|-------------|-------------|
| C    | 0.642197037 | -4.323148920 | -0.796574728 |
| C    | 1.872638361 | -4.851899841 | -0.087641583 |
| C    | 0.462252041 | -5.015345171 | -2.134528778 |
| C    | 2.760396964 | -5.650981011 | -0.703662342 |
| C    | 2.040204096 | -4.546939863 | 0.939839683 |
| C    | 1.417107741 | -5.804891282 | -2.656006615 |
| H    | -0.451521681 | -4.829604726 | -2.686159363 |
| H    | 3.656944314 | -6.000095946 | -0.20367666 |
| H    | 1.302002234 | -6.270098102 | -3.628637826 |
| N    | 2.591976482 | -6.084364179 | -1.99786187 |
| C    | -1.831084777 | 0.896018109 | -2.845366088 |
| C    | -0.568636302 | 1.467219025 | -3.402332829 |
| C    | -1.717143558 | -0.323086330 | -2.185859392 |
| C    | 0.528225519 | 0.784646499 | -3.299877775 |
| C    | 0.613899916 | -0.445950902 | -2.631481767 |
| C    | -0.549319954 | -1.015962052 | -2.045257778 |
| C    | 0.717656467 | -2.783827252 | -1.066122535 |
| C    | 1.895938796 | -2.361305019 | -1.853737726 |
| C    | 1.852380104 | -1.231942100 | -2.587538903 |
### Structure: INTS1

**Charge = 0 Multiplicity = 1**

**Number of imaginary frequencies: 0**

**SCF Energy: -781.487296587 hartree**

**SCF Energy + ZPVE: -781.232288587 hartree**

**Free Energy: -781.276421 hartree**

| Atom | x         | y         | z         |
|------|-----------|-----------|-----------|
| H    | -2.664982053 | -0.766146500 | -1.75490983 |
| H    | 1.422109137  | 1.210205844  | -3.746390772 |
| H    | 2.786008331  | -2.982506802 | -1.814909982 |
| N    | -0.559114050 | -2.222112174 | -1.374608060 |
| H    | 0.176967989  | -2.061333912 | -0.107496216 |
| H    | 1.029864478  | -2.405893646 | 0.201398771  |
| C    | 3.042934246  | -0.784030778 | -3.383237834 |
| H    | 2.787458978  | -0.679985645 | -4.442831764 |
| H    | 3.390477837  | 0.195085887  | -3.035770479 |
| H    | 3.863863723  | -1.497221543 | -3.285648734 |
| H    | -0.727422035 | 2.422360711  | -3.914923031 |
| H    | -2.784210008 | -1.411818050 | -2.926212318 |
| C    | -0.548629588 | -4.580189317 | 0.053743762  |
| N    | -1.446016719 | -4.836056899 | 0.737541156  |
| H    | 3.244573666  | -6.745494151 | -2.394490637 |
Structure: TSS2

Charge = 0  Multiplicity = 1

Number of imaginary frequencies: 1

SCF Energy: -689.138649852 hartree

SCF Energy + ZPVE: -688.891891852 hartree

Free Energy: -688.920135 hartree

| Atom | X       | Y       | Z       | Energy   | ZPE Energy | Corr. Energy |
|------|---------|---------|---------|----------|------------|--------------|
| H    | -2.150636074 | 0.044332087 | -1.047388093 |
| H    | 1.663376711  | 0.676695397  | -4.181677273  |
| H    | 2.435312308  | -3.458092092 | -1.776182135  |
| N    | -0.400977159 -1.854268423 | -0.931242806 |          |
| C    | 3.013513629  | -1.488491558 | -3.578269333  |
| H    | 2.697770276  | -1.458859644 | -4.626311972  |
| H    | 3.567546799  | -0.563791718 | -3.378288698  |
| H    | 3.688455072  | -2.33539484  | -3.442240767  |
| H    | -0.148182964 | 2.340410931  | -4.094432423  |
| H    | -2.061314216 | 2.038053115  | -2.530414483  |
| H    | 3.084419450  | -6.853517371 | 0.267867745   |

C    | 1.136294824  | -3.998550434 | -0.220285171  |
| C    | 2.062819601  | -4.270264761 | 0.785535903   |
| C    | 0.437693612  | -5.056525666 | -0.790292583  |
| C    | 2.248254140  | -5.591687600 | 1.177336346   |
| H    | 2.625428418  | -3.471625987 | 1.261981607   |
| C    | 0.701726737  | -6.346634168 | -0.329207687  |
| H    | -0.293381162 | -4.880187088 | -1.570803988  |
| H    | 2.959871918  | -5.833485523 | 1.962265690   |
| H    | 0.172354004  | -7.194636808 | -0.756120799  |
| N    | 1.585500718  | -6.621298193 | 0.634231792   |
| C    | -1.915654271 | 0.302358822  | -3.305125498  |
| C    | -0.820109886 | 1.085042726 | -3.698796440  |
| C    | -1.733773896 | -0.836825243 | -2.536359029  |
| C    | 0.457855539  | 0.691769320  | -3.322127508  |
| C    | 0.666015451  | -0.453404818 | -2.537246682  |
| C    | -0.445233965 | -1.234585637 | -2.11527284   |
| C    | 0.939881833  | -2.589593598 | -0.735879210  |
| C    | 2.139741580  | -1.992054773 | -1.369936034  |
| C    | 2.006543507  | -0.953977113 | -2.220336333  |
| H    | -2.582455195 | -1.443898794 | -2.232922094  |
| H    | 1.313875630  | 1.278673781  | -3.64334113   |
| H    | 3.110288166  | -2.411471790 | -1.124037902  |
| N    | -0.336206502 | -2.377728316 | -1.350734766  |
| H    | 0.055740913  | -1.922647271 | -0.013805220  |
| H    | 0.892352456  | -1.955052348 | 0.475622920   |
**Structure:** INTS2

Charge = 0 Multiplicity = 1

Number of imaginary frequencies: 0

SCF Energy: \(-688.096773033\) hartree

SCF Energy + ZPVE: \(-687.862201033\) hartree

Free Energy: \(-687.902002\) hartree

| Atom | X       | Y       | Z       | X       | Y       | Z       |
|------|---------|---------|---------|---------|---------|---------|
| C    | 3.206259985 | -0.328233533 | -2.868135913 | 3.116079145 | -0.348164871 | -3.95900681 |
| C    | 3.297979205 | 0.721649437 | -2.568962641 | 4.119827208 | -0.850926598 | -2.578160383 |
| C    | -0.966365686 | 1.978281882 | -4.297238484 | -2.920713266 | 0.590252477 | -3.601753304 |
| C    | 3.116079145 | -0.348164871 | -3.95900681 | 4.119827208 | -0.850926598 | -2.578160383 |
| C    | -0.966365686 | 1.978281882 | -4.297238484 | -2.920713266 | 0.590252477 | -3.601753304 |

| Atom | X       | Y       | Z       | X       | Y       | Z       |
|------|---------|---------|---------|---------|---------|---------|
| C    | 1.040633970 | -4.151070142 | -0.519455025 | 2.082346848 | -4.452284713 | 0.36205539 |
| C    | 0.008662157 | -5.085729912 | -0.645803043 | 2.044988092 | -5.654798712 | 1.063993279 |
| C    | 2.904988514 | -3.764510528 | 0.527718261 | 0.068073025 | -6.261205192 | 0.095208959 |
| C    | -0.822245877 | -4.902917241 | -1.318255046 | 2.843337285 | -5.901024019 | 1.759499628 |
| N    | -0.721451722 | -7.002858906 | 0.002920137 |
| C    | 1.064011602 | -6.554995118 | 0.940772375 |
| C    | -1.648045073 | 0.399002827 | -3.419067699 |
| C    | -0.495438338 | 1.128860914 | -3.802599563 |
| C    | -1.524522250 | -0.769144945 | -2.707127311 |
| C    | 0.758871526 | 0.675292659 | -3.467442730 |
| C    | 0.918203163 | -0.529002072 | -2.731864251 |
| C    | -0.240320736 | -1.259956884 | -2.347849031 |
| C    | 1.010258233 | -2.880387450 | -1.296960829 |
| C    | 2.223152278 | -2.223980519 | -1.644100708 |
| C    | 2.196161565 | -1.051736125 | -2.359637426 |
| H    | -2.395030901 | -1.343198921 | -2.402965911 |
| H    | 1.637764882 | 1.239292604 | -3.764102628 |
| H    | 3.174972439 | -2.662348641 | -1.361641566 |
| N    | -0.176218268 | -2.423794292 | -1.639882789 |
| C    | 3.461672614 | -0.343872399 | -2.746284392 |
| H    | 3.539288698 | -0.248662187 | -3.834319126 |
| H    | 4.333440806 | 0.667535599 | -2.328063054 |
| H    | -0.607029157 | 2.051319567 | -4.364054383 |
| H    | -2.631980046 | 0.768810171 | -3.691117698 |
Characterization data of products

2-(Pyridin-4-yl)quinoline (3aa)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 51% isolated yield (31.6 mg). 1H NMR (500 MHz, CDCl3) δ 8.77 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 8.00 (m, 2H), 7.83 (cd, J = 8.6 Hz, 1H), 7.65 (m, 3H), 7.51 (m, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 5.1 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 154.1, 150.4, 148.3, 146.7, 137.3, 130.1, 130.0, 127.8, 127.5, 127.2, 121.6, 118.4.

4-(Pyridin-4-yl)quinoline (3aa’)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 71% isolated yield (35.2 mg). 1H NMR (500 MHz, CDCl3) δ 8.81 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.6 Hz, 1H), 8.00 (m, 2H), 7.83 (cd, J = 8.6 Hz, 1H), 7.65 (m, 3H), 7.51 (m, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 5.1 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 154.1, 149.9, 148.6, 145.9, 145.5, 130.1, 129.7, 127.3, 125.7, 125.0, 124.2, 120.9.

2-Methyl-4-(pyridin-4-yl)quinoline (3ba)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 57% isolated yield (34.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.80 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.08 (m, 2H), 7.83 (cd, J = 8.6 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 5.1 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 154.1, 149.9, 148.6, 145.9, 145.5, 130.1, 129.7, 127.3, 125.7, 125.0, 124.2, 120.9.

2-Phenyl-4-(pyridin-4-yl)quinoline (3ca)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 67% isolated yield (36.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.78 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.74 (m, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.44 (d, J = 5.9 Hz, 2H), 7.23 (s, 1H), 2.80 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 158.5, 149.9, 148.2, 146.1, 145.6, 129.7, 129.2, 126.3, 124.7, 122.6, 121.8, 25.3.

3-Chloro-2-(pyridin-4-yl)quinoline and 3-chloro-4-(pyridin-4-yl)quinolone (3da)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 52% isolated yield (31.3 mg). 1H NMR (500 MHz, Chloroform-d) δ 9.07 (s, 1H), 8.82 (d, J = 26.3 Hz, 4H), 8.23 (s, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.00 (m, 2H), 7.83 (cd, J = 9.0, 2.2 Hz, 1H), 7.75 (m, 3H), 7.51 (m, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 5.5 Hz, 2H). 13C NMR (126 MHz, Chloroform-d) δ 151.9, 150.2, 149.7, 149.7, 146.7, 145.6, 144.9, 135.6, 133.9, 131.3, 129.9, 129.8, 129.1, 128.6, 128.1, 127.9, 125.4, 124.2, 124.0, 122.4.

4-Methyl-2-(pyridin-4-yl)quinoline (3ea)
(Hey and Williams, 1950, Nunn and Schofield, 1952; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 93% isolated yield (51.2 mg). 1H NMR (500 MHz, CDCl3) δ 8.77 (d, J = 6.0 Hz, 2H), 8.18 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 4.6 Hz, 2H), 8.01 (d, J = 8.3 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.72 (s, 1H), 7.59 (t, J = 7.6 Hz, 1H), 2.78 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 154.1, 150.4, 148.0, 146.8, 145.5, 130.5, 129.7, 127.8, 126.9, 123.7, 121.6, 119.2, 19.0.

5-Chloro-2-(pyridin-4-yl)quinoline (3fa)
yellow solid was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 76% isolated yield (45.7 mg). m. p. = 123-125°C. 1H NMR (500 MHz, CDCl3) δ 8.80 (d, J = 5.1 Hz, 2H), 8.69 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.08 (d, J = 5.8 Hz, 2H), 8.00 (d, J = 8.8 Hz, 1H), 7.71 (m, 2H). 13C NMR (126 MHz, CDCl3) δ 155.1, 150.5, 148.9, 146.0, 134.3, 131.3, 129.8, 129.1, 127.1, 126.0, 121.6, 119.2. HRMS (ESI) m/z: [M + H]+ calcld for C14H9ClN2: 283.0860, found: 283.0853.
5-Bromo-2-(pyridin-4-yl)quinoline (3ga)
yellow solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 84% isolated yield (59.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.80 (d, J = 5.0 Hz, 2H), 8.65 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 4.7 Hz, 2H), 7.98 (d, J = 8.8 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.61 (t, 1H). 13C NMR (126 MHz, CDCl3) δ 155.1, 150.5, 148.9, 145.9, 136.9, 130.8, 130.3, 129.9, 127.3, 121.8, 121.7, 119.5. HRMS (ESI) m/z: [M + H]+ calcd for C14H9BrN2: 285.0022, found: 285.0020.

6-Fluoro-2-(pyridin-4-yl)quinoline (3ha)
yellow oil was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 23% isolated yield (13.0 mg). 1H NMR (500 MHz, CDCl3) δ 8.80 (s, 2H), 8.26 (d, J = 8.6 Hz, 1H), 8.20 (dd, J = 9.2, 5.3 Hz, 1H), 8.08 (d, J = 5.6 Hz, 2H), 7.94 (d, J = 8.6 Hz, 1H), 7.57 (m, 1H), 7.49 (d, J = 8.7 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 160.9 (d, J = 249.6 Hz), 153.7 (d, J = 3.0 Hz), 150.2, 146.7, 145.4, 136.7, 132.5 (d, J = 9.2 Hz), 128.5 (d, J = 10.2 Hz), 121.4, 120.5 (d, J = 21.3 Hz), 119.1, 110.6 (d, J = 21.8 Hz). 19F NMR (471 MHz, CDCl3) δ -111.9. HRMS (ESI) m/z: [M + H]+ calcd for C14H9F2N2: 225.0823, found: 225.0822.

6-Fluoro-4-(pyridin-4-yl)quinoline (3ha’)
white solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 57% isolated yield (31.8 mg). 1H NMR (500 MHz, CDCl3) δ 8.96 (d, J = 4.3 Hz, 1H), 8.82 (d, J = 5.7 Hz, 2H), 8.24 (m, 1H), 7.57 (m, 1H), 7.46 (m, 3H), 7.37 (d, J = 4.3 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 160.9 (d, J = 249.1 Hz), 150.3, 149.2 (d, J = 2.7 Hz), 145.7, 145.3, 144.9, 132.7 (d, J = 9.3 Hz), 126.5 (d, J = 9.6 Hz), 124.0, 121.5, 120.0 (d, J = 25.7 Hz), 108.4 (d, J = 23.3 Hz). 19F NMR (471 MHz, CDCl3) δ -111.1 (s). HRMS (ESI) m/z: [M + H]+ calcd for C14H9F2N2: 225.0823, found: 225.0823.

7-Chloro-2-(pyridin-4-yl)quinoline (3ia)
yellow solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 29% isolated yield (17.5 mg). 1H NMR (500 MHz, CDCl3) δ 8.80 (d, J = 4.2 Hz, 2H), 8.28 (d, J = 8.5 Hz, 1H), 8.20 (s, 1H), 8.07 (d, J = 4.8 Hz, 2H), 7.92 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.7 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 155.3, 150.4, 148.6, 146.3, 137.1, 136.0, 128.9, 128.7, 128.3, 126.2, 121.6, 118.6. HRMS (ESI) m/z: [M + H]+ calcd for C14H9ClN2: 241.0527, found: 241.0525.

7-Chloro-4-(pyridin-4-yl)quinoline (3ia’)
yellow solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 55% isolated yield (33.1 mg). 1H NMR (500 MHz, CDCl3) δ 8.99 (d, J = 4.2 Hz, 1H), 8.81 (d, J = 4.1 Hz, 2H), 8.20 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 4.3 Hz, 2H), 7.34 (d, J = 4.3 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 150.9, 150.4, 150.2, 149.0, 145.6, 145.3, 135.8, 129.0, 128.3, 126.4, 124.1, 121.0. HRMS (ESI) m/z: [M + H]+ calcd for C14H9ClN2: 241.0527, found: 241.0515.

2,6-Dimethyl-4-(pyridin-4-yl)quinoline (3ja)
yellow oil was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 71% isolated yield (41.6 mg). 1H NMR (500 MHz, CDCl3) δ 8.78 (d, J = 4.8 Hz, 2H), 8.00 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.49 (s, 1H), 7.42 (d, J = 4.8 Hz, 2H), 7.17 (s, 1H), 2.77 (s, 3H), 2.46 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 157.4, 150.0, 146.8, 146.3, 144.9, 136.2, 131.9, 128.9, 124.2, 124.0, 123.5, 121.8, 25.1, 21.7. HRMS (ESI) m/z: [M + H]+ calcd for C14H9BrN2: 235.1230, found: 235.1224.

6-Bromo-2-methyl-4-(pyridin-4-yl)quinoline (3ka)
yellow solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 56% isolated yield (41.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.81 (d, J = 4.9 Hz, 2H), 7.97 (d, J = 9.0 Hz, 1H), 7.87 (s, 1H), 7.79 (d, J = 9.0 Hz, 1H), 7.41 (d, J = 5.5 Hz, 2H), 7.24 (s, 1H), 2.78 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 159.0, 150.2, 146.9, 145.3, 144.7, 133.2, 131.0, 126.9, 125.3, 124.1, 122.6, 120.4, 25.3. HRMS (ESI) m/z: [M + H]+ calcd for C14H11BrN2: 299.0178, found: 299.0172.

8-Methyl-2-(pyridin-4-yl)quinoline (3la)
yellow oil was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 27% isolated yield (14.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.78 (d, J = 4.6 Hz, 2H), 8.26 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 5.9 Hz, 2H), 7.93 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 6.9 Hz, 1H), 7.50–7.45 (m,
8-Methyl-4-(pyridin-4-yl)quinoline/8-methyl-6-(pyridin-4-yl)quinoline (3ia', C4: C6 = 1/1)

yellow oil was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 40% isolated yield (22.0 mg). 1H NMR (500 MHz, CDCl3) δ 8.99 (dd, J = 7.6, 4.3 Hz, 2H), 8.78 (dd, J = 11.7, 5.1 Hz, 4H), 7.75 (s, 1H), 7.70 (s, 1H), 7.62 (dd, J = 11.8, 7.7 Hz, 2H), 7.41 (dd, J = 13.3, 5.5 Hz, 6H), 7.31 (t, J = 4.3 Hz, 2H), 2.86 (s, 3H), 2.83 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 158.2, 154.6, 154.4, 145.4, 145.4 (d, J = 3.0 Hz), 138.9 (d, J = 11.7 Hz), 127.4, 126.9, 124.9, 122.3, 121.7, 119.3, 114.2 (d, J = 19.0 Hz). 19F NMR (471 MHz, CDCl3) δ -123.9. HRMS (ESI) m/z: [M + H]⁺ calcd for C14H9FN2: 225.0826, found: 225.0826.

8-Fluoro-2-(pyridin-4-yl)quinoline (3ma)

green solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 23% isolated yield (12.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.79 (d, J = 5.3 Hz, 2H), 8.32 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 5.8 Hz, 2H), 7.98 (d, J = 8.6 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.55 (m, 1H), 7.49 (m, 1H). 13C NMR (126 MHz, CDCl3) δ 158.2 (d, J = 257.3 Hz), 154.6, 154.4, 145.4, 145.4 (d, J = 3.0 Hz), 138.9 (d, J = 11.7 Hz), 127.4, 126.9, 124.9, 122.3, 121.8, 120.7 (d, J = 4.8 Hz), 113.8 (d, J = 19.0 Hz). 19F NMR (471 MHz, CDCl3) δ -123.9. HRMS (ESI) m/z: [M + H]⁺ calcd for C14H8FN2: 225.0823, found: 225.0826.

8-Fluoro-4-(pyridin-4-yl)quinoline (3ma')

green solid was obtained by column chromatography (elucent: EtOAc/petroleum ether = 1/4) with 43% isolated yield (35.3 mg). 1H NMR (500 MHz, CDCl3) δ 9.04 (d, J = 4.2 Hz, 1H), 8.81 (d, J = 5.2 Hz, 2H), 7.61 (d, J = 8.1 Hz, 1H), 7.52 (m, 4H), 7.42 (d, J = 4.3 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 158.2 (d, J = 257.3 Hz), 150.1, 150.0 (d, J = 1.0 Hz), 145.4, 145.4 (d, J = 3.0 Hz), 138.9 (d, J = 11.7 Hz), 127.4, 126.9, 124.9 (d, J = 8.3 Hz, 1H), 124.1, 121.8, 120.7 (d, J = 4.8 Hz), 113.8 (d, J = 19.0 Hz). 19F NMR (471 MHz, CDCl3) δ -123.9. HRMS (ESI) m/z: [M + H]⁺ calcd for C14H8FN2: 225.0823, found: 225.0824.

8-Chloro-2-(pyridin-4-yl)quinoline (3na)

[2,4'-bipyridine]-4-carbonitrile (4aa)

[2-(Pyridin-4-yl)quinazoline (3qa)]

(4aa, 2% - 3%)

[2-(Pyridin-4-yl)quinoline (3qa)]
7.99 (t, J = 7.7 Hz, 1H), 7.71 (d, J = 5.9 Hz, 2H), 7.68 (d, J = 8.1 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 165.7, 154.6, 151.1, 150.0, 144.7, 134.2, 129.2, 128.4, 126.0, 124.2.

2-(Isoquinolin-1-yl)quinazoline (3qb)
yellow solid was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 69% isolated yield (47.3 mg). 1H NMR (500 MHz, CDCl3) δ 8.84 (m, 2H), 8.71 (d, J = 9.3 Hz, 1H), 8.27 (d, J = 6.7 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.89 (m, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 158.4, 149.7, 147.6, 143.5, 131.0, 130.4, 129.1, 127.9, 127.6, 125.4, 124.2, 122.9, 122.5, 120.5. HRMS (ESI) m/z: [M + H]+ calcd for C22H14N2: 307.1230, found: 307.1230.

6-(Pyridin-4-yl)phenanthridine (3ra)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 62% isolated yield (35.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.84 (m, 2H), 8.71 (d, J = 9.3 Hz, 1H), 8.27 (d, J = 6.7 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.89 (m, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 148.5, 148.1, 147.8, 140.7, 137.0, 131.7, 130.4, 129.8, 127.6, 125.4, 124.2, 122.1, 121.2. HRMS (ESI) m/z: [M + H]+ calcd for C19H12N2: 271.1230, found: 271.1229.

6-(Isoquinolin-1-yl)phenanthridine (3rb)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 60% isolated yield (37.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.81 (m, 2H), 8.22 (d, J = 8.8 Hz, 2H), 7.79 (m, 2H), 7.51 (d, J = 8.7 Hz, 2H), 7.41 (m, 2H), 7.34 (d, J = 5.8 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 163.9, 148.5, 148.1 (d, J = 14.9 Hz), 142.2, 130.3, 129.9, 126.7, 125.5, 123.9, 123.3 (d, J = 4.7 Hz), 111.5 (d, J = 37.4 Hz). 19F NMR (471 MHz, CDCl3) δ -66.5. HRMS (ESI) m/z: [M + H]+ calcd for C18H13F2N2: 275.0979, found: 275.0977.

9-(2-Fluoropyridin-4-yl)acridine (3sc)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 51% isolated yield (35.9 mg). 1H NMR (500 MHz, CDCl3) δ 8.50 (d, J = 5.0 Hz, 1H), 8.32 (d, J = 8.8 Hz, 2H), 7.85 (m, 2H), 7.58 (d, J = 8.5 Hz, 2H), 7.53 (m, 2H), 7.31 (d, J = 4.9 Hz, 1H), 7.08 (s, 1H). 13C NMR (126 MHz, CDCl3) δ 163.9 (d, J = 141.6 Hz), 150.1 (d, J = 7.4 Hz, 1H), 148.5, 148.1 (d, J = 14.9 Hz), 142.2, 130.3, 129.9, 126.7, 125.5, 123.9, 123.3 (d, J = 4.7 Hz), 111.5 (d, J = 37.4 Hz). 19F NMR (471 MHz, CDCl3) δ -66.5. HRMS (ESI) m/z: [M + H]+ calcd for C19H12F2N2: 275.0979, found: 275.0977.

9-(3-Chloropyridin-4-yl)acridine (3sd)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 55% isolated yield (40.0 mg). 1H NMR (500 MHz, CDCl3) δ 8.92 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.35 (d, J = 8.8 Hz, 2H), 7.83 (t, J = 7.0 Hz, 2H), 7.51 (t, J = 8.2 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 4.8 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 150.2, 147.8, 140.7, 137.0, 131.7, 130.4, 129.8, 128.9, 126.2, 125.3, 123.8, 99.9. HRMS (ESI) m/z: [M + H]+ calcd for C18H13ClN2: 291.0684, found: 291.0681.

9-(4-Methylpyridin-2-yl)acridine (3se)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 70% isolated yield (47.3 mg). 1H NMR (500 MHz, CDCl3) δ 8.77 (d, J = 5.1 Hz, 1H), 8.29 (d, J = 8.8 Hz, 2H), 7.77 (t, J = 7.8 Hz, 2H), 7.65 (d, J = 8.7 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.37 (s, 1H), 7.33 (d, J = 5.0 Hz, 1H), 2.50 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 155.3, 149.8, 148.8, 147.7, 144.9, 130.0, 129.6, 127.0, 126.2, 126.0, 124.7, 124.1, 29.7. HRMS (ESI) m/z: [M + H]+ calcd for C19H14N2: 271.1230, found: 271.1229.
**methyl 2-(acridin-9-yl)isonicotinate (3sf)**

Yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 71% isolated yield (55.8 mg). $^1$H NMR (500 MHz, CDCl$_3$) δ 9.10 (d, $J = 5.0$ Hz, 1H), 8.34 (d, $J = 8.8$ Hz, 2H), 8.11 (s, 1H), 8.09 (d, $J = 5.0$ Hz, 1H), 7.80 (t, $J = 7.2$ Hz, 2H), 7.58 (d, $J = 8.7$ Hz, 2H), 7.48 (t, $J = 7.0$ Hz, 2H), 3.98 (d, $J = 12.1$ Hz, 3H), δ 3.99 (s, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 165.3, 156.6, 153.7, 151.1, 148.6, 138.0, 130.3, 129.5, 126.5, 125.8, 125.3, 124.5, 122.4, 52.9. HRMS (ESI) m/z: [M + H]$^+$ calcd for C$_{20}$H$_{14}$N$_2$: 315.1230, found: 315.1228.

**9-(4-(tert-butyl)pyridin-2-yl)acridine (3sg)**

Yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 72% isolated yield (42.2 mg). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.83 (s, 1H), 8.60 (d, $J = 4.9$ Hz, 1H), 8.47 (s, 1H), 8.39 (s, 1H), 8.19 (d, $J = 8.4$ Hz, 1H), 8.03 (d, $J = 8.3$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 4.6$ Hz, 1H), 2.80 (s, 3H), 2.49 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.2, 155.8, 148.9, 148.2, 147.7, 145.1, 141.5, 130.2, 129.2, 128.2, 126.4, 125.0, 123.8, 122.6, 119.7, 29.7, 18.9. HRMS (ESI) m/z: [M + H]$^+$ calcd for C$_{26}$H$_{20}$N$_2$: 357.1230, found: 357.1229.

**9-(4-Methyl-2-(4-methylpyridin-2-yl)quinoline (3ee)**

Yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 71% isolated yield (41.9 mg). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.93 (s, 1H), 8.75 (d, $J = 8.3$ Hz, 1H), 8.40 (s, 1H), 8.39 (s, 1H), 8.19 (d, $J = 8.5$ Hz, 1H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.88 (t, $J = 7.7$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 6.2$ Hz, 1H), 2.80 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.5, 155.6, 149.1, 147.8, 145.1, 137.0, 130.3, 129.2, 128.3, 126.5, 124.0, 123.8, 121.9, 119.5, 18.9.

**2-(Pyridin-2-yl)quinaline (3ai)**

(Hey and Williams, 1950, Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) Yellow solid was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 62% isolated yield (51.3 mg). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.93 (s, 1H), 8.75 (d, $J = 8.3$ Hz, 1H), 8.40 (s, 1H), 8.19 (d, $J = 8.5$ Hz, 1H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.88 (t, $J = 7.7$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 6.2$ Hz, 1H), 2.80 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.5, 155.6, 149.1, 147.9, 136.9, 136.8, 129.8, 129.5, 126.3, 126.0, 124.7, 123.2, 227.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for C$_{19}$H$_{14}$N$_2$: 291.1230, found: 291.1228.

**2-(Pyridin-2-yl)quinoline (3ei)**

(Hey and Williams, 1950, Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) Yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/6) with 62% isolated yield (51.3 mg). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.93 (s, 1H), 8.75 (d, $J = 8.3$ Hz, 1H), 8.40 (s, 1H), 8.19 (d, $J = 8.5$ Hz, 1H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.88 (t, $J = 7.7$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 6.2$ Hz, 1H), 2.80 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.5, 155.6, 149.1, 147.9, 136.9, 136.8, 129.8, 129.5, 128.2, 127.6, 126.7, 124.0, 121.8, 118.9.
2-(4-(tert-butyl)pyridin-2-yl)-4-methylquinoline (3eg)
yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 76% isolated yield (52.5 mg). ¹H NMR (500 MHz, CDCl₃) δ 8.65 (d, J = 5.8 Hz, 2H), 8.39 (s, 1H), 8.23 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.73 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 7.37 (d, J = 3.7 Hz, 1H), 2.80 (s, 3H), 1.44 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 161.2, 156.2, 155.9, 148.9, 147.6, 145.1, 130.3, 129.2, 128.2, 126.4, 123.7, 121.3, 119.8, 118.9, 30.6, 29.7, 18.9. HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₉H₂₀N₂: 277.1699, found: 277.1699.

4-Methyl-2-(6-methylpyridin-2-yl)quinoline (3eh)
(Hey and Williams, 1950; Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 63% isolated yield (36.9 mg). ¹H NMR (500 MHz, CDCl₃) δ 8.41 (d, J = 5.7 Hz, 2H), 8.18 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.3 Hz, 1H), 7.77–7.70 (m, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 7.6 Hz, 1H), 2.80 (s, 3H), 2.69 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 157.8, 156.0, 155.9, 147.8, 144.9, 137.1, 130.3, 129.1, 128.2, 123.7, 123.5, 119.6, 118.9, 29.7, 18.9.

4-Methyl-2,2'-biquinoline (3eb)
(Hey and Williams, 1950; Nunn and Schofield, 1952; Kouznetsov et al., 2012, 2017; Yamaguchi et al., 2016; Pang et al., 2017; Zhang et al., 2017a, 2017b; Roder et al., 2019) yellow oil was obtained by column chromatography (eluent: EtOAc/petroleum ether = 1/4) with 54% isolated yield (36.5 mg). ¹H NMR (500 MHz, CDCl₃) δ 8.85 (d, J = 8.6 Hz, 1H), 8.69 (s, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.25 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.79 (m, 2H), 7.63 (m, 2H), 2.86 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 154.8, 147.9, 141.7, 140.8, 136.8, 135.7, 131.3, 130.4, 129.8, 129.5, 129.3, 128.4, 127.7, 126.9, 126.7, 123.8, 119.9, 119.5, 19.0.