

博士論文

ヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体の合成と応用：
位置選択的トリフルオロメチル化およびその蛍光特性

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略語表

abs	absorbance
Ac	acetyl
aq.	aqueous
Ar	aryl
Bu	butyl
Bz	benzoyl
conc.	concentrated
DART	direct analysis in real time
DCE	1,2-dichloroethane
DFT	density functional theory
DME	1,2-dimethoxyethane
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
em	emission
eq	equivalent
ESI	electrospray ionization
Et	ethyl
FT	Fourier transform
h	hour
HOMO	highest occupied molecular orbital
IR	infrared
LUMO	lowest unoccupied molecular orbital
<i>m</i> -CPBA	<i>m</i> -chloroperbenzoic acid
Me	methyl
Ms	methanesulfonyl
MS	mass spectrometry
MS4A	molecular sieves 4A
NMP	<i>N</i> -methylpyrrolidone
NMR	nuclear magnetic resonance
Ph	phenyl
phen	phenanthroline
ppm	parts per million
Py	pyridyl
TBA	tetrabutylammonium

TBHP	<i>t</i> -butyl hydroperoxide
TD-DFT	time-dependent density functional theory
TG-DTA	thermogravimetry-differential thermal analysis
THF	tetrahydrofuran
TLC	thin-layer chromatography
Ts	<i>p</i> -toluenesulfonyl
UV-Vis	ultraviolet-visible

序論

1990年代までの創薬研究では低分子医薬品開発が主流であり、有機合成化学の進展が医薬品開発に大きく貢献してきた。2000年代に入り、バイオテクノロジーの進展とともに抗体医薬品の有用性が示され、近年では再生医療に関する研究が注目を集めている。それでは低分子医薬品が淘汰されていくかということ、決してそのようなことはないと考えられる。2000年代の分子標的薬としての抗がん剤や中枢神経系疾患の治療薬としての研究開発において、単剤で複数のターゲットに対する親和性を併せもつことが可能であること、服薬コンプライアンス、医療費や品質管理といった点で、低分子医薬品であることの利点が示されている。また、両者を組み合わせた抗体薬物複合体(ADC)の研究開発も進んでいる。そのため、低分子医薬品の研究開発に有用な有機合成化学の進展が、これまでと同様に強く求められている。天然物や医薬品をリード化合物とした創薬研究を考えると、高度に官能基化されたリード化合物に対する保護基を必要としない位置選択的な新規反応の開発は、低分子医薬品開発に貢献できる研究の一つであるといえる。今回、これまでの天然物ライブラリーに不足していると考えられる誘導体としてフッ素を含む化合物に着目した。

地殻におけるフッ素化合物の含有量は比較的高いにもかかわらず、天然に存在するフッ素を含む有機化合物は極めて少ない¹⁾。その一方で、現在では医薬品の2割、農薬の3割程度がフッ素を含む有機化合物として開発されてきており、天然には成しえない有機合成化学による重要な貢献であることは明らかである。医薬品の部分構造としては、主に芳香環上のフッ素原子またはトリフルオロメチル基として含まれており、化合物の物性や代謝安定性などの薬物動態パラメータに大きな影響を与えることが知られている。

従来、フッ素原子やトリフルオロメチル基の導入は、ハロゲン化アリアルを基質とした鈴木・宮浦カップリングをはじめとする種々のクロスカップリング反応では困難であったが、現在では触媒的な官能基化や、C-H結合の変換による種々の反応が開発され、ここ十数年の進展はめざましいものがある²⁾。トリフルオロメチル基は高い脂溶性および電子求引性を有しており、フッ素原子とは大きく異なる性質を示すため、その高効率かつ実用的な導入法の開発は重要である。以上の背景をふまえ、既存の方法では困難とされていた、ヘテロ芳香族化合物の位置選択的トリフルオロメチル化反応の開発に着手した。

本論文では、既存の方法によるヘテロ芳香族化合物の活性化に比べ、さらに求電子的な活性化体としての、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃錯体の設計と合成、およびその特性を活用した応用研究について述べる。

第1章では、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃錯体の設計、合成、および特性について述べる。第2章では、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃錯体の特性を活用した、6員環ヘテロ芳香族化合物の位置選択的なトリフルオロメチル化反応の開発について述べる。第3章では、新規機能性材料としての応用を志向した、ヘテロ芳香族化合物 *N*-オキ

シド-BF₂CF₃錯体の蛍光特性について述べる。

ヘテロ芳香族化合物 *N*-オキシドの活性化剤としてルイス酸であるボラン BF₂CF₃ を設計した。有機合成反応において汎用されているボラン BF₃ の一つのフッ素原子をトリフルオロメチル基に置換した化合物であり、1960年代にその合成法が報告されている³⁾。一方、合成法が非常に煩雑であることもあり、BF₂CF₃ はこれまで有機合成反応に活用されていない。今回、トリフルオロメチル基の特徴により、BF₂CF₃ がヘテロ芳香族化合物 *N*-オキシドの活性化剤として BF₃ とは大きく異なる特徴が見出された点が、非常に興味深い。

本研究による知見が世界中の研究者により活用され、革新的な創薬研究や反応開発の礎となれば幸いである。

References

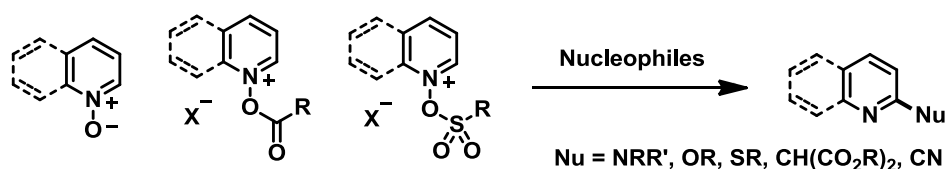
- 1) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881.
- 2) (a) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (b) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (c) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem. Int. Ed.* **2013**, *52*, 8214.
- 3) (a) Parsons, T. D.; Baker, E. D.; Burg, A. B.; Juvinall, G. L. *J. Am. Chem. Soc.* **1961**, *83*, 250. (b) Parsons, T. D.; Self, J. M.; Schaad, L. H. *J. Am. Chem. Soc.* **1967**, *89*, 3446.

本論

第1章 ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体の合成

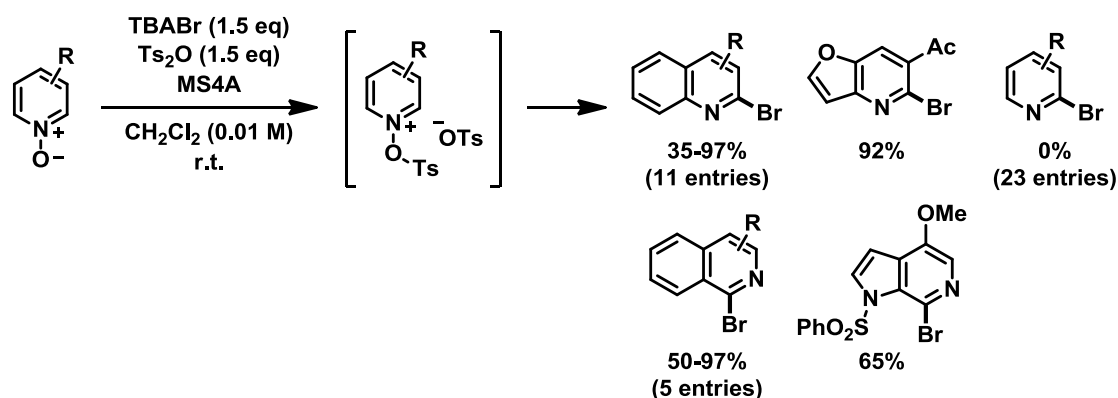
1-1 背景

ピリジン環、キノリン環、およびその類縁の含窒素ヘテロ芳香環は、天然物、医薬品や機能性材料の骨格として非常に重要である¹⁻³⁾。含窒素ヘテロ芳香環に対する位置選択的な反応は、種々の誘導体を効率的に合成するために有用であり、2位に置換基を導入する方法として、含窒素ヘテロ芳香族化合物 *N*-オキシドと求核剤との反応が古くから知られている (Scheme 1-1)⁴⁾。含窒素ヘテロ芳香族化合物 *N*-オキシドのさらなる求電子的な活性化法としては、アシル基やスルホニル基の導入が汎用されており、アミン、フェノール、チオール、活性メチレン化合物、およびシアン化物イオンを求核剤とした反応が報告されている。



Scheme 1-1. General approach to 2-position-selective functionalizations of pyridine and quinoline *N*-oxides and their derivatives

例えば、Baran らによって、含窒素ヘテロ芳香族化合物 *N*-オキシドの2位選択的なブROM化が報告されている (Scheme 1-2)⁵⁾。活性化剤として無水トシル酸を用いることで、比較的弱い求核剤である臭化物イオンとの反応が進行しており、本反応は種々の置換基を有するキノリン *N*-オキシド、イソキノリン *N*-オキシドといった芳香環と縮環した含窒素ヘテロ芳香族化合物に対して適用可能である。一方、種々の置換基を有するピリジン *N*-オキシドを基質とした場合には、目的物が全く得られないことが報告されている。これは、ピリジン *N*-オキシドの活性化体の求電子的性がキノリン *N*-オキシドの活性化体に比べて低いため、比較的弱い求核剤である臭化物イオンによる求核反応が進行しないことが原因であると考えられる。



Scheme 1-2. Regioselective bromination of fused heterocyclic *N*-oxides reported by Baran group

以上のことから、既存の方法に比べ、より強力な含窒素ヘテロ芳香族化合物 *N*-オキシドの求電子的な活性化が達成されれば、これまでに導入が困難であった弱い求核剤との反応による、多様な含窒素ヘテロ芳香環の合成が可能になると考えられた。

1-2 電子不足な新規ヘテロ芳香族化合物の設計

含窒素ヘテロ芳香族化合物 *N*-オキシドを求電子的に活性化する他のアプローチとして、ルイス酸との錯体へと変換する方法が報告されている。ピリジン *N*-オキシド- BF_3 錯体は、ピリジン *N*-オキシドに比べ、電子受容性が向上することが報告されている⁶⁾。そこで、DFT 計算を用いて、より求電子的性の高い、つまり LUMO エネルギー準位の低い活性化体を設計した。既存の酸塩化物や酸無水物によるピリジン *N*-オキシドの活性化体、および、ピリジン *N*-オキシドとボランとの錯体の LUMO エネルギー準位を Figure 1-1 に示す。ピリジン *N*-オキシド- BF_3 錯体 **G** の LUMO エネルギー準位は、既存の方法による活性化体(**C-F**)に比べて低いことがわかった。また、 BF_3 よりルイス酸性の高いボランである BF_2CF_3 との錯体 **H** の LUMO エネルギー準位は、 BF_3 との錯体 **G** に比べてさらに低いことがわかり、強力なピリジン *N*-オキシドの求電子的活性化体であることが示唆された⁷⁾。

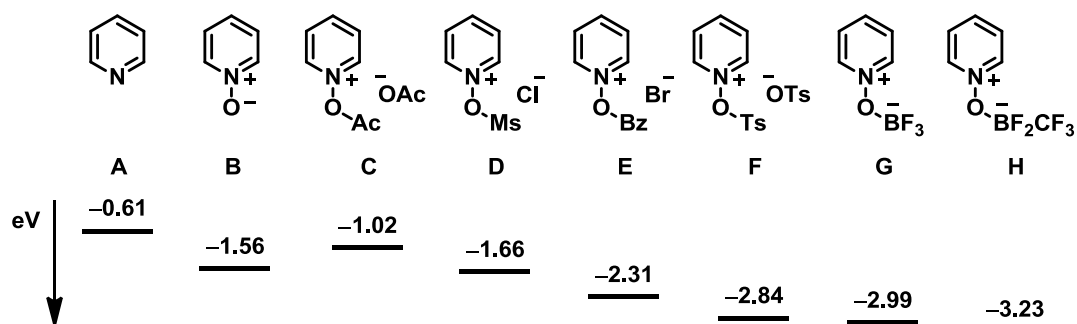
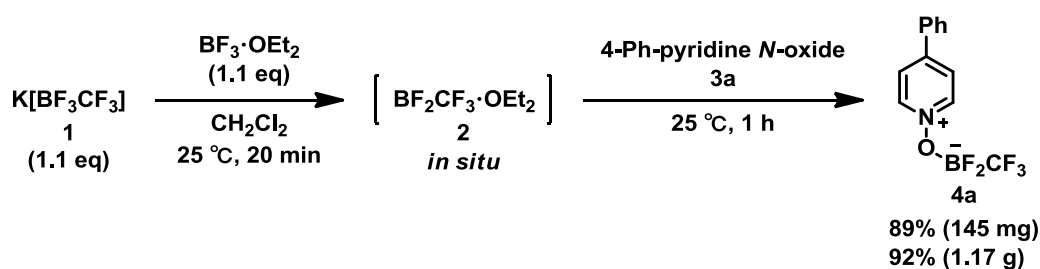


Figure 1-1. Comparison of LUMO levels of several pyridine derivatives (B3LYP/6-31G*)

for A; B3LYP/6-31+G* for B, C, D, F, G, and H; B3LYP/LAV3P+* for E)

1-3 ピリジン *N*-オキシド-ボラン錯体の合成検討

4-フェニルピリジン *N*-オキシドを基質とし、種々のボラン錯体を合成した。4-フェニルピリジン *N*-オキシド-BF₂CF₃ 錯体の合成法を示す(Scheme 1-3)。市販のカリウムトリフルオロメチルトリフルオロボレート **1** に BF₃·OEt₂ を反応させ、系中で BF₂CF₃·OEt₂ (**2**) を調製し、4-フェニルピリジン *N*-オキシド(**3a**) を反応させることにより、温和な条件下で目的とする錯体 **4a** が 89% の収率で得られた。また、本合成法はグラムスケールにおいても、同等の収率(92%)で進行することが確認された。



Scheme 1-3. Preparation of 4-phenylpyridine *N*-oxide-BF₂CF₃ complex **4a**

興味深いことに、ボラン BF₂CF₃ は空气中で分解するのに対し、錯体 **4a** は空气中で非常に安定であり、分液操作による後処理やシリカゲルカラムによる精製が可能であることがわかった⁷⁾。原料 **3a** は高極性化合物であるのに対し、錯体 **4a** は低極性化合物であり、ジクロロメタンを展開溶媒としたシリカゲルカラム精製により、高純度の化合物が得られた。ヘキサン/酢酸エチル系においても溶出させることは可能であったが、¹⁹F および ¹¹B NMR 測定により、TLC で確認できない原料 **1** に由来する不純物が分離できていないことが確認された。錯体 **4a** は、少なくとも固体状態で 3 ヶ月、THF-*d*₈ および CD₃CN 溶液中で 2 週間は分解しないことを確認している。

錯体 **4a** の ¹H NMR 測定により、**3a** に比べて芳香環上のプロトンに対応するシグナルが低磁場シフトしていることがわかり、ピリジン環上がより電子不足になっていることが示唆された。¹⁹F NMR 測定により、BF₂CF₃ 部位の 2 種のフッ素に対応する積分比 2:3 のシグナルが観測された。¹¹B NMR 測定により、BF₂CF₃ 部位のホウ素に対応するシグナルが観測され、その化学シフト値(δ 0.61 ppm)より、ボレートであることが支持された。

同様の方法にて、種々のボランと **3a** との錯体の合成を検討した(Figure 1-2)。トリフルオロメチル基をパーフルオロアルキル基へと変換した BF₂CF₂CF₃ 錯体(**5**)、パーフルオロフェニル基へと変換した BF₂C₆F₅ 錯体(**6**)、BF₂(*p*-CF₃C₆F₄) 錯体(**7**)、および BF₃ 錯体(**8**)のいずれもが、同様の方法で得られることが反応溶液の ¹H、¹⁹F、および ¹¹B NMR 測定により確認できた。一方、トリフルオロメチル基をメチル基、フェニル基、および 1-ヘキシニル

基へと変換した錯体は得られないことが確認され、本合成法は BF_3 よりもルイス酸性の高いボラン錯体の合成に適用可能であると考えられる。

得られた錯体(4a-8)の安定性を評価した結果、よりルイス酸性の高いパーフルオロアルキル基を有するボラン錯体(4a,5)のみが、分液操作による後処理、シリカゲルカラム精製による単離や空気中での保存が可能ほど安定であることがわかった。分液操作による後処理の結果より、パーフルオロフェニル基を有するボラン錯体(6,7)は、 BF_3 錯体(8)に比べて安定であることが示唆されたが、シリカゲルカラム精製により原料である 4-フェニルピリジン *N*-オキシド **3a** として回収されることが確認された。以上の結果より、ボランのルイス酸性が高くなるにつれ、酸-塩基相互作用が強くなり、錯体の安定性が向上していると考えられる。

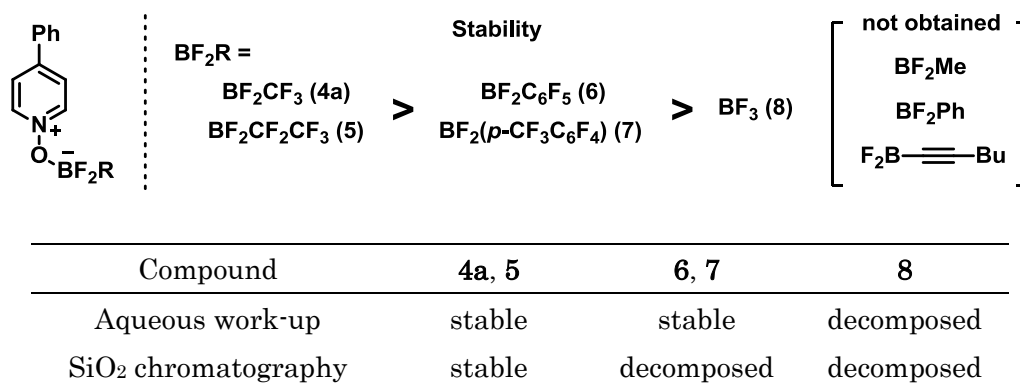
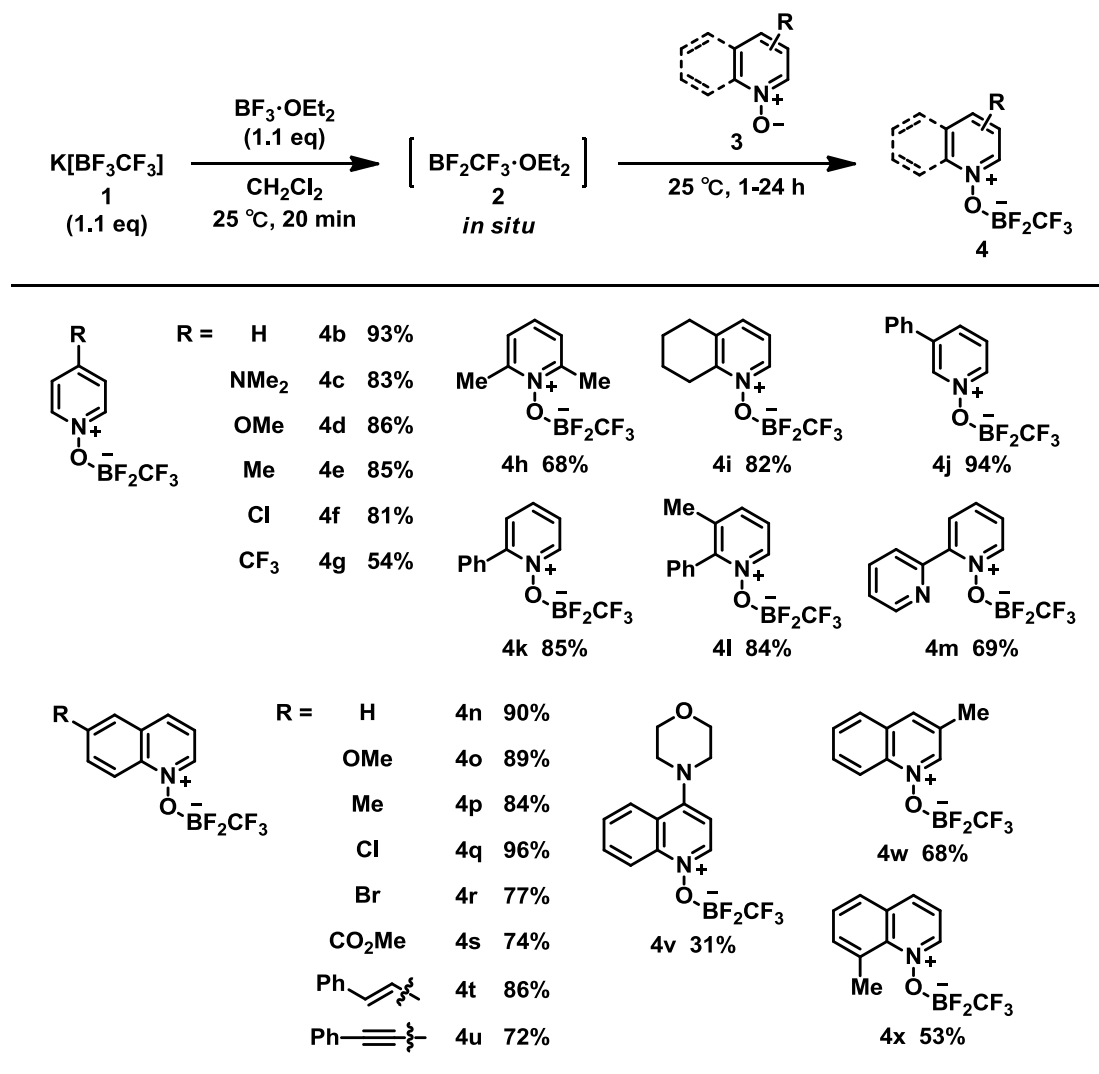


Figure 1-2. Relative stability of several 4-phenylpyridine *N*-oxide-borane complexes

1-4 基質一般性

本合成法の基質一般性を示す(Table 1-1)。電子供与性および電子求引性の置換基を有する種々のピリジン誘導体(4b-4m)やキノリン誘導体(4n-4x)が、良好な収率、高い官能基許容性で得られた。立体障害の大きい 2,6-ルチジン誘導体 **4h** についても良好な収率で目的物が得られた。

Table 1-1. Synthesis of various pyridine and quinoline *N*-oxide-BF₂CF₃ complexes



ピリジンやキノリン誘導体以外に、種々の含窒素ヘテロ芳香族化合物 *N*-オキッドを基質として用いた場合にも、同様の方法にて、イソキノリン誘導体 **4y**、フェナンスリジン誘導体 **4z**、アクリジン誘導体 **4aa**、ベンゾ[*h*]キノリン誘導体 **4ab**、フェナントロリン誘導体 **4ac**、フタラジン誘導体 **4ad**、ピリミジン誘導体 **4ae**、縮環ピリジン誘導体(**4af**, **4ag**)、およびイミダゾール誘導体(**4ah**, **4ai**)が得られた(Table 1-2)。

一方、Figure 1-3 に示すキノキサリン誘導体、ピラジン誘導体、およびピリダジン誘導体は、反応溶液の ¹H、¹⁹F、および ¹¹B NMR 測定により錯体の生成は確認できたが、シリカゲルカラムにより原料のヘテロ芳香族化合物 *N*-オキッドへと分解することが TLC により確認できた。置換基にもよるが、一般に、キノキサリン、ピラジン、およびピリダジンの塩基性は、ピリジンやキノリンに比べて低い。この結果より、ヘテロ芳香族化合物 *N*-オキッド-BF₂CF₃ 錯体の安定性は、ボランのルイス酸性だけではなく、ヘテロ芳香族化合物

N-オキシドのルイス塩基性にも依存していると考えられる。

Table 1-2. Synthesis of various heterocyclic *N*-oxide-BF₂CF₃ complexes

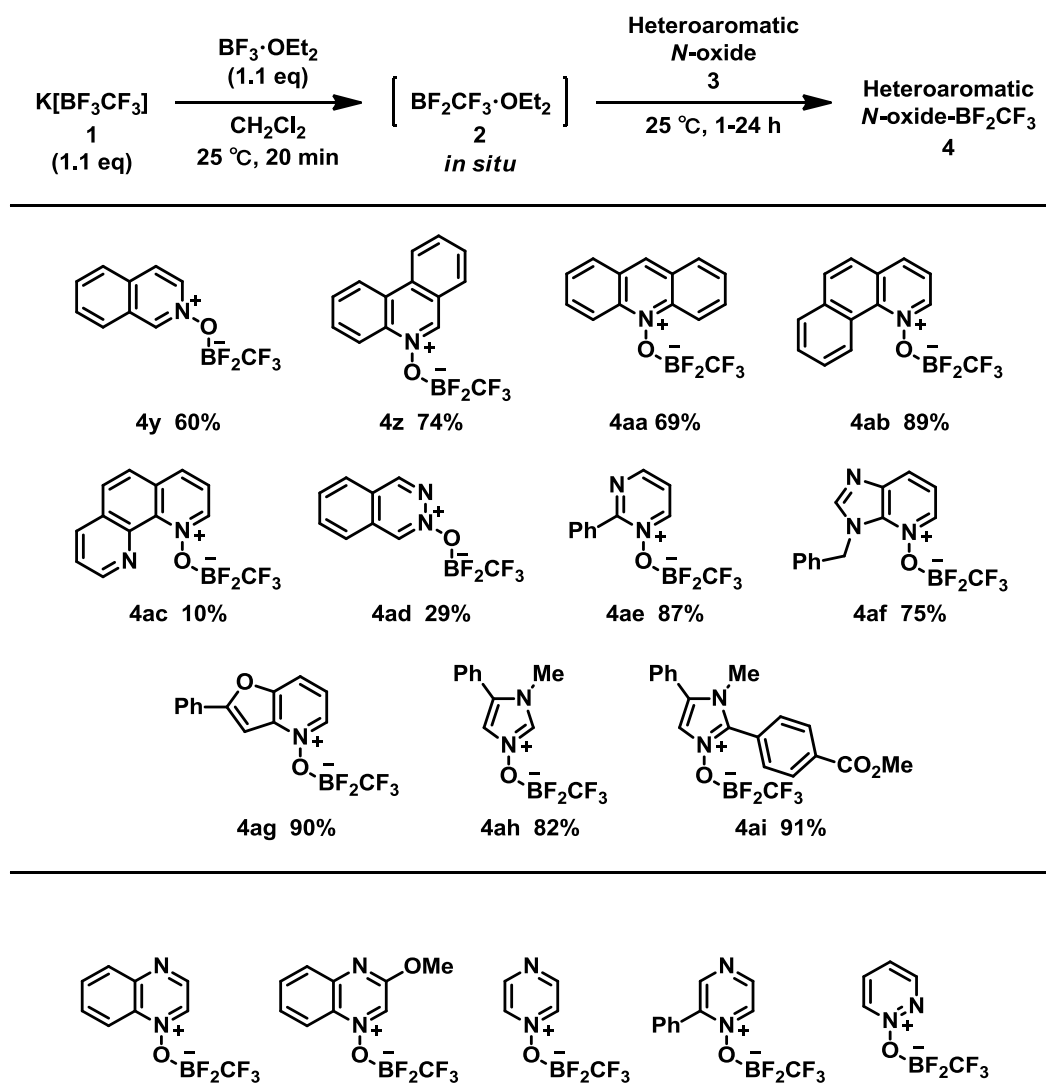


Figure 1-3. Decomposed heterocyclic *N*-oxide-BF₂CF₃ complexes by silica-gel chromatography

1-5 ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体の特性

アクリジン *N*-オキシド-BF₂CF₃ 錯体 **4aa** は、単結晶 X 線構造解析により、その構造を決定することができた。アクリジン *N*-オキシドの酸素原子は、BF₂CF₃ のホウ素原子に配位していることが確認された。化合物 **4aa** におけるホウ素原子と酸素原子の結合距離は 1.514 Å であり、一般的な B-O 配位結合に比べ、かなり短いことがわかった(e.g., B-O in BF₃·OMe₂, 1.719 Å)⁸⁾。ホウ素中心はわずかにひずんだ四面体構造をとっており、アクリジン *N*-オキシドと BF₂CF₃ 部位は、強いルイス酸-塩基相互作用により結合していることが示唆

された。

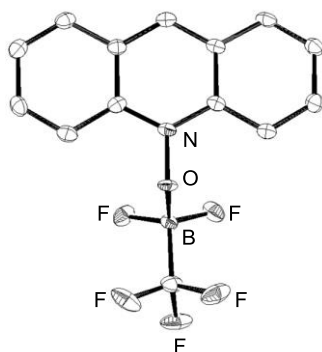


Figure 1-4. ORTEP drawing of acridine *N*-oxide- BF_2CF_3 complex **4aa** (50% probability for thermal ellipsoids. Hydrogen atoms are omitted for clarity.)

TG-DTA 分析により、得られたヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体の熱的安定性を評価した。その結果、ボランのルイス酸性を高めることにより、ヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体の熱的安定性が向上することがわかった。4-フェニルピリジン *N*-オキシド- BF_2CF_3 錯体 **4a** の熱分解点は 162 °C であるのに対し、よりルイス酸性の高いボランである $\text{BF}_2\text{CF}_2\text{CF}_3$ 錯体 **5** の熱分解点は 275 °C であった。さらに、ヘテロ芳香族化合物 *N*-オキシドのルイス塩基性を高めることによっても、ヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体の熱的安定性が向上することがわかった。ピリジン *N*-オキシド- BF_2CF_3 錯体 **4b** の熱分解点は 139 °C であるのに対し、電子供与性置換基であるジメチルアミノ基を有するピリジン *N*-オキシド- BF_2CF_3 錯体 **4c** の熱分解点は 176 °C であった。

種々のピリジン *N*-オキシド-ボラン錯体の NBO 計算により、結合長および結合次数の指標である Wiberg bond index を見積もった結果、O-B 結合の Wiberg bond index はボランのルイス酸性が高まるにつれて大きくなることがわかった (Table 1-3)。これは、4-フェニルピリジン *N*-オキシド-ボラン錯体 **8**、**4a** および **5** の安定性評価の結果を支持しているといえる。

Table 1-3. Selected bond lengths and the Wiberg bond indices of pyridine *N*-oxide complex with various boranes^a

compound	bond lengths [Å]		Wiberg bond index	
	N-O	O-B	N-O	O-B
PyO-BF ₃	1.34770	1.58717	1.0359	0.4711
PyO-BF ₂ CF ₃	1.35253	1.55893	1.0292	0.5226
PyO-BF ₂ C ₂ F ₅	1.35235	1.55710	1.0290	0.5304

^a Calculated at the MP2/6-31+G(d) level.

化合物 **4a** の THF 溶液中におけるサイクリックボルタンメトリー測定により、ピーク電位-1.87 V の不可逆的な還元波が観測され、LUMO エネルギー準位は-3.30 eV であると算出された(Figure 1-5)⁹⁾。Figure 1-1 に示したように、DFT 計算により見積もったピリジン *N*-オキシド-BF₂CF₃ 錯体の LUMO エネルギー準位は-3.23 eV であり、4-フェニルピリジン *N*-オキシド-BF₂CF₃ 錯体 **4a** の値とほぼ一致している。この結果より、ルイス酸性の高い BF₂CF₃ と結合することで、芳香環上の電子受容性が向上していることが支持された⁶⁾。

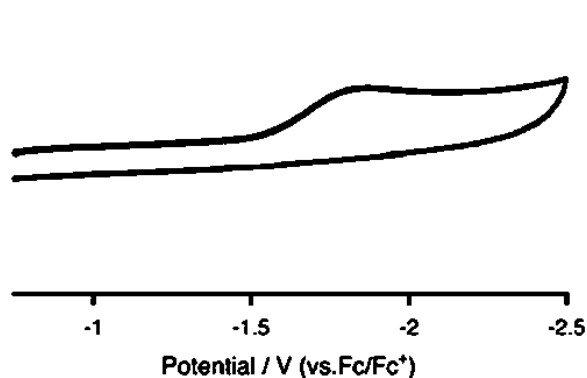


Figure 1-5. Cyclic voltammogram of **4a** in THF

1-6 小括

既存の方法によるピリジン誘導体の活性化に比べ、さらに求電子的な活性化体として、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体を見出した。本化合物群は、ヘテロ芳香族化合物 *N*-オキシドから、温和な条件下、高い官能基許容性で得ることが可能であり、分液操作やシリカゲルカラムによる単離精製が可能にほど安定であることがわかった。また、ボラン BF₂CF₃ の高いルイス酸性により、ヘテロ芳香環上が非常に電子不足になっていることが、¹H NMR のケミカルシフトやサイクリックボルタンメトリー測定による還元電位から支持された。本化合物の高い求電子的性を活用することにより、これまでに導入が困難であった弱い求核剤との反応による、多様な含窒素ヘテロ芳香環の合成が可能になると期待される。

Experimental

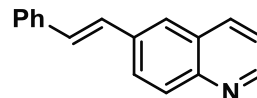
General. All reactions were carried out in a dry solvent under an argon atmosphere. Potassium trifluoro(trifluoromethyl)borate was purchased from Tokyo Chemical Industry Co., Ltd. Known heteroaromatic *N*-oxides **3g**¹⁰⁾, **3i**¹¹⁾, **3j**¹²⁾, **3k**¹³⁾, **3l**¹³⁾, **3q**⁵⁾, **3r**⁵⁾, **3s**¹⁴⁾, **3v**¹⁵⁾, **3w**¹⁶⁾, **3x**¹⁷⁾, **3ac**⁵⁾, **3ad**¹⁸⁾, **3ae**¹⁹⁾, **3af**²⁰⁾, **3ah**²¹⁾, **3ai**²²⁾, and potassium trifluoro(perfluorophenyl)borate²³⁾ were prepared according to the literature methods and identified by comparing these spectroscopic data with those of reported data. Other reagents and heteroaromatic compounds were purchased from commercial sources and

used without further purification unless otherwise noted. Column chromatography was performed with silica gel (230-400 mesh ASTM). NMR spectra were recorded on JEOL JNM-ECX500 (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) and JEOL JNM-ECS400 (400 MHz for ^1H NMR, 125 MHz for ^{13}C NMR, 368 MHz for ^{19}F NMR, and 125 MHz for ^{11}B NMR) spectrometers. Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. Fluorine and boron chemical shifts are reported relative to trifluoroacetic acid (δ -76.55 ppm) and $\text{BF}_3\cdot\text{OEt}_2$ (δ 0.00 ppm) as an external reference, respectively. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. ESI-MS spectra and DART-MS spectra were measured on a JEOL JMS-T100LC AccuTOF spectrometer for HRMS. Single crystal X-ray structure analysis was performed on a Rigaku R-Axis RAPID II imaging plate area detector with graphite-monochromated $\text{Cu-K}\alpha$ radiation. TG-DTA analysis was performed on a SHIMADZU DTG-60/60H system. Cyclic voltammetry (CV) was performed on an ALS/CHI-617A electrochemical analyzer. The CV cell consisted of a glassy carbon electrode, a Pt wire counter electrode, and an Ag/AgNO_3 reference electrode. The measurements were carried out under an argon atmosphere using a THF solution of sample with a concentration of 1.0 mM and 0.10 M tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) as a supporting electrolyte. The reduction potentials were calibrated with a ferrocene/ferrocenium ion couple.

Preparation of (*E*)-6-styrylquinoline.

A mixture of 6-bromoquinoline (2.08 g, 10.0 mmol), styrene (1.25 g, 12.0 mmol), potassium carbonate (5.10 g, 36.9 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (250 mg, 0.356 mmol), and DMF (9.1 mL) was heated at 160 °C for 24 h. Then the reaction mixture was filtered through a pad of Celite, evaporated in vacuo, and purified by column chromatography on silica gel (hexane/ethyl acetate = 3/1) to afford the title compound.

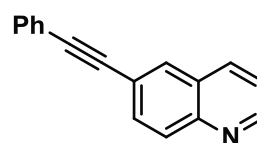
(*E*)-6-Styrylquinoline. 88% yield; yellow solid; R_f = 0.20 (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.32 (m, 3H), 7.38-7.42 (m, 3H), 7.57 (d, J = 7.9 Hz, 2H), 7.84 (d, J = 2.2 Hz, 1H), 7.99 (dd, J = 8.8, 2.2 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.87 (dd, J = 4.0, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 121.5, 126.0, 126.7, 127.3, 127.8, 128.0, 128.6, 128.8, 129.7, 130.2, 135.6, 136.0, 137.0, 148.0, 150.1; IR (KBr, ν / cm^{-1}) 1568, 1498, 1362, 1117, 1075, 962, 890, 799, 753, 693; HRMS (DART) Calcd for $\text{C}_{17}\text{H}_{14}\text{N}^+$ [$\text{M}+\text{H}^+$] 232.1121, Found 232.1129.



Preparation of 6-(phenylethynyl)quinoline.

To a solution of 6-bromoquinoline (2.08 g, 10.0 mmol) in Et₃N (25.0 mL) was added PdCl₂(PPh₃)₂ (35.1 mg, 0.0500 mmol) and CuI (19.1 mg, 0.100 mmol), and the mixture was stirred for 15 min. Ethynylbenzene (1.32 mL, 12.0 mmol) was added, and the mixture was stirred at 25 °C. After the reaction was completed, white precipitates were filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. Water (20 mL) was added, and the mixture was extracted with diethyl ether (3 x 20 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The product was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to give the title compound.

6-(Phenylethynyl)quinoline. 97% yield; white solid; R_f = 0.26 (hexane/ethyl acetate = 3/1); ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.40 (m, 4H), 7.57-7.60 (m, 2H), 7.82 (dd, *J* = 8.5, 1.8 Hz, 1H), 8.03 (d, *J* = 1.8 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* =



8.5 Hz, 1H), 8.92 (dd, *J* = 4.0, 1.8 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 89.1, 90.7, 121.6, 121.7, 123.0, 128.0, 128.5, 128.6, 129.6, 131.1, 131.7, 132.2, 125.7, 147.7, 150.9; IR (KBr, ν / cm⁻¹) 1371, 1128, 1070, 955, 919, 887, 839, 799, 758, 690; HRMS (DART) Calcd for C₁₇H₁₂N⁺ [M+H⁺] 230.0964, Found 230.0976.

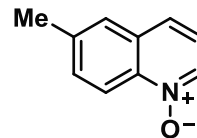
General procedure for preparation of heteroaromatic *N*-oxides.

Method A: To a 0 °C solution of a pyridine derivative (1.0 equiv) in CH₂Cl₂ (0.5 M) was added *m*-CPBA (77%, 1.0 equiv) and the mixture was stirred at 25 °C for 1-24 h. After the reaction mixture was diluted with CH₂Cl₂, powdered potassium carbonate (1.5 equiv) was added to the reaction mixture, and the mixture was stirred for 1 h. Insoluble solid was filtered off through a pad of Celite, washed with CH₂Cl₂, and then the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (CH₂Cl₂/MeOH = 10/1) to give the corresponding *N*-oxide of the pyridine derivative.

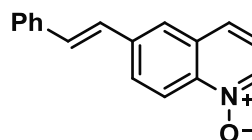
Method B: To a solution of a pyridine derivative (1.0 equiv) in CH₂Cl₂ (1.0 M) was successively added MeReO₃ (0.030 equiv) and aqueous hydrogen peroxide (30 wt%, 2.0 equiv), and then the mixture was stirred at 25 °C for 12 h. After excess amount of hydrogen peroxide was quenched with MnO₂, the reaction mixture was diluted with CH₂Cl₂ and water. The layers were separated, and the organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product

was purified by column chromatography on silica gel (CH₂Cl₂/MeOH = 10/1) to give the corresponding *N*-oxide of the pyridine derivative.

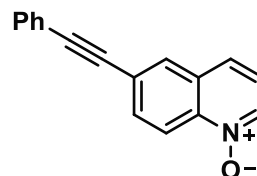
6-Methylquinoline 1-oxide (3p). 81% yield (Method A); white solid; R_f = 0.10 (ethyl acetate); ¹H NMR (500 MHz, CDCl₃) δ 2.55 (s, 3H), 7.38 (dd, *J* = 5.7, 5.7 Hz, 1H), 7.59 (s, 1H), 7.60 (d, *J* = 5.7 Hz, 1H), 7.69 (d, *J* = 8.9 Hz, 1H), 8.64 (d, *J* = 5.7 Hz, 1H), 8.72 (d, *J* = 8.9 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 20.0, 117.9, 119.8, 123.9, 125.8, 129.3, 131.0, 133.5, 137.5, 138.6; IR (KBr, ν / cm⁻¹) 3854, 3038, 1929, 1637, 1054, 969, 931, 893, 873, 627; HRMS (DART) Calcd for C₁₀H₁₀NO⁺ [M+H⁺] 160.0757, Found 160.0763.



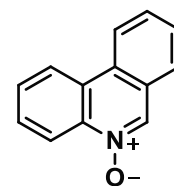
(*E*)-6-Styrylquinoline 1-oxide (3t). 61% yield (Method A); yellow solid; R_f = 0.31 (CH₂Cl₂/acetone = 1/1); ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.34 (m, 3H), 7.39-7.43 (m, 3H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.86 (s, 1H), 8.01 (dd, *J* = 9.2, 1.8 Hz, 1H), 8.49 (d, *J* = 6.3 Hz, 1H), 8.73 (d, *J* = 9.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 120.2, 121.5, 125.9, 126.0, 126.8, 126.9, 128.3, 128.5, 128.9, 131.1, 131.9, 135.5, 136.6, 138.0, 141.0; IR (KBr, ν / cm⁻¹) 2210, 1568, 1489, 1417, 1356, 1228, 893, 827, 759, 691; HRMS (DART) Calcd for C₁₇H₁₄NO⁺ [M+H⁺] 248.1070, Found 248.1067.



6-(Phenylethynyl)quinoline 1-oxide (3u). 67% yield (Method A); yellow solid; R_f = 0.38 (CH₂Cl₂/acetone = 1/1); ¹H NMR (500 MHz, CDCl₃) δ 7.32 (dd, *J* = 8.5, 6.3 Hz, 1H), 7.38-7.40 (m, 3H), 7.57-7.59 (m, 2H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.86 (dd, *J* = 9.0, 1.3 Hz, 1H), 8.04 (s, 1H), 8.51 (d, *J* = 6.3 Hz, 1H), 8.73 (d, *J* = 9.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 88.0, 92.3, 120.2, 121.8, 122.5, 124.4, 125.5, 128.6, 129.1, 130.1, 131.1, 131.9, 133.2, 136.1, 140.9; IR (neat ν / cm⁻¹) 1614, 1504, 1425, 1301, 1219, 1091, 959, 821, 734, 663; HRMS (DART) Calcd for C₁₇H₁₂NO⁺ [M+H⁺] 246.0913, Found 246.0918.

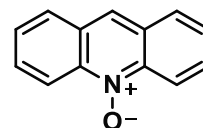


Phenanthridine 5-oxide (3z). 61% yield (Method B); pale pink solid; R_f = 0.34 (ethyl acetate); ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.73 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.78 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.86-7.93 (m, 2H), 7.99 (d, *J* = 7.4 Hz, 1H), 8.68-8.79 (m, 2H), 8.87 (dd, *J* = 5.8, 3.1 Hz, 1H), 9.15 (s, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 119.8, 122.5, 123.7, 125.6, 126.1, 126.3, 126.7, 129.0, 129.3, 129.5, 129.7, 133.7, 138.9; IR (KBr, ν / cm⁻¹) 1574, 1491, 1457, 1436,



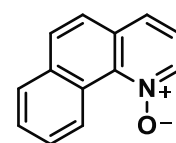
1310, 1236, 1195, 1113, 898, 766; HRMS (DART) Calcd for C₁₃H₁₀NO⁺ [M+H⁺] 196.0757, Found 196.0767.

Acridine 10-oxide (3aa). 53% yield (Method B); yellow solid; R_f = 0.41 (ethyl acetate); ¹H NMR (400 MHz, CD₃OD) δ 7.63 (dd, *J* = 8.0, 7.7 Hz, 2H), 7.89 (dd, *J* = 8.5, 7.7 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 2H), 8.64 (s, 1H), 8.71 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (100 MHz, CD₃OD) δ 119.5, 128.5,



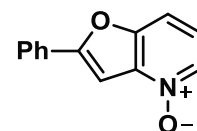
128.7, 129.9, 130.3, 133.8, 140.4; IR (KBr, ν / cm⁻¹) 3388, 1621, 1560, 1436, 1401, 1330, 1288, 1254, 1099, 835; HRMS (ESI) Calcd for C₁₃H₉NNaO⁺ [M+Na⁺] 218.0576, Found 218.0576.

Benzo[*h*]quinoline 1-oxide (3ab). 65% yield (Method B); orange solid; R_f = 0.25 (ethyl acetate); ¹H NMR (400 MHz, acetone-*d*₆) δ 7.57 (dd, *J* = 8.1, 6.3 Hz, 1H), 7.72-7.82 (m, 2H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.91 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 8.03 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.66



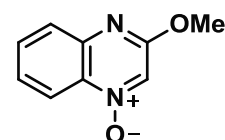
(dd, *J* = 6.3, 1.1 Hz, 1H), 10.91 (dd, *J* = 8.1, 1.1 Hz, 1H); ¹³C NMR (100 MHz, acetone-*d*₆) δ 122.9, 125.7, 126.4, 126.9, 128.0, 128.6, 129.0, 129.7, 131.0, 132.3, 134.9, 138.8, 140.0; IR (KBr, ν / cm⁻¹) 3039, 1570, 1433, 1409, 1321, 1258, 1231, 1208, 827, 805; HRMS (DART) Calcd for C₁₃H₁₀NO⁺ [M+H⁺] 196.0757, Found 196.0765.

2-Phenylfuro[3,2-*b*]pyridine 4-oxide (3ag). 71% yield (Method A); pale yellow solid; R_f = 0.49 (CH₂Cl₂/MeOH = 10/1); ¹H NMR (400 MHz, CD₃OD) δ 7.32 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.36-7.45 (m, 4H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.79-7.86 (m, 2H), 8.22 (d, *J* = 6.6 Hz, 1H); ¹³C NMR (100



MHz, CD₃OD) δ 96.8, 114.1, 121.6, 126.7, 129.2, 130.2, 131.7, 135.8, 140.5, 152.0, 161.6; IR (KBr, ν / cm⁻¹) 1616, 1490, 1434, 1270, 1240, 1061, 1015, 918, 856, 787; HRMS (DART) Calcd for C₁₃H₁₀NO₂⁺ [M+H⁺] 212.0706, Found 212.0708.

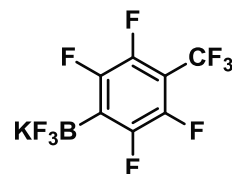
3-Methoxyquinoxaline 1-oxide. 72% yield (Method A); white amorphous; R_f = 0.45 (hexane/ethyl acetate = 2/1); ¹H NMR (400 MHz, CD₃CN) δ 4.01 (s, 3H), 7.54 (ddd, *J* = 8.5, 6.7, 1.6 Hz, 1H), 7.69-7.80 (m, 2H), 8.02 (s, 1H), 8.32 (dd, *J* = 8.5, 1.6 Hz, 1H); ¹³C NMR (100



MHz, CD₃CN) δ 54.8, 119.4, 122.9, 127.7, 128.7, 132.9, 135.4, 143.0, 161.2; IR (KBr, ν / cm⁻¹) 1585, 1557, 1507, 1478, 1420, 1376, 1209, 1092, 1035, 845; HRMS (DART) Calcd for C₉H₉N₂O₂⁺ [M+H⁺] 177.0659, Found 177.0661.

Preparation of potassium trifluoro

-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)borate. To a solution of 1,2,4,5-tetrafluoro-3-(trifluoromethyl)benzene (1.00 g, 4.59 mmol) in THF (18 mL) at -78 °C was added a hexane solution of *n*-butyllithium (2.69 M, 1.88 mL, 5.05 mmol, 1.1 equiv) slowly. The



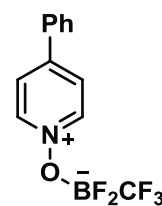
mixture was stirred for 1 h at -78 °C, followed by the addition of 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.57 g, 13.8 mmol, 3.0 equiv). The mixture was allowed to warm to room temperature and stirred for 3 h, and then saturated aq. KHF₂ (4.30 g, 55.1 mmol, 12 equiv) was added. After the mixture was stirred for 20 h, the solvent was removed under reduced pressure. The residue was diluted with acetone (20 mL) and insoluble solid was filtered off, washed with acetone, and then the solvent was removed under reduced pressure. The crude product was washed with diethyl ether (10 mL) to give the title compound (82.9 mg, 6% yield) as a white solid; ¹⁹F NMR (368 MHz, acetone-*d*₆) δ -146.4~-145.9 (m, 2F), -136.1~-135.6 (m, 3F), -133.7~-133.3 (m, 2F), -56.5 (t, *J* = 20.9 Hz, 3F); ¹¹B NMR (125 MHz, acetone-*d*₆) δ 0.99 (q, *J* = 48.0 Hz); IR (KBr, ν / cm⁻¹) 1452, 1423, 1383, 1342, 1159, 1062, 1010, 952, 805, 719.

Typical procedure for preparation of *N*-oxide-borane complexes of pyridine derivatives.

To a mixture of potassium trifluoro(trifluoromethyl)borate (96.8 mg, 0.550 mmol, 1.1 equiv) in CH₂Cl₂ (1.0 mL) was added BF₃·OEt₂ (77.6 mg, 0.550 mmol, 1.1 equiv), and the mixture was stirred at 25 °C for 20 min. Then, 4-phenylpyridine *N*-oxide (85.6 mg, 0.500 mmol) was added to the reaction mixture and the mixture was stirred at 25 °C for 1 h. After the reaction mixture was diluted with CH₂Cl₂/acetone (1/1), insoluble solid was filtered off, washed with CH₂Cl₂/acetone (1/1), and then the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (CH₂Cl₂ then CH₂Cl₂/acetone = 20/1) to give difluoro((4-phenyl-1-pyridinium-1-yl)oxy)(trifluoromethyl)borate (**4a**, 129 mg, 92% yield).

Difluoro((4-phenylpyridin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4a**).**

89% yield; white solid; R_f = 0.51 (CH₂Cl₂); ¹H NMR (400 MHz, acetone-*d*₆) δ 7.61-7.68 (m, 3H), 7.98-8.05 (m, 2H), 8.38-8.43 (m, 2H), 8.87 (d, *J* = 7.2 Hz, 2H); ¹³C NMR (100 MHz, acetone-*d*₆) δ 125.8, 128.8, 130.6, 132.5, 135.1, 143.4, 154.1; ¹⁹F NMR (368 MHz, acetone-*d*₆) δ -161.2 (q, *J* = 44.7

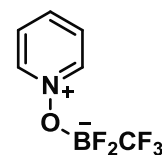


Hz, 2F), -75.3 (q, *J* = 29.8 Hz, 3F); ¹¹B NMR (125 MHz, acetone-*d*₆) δ 0.61 (m); IR (KBr, ν

/ cm^{-1}) 3138, 1624, 1561, 1516, 1483, 1431, 1222, 1067, 1011, 916; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_9\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 312.0590, Found 312.0592.

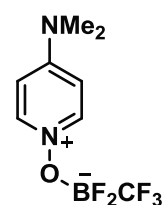
Difluoro(1-pyridinium-1-yloxy)(trifluoromethyl)borate (4b). 93% yield;

white solid; $R_f = 0.23$ (hexane/ethyl acetate = 1/3); ^1H NMR (400 MHz, acetone- d_6) δ 8.11-8.21 (m, 2H), 8.50-8.59 (m, 1H), 8.88 (d, $J = 6.3$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 129.1, 143.1, 143.5; ^{19}F NMR (368 MHz, acetone- d_6) δ -161.3 (q, $J = 47.7$ Hz, 2F), -75.5 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, acetone- d_6) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3133, 1621, 1483, 1260, 1205, 1169, 1065, 1014, 915, 783; HRMS (ESI) Calcd for $\text{C}_6\text{H}_5\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 236.0277, Found 236.0288.



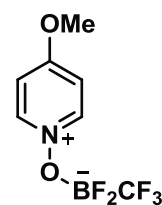
((4-(Dimethylamino)-1-pyridinium-1-yl)oxy)difluoro(trifluoromethyl)borate (4c). 4-(Dimethylamino)pyridine *N*-oxide hydrate was used. 83% yield;

white solid; $R_f = 0.35$ (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 3.27 (s, 6H), 6.92-6.97 (m, 2H), 8.10 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 40.3, 107.6, 141.4, 155.9; ^{19}F NMR (368 MHz, acetone- d_6) δ -162.0 (q, $J = 47.7$ Hz, 2F), -75.1 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.46 (m); IR (KBr, ν / cm^{-1}) 3152, 1641, 1561, 1446, 1402, 1330, 1223, 1083, 1018, 951; HRMS (ESI) Calcd for $\text{C}_8\text{H}_{10}\text{BF}_5\text{N}_2\text{NaO}^+$ $[\text{M}+\text{Na}^+]$ 279.0699, Found 279.0706.



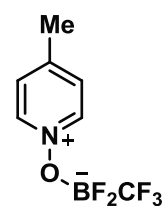
Difluoro((4-methoxy-1-pyridinium-1-yl)oxy)(trifluoromethyl)borate (4d).

4-Methoxypyridine *N*-oxide hydrate was used. 86% yield; white solid; $R_f = 0.36$ (hexane/ethyl acetate = 1/2); ^1H NMR (400 MHz, acetone- d_6) δ 4.19 (s, 3H), 7.53 (d, $J = 7.4$ Hz, 2H), 8.61 (d, $J = 7.4$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 58.4, 113.7, 144.6, 169.6; ^{19}F NMR (368 MHz, acetone- d_6) δ -161.8 (q, $J = 41.7$ Hz, 2F), -75.3 (q, $J = 29.8$ Hz, 3F); ^{11}B NMR (125 MHz, acetone- d_6) δ 0.46 (m); IR (KBr, ν / cm^{-1}) 3138, 1637, 1578, 1518, 1439, 1331, 1313, 1210, 1067, 918; HRMS (ESI) Calcd for $\text{C}_7\text{H}_7\text{BF}_5\text{NNaO}_2^+$ $[\text{M}+\text{Na}^+]$ 266.0382, Found 266.0391.



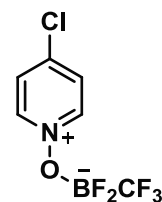
Difluoro((4-methyl-1-pyridinium-1-yl)oxy)(trifluoromethyl)borate (4e).

85% yield; white solid; $R_f = 0.60$ (CH_2Cl_2 /acetone = 19/1); ^1H NMR (400 MHz, acetone- d_6) δ 2.70 (s, 3H), 7.95 (d, $J = 7.2$ Hz, 2H), 8.68 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 21.5, 129.3, 142.5, 156.8; ^{19}F NMR (368 MHz, acetone- d_6) δ -161.4 (q, $J = 47.7$ Hz, 2F), -75.3 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, acetone- d_6) δ 0.76 (m); IR (KBr, ν / cm^{-1}) 3134, 1633, 1501, 1473, 1387, 1339, 1274, 1204, 1075, 911; HRMS (ESI) Calcd for $\text{C}_7\text{H}_7\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$

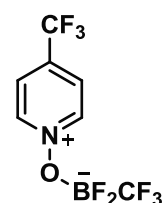


250.0433, Found 250.0442.

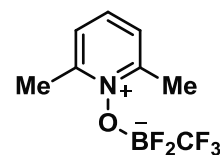
((4-Chloro-1-pyridinium-1-yl)oxy)difluoro(trifluoromethyl)borate (4f). 81% yield; white solid; $R_f = 0.58$ (hexane/ethyl acetate = 1/2); ^1H NMR (400 MHz, acetone- d_6) δ 8.24-8.29 (m, 2H), 8.86-8.91 (m, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 129.5, 144.6, 150.3; ^{19}F NMR (368 MHz, acetone- d_6) δ -161.2 (q, $J = 41.7$ Hz, 2F), -75.4 (q, $J = 29.8$ Hz, 3F); ^{11}B NMR (125 MHz, acetone- d_6) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3134, 1621, 1481, 1251, 1206, 1068, 1012, 944, 848, 714; HRMS (ESI) Calcd for $\text{C}_6\text{H}_4\text{BClF}_5\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 269.9887, Found 269.9900.



Difluoro(trifluoromethyl)((4-(trifluoromethyl)-1-pyridinium-1-yl)oxy)borate (4g). 54% yield; white solid; $R_f = 0.64$ (hexane/ethyl acetate = 1/1); ^1H NMR (400 MHz, CD_3CN) δ 8.26 (d, $J = 6.7$ Hz, 2H), 8.92 (d, $J = 6.7$ Hz, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ 122.4 (q, $J = 274$ Hz), 126.6 (q, $J = 3.6$ Hz), 142.6 (q, $J = 36.4$ Hz), 145.3; ^{19}F NMR (368 MHz, CD_3CN) δ -161.1 (q, $J = 45.5$ Hz, 2F), -75.8 (q, $J = 28.5$ Hz, 3F), -65.1 (s, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.76 (m); IR (KBr, ν / cm^{-1}) 3139, 1451, 1327, 1201, 1163, 1089, 1013, 903, 864, 721; HRMS (ESI) Calcd for $\text{C}_7\text{H}_4\text{BF}_8\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 304.0150, Found 304.0138.



((2,6-Dimethyl-1-pyridinium-1-yl)oxy)difluoro(trifluoromethyl)borate (4h). 68% yield; white solid; $R_f = 0.47$ (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 2.83 (s, 6H), 7.84 (d, $J = 8.0$ Hz, 2H), 8.19 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 18.9 (t, $J = 4.2$ Hz), 127.7, 141.4, 156.0; ^{19}F NMR (368 MHz, acetone- d_6) δ -156.5 (q, $J = 47.7$ Hz, 2F), -75.2 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, acetone- d_6) δ 0.76 (m); IR (KBr, ν / cm^{-1}) 1620, 1498, 1459, 1189, 1081, 1024, 899, 821, 797, 717; HRMS (ESI) Calcd for $\text{C}_8\text{H}_9\text{BF}_5\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 264.0590, Found 264.0601.



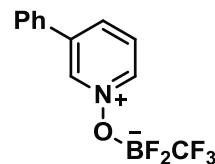
Difluoro((5,6,7,8-tetrahydroquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4i). 82% yield; white solid; $R_f = 0.53$ (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 1.77-1.85 (m, 2H), 1.86-1.95 (m, 2H), 2.94 (t, $J = 6.2$ Hz, 2H), 3.12 (t, $J = 6.2$ Hz, 2H), 7.61 (dd, $J = 7.0, 7.0$ Hz, 1H), 7.99 (d, $J = 7.0$ Hz, 1H), 8.48 (d, $J = 7.0$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 21.5, 21.5, 25.7, 28.9, 124.7, 140.9, 140.9, 142.5, 154.0; ^{19}F NMR (368 MHz, CD_3CN) δ -160.3 (q, $J = 45.5$ Hz, 2F), -76.0 (q, $J = 31.3$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3138, 2948, 2872, 1607, 1492, 1456, 1340, 1262, 1234, 1174; HRMS (ESI)



Calcd for C₁₀H₁₁BF₅NNaO⁺ [M+Na⁺] 290.0746, Found 290.0749.

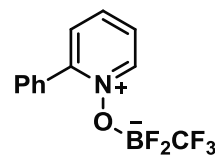
Difluoro((3-phenylpyridin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4j).

94% yield; white solid; R_f = 0.21 (CH₂Cl₂); ¹H NMR (400 MHz, acetone-*d*₆) δ 7.56-7.65 (m, 3H), 7.86-7.91 (m, 2H), 8.23 (dd, *J* = 8.1, 6.3 Hz, 1H), 8.75-8.81 (m, 1H), 8.82-8.87 (m, 1H), 9.10 (s, 1H); ¹³C NMR (100 MHz, acetone-*d*₆) δ 128.4, 128.9, 130.5, 131.2, 134.0, 140.7, 141.1, 141.6, 142.3; ¹⁹F NMR (368 MHz, acetone-*d*₆) δ -161.0 (q, *J* = 47.7 Hz, 2F), -75.2 (q, *J* = 29.8 Hz, 3F); ¹¹B NMR (125 MHz, CD₃CN) δ 0.76 (m); IR (KBr, ν / cm⁻¹) 3123, 1508, 1480, 1432, 1258, 1182, 1092, 1064, 1018, 921; HRMS (ESI) Calcd for C₁₂H₉BF₅NNaO⁺ [M+Na⁺] 312.0590, Found 312.0584.



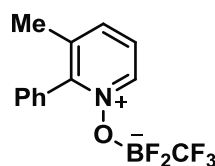
Difluoro((2-phenylpyridin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4k).

85% yield; white solid; R_f = 0.18 (hexane/ethyl acetate = 1/1); ¹H NMR (400 MHz, acetone-*d*₆) δ 7.52-7.63 (m, 3H), 7.81-7.87 (m, 2H), 8.08 (ddd, *J* = 8.0, 6.5, 1.3 Hz, 1H), 8.17 (dd, *J* = 8.0, 1.8 Hz, 1H), 8.51 (td, *J* = 8.0, 1.3 Hz, 1H), 8.95 (d, *J* = 6.5 Hz, 1H); ¹³C NMR (100 MHz, acetone-*d*₆) δ 127.3, 129.2, 130.8, 130.9, 131.1, 131.9, 142.6, 144.1, 154.0; ¹⁹F NMR (368 MHz, acetone-*d*₆) δ -159.1 (q, *J* = 41.7 Hz, 2F), -75.5 (q, *J* = 23.8 Hz, 3F); ¹¹B NMR (125 MHz, CD₃CN) δ 0.46 (m); IR (KBr, ν / cm⁻¹) 3141, 1616, 1574, 1508, 1485, 1429, 1243, 1191, 1168, 1082; HRMS (ESI) Calcd for C₁₂H₉BF₅NNaO⁺ [M+Na⁺] 312.0590, Found 312.0585.



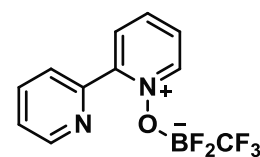
Difluoro((3-methyl-2-phenylpyridin-1-ium-1-yl)oxy)(trifluoromethyl)

borate (4l). 84% yield; white solid; R_f = 0.54 (ethyl acetate); ¹H NMR (400 MHz, CD₃CN) δ 2.24 (s, 3H), 7.41-7.47 (m, 2H), 7.53-7.59 (m, 3H), 7.81 (dd, *J* = 8.1, 6.7 Hz, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 8.69 (d, *J* = 6.7 Hz, 1H); ¹³C NMR (100 MHz, CD₃CN) δ 20.1, 126.8, 129.3, 130.06, 130.13, 131.1, 140.7, 140.99, 141.02, 141.03, 143.9, 153.6; ¹⁹F NMR (368 MHz, CD₃CN) δ -159.0 (q, *J* = 39.9 Hz, 2F), -76.0 (q, *J* = 28.5 Hz, 3F); ¹¹B NMR (125 MHz, CD₃CN) δ 0.46 (m); IR (KBr, ν / cm⁻¹) 3140, 1599, 1478, 1453, 1338, 1243, 1173, 1072, 1025, 958; HRMS (ESI) Calcd for C₁₃H₁₁BF₅NNaO⁺ [M+Na⁺] 326.0746, Found 326.0758.



[(2,2'-Bipyridin]-1-ium-1-yloxy)difluoro(trifluoromethyl)borate

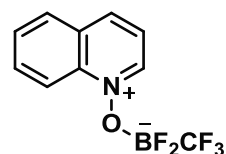
(4m). 69% yield; white solid; R_f = 0.26 (ethyl acetate); ¹H NMR (400 MHz, acetone-*d*₆) δ 7.60 (ddd, *J* = 7.6, 4.7, 1.0 Hz, 1H), 8.02 (ddd, *J* = 8.0, 8.0, 2.0 Hz, 1H), 8.17 (ddd, *J* = 6.9, 6.9, 2.0 Hz, 1H),



8.39 (dd, $J = 8.0, 1.0$ Hz, 1H), 8.54-8.64 (m, 2H), 8.79-8.84 (m, 1H), 8.95 (d, $J = 6.9$ Hz, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 126.6, 127.8, 128.2, 131.1, 137.3, 142.8, 144.1, 148.3, 150.9, 152.0; ^{19}F NMR (368 MHz, acetone- d_6) δ -159.6 (q, $J = 47.7$ Hz, 2F), -75.6 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.46 (m); IR (KBr, ν / cm^{-1}) 3141, 1618, 1581, 1497, 1464, 1449, 1423, 1253, 1190, 1083; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_8\text{BF}_5\text{N}_2\text{NaO}^+ [\text{M}+\text{Na}^+]$ 313.0542, Found 313.0533.

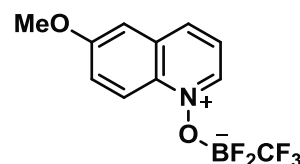
Difluoro((quinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4n). 90%

yield; white solid; $R_f = 0.53$ (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 8.01-8.08 (m, 1H), 8.15 (dd, $J = 8.5, 6.1$ Hz, 1H), 8.23-8.30 (m, 1H), 8.43 (d, $J = 8.5$ Hz, 1H), 8.62 (d, $J = 8.5$ Hz, 1H), 9.12 (d, $J = 8.5$ Hz, 1H), 9.29 (d, $J = 6.1$ Hz, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 119.3, 122.3, 130.1, 131.3, 131.5, 136.0, 139.6, 143.9, 145.1; ^{19}F NMR (368 MHz, acetone- d_6) δ -160.4 (q, $J = 41.7$ Hz, 2F), -75.5 (q, $J = 35.8$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.92 (m); IR (KBr, ν / cm^{-1}) 3130, 1591, 1523, 1400, 1386, 1325, 1227, 1158, 1070, 1027; HRMS (ESI) Calcd for $\text{C}_{10}\text{H}_7\text{BF}_5\text{NNaO}^+ [\text{M}+\text{Na}^+]$ 286.0433, Found 286.0436.



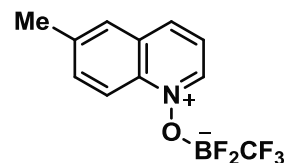
Difluoro((6-methoxyquinolin-1-ium-1-yl)oxy)(trifluoromethyl)

borate (4o). 89% yield; white solid; $R_f = 0.57$ (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 4.00 (s, 3H), 7.61 (s, 1H), 7.77 (d, $J = 9.5$ Hz, 1H), 7.84 (dd, $J = 8.5, 6.1$ Hz, 1H), 8.45 (d, $J = 9.5$ Hz, 1H), 8.74 (d, $J = 8.5$ Hz, 1H), 8.89 (d, $J = 6.1$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 57.2, 107.4, 120.9, 122.7, 129.0, 133.6, 135.3, 142.0, 142.2, 161.5; ^{19}F NMR (368 MHz, CD_3CN) δ -160.8 (q, $J = 42.7$ Hz, 2F), -75.8 (q, $J = 28.5$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.07 (m); IR (KBr, ν / cm^{-1}) 3131, 3101, 3025, 2963, 1899, 1719, 1339, 747, 724, 703; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_9\text{BF}_5\text{NNaO}_2^+ [\text{M}+\text{Na}^+]$ 316.0539, Found 316.0526.



Difluoro((6-methylquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4p). 84% yield; white solid; $R_f = 0.56$ (ethyl acetate); ^1H

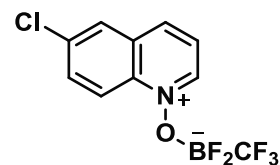
NMR (400 MHz, CD_3CN) δ 2.58 (s, 3H), 7.87 (dd, $J = 8.7, 6.2$ Hz, 1H), 8.02 (d, $J = 9.4$ Hz, 1H), 8.06 (s, 1H), 8.46 (d, $J = 9.4$ Hz, 1H), 8.79 (d, $J = 8.7$ Hz, 1H), 9.00 (d, $J = 6.2$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 21.6, 118.8, 122.1, 128.6, 131.8, 138.1, 138.4, 142.6, 143.2, 143.8; ^{19}F NMR (368 MHz, CD_3CN) δ -160.8 (q, $J = 45.5$ Hz, 2F), -75.8 (q, $J = 31.3$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.07 (m); IR (KBr, ν / cm^{-1}) 3104, 1590, 1520, 1435, 1382, 1330, 1278, 1221, 741, 689; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_9\text{BF}_5\text{NNaO}^+ [\text{M}+\text{Na}^+]$ 300.0590, Found 300.0582.



((6-Chloroquinolin-1-ium-1-yl)oxy)difluoro(trifluoromethyl)borate (4q). 96% yield; white solid; $R_f = 0.57$ (ethyl acetate); ^1H NMR

(400 MHz, CD_3CN) δ 7.96 (dd, $J = 8.5, 6.3$ Hz, 1H), 8.12 (dd, $J = 9.4, 2.2$ Hz, 1H), 8.35 (d, $J = 2.2$ Hz, 1H), 8.54 (d, $J = 9.4$ Hz, 1H), 8.83 (d, $J = 8.5$ Hz, 1H), 9.09 (d, $J = 6.3$ Hz, 1H); ^{13}C NMR (125

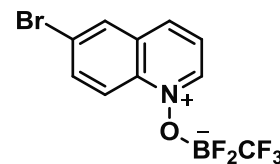
MHz, CD_3CN) δ 121.3, 123.6, 128.8, 132.3, 136.7, 137.1, 138.3, 143.3, 145.2; ^{19}F NMR (368 MHz, CD_3CN) δ -160.7 (q, $J = 45.5$ Hz, 2F), -68.3 (q, $J = 28.5$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.92 (m); IR (KBr, ν / cm^{-1}) 3127, 1588, 1518, 1379, 1205, 1172, 829, 812, 742, 690; HRMS (ESI) Calcd for $\text{C}_{10}\text{H}_6\text{BClF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 320.0043, Found 320.0055.



((6-Bromoquinolin-1-ium-1-yl)oxy)difluoro(trifluoromethyl)borate (4r). 77% yield; white solid; $R_f = 0.63$ (ethyl acetate); ^1H NMR

(400 MHz, CD_3CN) δ 7.95 (dd, $J = 8.5, 6.0$ Hz, 1H), 8.23-8.26 (m, 1H), 8.46 (d, $J = 9.8$ Hz, 1H), 8.53 (d, $J = 2.2$ Hz, 1H), 8.82 (d, $J =$

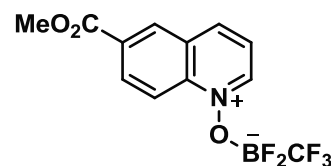
8.5 Hz, 1H), 9.10 (d, $J = 6.0$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 121.3, 123.7, 125.4, 132.3, 132.7, 138.7, 139.4, 143.3, 145.5; ^{19}F NMR (368 MHz, CD_3CN) δ -160.7 (q, $J = 45.5$ Hz, 2F), -75.8 (q, $J = 28.5$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.91 (m); IR (KBr, ν / cm^{-1}) 3093, 1585, 1435, 1377, 1239, 1204, 1176, 804, 739, 691; HRMS (ESI) Calcd for $\text{C}_{10}\text{H}_6\text{BBrF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 363.9538, Found 363.9555.



Difluoro((6-(methoxycarbonyl)quinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4s). 74% yield; white solid; $R_f = 0.17$

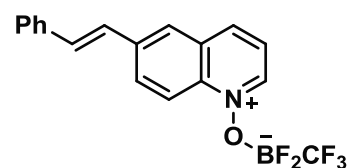
(ethyl acetate); ^1H NMR (500 MHz, CD_3CN) δ 4.01 (s, 3H), 8.01 (dd, $J = 8.1, 6.2$ Hz, 1H), 8.65 (m, 2H), 8.96 (d, $J = 1.2$

Hz, 1H), 9.05 (d, $J = 8.1$ Hz, 1H) 9.18 (d, $J = 6.2$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 53.7, 120.0, 123.3, 131.2, 132.3, 132.8, 135.1, 141.3, 145.5, 146.7, 165.8; ^{19}F NMR (368 MHz, CD_3CN) δ -161.7 (q, $J = 39.9$ Hz, 2F), -76.9 (q, $J = 34.2$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.92 (m); IR (KBr, ν / cm^{-1}) 3052, 2965, 1587, 1389, 1368, 977, 794, 738, 692, 609; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_9\text{BF}_5\text{NNaO}_3^+$ $[\text{M}+\text{Na}^+]$ 344.0488, Found 344.0494.



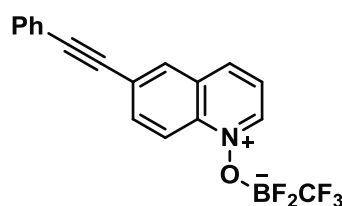
(E)-Difluoro((6-styryl-1-quinolinium-1-yl)oxy)(trifluoromethyl)borate (4t). 86% yield; yellow solid; $R_f = 0.74$ (ethyl

acetate); ^1H NMR (400 MHz, CD_3CN) δ 7.35-7.39 (m, 1H), 7.42-7.47 (m, 3H), 7.55 (d, $J = 16.6$ Hz, 1H), 7.68 (d, $J = 7.6$



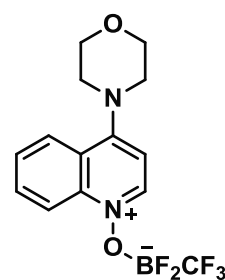
Hz, 2H), 7.89 (dd, $J = 8.5, 6.1$ Hz, 1H), 8.30 (s, 1H), 8.44 (d, $J = 9.2$ Hz, 1H), 8.54 (d, $J = 9.2$ Hz, 1H), 8.84 (d, $J = 8.5$ Hz, 1H), 8.99 (d, $J = 6.1$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 119.5, 122.6, 126.7, 126.9, 128.1, 129.8, 129.9, 132.2, 134.0, 134.5, 137.4, 139.0, 140.6, 143.5, 143.9; ^{19}F NMR (368 MHz, CD_3CN) δ -161.7 (q, $J = 45.5$ Hz, 2F), -76.9~-76.7 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.89 (m); IR (KBr, ν / cm^{-1}) 1596, 1518, 1389, 1337, 1074, 1022, 964, 900, 825, 744; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{13}\text{BF}_5\text{NNaO}^+ [\text{M}+\text{Na}^+]$ 388.0903, Found 388.0897.

Difluoro((6-(phenylethynyl)-1-quinolinium-1-yl)oxy)(trifluoromethyl)borate (4u). 72% yield; white solid; $R_f = 0.56$ (CH_2Cl_2); ^1H NMR (400 MHz, CD_3CN) δ 7.44-7.50 (m, 3H), 7.64-7.67 (m, 2H), 7.94 (dd, $J = 8.5, 6.3$ Hz, 1H), 8.23 (dd, $J = 9.0, 1.6$ Hz, 1H), 8.43 (d, $J = 1.6$ Hz, 1H), 8.56 (d, $J = 9.0$



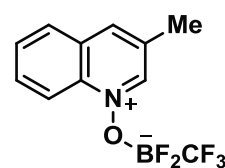
Hz, 1H), 8.87 (d, $J = 8.5$ Hz, 1H), 9.07 (d, $J = 5.4$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 87.7, 94.5, 119.8, 122.7, 123.1, 126.4, 129.8, 130.6, 131.6, 132.5, 132.8, 138.8, 139.0, 143.7, 145.2; ^{19}F NMR (368 MHz, CD_3CN) δ -161.7 (q, $J = 39.9$ Hz, 2F), -76.9~-76.7 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.89 (m); IR (KBr, ν / cm^{-1}) 3127, 2212, 1587, 1513, 1436, 1383, 1337, 1235, 757, 691; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{11}\text{BF}_5\text{NNaO}^+ [\text{M}+\text{Na}^+]$ 386.0746, Found 386.0761.

Difluoro((4-morpholino-1-quinolinium-1-yl)oxy)(trifluoromethyl)borate (4v). 31% yield; yellow solid; $R_f = 0.46$ (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 3.69 (t, $J = 4.7$ Hz, 4H), 3.91 (t, $J = 4.7$ Hz, 4H), 7.00 (d, $J = 7.3$ Hz, 1H), 7.71-7.75 (m, 1H), 7.98-8.02 (m, 1H), 8.17 (d, $J = 8.8$ Hz, 1H), 8.36 (d, $J = 8.8$ Hz, 1H), 8.58 (d, $J = 7.3$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 53.4, 66.9, 106.2, 119.3, 122.1, 127.0, 128.2, 134.8, 140.6, 143.4, 160.5; ^{19}F NMR (368 MHz, CD_3CN) δ



-162.1 (q, $J = 40.0$ Hz, 2F), -76.9~-76.6 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.90 (m); IR (KBr, ν / cm^{-1}) 3113, 2868, 1369, 1335, 1312, 1243, 817, 685, 657, 620; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{BF}_5\text{N}_2\text{NaO}_2^+ [\text{M}+\text{Na}^+]$ 371.0961, Found 371.0973.

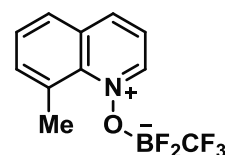
Difluoro((3-methylquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (4w). 68% yield; white solid; $R_f = 0.57$ (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 2.65 (s, 3H), 7.93 (dd, $J = 8.2, 7.0$ Hz, 1H), 8.12-8.18 (m, 1H), 8.18 (d, $J = 8.2$ Hz, 1H), 8.50 (d, $J = 9.0$ Hz, 1H), 8.70 (s, 1H), 8.99 (s, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 18.6, 118.9, 129.3, 131.1, 131.3, 133.5, 135.1,



137.9, 143.2, 145.6; ^{19}F NMR (368 MHz, CD_3CN) δ -161.8 (q, J = 45.5 Hz, 2F), -76.8 (q, J = 31.3 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.22 (m); IR (KBr, ν / cm^{-1}) 3854, 3735, 3649, 3126, 1598, 1520, 1381, 1336, 1285, 732; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_9\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 300.0590, Found 300.0580.

Difluoro((8-methylquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate

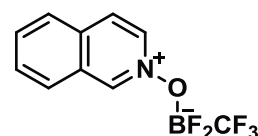
(4x). 53% yield; white solid; R_f = 0.54 (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 3.06 (s, 3H), 7.78-7.87 (m, 2H), 7.93 (d, J = 6.5 Hz, 1H), 8.11 (d, J = 7.6 Hz, 1H), 8.85 (d, J = 8.5 Hz, 1H), 9.05 (d, J = 6.5



Hz, 1H); ^{13}C NMR (125 MHz, CD_3CN) δ 23.9, 121.6, 129.0, 130.8, 132.1, 133.2, 139.2, 139.6, 145.2, 146.5; ^{19}F NMR (368 MHz, CD_3CN) δ -161.3 (q, J = 45.6 Hz, 2F), -76.1 (q, J = 31.3 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.92 (m); IR (KBr, ν / cm^{-1}) 3127, 1524, 1211, 1163, 1078, 1022, 973, 896, 830, 755; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_9\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 300.0590, Found 300.0589.

Difluoro(isoquinolin-2-ium-2-yloxy)(trifluoromethyl)borate (4y).

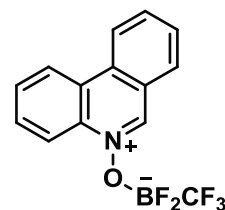
60% yield; white solid; R_f = 0.61 (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 8.02-8.08 (m, 1H), 8.15-8.22 (m, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.49-8.62 (m, 3H), 9.77 (s, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 127.2, 128.3, 128.6, 130.3, 132.2, 135.6, 136.6, 136.6, 146.1; ^{19}F NMR (368



MHz, acetone- d_6) δ -160.8 (q, J = 41.7 Hz, 2F), -75.2 (q, J = 29.8 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.76 (m); IR (KBr, ν / cm^{-1}) 3127, 1639, 1508, 1389, 1351, 1257, 1216, 1072, 1021, 945; HRMS (ESI) Calcd for $\text{C}_{10}\text{H}_7\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 286.0433, Found 286.0444.

Difluoro(phenanthridin-5-ium-5-yloxy)(trifluoromethyl)borate (4z).

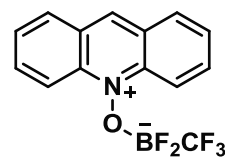
74% yield; white solid; R_f = 0.47 (hexane/ CH_2Cl_2 = 1/3); ^1H NMR (400 MHz, CD_3CN) δ 7.86-7.98 (m, 2H), 8.02 (ddd, J = 8.7, 7.2, 1.3 Hz, 1H), 8.13 (ddd, J = 8.7, 7.2, 1.3 Hz, 1H), 8.35 (d, J = 7.6 Hz, 1H), 8.60 (d, J = 8.5 Hz, 1H), 8.66-8.76 (m, 2H), 9.64 (s, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 120.3, 123.9, 124.4, 124.6, 127.6, 131.3, 131.9, 132.4, 132.8, 133.8, 135.7,



137.6, 148.3; ^{19}F NMR (368 MHz, CD_3CN) δ -160.21 (q, J = 39.9 Hz, 2F), -75.9~-75.3 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.01 (m); IR (KBr, ν / cm^{-1}) 3091, 1877, 1622, 1528, 1505, 1461, 1398, 1342, 1312, 1116; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_9\text{BF}_5\text{NNaO}^+$ $[\text{M}+\text{Na}^+]$ 336.0590, Found 336.0606.

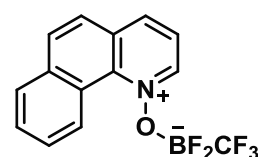
(Acridin-10-ium-10-yloxy)difluoro(trifluoromethyl)borate (4aa).

69% yield; yellow solid; $R_f = 0.62$ (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 7.95-8.01 (m, 2H), 8.34-8.41 (m, 2H), 8.54 (d, $J = 8.5$ Hz, 2H), 8.82 (d, $J = 9.4$ Hz, 2H), 9.85 (s, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 119.2, 127.6, 128.8, 130.5, 138.1, 141.1, 145.8; ^{19}F NMR (368 MHz, acetone- d_6) δ -156.9 (q, $J = 44.7$ Hz, 2F), -74.9 (q, $J = 29.8$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.22 (m); IR (KBr, ν / cm^{-1}) 3069, 1623, 1543, 1397, 1146, 1075, 1022, 888, 863, 772; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_9\text{BF}_5\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 336.0590, Found 336.0581.



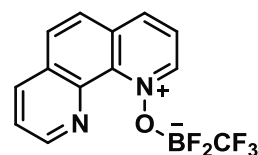
(Benzo[h]quinolin-1-ium-1-yloxy)difluoro(trifluoromethyl)borate

(4ab). 89% yield; pale yellow solid; $R_f = 0.54$ (ethyl acetate); ^1H NMR (400 MHz, acetone- d_6) δ 7.85-7.92 (m, 1H), 7.94-8.01 (m, 1H), 8.12 (d, $J = 8.5$ Hz, 1H), 8.19 (d, $J = 8.1$ Hz, 1H), 8.21-8.27 (m, 2H), 9.08 (d, $J = 8.1$ Hz, 1H), 9.29 (d, $J = 6.3$ Hz, 1H), 10.04 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, acetone- d_6) δ 123.3, 124.1, 125.5, 129.2, 130.1, 130.5, 132.2, 132.6, 133.1, 137.1, 138.9, 143.4, 145.6; ^{19}F NMR (368 MHz, acetone- d_6) δ -159.0 (q, $J = 41.7$ Hz, 2F), -75.0 (q, $J = 29.8$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.07 (m); IR (KBr, ν / cm^{-1}) 3133, 1591, 1498, 1456, 1413, 1335, 1081, 1026, 887, 839; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_9\text{BF}_5\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 336.0590, Found 336.0591.



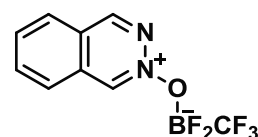
((1,10-Phenanthrolin-1-ium-1-yloxy)difluoro(trifluoromethyl)borate

(4ac). 10% yield; white solid; $R_f = 0.58$ ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 10/1$); In NMR chart, some signals arise from impurities were observed because this compound was gradually decomposed in CD_3CN . ^1H NMR (400 MHz, CD_3CN) δ 7.88 (dd, $J = 8.3, 4.3$ Hz, 1H), 8.12 (dd, $J = 8.3, 6.3$ Hz, 1H), 8.14 (d, $J = 9.0$ Hz, 1H), 8.22 (d, $J = 9.0$ Hz, 1H), 8.52 (dd, $J = 8.3, 1.8$ Hz, 1H), 8.98 (dd, $J = 8.3, 1.8$ Hz, 1H), 9.14-9.19 (m, 1H), 9.22 (dd, $J = 4.0, 1.8$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 124.5, 126.3, 126.5, 132.1, 132.3, 134.1, 137.5, 138.4, 141.0, 143.7, 146.9, 151.2; ^{19}F NMR (368 MHz, CD_3CN) δ -159.6 (q, $J = 45.5$ Hz, 2F), -74.4 (q, $J = 34.2$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.89 (m); IR (KBr, ν / cm^{-1}) 3062, 1590, 1523, 1434, 1337, 1070, 891, 850, 715, 700; HRMS (ESI): A target mass was not detected due to the decomposition of **4ac** to the corresponding *N*-oxide.



Difluoro(2-phthalazininium-2-yloxy)(trifluoromethyl)borate (4ad).

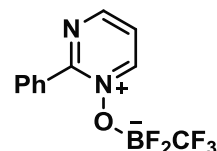
29% yield; white solid; $R_f = 0.54$ (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 8.26-8.40 (m, 2H), 8.42-8.51 (m, 2H), 9.64 (s, 1H), 9.80 (s,



1H); ^{13}C NMR (100 MHz, CD_3CN) δ 128.3, 129.2, 130.0, 131.0, 137.3, 138.8, 143.9, 155.4; ^{19}F NMR (368 MHz, CD_3CN) δ -160.4 (q, J = 45.5 Hz, 2F), -75.8 (q, J = 34.2 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.89 (m); IR (KBr, ν / cm^{-1}) 3097, 1620, 1577, 1460, 1385, 1351, 1282, 1223, 937, 760; HRMS (ESD): A target mass was not detected due to the decomposition of **4ad** to the corresponding *N*-oxide.

Difluoro((2-phenyl-1-pyrimidinium-1-yl)oxy)(trifluoromethyl)borate

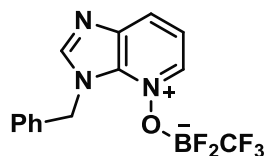
(4ae). 87% yield; white solid; R_f = 0.43 (CH_2Cl_2); ^1H NMR (400 MHz, CD_3CN) δ 7.57-7.64 (m, 2H), 7.66-7.73 (m, 1H), 7.90 (dd, J = 6.7, 4.6 Hz, 1H), 8.18-8.24 (m, 2H), 8.99-9.05 (m, 1H), 9.22 (dd, J = 4.6, 1.6 Hz,



1H); ^{13}C NMR (100 MHz, CD_3CN) δ 122.7, 129.4, 130.6, 132.1, 134.1, 151.9, 160.2, 161.7; ^{19}F NMR (368 MHz, CD_3CN) δ -159.2 (q, J = 45.5 Hz, 2F), -75.9 (q, J = 34.2 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3119, 1600, 1552, 1497, 1466, 1247, 1188, 1089, 908, 841; HRMS (ESD): A target mass was not detected due to the decomposition of **4ae** to the corresponding *N*-oxide.

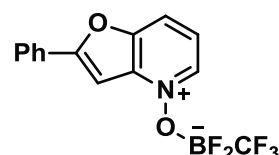
((3-Benzyl-3H-imidazo[4,5-b]-4-pyridinium-4-yl)oxy)difluoro(trifluoromethyl)borate (4af). 75% yield; white solid; R_f = 0.57 (ethyl acetate); ^1H NMR (400 MHz, CD_3CN) δ 5.87 (s, 2H), 7.30-7.41 (m,

5H), 7.67 (dd, J = 8.3, 6.3 Hz, 1H), 8.37 (s, 1H), 8.56 (d, J = 8.3 Hz, 1H), 8.57 (d, J = 6.3 Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 51.3, 119.7, 128.8, 129.5, 130.0, 134.8, 136.4, 138.4, 138.5, 143.8, 149.9; ^{19}F NMR (368 MHz, CD_3CN) δ -160.5 (q, J = 45.5 Hz, 2F), -75.3 (q, J = 34.2 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.98 (m); IR (KBr, ν / cm^{-1}) 3109, 1634, 1508, 1454, 1409, 1350, 1292, 1091, 896, 798; HRMS (ESD): A target mass was not detected due to the decomposition of **2B** to the corresponding *N*-oxide.

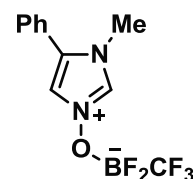


Difluoro((2-phenylfuro[3,2-b]pyridin-4-ium-4-yl)oxy)(trifluoromethyl)borate (4ag). 90% yield; white solid; R_f = 0.49 (hexane/ethyl acetate = 1/1); ^1H NMR (400 MHz, CD_3CN) δ 7.52-7.61 (m, 4H),

7.68 (dd, J = 8.5, 6.7 Hz, 1H), 7.99-8.05 (m, 2H), 8.35 (d, J = 8.5 Hz, 1H), 8.56 (dd, J = 6.7, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 97.1, 121.1, 124.2, 127.7, 128.0, 130.4, 133.2, 138.9, 142.7, 152.1, 165.8; ^{19}F NMR (368 MHz, CD_3CN) δ -160.4 (q, J = 45.5 Hz, 2F), -75.6 (q, J = 45.5 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.89 (m); IR (KBr, ν / cm^{-1}) 3140, 1561, 1477, 1443, 1389, 1282, 1168, 1092, 904, 791; HRMS (ESD) Calcd for $\text{C}_{14}\text{H}_9\text{BF}_5\text{NNaO}_2^+$ [M+Na $^+$] 352.0539, Found 352.0552.



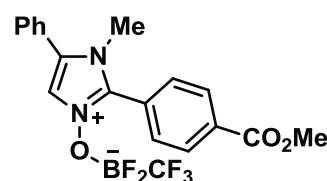
Difluoro((1-methyl-5-phenyl-1*H*-imidazol-3-ium-3-yl)oxy)(trifluoromethyl)borate (4ah). 82% yield; white solid; $R_f = 0.34$ (CH_2Cl_2); ^1H NMR (400 MHz, CD_3CN) δ 3.71 (s, 3H), 7.44-7.60 (m, 6H), 8.53 (s, 1H); ^{19}F NMR (368 MHz, CD_3CN) δ -162.5 (q, $J = 39.9$ Hz, 2F), -75.4 (q, $J = 28.5$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.28 (m).



Difluoro((2-(4-(methoxycarbonyl)phenyl)-1-methyl-5-phenyl-1*H*-imidazol-3-ium-3-yl)oxy)(trifluoromethyl)borate (4ai).

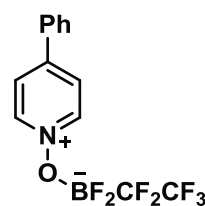
91% yield; white solid; $R_f = 0.62$ (hexane/ethyl acetate = 1/3); ^1H NMR (400 MHz, CD_3CN) δ 3.57 (s, 3H), 3.93 (s, 3H), 7.57-7.63 (m, 5H), 7.69 (s, 1H), 7.90 (d, $J = 8.1$ Hz, 2H), 8.23

(d, $J = 8.1$ Hz, 2H); ^{19}F NMR (368 MHz, CD_3CN) δ -161.1 (q, $J = 39.9$ Hz, 2F), -75.8 (q, $J = 45.5$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.31 (m).



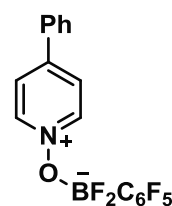
Difluoro(perfluoroethyl)((4-phenyl-1-pyridinium-1-yl)oxy)borate (5).

87% yield; white solid; $R_f = 0.56$ (hexane/ethyl acetate = 1/1); ^1H NMR (500 MHz, acetone- d_6) δ 7.61-7.67 (m, 3H), 7.98-8.04 (m, 2H), 8.41 (d, $J = 7.2$ Hz, 2H), 8.85 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (125 MHz, acetone- d_6) δ 125.9, 128.8, 130.6, 132.5, 135.1, 143.4, 154.1; ^{19}F NMR (368 MHz, CD_3CN) δ -158.8 (q, $J = 45.5$ Hz, 2F), -136.4~-136.0 (m, 2F), -84.0 (s, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.37 (s); IR (KBr, ν / cm^{-1}) 3141, 1630, 1517, 1484, 1435, 1337, 1204, 1071, 979, 900; HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_9\text{BF}_5\text{NNaO}^+$ [$\text{M}+\text{Na}^+$] 362.0558, Found 362.0565.

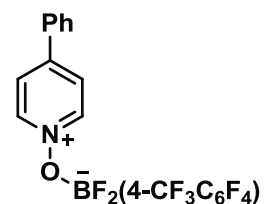


Difluoro(perfluorophenyl)((4-phenyl-1-pyridinium-1-yl)oxy)borate (6).

This compound was purified by recrystallization from ethyl acetate at 60 °C instead of column chromatography on silica gel. 55% yield; white solid; ^1H NMR (400 MHz, acetone- d_6) δ 7.62-7.67 (m, 3H), 7.99-8.05 (m, 2H), 8.37-8.41 (m, 2H), 8.88 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 125.7, 128.8, 130.6, 132.4, 135.3, 143.6, 153.6; ^{19}F NMR (368 MHz, acetone- d_6) δ -166.1~-165.8 (m, 2F), -159.5 (t, $J = 19.9$ Hz, 1F), -144.1~-143.3 (m, 2F), -135.2~-134.9 (m, 2F); ^{11}B NMR (125 MHz, CD_3CN) δ 4.28 (m); IR (KBr, ν / cm^{-1}) 3142, 1634, 1520, 1468, 1430, 1298, 1130, 1046, 966, 887; HRMS (ESI): A target mass was not detected due to the decomposition to 4-phenylpyridine *N*-oxide.



Difluoro((4-phenyl-1-pyridinium-1-yl)oxy)(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)borate (7). This compound was purified by recrystallization from ethyl acetate at 60 °C instead of column chromatography on silica gel. 63% yield; white solid; ^1H NMR (400 MHz, acetone- d_6) δ 7.60-7.68 (m, 3H), 7.98-8.06 (m, 2H), 8.42 (d, J = 7.0 Hz, 2H), 8.91 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 125.8, 128.8, 130.6, 132.4, 135.2, 143.6, 153.8; ^{19}F NMR (368 MHz, acetone- d_6) δ -145.0~-144.6 (m, 2F), -144.6~-143.9 (m, 2F), -133.4 (s, 2F), -56.7 (t, J = 20.3 Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 3.97 (m); IR (KBr, ν / cm^{-1}) 3136, 1632, 1563, 1460, 1431, 1323, 1224, 1152, 1050, 970; HRMS (ESI): A target mass was not detected due to the decomposition to 4-phenylpyridine *N*-oxide.



Computational Method. The geometry optimization of **A-H** was performed using the B3LYP functional with the 6-31G(d) basis set for **A**, 6-31+G(d) basis set for **B-D** and **F-H**, or LAV3P (+,d) basis set for **E**, implemented in the Jaguar program²⁴). A stationary point was optimized without any symmetry assumptions and characterized by frequency analysis at the same level of theory (the number of imaginary frequencies, NIMAG, was 0.) The Cartesian coordinates for **A-H** are given in Tables 1-4 to 1-11.

Table 1-4. Cartesian Coordinates of **A**.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C1	2.1413524835	-0.4966349420	0.2708214210
N2	1.5054670538	0.6774958783	0.2633168790
C3	0.1706871841	0.6413622678	0.2612830240
C4	-0.5743095123	-0.5356952241	0.2664654438
C5	0.1047523034	-1.7480854244	0.2743807394
C6	1.4942780966	-1.7302024196	0.2767583818
H7	3.2287036687	-0.4456243201	0.2723032895
H9	-0.3286826271	1.6085969339	0.2554044059
H10	-1.6601961522	-0.5001127407	0.2643064945
H11	-0.4386771799	-2.6892366784	0.2789030587
H12	2.0678419178	-2.6529270622	0.2829643810

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-5. Cartesian Coordinates of **B**.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C1	3.2925223154	-1.2513678441	0.2746003848
N2	2.6161392574	-0.0600469462	0.3081000349
C3	1.2458922458	-0.0720561710	0.3092933260
C4	0.5440435189	-1.2574337800	0.2779183958
C5	1.2238305647	-2.4744538411	0.2441306994
C6	2.6181046204	-2.4525503651	0.2428024188
H7	4.3697090892	-1.1480188195	0.2759946743
H9	0.7954799876	0.9115081395	0.3365219202
H10	-0.5403253211	-1.2204451964	0.2803655910
H11	0.6818169572	-3.4144450217	0.2192900632
H12	3.1934912558	-3.3720631870	0.2170713193
O12	3.2584433419	1.0535987940	0.3382511806

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-6. Cartesian Coordinates of **C**.^a

atom	x	y	z
C1	-0.1962056030	-2.0367790472	0.3471617424
N2	-0.5668337588	-0.9202910527	-0.3128344769
C3	-1.8292460262	-0.6348814476	-0.6751964908
C4	-2.8305584234	-1.5053803364	-0.2837205302
C5	-2.5070814933	-2.6490603190	0.4412132461
C6	-1.1699650471	-2.9213168902	0.7498632719
H7	0.8597675641	-2.1763128018	0.5246310089
H8	-1.9946547369	0.2787778928	-1.2384759025
H9	-3.8540501195	-1.2603689236	-0.5382383199
H10	-3.2880529410	-3.3318444159	0.7599975114
H11	-0.8797527308	-3.8061005291	1.3032030390
O12	0.3913269560	-0.0726163036	-0.8393054445
C13	1.1945337534	0.5661459694	0.0887113296
C14	1.8672526006	1.7642962499	-0.5214846035
O15	1.3831800404	0.1348923566	1.1950383571
O16	-1.8801162662	1.2176642152	1.2017616320
C17	-1.7646982308	2.3018387373	0.5404512578
O18	-1.2685489217	2.3867192894	-0.6265199464
C19	-2.2901375133	3.5854253117	1.1988644443
H20	-3.3812911732	3.6303687746	1.1033695775
H21	-2.0498481748	3.5975046273	2.2673335759
H22	-1.8663645028	4.4707955136	0.7153478463
H23	2.9178151449	1.5312162533	-0.7228482973
H24	1.3679824210	2.0840474884	-1.4392066071
H25	1.8116499428	2.5726044747	0.2097307290

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-7. Cartesian Coordinates of **D**.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C1	1.3831902397	-0.9069290996	0.0980980321
N2	1.1965679363	0.3338407085	0.5956931823
C3	-0.0021801313	0.8386986175	0.9487630739
C4	-1.1137283006	0.0390132156	0.8194711989
C5	-0.9695261274	-1.2602015907	0.3380050053
C6	0.2900377545	-1.7279728722	-0.0381745981
H7	2.3957053531	-1.1740835164	-0.1712951232
H8	-0.0102419048	1.8590789031	1.3076950080
H9	-2.0867252012	0.4496294921	1.0586036098
H10	-1.8420869044	-1.8913799477	0.2111749850
H11	0.4229014947	-2.7107513537	-0.4729879077
O12	2.3196371356	1.0639755256	0.9815784578
S13	3.0625001328	2.0700009555	-0.2294269444
O14	2.2088023771	3.2278736961	-0.4148184741
O15	3.5211575100	1.1782479989	-1.2814270551
C16	4.4517490420	2.5140012074	0.8255718315
Cl17	-0.1065725103	0.8933441280	-2.3597711760
H18	5.0026586364	1.6157146377	1.1101596364
H19	5.0668442409	3.1609739503	0.1969144346
H20	4.0869154168	3.0612519280	1.6967493848

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-8. Cartesian Coordinates of **E**.^a

atom	x	y	z
C1	1.6110669007	-1.2551901760	1.3149269251
N2	1.4825822106	-0.3476787037	0.3379510271
C3	0.6239752577	-0.4428498126	-0.6861379316
C4	-0.1522550547	-1.5747449474	-0.7856841939
C5	-0.0323785379	-2.5688685896	0.1830858815
C6	0.8521491091	-2.4008112753	1.2466918694
H7	2.2983804329	-1.0126224025	2.1143025932
H9	0.5814122215	0.4006841670	-1.3621982062
H10	-0.8624036072	-1.6549378582	-1.5997376134
H11	-0.6495163967	-3.4595080057	0.1263114163
H12	0.9370360843	-3.1349838001	2.0386145216
O12	2.2445955636	0.7988204835	0.4282785124
C13	3.4769261563	0.7529218668	-0.1864086491
O14	3.8915782980	-0.2226021286	-0.7735395021
Br15	-0.4830818185	1.5349636895	2.0538549831
C16	5.5141637048	4.4541693059	0.3166669853
C17	6.1233763059	3.3977771749	-0.3687272859
C18	5.4518962780	2.1934536034	-0.5301933444
C19	4.1650721112	2.0425368081	-0.0021804113
C20	3.5514331874	3.0987233464	0.6901332361
C21	4.2298642396	4.3023234613	0.8439575164
H22	6.0414363344	5.3965758902	0.4395349810
H23	7.1224060888	3.5138673839	-0.7782325110
H24	5.9178699115	1.3697143665	-1.0619288189
H25	2.5533845869	2.9841789581	1.1069967418
H26	3.7534697017	5.1195854204	1.3769881056

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-9. Cartesian Coordinates of **F**.^a

atom	x	y	z
C1	1.5569853285	-0.9196896782	-0.7198502319
N2	1.2216590349	0.2575120478	-0.1529431187
C3	0.6767012630	0.3731791878	1.0805199837
C4	0.4017453754	-0.7756157514	1.7930012320
C5	0.6912835165	-2.0223607167	1.2279233936
C6	1.2669432045	-2.0903589921	-0.0383482474
H7	2.0578154829	-0.8678891476	-1.6757935558
H8	0.4999304471	1.3816376605	1.4268806313
H9	-0.0128253969	-0.6871897602	2.7906951779
H10	0.5111143978	-2.9327293566	1.7885449951
H11	1.5749046521	-3.0315355217	-0.4746275092
O12	1.3790752008	1.4025518369	-0.9094480492
S13	2.8292148953	2.4188866774	-0.5412761115
O14	2.6994280190	2.7874739043	0.8600493550
O15	3.9858482929	1.7570296841	-1.1118953504
O16	3.6335294777	-3.0171799851	1.6864193298
S17	4.2226560302	-1.8244007063	1.0060037896
O18	3.6161928598	-0.5281417291	1.4529132225
O19	4.2300343739	-1.9485914188	-0.4902138934
C20	1.4571541005	5.8350611824	-3.2462955193
C21	1.0954765045	5.8062961856	-1.8893214050
C22	1.5027349208	4.7674310758	-1.0552894934
C23	2.2873002545	3.7447033381	-1.5946387869
C24	2.6643318704	3.7387527853	-2.9402465331
C25	2.2421074610	4.7870418083	-3.7550457289
C26	1.0403605616	6.9849174782	-4.1309444200
H27	0.4900142170	6.6100997802	-1.4779359409
H28	1.2311829248	4.7549937508	-0.0048478054
H29	3.2801543622	2.9366321957	-3.3338314910
H30	2.5315263401	4.7928732599	-4.8029165823
C31	8.6694708033	-1.7067746807	2.2559610237
C32	8.1080205627	-0.6776646971	1.4814713862

C33	6.7645029312	-0.7036859801	1.1092537859
C34	5.9580040989	-1.7727379834	1.5095817203
C35	6.4932419522	-2.8061721005	2.2763474082
C36	7.8419637279	-2.7680384760	2.6435287908
C37	10.1209672138	-1.6539914018	2.6785089651
H38	8.7338548144	0.1548902207	1.1639231499
H39	6.3404370975	0.0962843203	0.5093479590
H40	5.8523768729	-3.6296818064	2.5747369599
H41	8.2554003918	-3.5802977649	3.2390424883
H42	0.8983055295	6.6627768277	-5.1676827036
H43	0.1089533453	7.4427246283	-3.7825879456
H44	1.8107318812	7.7678181927	-4.1335209879
H45	10.5006356266	-2.6505503935	2.9302197408
H46	10.7560091990	-1.2413534826	1.8855592705
H47	10.2545217302	-1.0188478030	3.5653527180

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-10. Cartesian Coordinates of **G**.^a

atom	x	y	z
C1	-2.0038002023	-2.2784266912	-0.2719143725
N2	-2.3930351627	-0.9918444997	-0.2901627053
C3	-3.6337940404	-0.5910407505	0.0388182489
C4	-4.5631160718	-1.5325641701	0.4292005013
C5	-4.1983947223	-2.8757134281	0.4682469847
C6	-2.9050852233	-3.2489312022	0.1114253779
H7	-0.9748175697	-2.4577311105	-0.5517994063
H9	-3.8084255918	0.4748199667	-0.0126620740
H10	-5.5593102505	-1.2078701378	0.7059143944
H11	-4.9165027531	-3.6276175617	0.7793152255
H12	-2.5871099318	-4.2845771873	0.1363594378
O12	-1.5030493403	-0.0562485190	-0.7178419840
B13	-0.7186088607	0.5397825933	0.4675564210
F14	-1.6463262834	1.1824031342	1.3083725874
F15	0.1857942052	1.4141682089	-0.1111930414
F16	-0.0966796469	-0.5290593992	1.1382862952

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-11. Cartesian Coordinates of **H**.^a

atom	x	y	z
C1	1.3014580000	-1.9130090000	-0.4061580000
N2	0.8427570000	-0.6524730000	-0.2489900000
C3	-0.4012640000	-0.3782550000	0.1997490000
C4	-1.2622450000	-1.4222490000	0.5023020000
C5	-0.8279530000	-2.7401990000	0.3447170000
C6	0.4688900000	-2.9825960000	-0.1133680000
H7	2.3231630000	-1.9895660000	-0.7531700000
H9	-0.6315900000	0.6740440000	0.2985390000
H10	-2.2594690000	-1.1926170000	0.8611250000
H11	-1.4909250000	-3.5676030000	0.5776320000
H12	0.8452730000	-3.9912390000	-0.2435250000
O12	1.6582990000	0.3785630000	-0.5677140000
B13	2.5072160000	0.8294410000	0.6609960000
C14	3.4143500000	2.0663270000	0.0952290000
F15	4.2339380000	1.7064390000	-0.9406320000
F16	4.2301330000	2.5779100000	1.0626010000
F17	2.6675220000	3.1170140000	-0.3659420000
F18	1.6201910000	1.2232820000	1.6611170000
F19	3.2732220000	-0.2626040000	1.0644760000

^a Calculated at the B3LYP/6-31+G(d) level.

The geometry optimization of pyridine *N*-oxide adducts with BF₃, BF₂CF₃, and BF₂CF₂CF₃ were performed using the B3LYP functional with the 6-31+G(d) basis set, implemented in the Gaussian 09²⁵). A stationary point was optimized without any symmetry assumptions and characterized by frequency analysis at the same level of theory (the number of imaginary frequencies, NIMAG, was 0.) The Cartesian coordinates for all calculated compounds are given in Tables 1-12 to 1-14. For pyridine *N*-oxide adducts with BF₃, BF₂CF₃, and BF₂CF₂CF₃, natural bond orbital (NBO) analysis were performed with the MP2 theory and 6-31+G(d) basis set using the optimized structures as initial geometries.

Table 1-12. Cartesian Coordinates of Pyridine *N*-Oxide–BF₃ complex.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C	3.03697055	0.00554259	0.34039600
C	1.06049574	-1.18701372	-0.33421080
C	1.05192444	1.18147269	-0.33854711
C	2.36376722	1.20754573	0.11112415
C	2.37255538	-1.20210518	0.11478616
H	0.43727955	2.05042737	-0.53130129
H	2.84086118	2.16653102	0.28113911
H	2.85692867	-2.15696836	0.28744734
H	4.06377231	0.00977752	0.69261739
N	0.44414895	-0.00541888	-0.55498141
H	0.45216098	-2.06105509	-0.52409737
O	-0.81874462	-0.01168269	-1.02546104
B	-1.88194827	0.00023497	0.15288667
F	-1.62443088	-1.13623016	0.91862318
F	-3.08444290	-0.01557491	-0.49717380
F	-1.63719589	1.16167769	0.88488721

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-13. Cartesian Coordinates of Pyridine *N*-Oxide–BF₂CF₃ complex.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C	3.95858502	0.00067133	0.14902300
C	1.92073667	-1.18491430	-0.32536587
C	1.92019805	1.18627721	-0.32290930
C	3.27091601	1.20623575	-0.00896470
C	3.27147995	-1.20485510	-0.01135539
H	1.29326565	2.05793682	-0.45507481
H	3.76699154	2.16291085	0.11239401
H	3.76798219	-2.16154610	0.10813984
H	5.01573455	0.00066326	0.39561842
N	1.29216512	0.00067830	-0.47695801
H	1.29432581	-2.05667016	-0.45934006
O	-0.01735800	0.00088662	-0.81531311
B	-0.92809189	-0.00237874	0.44992357
F	-0.63381484	-1.15553229	1.17521693
F	-0.63101124	1.14506045	1.18304099
C	-2.44741130	0.00124019	-0.15332220
F	-2.71674773	-1.08690050	-0.93949840
F	-3.38748670	-0.00431415	0.83582263
F	-2.71662377	1.09822288	-0.92711298

^a Calculated at the B3LYP/6-31+G(d) level.

Table 1-14. Cartesian Coordinates of Pyridine *N*-Oxide–BF₂C₂F₅ complex.^a

atom	<i>x</i>	<i>y</i>	<i>z</i>
C	-4.69280869	-0.00199049	-0.38548935
C	-2.70524279	-1.18792675	0.26715068
C	-2.70981406	1.18358342	0.28173995
C	-4.02559378	1.20352459	-0.15612401
C	-4.02091079	-1.20763273	-0.17080353
H	-2.09990093	2.05523882	0.47812166
H	-4.51043203	2.16022259	-0.31637156
H	-4.50209386	-2.16413573	-0.34285523
H	-5.72258913	-0.00192949	-0.72888717
N	-2.09630859	-0.00229557	0.48518156
H	-2.09188852	-2.05949505	0.45283336
O	-0.82441675	-0.00306280	0.94467438
B	0.19873119	0.00959333	-0.22902185
F	-0.03320432	-1.12777304	-0.99950701
F	-0.02311454	1.17039638	-0.96672900
C	1.64778316	-0.00888212	0.54619366
F	1.75657652	-1.13253537	1.34552914
F	1.76523938	1.08290684	1.38703670
C	2.91889470	0.00266575	-0.33489267
F	4.04029864	-0.02404563	0.41544687
F	2.96278787	1.11197868	-1.10036843
F	2.94573823	-1.06952189	-1.15230228

^a Calculated at the B3LYP/6-31+G(d) level.

X-ray Structure Report (4aa)

Experimental

Data Collection

A yellow block crystal of $C_{14}H_9BF_5NO$ having approximate dimensions of 0.466 x 0.344 x 0.178 mm was mounted on a glass fiber. All measurements were made on a Rigaku R-Axis RAPID diffractometer using graphite monochromated Cu-K α radiation.

The crystal-to-detector distance was 127.40 mm.

Cell constants and an orientation matrix for data collection corresponded to a primitive triclinic cell with dimensions:

$$\begin{array}{ll} a = 9.3821(2) \text{ \AA} & \alpha = 89.3186(7)^\circ \\ b = 10.5283(2) \text{ \AA} & \beta = 86.5533(7)^\circ \\ c = 12.8919(3) \text{ \AA} & \gamma = 84.1267(7)^\circ \\ V = 1264.44(4) \text{ \AA}^3 & \end{array}$$

For $Z = 4$ and F.W. = 313.03, the calculated density is 1.644 g/cm³. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

P-1 (#2)

The data were collected at a temperature of $-165 \pm 1^\circ\text{C}$ to a maximum 2θ value of 136.4° . A total of 45 oscillation images were collected. A sweep of data was done using ω scans from 80.0 to 260.0° in 20.0° step, at $\chi=54.0^\circ$ and $\phi = 60.0^\circ$. The exposure rate was 60.0 [sec./ $^\circ$]. A second sweep was performed using ω scans from 80.0 to 260.0° in 20.0° step, at $\chi=54.0^\circ$ and $\phi = 150.0^\circ$. The exposure rate was 60.0 [sec./ $^\circ$]. Another sweep was performed using ω scans from 80.0 to 260.0° in 20.0° step, at $\chi=54.0^\circ$ and $\phi = 240.0^\circ$. The exposure rate was 60.0 [sec./ $^\circ$]. Another sweep was performed using ω scans from 80.0 to 260.0° in 20.0° step, at $\chi=54.0^\circ$ and $\phi = 330.0^\circ$. The exposure rate was 60.0 [sec./ $^\circ$]. Another sweep was performed using ω scans from 80.0 to 260.0° in 20.0° step, at $\chi=0.0^\circ$ and $\phi = 60.0^\circ$. The exposure rate was 60.0 [sec./ $^\circ$]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 14047 reflections that were collected, 4542 were unique ($R_{\text{int}} = 0.0443$); equivalent reflections were merged.

The linear absorption coefficient, μ , for Cu-K α radiation is 13.531 cm⁻¹. An empirical absorption correction was applied which resulted in transmission factors ranging from 0.523 to 0.786. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods¹ and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement² on F^2 was based on 4542 observed reflections and 397 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.0415$$

$$wR2 = [\sum (w (F_o^2 - F_c^2)^2) / \sum w(F_o^2)^2]^{1/2} = 0.1296$$

The standard deviation of an observation of unit weight³ was 1.13. Unit weights were used. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.39 and -0.35 e⁻/Å³, respectively.

Neutral atom scattering factors were taken from Cromer and Waber⁴. Anomalous dispersion effects were included in F_{calc} ⁵; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley⁶. The values for the mass attenuation coefficients are those of Creagh and Hubbell⁷. All calculations were performed using the CrystalStructure⁸ crystallographic software package except for refinement, which was performed using SHELXL-97⁹.

References for X-ray structure report

(1) SHELX97: Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122.

(2) Least Squares function minimized: (SHELXL97)

$$\sum w(F_o^2 - F_c^2)^2 \quad \text{where } w = \text{Least Squares weights.}$$

(3) Standard deviation of an observation of unit weight:

$$[\sum w(F_o^2 - F_c^2)^2 / (N_o - N_v)]^{1/2}$$

where: N_o = number of observations
 N_v = number of variables

(4) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(5) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

(6) Creagh, D. C. & McAuley, W.J. ; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(7) Creagh, D. C. & Hubbell, J.H.; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(8) CrystalStructure 4.0: Crystal Structure Analysis Package, Rigaku Corporation (2000-2010). Tokyo 196-8666, Japan.

(9) SHELX97: Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122.

EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	C ₁₄ H ₉ BF ₅ NO
Formula Weight	313.03
Crystal Color, Habit	yellow, block
Crystal Dimensions	0.466 X 0.344 X 0.178 mm
Crystal System	triclinic
Lattice Type	Primitive
Lattice Parameters	a = 9.3821(2) Å b = 10.5283(2) Å c = 12.8919(3) Å α = 89.3186(7) ° β = 86.5533(7) ° γ = 84.1267(7) ° V = 1264.44(4) Å ³
Space Group	P-1 (#2)
Z value	4
D _{calc}	1.644 g/cm ³
F ₀₀₀	632.00
μ(CuKα)	13.531 cm ⁻¹

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuK α ($\lambda = 1.54187 \text{ \AA}$) graphite monochromated
Voltage, Current	50kV, 40mA
Temperature	-165.0°C
Detector Aperture	460 x 256 mm
Data Images	45 exposures
ω oscillation Range ($\chi=54.0, \phi=60.0$)	80.0 - 260.0°
Exposure Rate	60.0 sec./°
ω oscillation Range ($\chi=54.0, \phi=150.0$)	80.0 - 260.0°
Exposure Rate	60.0 sec./°
ω oscillation Range ($\chi=54.0, \phi=240.0$)	80.0 - 260.0°
Exposure Rate	60.0 sec./°
ω oscillation Range ($\chi=54.0, \phi=330.0$)	80.0 - 260.0°
Exposure Rate	60.0 sec./°
ω oscillation Range ($\chi=0.0, \phi=60.0$)	80.0 - 260.0°
Exposure Rate	60.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{\max}$	136.4°
No. of Reflections Measured	Total: 14047

Corrections

Unique: 4542 ($R_{\text{int}} = 0.0443$)

Lorentz-polarization

Absorption

(trans. factors: 0.523 - 0.786)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	$\sum w (F_o^2 - F_c^2)^2$
Least Squares Weights	$w = 1 / [\sigma^2(F_o^2) + (0.0707 \cdot P)^2 + 0.0625 \cdot P]$ where $P = (\text{Max}(F_o^2, 0) + 2F_c^2)/3$
$2\theta_{\text{max}}$ cutoff	136.4°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	4542
No. Variables	397
Reflection/Parameter Ratio	11.44
Residuals: R1 ($I > 2.00\sigma(I)$)	0.0415
Residuals: R (All reflections)	0.0538
Residuals: wR2 (All reflections)	0.1296
Goodness of Fit Indicator	1.129
Max Shift/Error in Final Cycle	0.001
Maximum peak in Final Diff. Map	0.39 e ⁻ /Å ³
Minimum peak in Final Diff. Map	-0.35 e ⁻ /Å ³

Table 1. Atomic coordinates and $B_{\text{iso}}/B_{\text{eq}}$

atom	x	y	z	B_{eq}
F1	0.1986(2)	0.6290(1)	0.33403(8)	2.29(3)
F2	0.3941(2)	0.6398(1)	0.22354(9)	2.16(3)
F3	0.2366(2)	0.5512(2)	0.05615(9)	3.48(3)
F4	0.1175(2)	0.7155(1)	0.1290(1)	3.10(3)
F5	0.0518(2)	0.5271(1)	0.1596(1)	3.06(3)
F6	0.2417(2)	0.9543(1)	0.21171(8)	1.69(3)
F7	0.4141(1)	0.8929(1)	0.32404(9)	2.06(3)
F8	0.1244(2)	0.9115(1)	0.42508(9)	2.71(3)
F9	0.2481(2)	1.0544(2)	0.48358(9)	2.65(3)
F10	0.0845(2)	1.1080(1)	0.37597(9)	2.17(3)
O1	0.3087(2)	0.4369(2)	0.25535(9)	1.47(3)
O2	0.3717(2)	1.1132(2)	0.28150(9)	1.24(3)
N1	0.3933(2)	0.4018(2)	0.3372(2)	1.34(3)
N2	0.4472(2)	1.1211(2)	0.1870(2)	1.22(3)
C1	0.3245(2)	0.3746(2)	0.4300(2)	1.25(4)
C2	0.1741(2)	0.3852(2)	0.4434(2)	1.48(4)
C3	0.1115(3)	0.3577(2)	0.5376(2)	1.66(4)
C4	0.1948(3)	0.3210(2)	0.6232(2)	1.73(4)
C5	0.3404(3)	0.3090(2)	0.6118(2)	1.65(4)
C6	0.4114(2)	0.3335(2)	0.5143(2)	1.28(4)
C7	0.5597(2)	0.3169(2)	0.4973(2)	1.46(4)
C8	0.6253(2)	0.3408(2)	0.3999(2)	1.41(4)
C9	0.7770(2)	0.3200(2)	0.3785(2)	1.67(4)
C10	0.8362(3)	0.3434(2)	0.2825(2)	1.83(4)
C11	0.7478(3)	0.3880(2)	0.2014(2)	1.73(4)
C12	0.6017(3)	0.4075(2)	0.2168(2)	1.55(4)
C13	0.5384(2)	0.3852(2)	0.3166(2)	1.35(4)
C14	0.1699(3)	0.5922(2)	0.1474(2)	1.96(4)
C15	0.3734(2)	1.1720(2)	0.1055(2)	1.28(4)
C16	0.2241(2)	1.2096(2)	0.1168(2)	1.51(4)
C17	0.1558(3)	1.2579(2)	0.0320(2)	1.80(4)
C18	0.2301(3)	1.2700(2)	-0.0660(2)	2.06(4)
C19	0.3735(3)	1.2357(2)	-0.0782(2)	1.84(4)
C20	0.4511(2)	1.1847(2)	0.0080(2)	1.43(4)
C21	0.5981(2)	1.1502(2)	-0.0001(2)	1.48(4)
C22	0.6706(2)	1.1012(2)	0.0853(2)	1.39(4)
C23	0.8218(2)	1.0670(2)	0.0808(2)	1.72(4)

Table 1. Atomic coordinates and $B_{\text{iso}}/B_{\text{eq}}$ (continued)

atom	x	y	z	B_{eq}
C24	0.8886(3)	1.0214(2)	0.1664(2)	1.87(4)
C25	0.8080(2)	1.0094(2)	0.2621(2)	1.77(4)
C26	0.6630(2)	1.0409(2)	0.2716(2)	1.46(4)
C27	0.5921(2)	1.0874(2)	0.1827(2)	1.31(4)
C28	0.1919(2)	1.0154(2)	0.3960(2)	1.64(4)
B1	0.2718(3)	0.5791(2)	0.2449(2)	1.39(4)
B2	0.3080(3)	0.9871(2)	0.2995(2)	1.42(4)

$$B_{\text{eq}} = 8/3 \pi^2 (U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos \gamma + 2U_{13}(aa^*cc^*)\cos \beta + 2U_{23}(bb^*cc^*)\cos \alpha)$$

Table 2. Atomic coordinates and B_{iso} involving hydrogen atoms

atom	x	y	z	B_{iso}
H2	0.1168	0.4113	0.3871	1.78
H3	0.0098	0.3632	0.5463	2.00
H4	0.1485	0.3047	0.6889	2.08
H5	0.3952	0.2840	0.6695	1.97
H7	0.6175	0.2888	0.5528	1.75
H9	0.8370	0.2895	0.4321	2.01
H10	0.9373	0.3298	0.2695	2.19
H11	0.7911	0.4047	0.1348	2.08
H12	0.5438	0.4356	0.1613	1.86
H16	0.1726	1.2014	0.1819	1.82
H17	0.0557	1.2841	0.0390	2.16
H18	0.1791	1.3024	-0.1237	2.48
H19	0.4225	1.2454	-0.1440	2.21
H21	0.6502	1.1602	-0.0647	1.77
H23	0.8767	1.0762	0.0173	2.07
H24	0.9892	0.9975	0.1621	2.25
H25	0.8564	0.9784	0.3214	2.12
H26	0.6109	1.0318	0.3363	1.75

Table 3. Anisotropic displacement parameters

atom	U ₁₁	U ₂₂	U ₃₃	U ₁₂	U ₁₃	U ₂₃
F1	0.0400(8)	0.0233(7)	0.0223(7)	0.0015(6)	0.0019(6)	0.0029(5)
F2	0.0203(6)	0.0206(6)	0.0424(8)	-0.0057(5)	-0.0060(6)	0.0025(5)
F3	0.068(1)	0.0490(9)	0.0165(8)	-0.0109(8)	-0.0077(7)	0.0040(6)
F4	0.0445(9)	0.0240(7)	0.0528(9)	-0.0072(6)	-0.0295(7)	0.0164(6)
F5	0.0279(7)	0.0314(7)	0.061(1)	-0.0122(6)	-0.0230(7)	0.0134(6)
F6	0.0259(7)	0.0239(6)	0.0152(6)	-0.0082(5)	0.0014(5)	-0.0028(5)
F7	0.0190(6)	0.0180(6)	0.0405(8)	0.0006(5)	0.0001(6)	0.0073(5)
F8	0.0379(8)	0.0284(7)	0.0355(8)	-0.0107(6)	0.0183(6)	0.0045(6)
F9	0.0415(8)	0.0463(8)	0.0134(7)	-0.0068(7)	-0.0002(6)	-0.0020(6)
F10	0.0190(7)	0.0299(7)	0.0315(8)	0.0032(5)	0.0049(6)	-0.0022(6)
O1	0.0199(8)	0.0215(7)	0.0150(8)	-0.0008(6)	-0.0094(6)	0.0043(6)
O2	0.0175(7)	0.0198(7)	0.0094(7)	-0.0023(6)	0.0046(6)	0.0008(5)
N1	0.0203(9)	0.0179(8)	0.0127(9)	-0.0004(7)	-0.0047(7)	0.0021(7)
N2	0.0146(8)	0.0171(8)	0.0143(9)	-0.0025(7)	0.0024(7)	0.0022(7)
C1	0.022(1)	0.0109(9)	0.015(1)	-0.0021(8)	-0.0033(9)	-0.0003(8)
C2	0.022(1)	0.019(1)	0.016(1)	-0.0011(9)	-0.0045(9)	0.0012(8)
C3	0.021(1)	0.021(1)	0.020(2)	0.0003(9)	0.0007(9)	-0.0013(8)
C4	0.028(2)	0.022(1)	0.015(1)	0.0015(9)	0.0013(9)	0.0012(8)
C5	0.030(2)	0.020(1)	0.012(1)	0.0026(9)	-0.0052(9)	0.0001(8)
C6	0.024(1)	0.0117(9)	0.013(1)	-0.0008(8)	-0.0041(9)	-0.0008(8)
C7	0.022(1)	0.015(1)	0.018(1)	0.0006(8)	-0.0068(9)	0.0004(8)
C8	0.020(1)	0.0134(9)	0.020(1)	-0.0014(8)	-0.0036(9)	0.0014(8)
C9	0.021(1)	0.016(1)	0.027(2)	-0.0021(9)	-0.0061(9)	0.0033(8)
C10	0.019(1)	0.024(1)	0.027(2)	0.0003(9)	-0.0010(9)	-0.0004(9)
C11	0.026(2)	0.022(1)	0.017(1)	-0.0010(9)	0.0042(9)	-0.0025(8)
C12	0.027(1)	0.015(1)	0.018(1)	-0.0024(9)	-0.0049(9)	0.0005(8)
C13	0.017(1)	0.0114(9)	0.023(1)	-0.0017(8)	-0.0035(9)	0.0001(8)
C14	0.027(2)	0.021(1)	0.028(2)	-0.0067(9)	-0.009(1)	0.0103(9)
C15	0.019(1)	0.0117(9)	0.019(1)	-0.0046(8)	-0.0034(9)	0.0035(8)
C16	0.019(1)	0.018(1)	0.021(1)	-0.0015(8)	-0.0012(9)	0.0015(8)
C17	0.021(1)	0.021(1)	0.027(2)	-0.0012(9)	-0.0052(9)	0.0034(9)
C18	0.031(2)	0.025(1)	0.024(2)	-0.006(1)	-0.010(1)	0.0076(9)
C19	0.032(2)	0.024(1)	0.015(1)	-0.009(1)	-0.0025(9)	0.0056(9)
C20	0.023(1)	0.015(1)	0.018(1)	-0.0073(9)	-0.0004(9)	0.0012(8)
C21	0.023(1)	0.018(1)	0.015(1)	-0.0064(9)	0.0035(9)	-0.0011(8)
C22	0.018(1)	0.0143(9)	0.020(1)	-0.0042(8)	0.0045(9)	-0.0027(8)
C23	0.018(1)	0.026(1)	0.021(2)	-0.0044(9)	0.0050(9)	-0.0032(9)

Table 3. Anisotropic displacement parameters (continued)

atom	U ₁₁	U ₂₂	U ₃₃	U ₁₂	U ₁₃	U ₂₃
C24	0.014(1)	0.026(1)	0.031(2)	-0.0025(9)	0.0015(9)	-0.0020(9)
C25	0.020(1)	0.020(1)	0.028(2)	-0.0049(9)	-0.0063(9)	0.0026(9)
C26	0.018(1)	0.019(1)	0.019(1)	-0.0056(8)	-0.0012(9)	0.0015(8)
C27	0.016(1)	0.0116(9)	0.023(1)	-0.0041(8)	-0.0006(9)	0.0003(8)
C28	0.022(1)	0.021(1)	0.020(1)	-0.0047(9)	0.0003(9)	0.0032(8)
B1	0.020(1)	0.020(1)	0.012(1)	-0.0019(9)	-0.0020(9)	0.0005(9)
B2	0.016(2)	0.016(1)	0.021(2)	-0.0019(9)	0.001(1)	0.0042(9)

The general temperature factor expression: $\exp(-2\pi^2(a^2U_{11}h^2 + b^2U_{22}k^2 + c^2U_{33}l^2 + 2a*b*U_{12}hk + 2a*c*U_{13}hl + 2b*c*U_{23}kl))$

Table 4. Fragment Analysis

fragment: 1

F(1)	F(2)	F(3)	F(4)	F(5)
O(1)	N(1)	C(1)	C(2)	C(3)
C(4)	C(5)	C(6)	C(7)	C(8)
C(9)	C(10)	C(11)	C(12)	C(13)
C(14)	B(1)			

fragment: 2

F(6)	F(7)	F(8)	F(9)	F(10)
O(2)	N(2)	C(15)	C(16)	C(17)
C(18)	C(19)	C(20)	C(21)	C(22)
C(23)	C(24)	C(25)	C(26)	C(27)
C(28)	B(2)			

Table 5. Bond lengths (Å)

atom	atom	distance	atom	atom	distance
F1	B1	1.383(3)	F2	B1	1.382(3)
F3	C14	1.353(3)	F4	C14	1.363(3)
F5	C14	1.361(3)	F6	B2	1.388(3)
F7	B2	1.379(3)	F8	C28	1.357(3)
F9	C28	1.359(3)	F10	C28	1.363(3)
O1	N1	1.383(2)	O1	B1	1.508(3)
O2	N2	1.3788(19)	O2	B2	1.520(3)
N1	C1	1.365(3)	N1	C13	1.365(3)
N2	C15	1.367(3)	N2	C27	1.367(3)
C1	C2	1.405(3)	C1	C6	1.435(3)
C2	C3	1.358(3)	C3	C4	1.418(3)
C4	C5	1.358(3)	C5	C6	1.420(3)
C6	C7	1.389(3)	C7	C8	1.397(3)
C8	C9	1.428(3)	C8	C13	1.433(3)
C9	C10	1.356(3)	C10	C11	1.420(3)
C11	C12	1.367(3)	C12	C13	1.411(3)
C14	B1	1.622(3)	C15	C16	1.414(3)
C15	C20	1.426(3)	C16	C17	1.368(3)
C17	C18	1.417(3)	C18	C19	1.357(3)
C19	C20	1.435(3)	C20	C21	1.388(3)
C21	C22	1.394(3)	C22	C23	1.426(3)
C22	C27	1.431(3)	C23	C24	1.360(3)
C24	C25	1.419(3)	C25	C26	1.365(3)
C26	C27	1.417(3)	C28	B2	1.613(3)

Table 6. Bond lengths involving hydrogens (Å)

atom	atom	distance	atom	atom	distance
C2	H2	0.950	C3	H3	0.950
C4	H4	0.950	C5	H5	0.950
C7	H7	0.950	C9	H9	0.950
C10	H10	0.950	C11	H11	0.950
C12	H12	0.950	C16	H16	0.950
C17	H17	0.950	C18	H18	0.950
C19	H19	0.950	C21	H21	0.950
C23	H23	0.950	C24	H24	0.950
C25	H25	0.950	C26	H26	0.950

Table 7. Bond angles (°)

atom	atom	atom	angle	atom	atom	atom	angle
N1	O1	B1	113.86(14)	N2	O2	B2	113.77(13)
O1	N1	C1	117.22(15)	O1	N1	C13	117.47(15)
C1	N1	C13	124.99(17)	O2	N2	C15	117.24(14)
O2	N2	C27	118.18(15)	C15	N2	C27	124.36(16)
N1	C1	C2	121.87(17)	N1	C1	C6	117.65(17)
C2	C1	C6	120.48(17)	C1	C2	C3	119.31(18)
C2	C3	C4	121.35(19)	C3	C4	C5	120.32(18)
C4	C5	C6	120.68(18)	C1	C6	C5	117.80(17)
C1	C6	C7	119.27(17)	C5	C6	C7	122.91(18)
C6	C7	C8	121.07(18)	C7	C8	C9	122.60(18)
C7	C8	C13	119.50(18)	C9	C8	C13	117.89(17)
C8	C9	C10	120.71(19)	C9	C10	C11	120.31(19)
C10	C11	C12	121.57(19)	C11	C12	C13	118.89(19)
N1	C13	C8	117.39(17)	N1	C13	C12	121.97(18)
C8	C13	C12	120.62(17)	F3	C14	F4	104.99(16)
F3	C14	F5	105.24(17)	F3	C14	B1	114.15(17)
F4	C14	F5	104.97(16)	F4	C14	B1	112.46(17)
F5	C14	B1	114.13(17)	N2	C15	C16	121.23(17)
N2	C15	C20	117.90(17)	C16	C15	C20	120.86(18)
C15	C16	C17	118.49(18)	C16	C17	C18	121.75(19)
C17	C18	C19	120.66(19)	C18	C19	C20	120.10(18)
C15	C20	C19	118.13(17)	C15	C20	C21	119.58(18)
C19	C20	C21	122.28(18)	C20	C21	C22	120.92(18)
C21	C22	C23	122.69(18)	C21	C22	C27	119.37(17)
C23	C22	C27	117.92(18)	C22	C23	C24	120.78(19)
C23	C24	C25	120.01(19)	C24	C25	C26	122.04(19)
C25	C26	C27	118.48(18)	N2	C27	C22	117.79(17)
N2	C27	C26	121.46(17)	C22	C27	C26	120.75(17)
F8	C28	F9	105.42(15)	F8	C28	F10	105.04(15)
F8	C28	B2	112.72(16)	F9	C28	F10	104.93(15)
F9	C28	B2	114.20(17)	F10	C28	B2	113.65(16)
F1	B1	F2	110.04(17)	F1	B1	O1	110.99(16)
F1	B1	C14	110.81(16)	F2	B1	O1	110.82(16)
F2	B1	C14	110.63(17)	O1	B1	C14	103.40(16)
F6	B2	F7	110.66(16)	F6	B2	O2	109.99(16)
F6	B2	C28	110.79(17)	F7	B2	O2	109.97(16)
F7	B2	C28	111.20(16)	O2	B2	C28	104.03(15)

Table 8. Bond angles involving hydrogens (°)

atom	atom	atom	angle	atom	atom	atom	angle
C1	C2	H2	120.3	C3	C2	H2	120.3
C2	C3	H3	119.3	C4	C3	H3	119.3
C3	C4	H4	119.8	C5	C4	H4	119.8
C4	C5	H5	119.7	C6	C5	H5	119.7
C6	C7	H7	119.5	C8	C7	H7	119.5
C8	C9	H9	119.6	C10	C9	H9	119.6
C9	C10	H10	119.8	C11	C10	H10	119.8
C10	C11	H11	119.2	C12	C11	H11	119.2
C11	C12	H12	120.6	C13	C12	H12	120.6
C15	C16	H16	120.8	C17	C16	H16	120.7
C16	C17	H17	119.1	C18	C17	H17	119.1
C17	C18	H18	119.7	C19	C18	H18	119.7
C18	C19	H19	120.0	C20	C19	H19	119.9
C20	C21	H21	119.5	C22	C21	H21	119.5
C22	C23	H23	119.6	C24	C23	H23	119.6
C23	C24	H24	120.0	C25	C24	H24	120.0
C24	C25	H25	119.0	C26	C25	H25	119.0
C25	C26	H26	120.8	C27	C26	H26	120.8

Table 9. Torsion Angles($^{\circ}$)(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
N1	O1	B1	F1	-59.4(2)	N1	O1	B1	F2	63.22(19)
N1	O1	B1	C14	-178.22(12)	B1	O1	N1	C1	92.44(16)
B1	O1	N1	C13	-93.71(16)	N2	O2	B2	F6	-45.97(18)
N2	O2	B2	F7	76.15(18)	N2	O2	B2	C28	-164.68(12)
B2	O2	N2	C15	91.73(16)	B2	O2	N2	C27	-93.40(17)
O1	N1	C1	C2	-1.9(3)	O1	N1	C1	C6	177.73(12)
O1	N1	C13	C8	-176.05(13)	O1	N1	C13	C12	2.5(3)
C1	N1	C13	C8	-2.7(3)	C1	N1	C13	C12	175.80(15)
C13	N1	C1	C2	-175.20(15)	C13	N1	C1	C6	4.4(3)
O2	N2	C15	C16	-2.8(3)	O2	N2	C15	C20	178.00(13)
O2	N2	C27	C22	-177.31(13)	O2	N2	C27	C26	2.4(3)
C15	N2	C27	C22	-2.8(3)	C15	N2	C27	C26	176.87(15)
C27	N2	C15	C16	-177.34(15)	C27	N2	C15	C20	3.5(3)
N1	C1	C2	C3	-179.58(15)	N1	C1	C6	C5	178.08(14)
N1	C1	C6	C7	-3.2(3)	C2	C1	C6	C5	-2.3(3)
C2	C1	C6	C7	176.36(15)	C6	C1	C2	C3	0.8(3)
C1	C2	C3	C4	1.3(3)	C2	C3	C4	C5	-1.9(3)
C3	C4	C5	C6	0.3(3)	C4	C5	C6	C1	1.8(3)
C4	C5	C6	C7	-176.89(16)	C1	C6	C7	C8	0.7(3)
C5	C6	C7	C8	179.31(16)	C6	C7	C8	C9	-177.48(15)
C6	C7	C8	C13	1.0(3)	C7	C8	C9	C10	179.38(16)
C7	C8	C13	N1	-0.1(3)	C7	C8	C13	C12	-178.65(15)
C9	C8	C13	N1	178.45(15)	C9	C8	C13	C12	-0.1(3)
C13	C8	C9	C10	0.9(3)	C8	C9	C10	C11	-0.5(3)
C9	C10	C11	C12	-0.6(3)	C10	C11	C12	C13	1.4(3)
C11	C12	C13	N1	-179.49(16)	C11	C12	C13	C8	-1.0(3)
F3	C14	B1	F1	176.86(15)	F3	C14	B1	F2	54.5(2)
F3	C14	B1	O1	-64.2(2)	F4	C14	B1	F1	57.4(2)
F4	C14	B1	F2	-64.9(2)	F4	C14	B1	O1	176.37(14)
F5	C14	B1	F1	-62.0(2)	F5	C14	B1	F2	175.62(14)
F5	C14	B1	O1	56.93(19)	N2	C15	C16	C17	-178.91(15)
N2	C15	C20	C19	178.76(14)	N2	C15	C20	C21	-2.5(3)
C16	C15	C20	C19	-0.4(3)	C16	C15	C20	C21	178.28(16)
C20	C15	C16	C17	0.2(3)	C15	C16	C17	C18	0.6(3)
C16	C17	C18	C19	-1.2(3)	C17	C18	C19	C20	1.0(3)
C18	C19	C20	C15	-0.2(3)	C18	C19	C20	C21	-178.88(17)
C15	C20	C21	C22	1.2(3)	C19	C20	C21	C22	179.82(16)

Table 9. Torsion angles ($^{\circ}$) (continued)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C20	C21	C22	C23	-178.76(16)	C20	C21	C22	C27	-0.5(3)
C21	C22	C23	C24	178.99(17)	C21	C22	C27	N2	1.2(3)
C21	C22	C27	C26	-178.46(16)	C23	C22	C27	N2	179.57(16)
C23	C22	C27	C26	-0.1(3)	C27	C22	C23	C24	0.7(3)
C22	C23	C24	C25	-1.1(3)	C23	C24	C25	C26	0.9(3)
C24	C25	C26	C27	-0.3(3)	C25	C26	C27	N2	-179.78(16)
C25	C26	C27	C22	-0.1(3)	F8	C28	B2	F6	62.9(2)
F8	C28	B2	F7	-60.7(3)	F8	C28	B2	O2	-178.98(14)
F9	C28	B2	F6	-176.86(14)	F9	C28	B2	F7	59.6(2)
F9	C28	B2	O2	-58.70(19)	F10	C28	B2	F6	-56.5(2)
F10	C28	B2	F7	179.98(15)	F10	C28	B2	O2	61.7(2)

Table 10. Intramolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
F1	F4	2.9047(17)	F1	F5	2.9722(18)
F1	N1	2.8584(18)	F1	C1	3.089(2)
F1	C2	2.936(3)	F2	F3	2.9031(19)
F2	F4	2.9648(18)	F2	N1	2.8884(19)
F2	C12	2.965(2)	F2	C13	3.136(2)
F3	O1	2.9102(17)	F5	O1	2.8452(18)
F6	F8	2.9475(16)	F6	F10	2.9142(15)
F6	N2	2.741(2)	F6	C15	2.993(2)
F6	C16	2.933(3)	F7	F8	2.9315(16)
F7	F9	2.9502(16)	F7	N2	2.9961(19)
F7	C26	2.978(3)	F7	C27	3.247(3)
F9	O2	2.8740(17)	F10	O2	2.8950(17)
O1	C2	2.740(3)	O1	C12	2.750(3)
O2	C16	2.732(3)	O2	C26	2.757(3)
N1	C7	2.748(3)	N2	C21	2.752(3)
C1	C4	2.784(3)	C1	C8	2.812(3)
C1	B1	3.220(3)	C2	C5	2.810(3)
C2	B1	3.395(3)	C3	C6	2.798(3)
C6	C13	2.820(3)	C8	C11	2.802(3)
C9	C12	2.820(3)	C10	C13	2.793(3)
C12	B1	3.422(3)	C13	B1	3.234(3)
C15	C18	2.789(3)	C15	C22	2.809(3)
C15	B2	3.220(3)	C16	C19	2.828(3)
C16	B2	3.372(3)	C17	C20	2.799(3)
C20	C27	2.810(3)	C22	C25	2.800(3)
C23	C26	2.823(3)	C24	C27	2.794(3)
C26	B2	3.432(3)	C27	B2	3.246(3)

Table 11. Intramolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
F1	H2	2.563	F2	H12	2.555
F3	H12	3.368	F5	H2	3.231
F6	H16	2.645	F7	H26	2.483
F10	H16	2.788	O1	H2	2.434
O1	H12	2.451	O2	H16	2.430
O2	H26	2.461	N1	H2	2.627
N1	H12	2.639	N2	H16	2.633
N2	H26	2.639	C1	H3	3.244
C1	H5	3.307	C1	H7	3.296
C2	H4	3.268	C3	H5	3.267
C4	H2	3.280	C5	H3	3.255
C5	H7	2.653	C6	H2	3.325
C6	H4	3.273	C7	H5	2.667
C7	H9	2.674	C8	H10	3.280
C8	H12	3.331	C9	H7	2.661
C9	H11	3.255	C10	H12	3.293
C11	H9	3.267	C12	H10	3.281
C13	H7	3.302	C13	H9	3.313
C13	H11	3.252	C15	H17	3.252
C15	H19	3.316	C15	H21	3.291
C16	H18	3.279	C17	H19	3.269
C18	H16	3.292	C19	H17	3.255
C19	H21	2.651	C20	H16	3.330
C20	H18	3.279	C21	H19	2.674
C21	H23	2.671	C22	H24	3.282
C22	H26	3.336	C23	H21	2.659
C23	H25	3.254	C24	H26	3.295
C25	H23	3.266	C26	H24	3.282
C27	H21	3.298	C27	H23	3.309
C27	H25	3.250	C28	H16	3.369
B1	H2	2.954	B1	H12	2.979
B2	H16	2.928	B2	H26	2.994
H2	H3	2.304	H3	H4	2.356
H4	H5	2.301	H5	H7	2.502
H7	H9	2.507	H9	H10	2.299
H10	H11	2.357	H11	H12	2.314
H16	H17	2.316	H17	H18	2.349

Table 11. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H18	H19	2.301	H19	H21	2.502
H21	H23	2.505	H23	H24	2.304
H24	H25	2.354	H25	H26	2.311

Table 12. Intermolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
F1	F7	3.5966(16)	F1	F8	3.2046(16)
F1	C3 ¹	3.251(3)	F1	C7 ²	3.328(3)
F2	F6	3.4755(15)	F2	F7	3.0047(16)
F2	C5 ²	3.456(3)	F2	C19 ³	3.165(3)
F3	C11 ⁴	3.371(3)	F3	C17 ⁵	3.276(3)
F3	C18 ⁵	3.377(3)	F4	F6	3.1032(17)
F4	C17 ⁶	3.382(3)	F4	C18 ⁶	3.396(3)
F4	C21 ³	3.473(3)	F4	C23 ³	3.580(3)
F5	C10 ⁷	3.269(3)	F5	C11 ⁷	3.351(3)
F5	C16 ⁵	3.595(3)	F5	C17 ⁵	3.323(3)
F5	C18 ⁶	3.491(3)	F6	F2	3.4755(15)
F6	F4	3.1032(17)	F6	C21 ³	3.187(2)
F6	C24 ⁷	3.400(3)	F7	F1	3.5966(16)
F7	F2	3.0047(16)	F7	C5 ²	3.114(3)
F7	C6 ²	3.492(2)	F7	C7 ²	3.175(3)
F8	F1	3.2046(16)	F8	F8 ⁸	3.3631(16)
F8	F10 ⁸	3.1507(16)	F8	C9 ²	3.589(3)
F9	C1 ⁹	3.569(3)	F9	C2 ⁹	3.519(3)
F9	C3 ⁹	3.381(3)	F9	C4 ⁹	3.330(3)
F9	C5 ⁹	3.379(3)	F9	C6 ⁹	3.488(3)
F9	C25 ¹⁰	3.360(3)	F9	C26 ¹⁰	3.426(3)
F10	F8 ⁸	3.1507(16)	F10	C2 ⁹	3.261(3)
F10	C3 ⁹	3.413(3)	F10	C9 ¹¹	3.461(3)
F10	C10 ¹¹	3.479(3)	F10	C24 ⁷	3.536(3)
F10	C25 ⁷	3.318(3)	O1	O2 ⁵	3.4148(18)
O1	N2 ⁵	3.5453(19)	O1	C15 ⁵	3.394(3)
O1	C16 ⁵	3.195(3)	O2	O1 ⁹	3.4148(18)
O2	N1 ⁹	3.160(2)	O2	C1 ⁹	3.348(3)
O2	C13 ⁹	3.447(3)	N1	O2 ⁵	3.160(2)
N1	N2 ⁵	3.529(2)	N2	O1 ⁹	3.5453(19)
N2	N1 ⁹	3.529(2)	N2	C12 ⁹	3.511(3)
N2	C13 ⁹	3.467(3)	C1	F9 ⁵	3.569(3)
C1	O2 ⁵	3.348(3)	C2	F9 ⁵	3.519(3)
C2	F10 ⁵	3.261(3)	C3	F1 ¹	3.251(3)
C3	F9 ⁵	3.381(3)	C3	F10 ⁵	3.413(3)
C4	F9 ⁵	3.330(3)	C5	F2 ²	3.456(3)
C5	F7 ²	3.114(3)	C5	F9 ⁵	3.379(3)

Table 12. Intermolecular contacts less than 3.60 Å (continued)

atom	atom	distance	atom	atom	distance
C6	F7 ²	3.492(2)	C6	F9 ⁵	3.488(3)
C6	C8 ²	3.591(3)	C7	F1 ²	3.328(3)
C7	F7 ²	3.175(3)	C8	C6 ²	3.591(3)
C8	C26 ⁵	3.559(3)	C9	F8 ²	3.589(3)
C9	F10 ¹²	3.461(3)	C9	C25 ⁵	3.592(3)
C9	C26 ⁵	3.550(3)	C10	F5 ¹³	3.269(3)
C10	F10 ¹²	3.479(3)	C10	C25 ⁵	3.568(3)
C11	F3 ⁴	3.371(3)	C11	F5 ¹³	3.351(3)
C11	C22 ⁵	3.545(3)	C12	N2 ⁵	3.511(3)
C12	C27 ⁵	3.415(3)	C13	O2 ⁵	3.447(3)
C13	N2 ⁵	3.467(3)	C13	C27 ⁵	3.572(3)
C15	O1 ⁹	3.394(3)	C16	F5 ⁹	3.595(3)
C16	O1 ⁹	3.195(3)	C17	F3 ⁹	3.276(3)
C17	F4 ⁶	3.382(3)	C17	F5 ⁹	3.323(3)
C18	F3 ⁹	3.377(3)	C18	F4 ⁶	3.396(3)
C18	F5 ⁶	3.491(3)	C19	F2 ³	3.165(3)
C20	C22 ³	3.573(3)	C21	F4 ³	3.473(3)
C21	F6 ³	3.187(2)	C22	C11 ⁹	3.545(3)
C22	C20 ³	3.573(3)	C23	F4 ³	3.580(3)
C24	F6 ¹³	3.400(3)	C24	F10 ¹³	3.536(3)
C25	F9 ¹⁰	3.360(3)	C25	F10 ¹³	3.318(3)
C25	C9 ⁹	3.592(3)	C25	C10 ⁹	3.568(3)
C26	F9 ¹⁰	3.426(3)	C26	C8 ⁹	3.559(3)
C26	C9 ⁹	3.550(3)	C27	C12 ⁹	3.415(3)
C27	C13 ⁹	3.572(3)			

Symmetry Operators:

- | | |
|------------------|---------------------|
| (1) -X,-Y+1,-Z+1 | (2) -X+1,-Y+1,-Z+1 |
| (3) -X+1,-Y+2,-Z | (4) -X+1,-Y+1,-Z |
| (5) X,Y-1,Z | (6) -X,-Y+2,-Z |
| (7) X-1,Y,Z | (8) -X,-Y+2,-Z+1 |
| (9) X,Y+1,Z | (10) -X+1,-Y+2,-Z+1 |
| (11) X-1,Y+1,Z | (12) X+1,Y-1,Z |
| (13) X+1,Y,Z | |

Table 13. Intermolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
F1	H3 ¹	2.412	F1	H4 ¹	3.291
F1	H7 ²	2.547	F1	H9 ²	3.134
F2	H5 ²	2.670	F2	H7 ²	2.981
F2	H19 ³	2.378	F2	H21 ³	2.936
F3	H11 ⁴	2.523	F3	H12 ⁴	3.388
F3	H17 ⁵	3.445	F3	H17 ⁶	3.378
F3	H21 ³	3.326	F4	H4 ¹	3.343
F4	H17 ⁶	2.785	F4	H18 ⁶	2.813
F4	H21 ³	2.738	F4	H23 ³	2.878
F4	H24 ⁷	3.112	F5	H4 ¹	3.073
F5	H10 ⁷	2.771	F5	H11 ⁷	2.915
F5	H16 ⁵	3.514	F5	H17 ⁵	3.006
F5	H17 ⁶	3.362	F5	H18 ⁶	2.727
F6	H21 ³	2.377	F6	H23 ³	3.246
F6	H24 ⁷	2.486	F7	H5 ²	2.451
F7	H7 ²	2.501	F7	H19 ³	3.009
F7	H21 ³	3.494	F8	H3 ¹	3.278
F8	H7 ²	3.068	F8	H9 ²	2.798
F8	H25 ⁷	2.937	F8	H25 ⁸	3.502
F9	H25 ⁸	2.675	F9	H26 ⁸	2.836
F10	H2 ⁹	3.245	F10	H3 ⁹	3.479
F10	H9 ¹⁰	2.913	F10	H10 ¹⁰	2.956
F10	H24 ⁷	3.215	F10	H25 ⁷	2.781
O1	H16 ⁵	3.086	N1	H7 ²	3.557
N2	H12 ⁹	3.528	N2	H21 ³	3.595
C2	H3 ¹	3.010	C2	H9 ⁷	3.428
C2	H10 ⁷	3.346	C3	H2 ¹	3.191
C3	H3 ¹	3.239	C3	H9 ⁷	3.134
C4	H18 ¹¹	3.262	C4	H25 ²	3.300
C5	H19 ¹¹	3.331	C8	H26 ⁵	3.383
C9	H2 ¹²	3.431	C9	H3 ¹²	3.233
C10	H2 ¹²	3.178	C10	H16 ¹³	3.531
C11	H17 ¹³	3.551	C11	H18 ³	3.521
C12	H5 ²	3.583	C14	H17 ⁶	3.452
C14	H18 ⁶	3.378	C14	H21 ³	3.376
C15	H12 ⁹	3.446	C15	H21 ³	3.574
C16	H10 ¹⁰	3.382	C16	H24 ⁷	3.318

Table 13. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C17	H23 ⁷	3.412	C18	H4 ¹⁴	3.303
C18	H11 ³	3.516	C19	H5 ¹⁴	3.283
C20	H12 ⁹	3.528	C22	H11 ⁹	3.573
C23	H17 ¹²	3.344	C23	H23 ¹⁵	3.258
C23	H24 ¹⁵	3.543	C24	H16 ¹²	3.441
C24	H18 ³	3.585	C24	H23 ¹⁵	3.237
C25	H4 ²	3.347	C26	H5 ²	3.584
C27	H19 ³	3.563	C28	H7 ²	3.579
C28	H25 ⁷	3.408	B1	H7 ²	3.243
B2	H7 ²	3.487	B2	H21 ³	3.401
B2	H24 ⁷	3.559	H2	F10 ⁵	3.245
H2	C3 ¹	3.191	H2	C9 ⁷	3.431
H2	C10 ⁷	3.178	H2	H3 ¹	2.670
H2	H9 ⁷	3.059	H2	H10 ⁷	2.551
H2	H16 ⁵	3.449	H3	F1 ¹	2.412
H3	F8 ¹	3.278	H3	F10 ⁵	3.479
H3	C2 ¹	3.010	H3	C3 ¹	3.239
H3	C9 ⁷	3.233	H3	H2 ¹	2.670
H3	H3 ¹	3.098	H3	H9 ⁷	2.443
H4	F1 ¹	3.291	H4	F4 ¹	3.343
H4	F5 ¹	3.073	H4	C18 ¹¹	3.303
H4	C25 ²	3.347	H4	H18 ¹¹	2.450
H4	H19 ¹¹	3.456	H4	H25 ²	2.990
H5	F2 ²	2.670	H5	F7 ²	2.451
H5	C12 ²	3.583	H5	C19 ¹¹	3.283
H5	C26 ²	3.584	H5	H18 ¹¹	3.246
H5	H19 ¹¹	2.457	H5	H26 ²	3.333
H7	F1 ²	2.547	H7	F2 ²	2.981
H7	F7 ²	2.501	H7	F8 ²	3.068
H7	N1 ²	3.557	H7	C28 ²	3.579
H7	B1 ²	3.243	H7	B2 ²	3.487
H9	F1 ²	3.134	H9	F8 ²	2.798
H9	F10 ¹³	2.913	H9	C2 ¹²	3.428
H9	C3 ¹²	3.134	H9	H2 ¹²	3.059
H9	H3 ¹²	2.443	H9	H25 ⁵	3.571
H10	F5 ¹²	2.771	H10	F10 ¹³	2.956
H10	C2 ¹²	3.346	H10	C16 ¹³	3.382

Table 13. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H10	H2 ¹²	2.551	H10	H16 ¹³	2.665
H10	H17 ¹³	3.134	H11	F3 ⁴	2.523
H11	F5 ¹²	2.915	H11	C18 ³	3.516
H11	C22 ⁵	3.573	H11	H17 ¹³	2.885
H11	H18 ³	3.126	H12	F3 ⁴	3.388
H12	N2 ⁵	3.528	H12	C15 ⁵	3.446
H12	C20 ⁵	3.528	H12	H19 ³	3.408
H16	F5 ⁹	3.514	H16	O1 ⁹	3.086
H16	C10 ¹⁰	3.531	H16	C24 ⁷	3.441
H16	H2 ⁹	3.449	H16	H10 ¹⁰	2.665
H16	H24 ⁷	2.908	H17	F3 ⁹	3.445
H17	F3 ⁶	3.378	H17	F4 ⁶	2.785
H17	F5 ⁹	3.006	H17	F5 ⁶	3.362
H17	C11 ¹⁰	3.551	H17	C14 ⁶	3.452
H17	C23 ⁷	3.344	H17	H10 ¹⁰	3.134
H17	H11 ¹⁰	2.885	H17	H23 ⁷	2.918
H17	H24 ⁷	3.488	H18	F4 ⁶	2.813
H18	F5 ⁶	2.727	H18	C4 ¹⁴	3.262
H18	C11 ³	3.521	H18	C14 ⁶	3.378
H18	C24 ³	3.585	H18	H4 ¹⁴	2.450
H18	H5 ¹⁴	3.246	H18	H11 ³	3.126
H19	F2 ³	2.378	H19	F7 ³	3.009
H19	C5 ¹⁴	3.331	H19	C27 ³	3.563
H19	H4 ¹⁴	3.456	H19	H5 ¹⁴	2.457
H19	H12 ³	3.408	H21	F2 ³	2.936
H21	F3 ³	3.326	H21	F4 ³	2.738
H21	F6 ³	2.377	H21	F7 ³	3.494
H21	N2 ³	3.595	H21	C14 ³	3.376
H21	C15 ³	3.574	H21	B2 ³	3.401
H23	F4 ³	2.878	H23	F6 ³	3.246
H23	C17 ¹²	3.412	H23	C23 ¹⁵	3.258
H23	C24 ¹⁵	3.237	H23	H17 ¹²	2.918
H23	H23 ¹⁵	2.695	H23	H24 ¹⁵	2.651
H24	F4 ¹²	3.112	H24	F6 ¹²	2.486
H24	F10 ¹²	3.215	H24	C16 ¹²	3.318
H24	C23 ¹⁵	3.543	H24	B2 ¹²	3.559
H24	H16 ¹²	2.908	H24	H17 ¹²	3.488

Table 13. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H24	H23 ¹⁵	2.651	H25	F8 ¹²	2.937
H25	F8 ⁸	3.502	H25	F9 ⁸	2.675
H25	F10 ¹²	2.781	H25	C4 ²	3.300
H25	C28 ¹²	3.408	H25	H4 ²	2.990
H25	H9 ⁹	3.571	H26	F9 ⁸	2.836
H26	C8 ⁹	3.383	H26	H5 ²	3.333

Symmetry Operators:

- | | |
|-------------------|--------------------|
| (1) -X,-Y+1,-Z+1 | (2) -X+1,-Y+1,-Z+1 |
| (3) -X+1,-Y+2,-Z | (4) -X+1,-Y+1,-Z |
| (5) X,Y-1,Z | (6) -X,-Y+2,-Z |
| (7) X-1,Y,Z | (8) -X+1,-Y+2,-Z+1 |
| (9) X,Y+1,Z | (10) X-1,Y+1,Z |
| (11) X,Y-1,Z+1 | (12) X+1,Y,Z |
| (13) X+1,Y-1,Z | (14) X,Y+1,Z-1 |
| (15) -X+2,-Y+2,-Z | |

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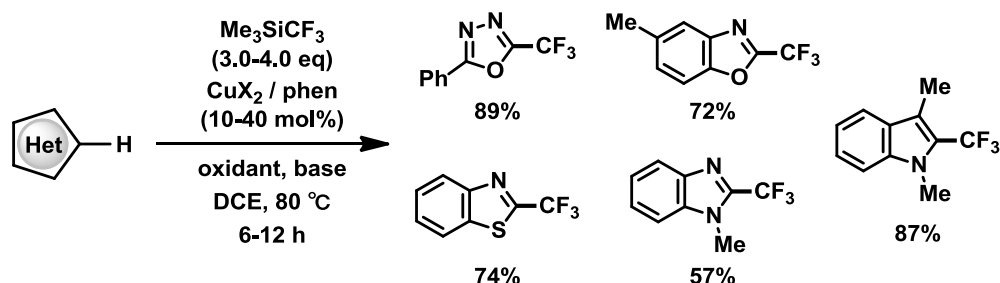
第2章 ヘテロ芳香族化合物の位置選択的トリフルオロメチル化反応

2-1 背景

トリフルオロメチル基は医薬品、農薬、機能性材料などに含まれる重要な官能基であり、特に医薬品開発においては、高い脂溶性および電子求引性を有するトリフルオロメチル基の導入により、リード化合物の物性や代謝安定性などの薬物動態パラメータの改善が期待できる¹⁾。そのため、高度に官能基化された芳香族母核に対し、トリフルオロメチル基を導入する方法は高効率的な創薬研究に非常に有用であり、その開発研究がここ数年の間に急速に進展している²⁾。従来の方法によるトリフルオロメチル基の導入は過酷な反応条件や低い基質一般性が問題であり、トリフルオロメチル基が導入されているビルディングブロックを原料とする合成に頼る必要があった^{2e)}。一般的に利用されてきた合成法としては、有機ハロゲン化物やボロン酸誘導体とトリフルオロメチル化剤を用いたクロスカップリング反応が挙げられる^{3,4)}。この場合、位置選択的に反応が進行し、望みの位置異性体のみを得ることができるが、原料である有機ハロゲン化物やボロン酸誘導体の合成に多段階を必要とする点、化学量論量の金属廃棄物が副生成物として生じる点が課題である。

近年、これらの課題を解決する方法として、C-H結合活性化によるトリフルオロメチル化が注目されており、芳香族化合物C-H結合のトリフルオロメチル化が活発に研究されている⁵⁻⁷⁾。C-H結合活性化による位置選択的なトリフルオロメチル化として、ピリジンなどのヘテロ芳香環やアミド基を配向基として用いた例が報告されている⁵⁾。配向基を用いた方法は高い位置選択性でトリフルオロメチル化を可能とする有用な方法であるが、最終的に不要となる配向基の除去が必要である点が課題である。

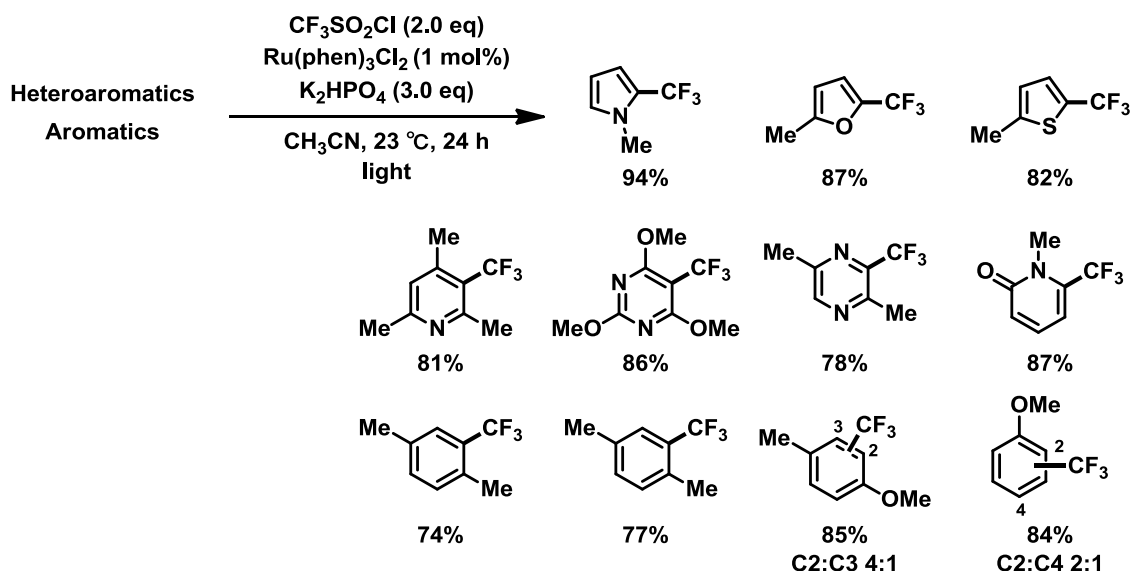
配向基を用いない例として、Qingらは、トリフルオロメチル銅を活性種とした、酸性度の高い5員環ヘテロ芳香族化合物の2位C-H結合の酸化的トリフルオロメチル化を報告している(Scheme 2-1)^{6e)}。ヘテロ芳香環の種類により最適な触媒系、酸化剤、および塩基が異なるが、種々のヘテロ芳香環に適用可能であり、基質の活性化を必要としない有用な方法である。



Scheme 2-1. Oxidative trifluoromethylation of various 5-membered heterocycles

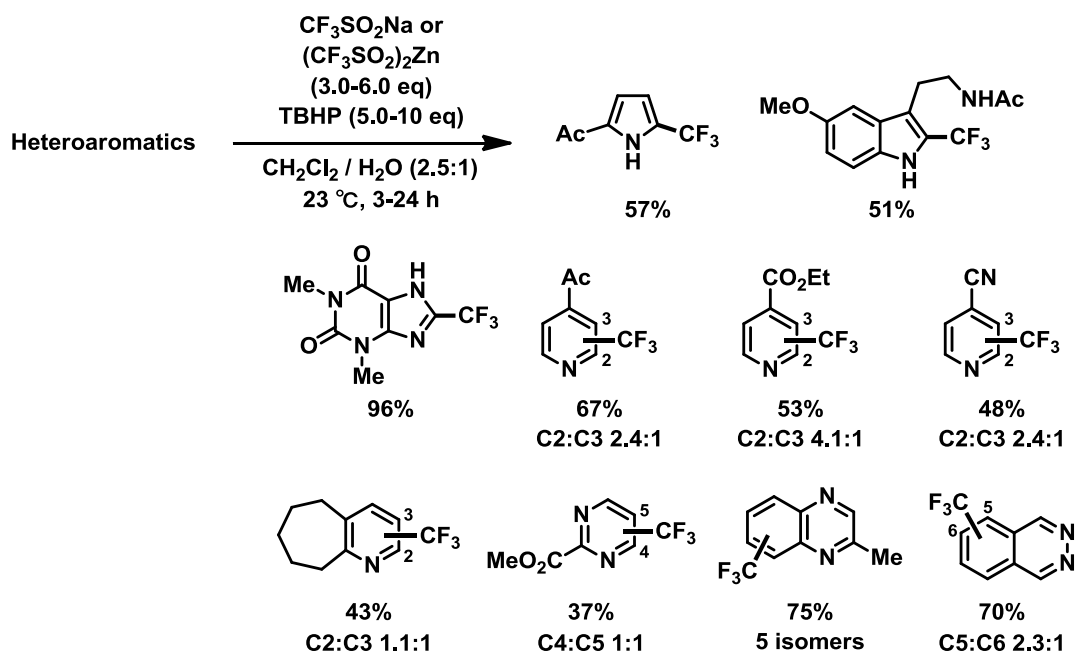
さらに別のアプローチとしては、反応性の高いトリフルオロメチルラジカルを用いた

C-H 結合の直接的なトリフルオロメチル化が報告されている⁷⁾。MacMillan らは光触媒を用いた種々のヘテロ芳香族化合物や芳香族化合物のトリフルオロメチル化を報告している (Scheme 2-2)^{7b)}。発生するトリフルオロメチルラジカルは求電子的であるため、5員環ヘテロ芳香族化合物においては2位、6員環の芳香族化合物ではより電子密度の高い位置で反応が進行する。5員環ヘテロ芳香族化合物の反応では高い位置選択性を示すが、6員環芳香族化合物の反応における位置選択性は基質の構造に大きく依存しており、単一の生成物としてトリフルオロメチル化体を得るには、置換基によりいくつかある反応部位のうち望みの反応点以外をブロックすることが必要となる。ピリジン誘導体は電子不足なヘテロ芳香環であるため、求電子的なトリフルオロメチルラジカルとの反応性は高くないと考えられる。相対的に最も求核的である3位で反応する傾向があるが、電子供与性置換基により環上の電子密度を高めるとともに、他の反応部位をブロックしていることがうかがえ、6員環ヘテロ芳香族化合物の位置選択的トリフルオロメチル化は課題であるといえる。



Scheme 2-2. Electrophilic radical trifluoromethylation by photoredox catalyst

その後、Baran らによっても求電子的トリフルオロメチルラジカルを用いた、ヘテロ芳香族化合物のトリフルオロメチル化が報告されている (Scheme 2-3)^{7c,d)}。MacMillan らの方法と同様に、5員環ヘテロ芳香族化合物の反応においては高い位置選択性を示し、天然物や医薬品の官能基化が可能である。一方で、ピリジンを代表とする6員環ヘテロ芳香族化合物の反応においては、多くの場合において位置異性体の混合物として得られることが報告されている。



Scheme 2-3. Electrophilic radical trifluoromethylation of several heteroaromatics

以上のように、既存の方法によるピリジンをはじめとする 6 員環ヘテロ芳香族化合物の位置選択的なトリフルオロメチル化は困難であり、そのような反応の実現は重要な課題である。2 位にトリフルオロメチル基を有するピリジンやキノリン誘導体は、医薬品や農薬として有用な化合物群であり、種々のヘテロ芳香族化合物に適応可能な合成法の開発により、効率的な創薬研究が可能になると考えられる(Figure 2-1)^{2e)}。

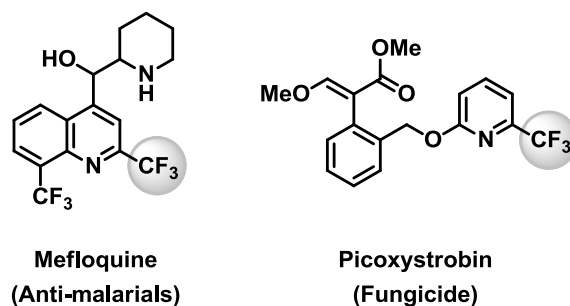
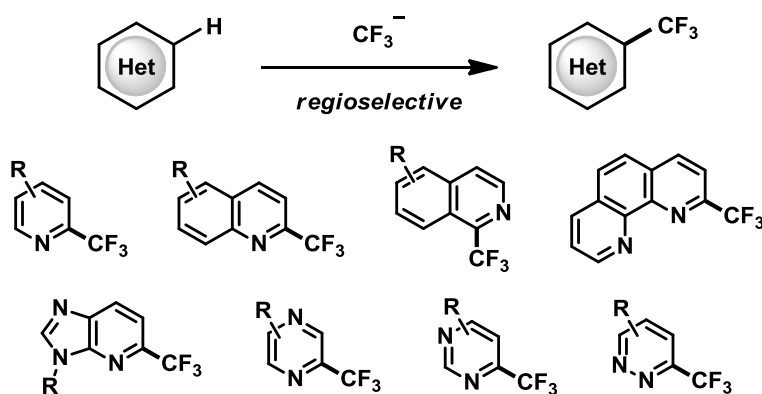


Figure 2-1. 2-Trifluoromethylated heteroaromatics as drugs and agrochemicals

2-2 位置選択的トリフルオロメチル化反応の設計と反応条件の最適化

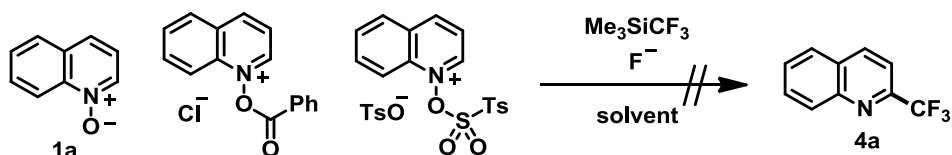
既存の方法における課題は低い位置選択性であり、これは高い反応性を有するトリフルオロメチルラジカルを活性種として用いることに起因している。そこで、求電子的に活性化されたヘテロ芳香族化合物に対する、脱芳香族化を伴う求核付加反応によるトリフルオロメチル基の導入を設計した(Scheme 2-4)⁸⁾。近年、求電子的なトリフルオロメチル化剤を

用いた反応が数多く報告されているが、試薬が高価で、爆発性の懸念が報告されている試薬もあることが課題として挙げられる⁹⁾。求核的なトリフルオロメチル化剤を用いることで、工業的にも応用可能な実用的な反応になりうると考えた。



Scheme 2-4. Our goal: regioselective trifluoromethylation of various heteroaromatics

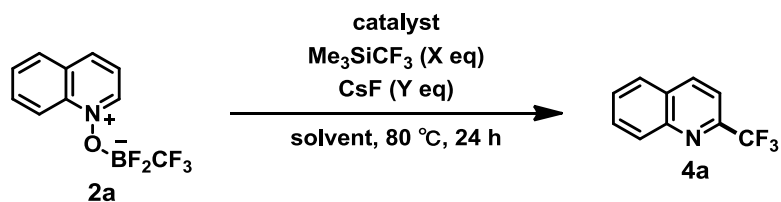
初期検討として、求電子的に活性化されたキノリン誘導体を用いた 2 位選択的トリフルオロメチル化を選択した。求核的なトリフルオロメチル化剤としては比較的安価な Ruppert-Prakash 試薬 (Me_3SiCF_3) を、その活性化剤としてはフッ化カリウム、フッ化セシウム、およびフッ化テトラブチルアンモニウムを用いて検討を行ったが、目的の反応は進行しなかった (Scheme 2-5)。その原因としては、トリフルオロメチルアニオンの求核性が低いためであると考えられる。



Scheme 2-5. Initial trials for the trifluoromethylation of quinoline derivatives

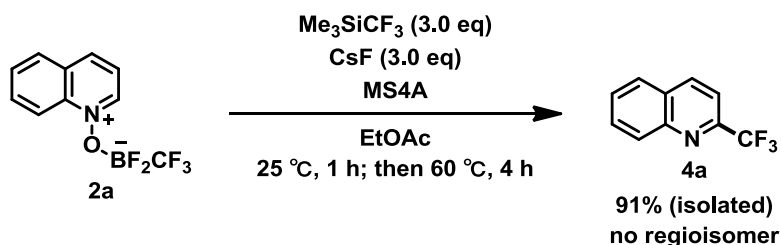
求電子性が高い活性化体であることが示唆されたキノリン *N*-オキシド- BF_2CF_3 錯体 (**2a**) を用いて、求核的トリフルオロメチル化を検討した (Table 2-1)¹⁰⁾。活性種としてトリフルオロメチル銅を用いた報告例を参考に、銅触媒存在下、 Me_3SiCF_3 およびフッ化セシウムを用いた条件で反応を行ったところ、42%の収率で目的物 (**4a**) が得られた (entry 1)。興味深いことに、本反応においては銅触媒による活性化が必要ないことがわかり、基質の求電子性が非常に高いことが示唆された (entry 2)。試薬の当量と溶媒を検討した結果、酢酸エチル中での反応が最も収率が高く、副生成物が少ないことがわかった (entry 4)。

Table 2-1. Optimization of reaction conditions



entry	catalyst	Me ₃ SiCF ₃ (X eq)	CsF (Y eq)	solvent	yield (¹ H NMR)
1	CuCl + phen (20 mol%)	3.0	1.5	THF	42
2	none	3.0	1.5	THF	45
3	none	2.0	3.0	THF	81
4	none	2.0	3.0	EtOAc	82
5	none	2.0	3.0	DCE	81
6	none	2.0	3.0	DMF	76
7	none	2.0	3.0	dioxane	70
8	none	2.0	3.0	MeCN	69
9	none	2.0	3.0	NMP	69
10	none	2.0	3.0	DME	53
11	none	2.0	3.0	toluene	22
12	none	2.0	3.0	DMSO	9

最適化した反応条件を Scheme 2-6 に示す。Table 2-1, entry 4 の反応条件をもとに、添加剤として MS4A を用い、25 °C で 1 時間、昇温して 60 °C で 4 時間加熱攪拌することにより、収率が 91% に向上した。本反応では、他の位置異性体は確認されておらず、高い位置選択性を実現することができた。



Scheme 2-6. Optimized conditions for the introduction of the CF₃ group

最適化条件を用いて、他の活性化体を用いて比較検討を行ったところ、キノリン *N*-オキシド-BF₃ 錯体(5)からは 45%、トシル酸無水物による活性化体(6)やキノリン *N*-オキシド(1a)

からは痕跡量の目的物しか得られなかった(Figure 2-2)。この結果より、トリフルオロメチル化反応の収率はLUMOエネルギー準位より見積もった種々の活性化体の求電子性の高さに相関しているといえる。

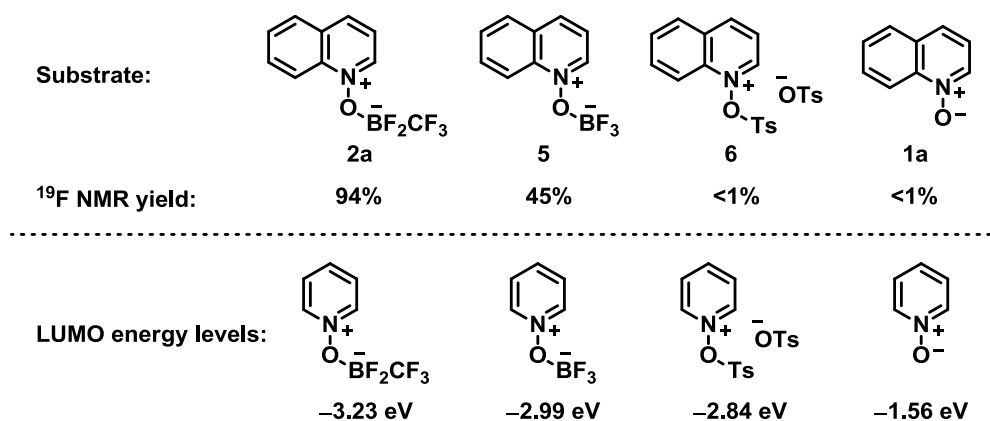


Figure 2-2. Comparison of yields and LUMO energy levels under optimized conditions

2-3 基質一般性

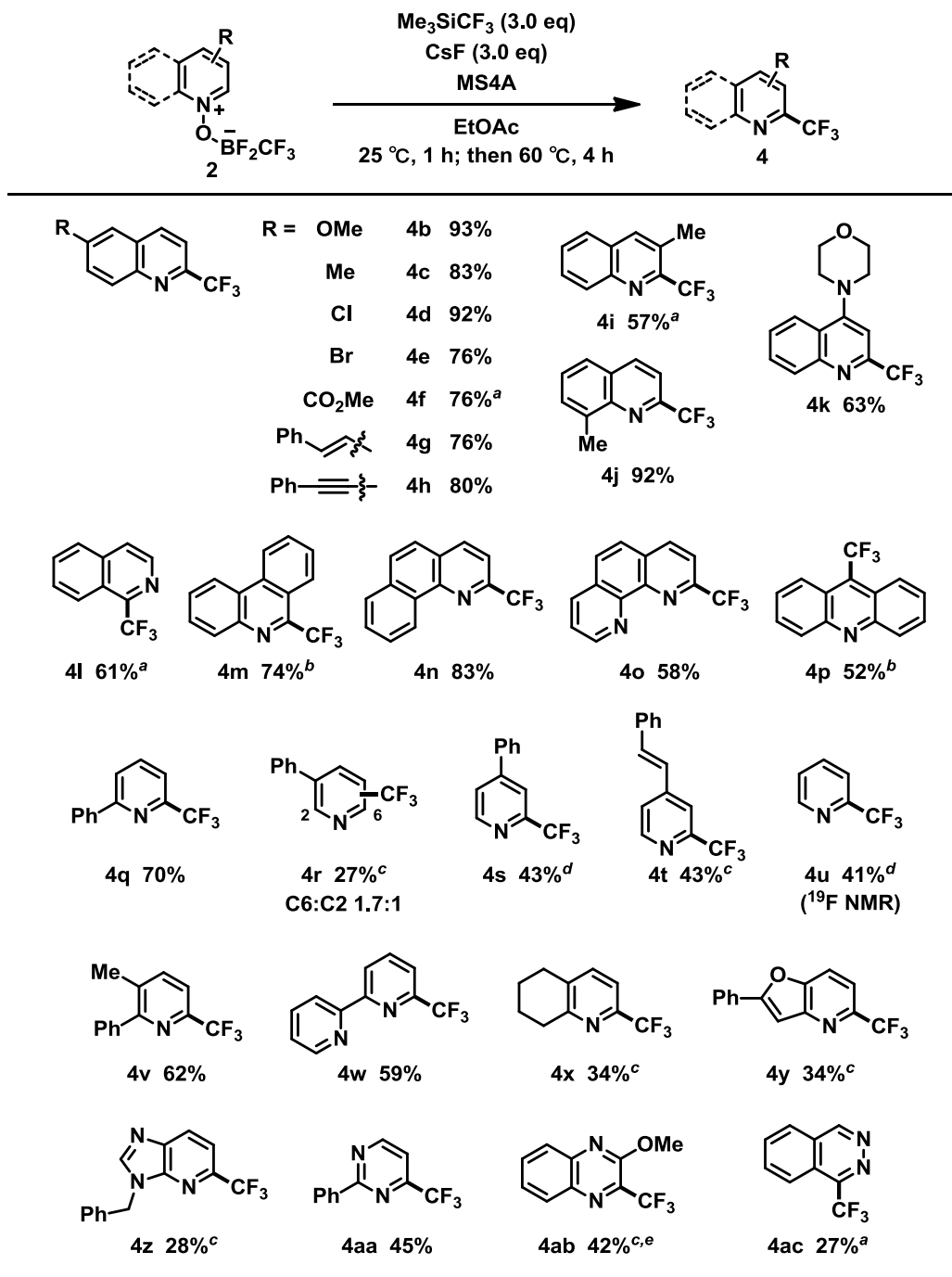
電子供与性および電子求引性の種々の置換基を有するトリフルオロメチル化されたキノリン誘導体(4b-4k)が、良好な収率、高い位置選択性、および高い官能基許容性で得られた(Table 2-2)。同様の方法にて、イソキノリン誘導体 4l、フェナンスリジン誘導体 4m、ベンゾ[h]キノリン誘導体 4n、フェナントロリン誘導体 4o、アクリジン誘導体 4p が良好な収率、高い位置選択性にて得られた。本反応は、最も電子密度が低い位置で反応が進行するため、イソキノリン誘導体は1位、アクリジン誘導体は9位において反応が進行する。実際に、¹H NMR 測定より、それぞれの原料である 2l の1位、および、4p の9位のプロトンは、最も低磁場に観測されることを確認している。化合物 4m および 4p の反応においては、トリフルオロメチル基の付加体からの再芳香族化を促進するため、塩酸/メタノール溶液による後処理により、良好な収率で目的物が得られることがわかった。

種々の置換基を有するピリジン誘導体(4q-4w)、縮環ピリジン誘導体(4x-4z)、ピリミジン誘導体 4aa、キノキサリン誘導体 4ab、およびフタラジン誘導体 4ac についても、高い位置選択性にて目的とするトリフルオロメチル化体が得られた。第1章で示したように、ヘテロ芳香族化合物 N-オキシド誘導体と求核剤との反応においては、キノリン誘導体に比べてピリジン誘導体は反応性が低いため、中程度の収率で反応が進行していると考えられる。

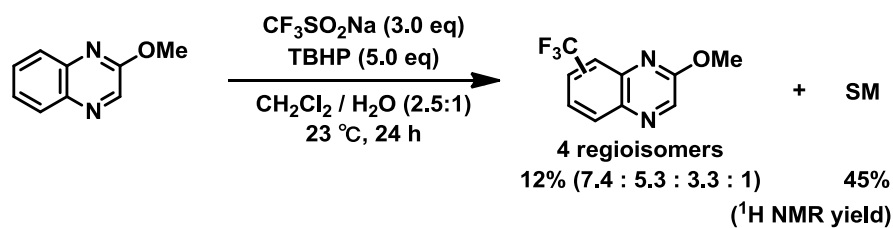
キノキサリン誘導体 4ab の反応においては、シリカゲルカラム精製による原料 2ab の単離が行えないため、ヘキサン/ジクロロメタン溶液による洗浄で精製した原料を用いて反応を行った。対照実験として Baran らによる求電子的トリフルオロメチル化を行った結果、トリフルオロメチル化生成物が4種類の位置異性体の混合物として得られることがわかつ

た(Scheme 2-7)。今回見出した方法においては、他の位置異性体は GC/MS 解析により観測されないことを確認しており、有用な合成法であるといえる。

Table 2-2. Trifluoromethylation reactions of several heterocyclic *N*-oxide-BF₂CF₃ complexes



^a 25 °C, 1 h; then 60 °C, 24 h. ^b After trifluoromethylation, the reaction mixture was treated with aq. HCl/MeOH. ^c Me₃SiCF₃ (5.0 eq), CsF (5.0 eq). ^d 25 °C, 24 h. ^e Trifluoromethylation was conducted without isolation of an *N*-oxide-BF₂CF₃ complex.



Scheme 2-7. Control experiment under Baran's conditions

一方で、Figure 2-3 に示すイミダゾール *N*-オキシド- BF_2CF_3 錯体を原料とした反応においては、トリフルオロメチル化体が全く得られなかった。その原因としては、イミダゾール環は 6 員環ヘテロ芳香環とは異なり電子不足な環ではないため、 BF_2CF_3 基による活性化体であっても、求核性の低いトリフルオロメチルアニオンとの反応が可能なほど求電子性が高くないことが考えられる。

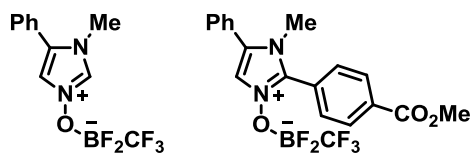
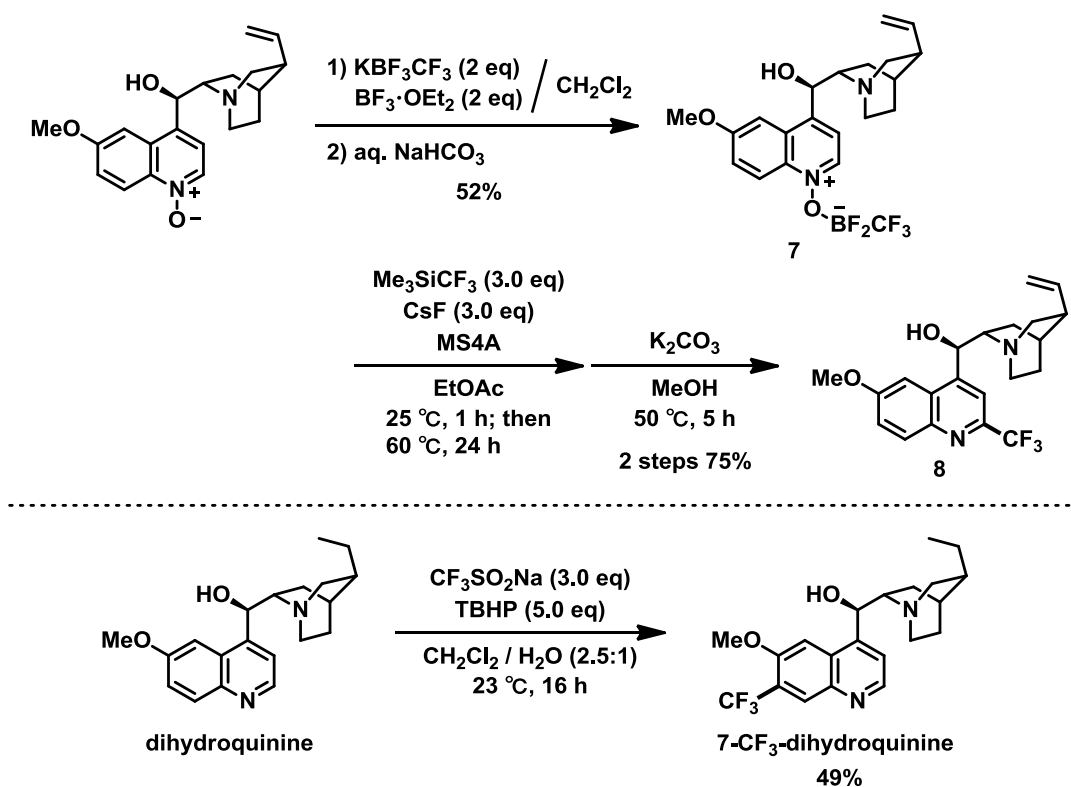


Figure 2-3. Structures of imidazole *N*-oxide- BF_2CF_3 complexes

高度に官能基化された基質への応用例として、キニーネのトリフルオロメチル化反応の検討を行った(Scheme 2-8)。定法に従い、2当量の $\text{BF}_2\text{CF}_3 \cdot \text{OEt}_2$ を用いることでキニーネ *N*-オキシド- BF_2CF_3 錯体 **7** を 52% の収率で得た。キヌクリジン部位に結合した BF_2CF_3 基は、重曹水溶液を用いた分液処理により除去可能であり、化合物 **7** も他のヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体と同様に、シリカゲルカラム精製による単離が可能であった。最適化した条件によるトリフルオロメチル化の後、反応により導入された水酸基上のトリメチルシリル基を除去することにより、2-トリフルオロメチルキニーネ **8** が 75% の収率で得られた。Baran らによって報告されている、求電子的トリフルオロメチルラジカルを用いた反応では、ジヒドロキニーネの 7 位トリフルオロメチル体が得られる⁷⁶⁾。今回見出した反応では 2 位選択的に求核的な反応が可能であるため、相補的で有用な合成法であるといえる。

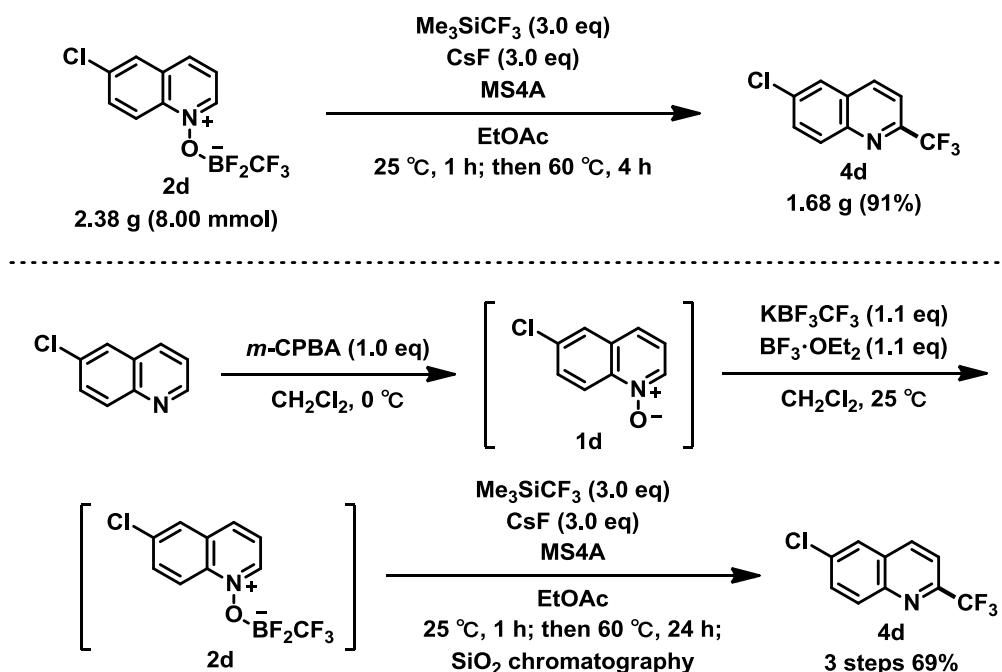


Scheme 2-8. Trifluoromethylation reactions of quinine derivatives

2-4 実用化に向けた合成検討

6-クロロキノリン *N*-オキシド- BF_2CF_3 錯体 **2d** を用いて、グラムスケールで反応を行ったところ、0.25 mmol (74.4 mg) スケールと同等の収率でトリフルオロメチル化生成物 **4d** が得られた(Scheme 2-9)。また、6-クロロキノリンを出発物質とし、*m*-CPBA による酸化、 BF_2CF_3 錯体への変換、2 位トリフルオロメチル化の 3 工程を、中間体をシリカゲルカラム

精製することなく行った。その結果、収率をあまり損なうことなく、目的物 **4d** が得られることを確認しており、医薬品製造にも適用可能な実用的な合成法であるといえる。



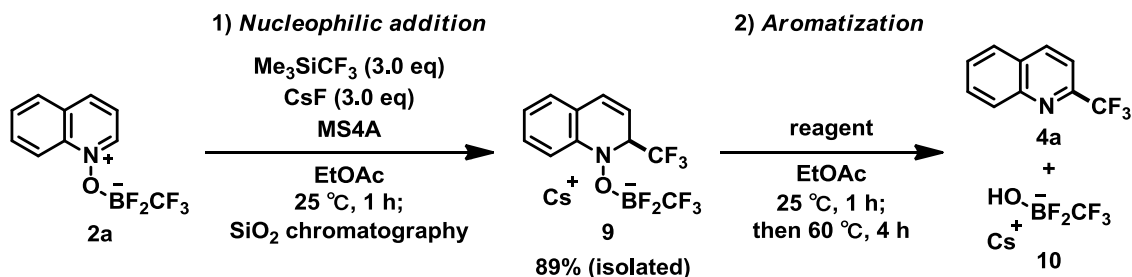
Scheme 2-9. Scale-up and sequential operation studies

2-5 推定反応機構

本反応は脱芳香族化を伴うトリフルオロメチルアニオンの求核付加ののち、再芳香族化することにより進行していることが確認された (Table 2-3)。キノリン *N*-オキシド- BF_2CF_3 錯体 **2a** を用いた反応では、1段階目の求核付加は室温、1時間で完了し、良好な収率で付加体 **9** が得られた。興味深いことに、付加体 **9** はシリカゲルカラム精製による単離が可能であり、 ^1H 、 ^{19}F 、 ^{11}B NMR により構造を決定した。

単離した付加体を用いて、2段階目の再芳香族化を検討した。最適化したトリフルオロメチル化条件を適用したところ、良好な収率で目的物 **4a** が得られたことから、本付加体を經由して反応が進行していることが確認できた (entry 1)。一方、再芳香族化はトリメチルシリルトリフルオロメタンやフッ化セシウム単独ではほとんど進行しなかった (entries 2 and 3)。そのため、系中で発生するフルオロトリメチルシランがルイス酸として作用することにより再芳香族化が促進していると考えられる。これを支持する実験として、フルオロトリフェニルシランを用いることにより、触媒的に再芳香族化が進行することを確認している (entries 4 and 5)。また、反応溶液の ^{19}F NMR による解析により、目的物 **4a** と等量のボレート塩 **10** が生成していることが確認できた。

Table 2-3. Proposed reaction mechanism



entry	reagent	^{19}F NMR yield (isolated yield)
1	Me_3SiCF_3 (3.0 eq), CsF (3.0 eq), MS4A	89% (79%)
2	Me_3SiCF_3 (3.0 eq)	trace
3	CsF (3.0 eq)	11%
4	Ph_3SiF (3.0 eq)	82%
5	Ph_3SiF (0.30 eq)	92%

2-6 小括

ボラン BF_2CF_3 による活性化により、種々の 6 員環ヘテロ芳香族化合物の位置選択的なトリフルオロメチル化を達成した。反応は BF_2CF_3 基により求電子的に活性化された基質に対する脱芳香族化をともなうトリフルオロメチルアニオンの求核付加ののち、ボレート塩の脱離をともなう再芳香族化により進行することが確認できた。本反応は遷移金属触媒を必要とせず、温和な条件下、高い位置選択性、および高い官能基許容性で進行する。また、グラムスケールにおいても反応は進行し、中間体を単離することなくヘテロ芳香環の酸化、 BF_2CF_3 基による活性化、トリフルオロメチル化の 3 工程を行うことが可能である。既存の求電子的トリフルオロメチルラジカルを用いた方法と相補的な特徴を有しており、二つの方法を使い分けることにより、種々のヘテロ芳香族化合物の位置選択的なトリフルオロメチル化が可能になったといえる。

Experimental

General. All reactions were carried out in a dry solvent under an argon atmosphere. Ethyl acetate was purchased, dried and stored with activated molecular sieves 4A before use. All reagents were purchased from commercial sources and used without further purification unless otherwise noted. Quinine *N*-oxide were prepared according to the literature methods and identified by comparing these spectroscopic data with those of reported data^{8b}). The known target materials **4b**¹¹), **4c**¹²), **4d**¹²), **4l**¹³), **4p**¹⁴), **4r**¹⁵), and **4s**¹⁶) were identified by comparing these spectroscopic data with those of reported

data. Column chromatography was performed with silica gel (230-400 mesh ASTM). NMR spectra were recorded on JEOL JNM-ECX500 (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) and JEOL JNM-ECS400 (400 MHz for ^1H NMR, 125 MHz for ^{13}C NMR, 368 MHz for ^{19}F NMR, and 125 MHz for ^{11}B NMR) spectrometers. Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. Fluorine and boron chemical shifts are reported relative to trifluoroacetic acid (δ -76.55 ppm) and $\text{BF}_3\cdot\text{OEt}_2$ (δ 0.00 ppm) as an external reference, respectively. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. ESI-MS spectra and DART-MS spectra were measured on a JEOL JMS-T100LC AccuTOF spectrometer for HRMS.

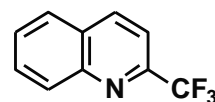
General procedure for the preparation of 2-trifluoromethylated *N*-heteroaromatics.

A mixture of CsF (3.65 g, 24.0 mmol, 3.0 equiv) and MS4A (800 mg, 100 mg/mmol) was flame-dried under vacuum. After cooling to room temperature, ((6-chloroquinolin-1-ium-1-yl)oxy)difluoro(trifluoromethyl)borate (2.38 g, 8.00 mmol) and ethyl acetate (80 mL) were added. To the mixture, Me_3SiCF_3 (3.56 mL, 24.0 mmol, 3.0 equiv) was added dropwisely with vigorous stirring. After stirring at 25 °C for 1 h, the mixture was heated at 60 °C for 4 h, and then cooled to room temperature. Insoluble solid was filtered off, washed with ethyl acetate, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to give 6-chloro-2-(trifluoromethyl)quinoline (**4d**, 1.68 g, 91% yield).

Technical note for the preparation of 2-trifluoromethylated *N*-heteroaromatics.

When Me_3SiCF_3 was added along the lateral wall of a glassware, the yields of 2-trifluoromethylated products were decreased slightly maybe due to the decomposition of Me_3SiCF_3 by CsF on the wall. Therefore, it would be better to add Me_3SiCF_3 directly to the reaction mixture. All reactions were carried out in 0.250 mmol scale unless otherwise noted.

2-(Trifluoromethyl)quinoline (4a). 91%; white solid; R_f = 0.61 (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.69 (dd, J = 8.1, 8.1 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.80-7.87 (m, 1H), 7.92 (d, J = 8.1 Hz, 1H), 8.24 (d, J = 8.1 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 116.9 (q, J = 1.9 Hz), 121.7 (q, J = 275 Hz), 127.8, 128.7, 129.0, 130.2, 131.0, 138.3, 147.3, 148.0 (q, J = 34.8 Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -68.3 (s, 3F); IR (KBr, ν

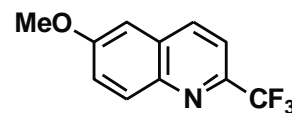


/ cm^{-1}) 2925, 1619, 1599, 1575, 1509, 1478, 1434, 1119, 945, 887; HRMS (DART) Calcd for $\text{C}_{10}\text{H}_7\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 198.0525, Found 198.0533.

6-Methoxy-2-(trifluoromethyl)quinoline (4b). 93% yield; yellow

solid; $R_f = 0.53$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 3.96 (s, 3H), 7.12 (d, $J = 1.8$ Hz, 1H), 7.46 (m, 1H), 7.68

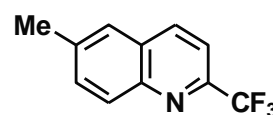
(d, $J = 8.5$ Hz, 1H), 8.10 (d, $J = 9.0$ Hz, 1H), 8.21 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 55.7, 104.8, 117.2 (q, $J = 2.4$ Hz), 121.9 (q, $J = 275$ Hz), 124.1, 130.4, 131.6, 136.5, 143.4, 145.5 (q, $J = 34.4$ Hz), 159.4; ^{19}F NMR (368 MHz, CDCl_3) δ -69.0 (s, 3F).



6-Methyl-2-(trifluoromethyl)quinoline (4c). 75% yield; white

solid; $R_f = 0.63$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 2.58 (s, 3H), 7.66 (m, 2H), 7.70 (d, $J = 8.5$ Hz, 1H), 8.12

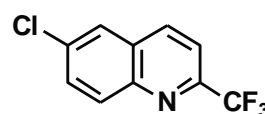
(d, $J = 9.4$ Hz, 1H), 8.26 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.8, 116.8 (q, $J = 2.4$ Hz), 121.8 (q, $J = 275$ Hz), 126.5, 129.0, 129.8, 133.3, 137.4, 139.0, 145.9, 147.1 (q, $J = 34.4$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -69.2 (s, 3F).



6-Chloro-2-(trifluoromethyl)quinoline (4d). 92% yield; white solid;

$R_f = 0.68$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 8.5$ Hz, 2H), 7.90 (s, 1H), 8.17 (d, $J = 9.0$ Hz, 1H),

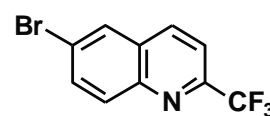
8.28 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 117.9 (q, $J = 2.2$ Hz), 121.5 (q, $J = 275$ Hz), 126.4, 129.5, 131.8, 132.1, 134.8, 137.4, 145.7, 148.3 (q, $J = 35.1$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -69.5 (s, 3F).



6-Bromo-2-(trifluoromethyl)quinoline (4e). 76% yield; white solid;

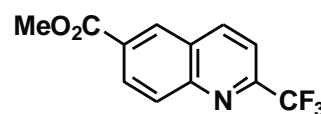
$R_f = 0.70$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.77 (d, $J = 8.5$ Hz, 1H), 7.90 (dd, $J = 8.5, 2.2$ Hz, 1H), 8.09 (s,

1H), 8.10 (d, $J = 9.0$ Hz, 1H), 8.28 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 117.8 (q, $J = 2.2$ Hz), 121.5 (q, $J = 275$ Hz), 123.1, 129.9, 129.9, 131.8, 134.6, 137.3, 145.8, 148.4 (q, $J = 35.1$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -68.5 (s, 3F); IR (KBr, ν / cm^{-1}) 1610, 1493, 1341, 1202, 1184, 1134, 1088, 950, 836, 745; HRMS (DART) Calcd for $\text{C}_{10}\text{H}_6\text{BrF}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 275.9630, Found 275.9628.



Methyl 2-(trifluoromethyl)quinoline-6-carboxylate (4f). 76%

yield; white solid; $R_f = 0.79$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 4.02 (s, 3H), 7.82 (d, $J = 8.5$ Hz, 1H),

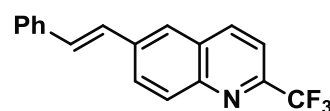


8.28 (d, $J = 9.0, 2.2$ Hz, 1H), 8.41 (dd, $J = 9.0, 1.8$ Hz, 1H), 8.49 (d, $J = 8.5$ Hz, 1H), 8.68 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 52.7, 117.6, 121.3 (q, $J = 275$ Hz), 128.0, 130.0, 130.2, 130.5, 130.7, 139.5, 148.9, 149.9, (q, $J = 34.8$ Hz), 166.1; ^{19}F NMR (368 MHz, CDCl_3) δ -69.6 (s, 3F); IR (KBr, ν / cm^{-1}) 1723, 1437, 1341, 1269, 1202, 1084, 990, 953, 833, 759; HRMS (DART) Calcd for $\text{C}_{12}\text{H}_9\text{F}_3\text{NO}_2^+$ $[\text{M}+\text{H}^+]$ 256.0580, Found 256.0580.

(E)-6-Styryl-2-(trifluoromethyl)quinoline (4g). 76% yield;

yellow solid; $R_f = 0.72$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.35 (m, 3H), 7.39-7.42 (m, 2H),

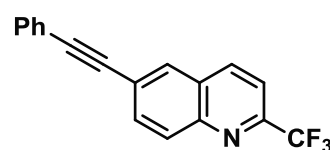
7.57-7.59 (m, 2H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.89 (s, 1H), 8.09 (dd, $J = 8.8, 2.2$ Hz, 1H), 8.21 (d, $J = 8.8$ Hz, 1H), 8.33 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 117.4 (q, $J = 2.4$ Hz), 121.8 (q, $J = 275$ Hz), 125.6, 127.0, 127.4, 128.5, 128.8, 129.0, 129.4, 130.5, 131.7, 136.8, 137.8, 137.9, 147.1, 147.6 (q, $J = 34.4$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -69.3 (s, 3F); IR (neat, ν / cm^{-1}) 1506, 1341, 1176, 1118, 1087, 960, 835, 754, 690, 634; HRMS (DART) Calcd for $\text{C}_{18}\text{H}_{13}\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 300.0995, Found 300.1002.



6-(Phenylethynyl)-2-(trifluoromethyl)quinoline (4h). 80%

yield; yellow solid; $R_f = 0.70$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.40 (m, 3H), 7.58-7.60 (m, 2H), 7.76 (d, $J = 8.5$ Hz, 1H), 7.92 (dd, $J = 9.0, 1.8$ Hz, 1H),

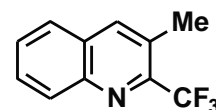
8.03 (s, 1H), 8.20 (d, $J = 9.0$ Hz, 1H), 8.33 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 88.6, 92.2, 117.6 (q, $J = 2.4$ Hz), 121.6 (q, $J = 275$ Hz), 122.7, 124.0, 128.6, 128.8, 129.0, 130.3, 130.8, 131.9, 133.6, 137.8, 146.6, 148.4 (q, $J = 34.8$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -69.4 (s, 3F); IR (neat, ν / cm^{-1}) 1497, 1348, 1193, 1176, 1087, 918, 893, 849, 689, 635; HRMS (DART) Calcd for $\text{C}_{18}\text{H}_{11}\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 298.0838, Found 298.0851.



3-Methyl-2-(trifluoromethyl)quinoline (4i). 57% yield; white solid; $R_f =$

0.71 (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 2.64 (q, $J = 0.9$ Hz, 3H), 7.60-7.64 (m, 1H), 7.71-7.75 (m, 1H), 7.80 (d, $J = 8.1$

Hz, 1H), 8.07 (s, 1H), 8.17 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 18.4 (q, $J = 3.2$ Hz), 122.3 (q, $J = 276$ Hz), 126.9, 128.3, 128.8, 129.2, 129.9, 130.0, 139.2, 145.1, 146.8 (q, $J = 32.4$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -67.8 (s, 3F); IR (KBr, ν / cm^{-1}) 1721, 1601, 1566, 1494, 1319, 1125, 1034, 910, 872, 761; HRMS (DART) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 212.0682, Found 212.0689.

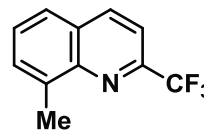


8-Methyl-2-(trifluoromethyl)quinoline (4j). 92% yield; white solid; $R_f =$

0.71 (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.84 (s, 1H), 7.55 (d, $J = 7.2$ Hz, 1H), 7.66 (d, $J = 7.2$ Hz, 1H), 7.72 (dd, $J = 8.3,$

8.1 Hz, 1H), 7.73 (d, $J = 8.1$ Hz, 1H), 8.31 (d, $J = 8.3$ Hz, 1H); $^{13}\text{C NMR}$

(125 MHz, CDCl_3) δ 17.8, 116.6 (q, $J = 2.4$ Hz), 121.9 (q, $J = 275$ Hz), 125.6, 128.5, 129.0, 130.8, 138.2, 138.6, 146.5, 146.8 (q, $J = 34.4$ Hz); $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -69.3 (s, 3F); IR (neat, ν / cm^{-1}) 1475, 1337, 1305, 1250, 1185, 1136, 1101, 886, 838, 764; HRMS (DART) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3\text{N}^+$ [$\text{M}+\text{H}^+$] 212.0682, Found 212.0691.



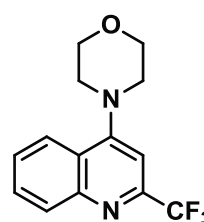
4-(2-(Trifluoromethyl)-4-quinolinyl)morpholine (4k). 63% yield; yellow

solid; $R_f = 0.66$ (ethyl acetate); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.31 (t, $J = 4.6$ Hz, 4H), 4.01 (t, $J = 4.6$ Hz, 4H), 7.15 (s, 1H), 7.60 (dd, $J = 7.6,$

7.6 Hz, 1H), 7.74-7.78 (m, 1H), 8.05 (d, $J = 8.3$ Hz, 1H), 8.18 (d, $J = 8.3$ Hz, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 52.7, 66.9, 104.4 (m), 121.8 (q,

$J = 276$ Hz), 123.7, 123.7, 127.4, 130.4, 131.0, 148.8, 148.9 (q, $J = 34.0$

Hz), 158.7; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -69.6 (s, 3F); IR (neat, ν / cm^{-1}) 2965, 1579, 1508, 1403, 1296, 1097, 946, 873, 776, 719; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_{14}\text{F}_3\text{N}_2\text{O}^+$ [$\text{M}+\text{H}^+$] 283.1053, Found 283.1055.

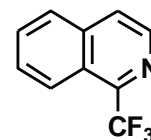


1-(Trifluoromethyl)isoquinoline (4l). 61%; colorless oil; $R_f = 0.58$

(hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.73 (dd, $J = 8.0,$

8.0 Hz, 1H), 7.79 (dd, $J = 8.0, 8.0$ Hz, 1H), 7.86 (d, $J = 5.4$ Hz, 1H), 7.94 (d, $J = 8.0$ Hz, 1H), 8.31 (d, $J = 8.0$ Hz, 1H), 8.60 (d, $J = 5.4$ Hz, 1H); $^{13}\text{C NMR}$

(125 MHz, CDCl_3) δ 122.4 (q, $J = 276$ Hz), 124.7, 124.8 (q, $J = 2.4$ Hz), 124.8, 127.6, 129.0, 131.0, 137.3, 140.8, 146.5 (q, $J = 33.2$ Hz); $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -63.9 (s, 3F).



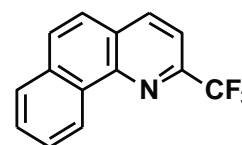
2-(Trifluoromethyl)benzo[*b*]quinoline (4n). 83%; white solid; $R_f =$

0.62 (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.70

(d, $J = 8.6$ Hz, 1H), 7.72-7.80 (m, 2H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.89

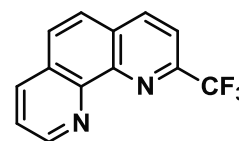
(d, $J = 8.0$ Hz, 1H), 7.90-7.94 (m, 1H), 8.30 (d, $J = 8.0$ Hz, 1H), 9.35

(dd, $J = 8.0, 1.7$ Hz, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 117.7 (q, $J = 2.4$ Hz), 122.0 (q, $J = 273$ Hz), 124.6, 125.0, 127.7, 127.8, 128.0, 129.2, 130.1, 131.3, 134.0, 137.3, 146.1, 146.5 (q, $J = 34.6$ Hz); $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -67.9 (s, 3F); IR (KBr, ν / cm^{-1}) 1339, 1278, 1182, 1131, 1109, 1079, 848, 796, 762, 669; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{N}^+$ [$\text{M}+\text{H}^+$] 248.0682, Found 248.0689.



2-(Trifluoromethyl)-1,10-phenanthroline (4o). 58%; white solid; $R_f =$

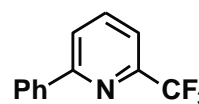
0.35 (hexane/ethyl acetate = 1/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.67 (dd, $J = 8.1, 4.5$ Hz, 1H), 7.81 (d, $J = 8.8$ Hz, 1H), 7.87 (d, $J = 8.8$ Hz, 1H), 7.95 (d, $J = 8.5$ Hz, 1H), 8.25 (dd, $J = 8.1, 1.8$ Hz, 1H), 8.40 (d, $J = 8.5$ Hz, 1H), 9.26 (dd, $J = 4.5, 1.8$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 119.2 (q, $J = 2.4$ Hz), 121.8 (q, $J = 275$ Hz), 123.8, 125.9, 129.0, 129.3, 129.9, 136.3, 138.0, 145.7, 145.9, 147.9 (q, $J = 35.3$ Hz), 151.2; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -67.3 (s, 3F); IR (neat, ν / cm^{-1}) 2965, 1560, 1496, 1456, 1397, 1339, 1290, 1179, 1118, 883; HRMS (DART) Calcd for $\text{C}_{13}\text{H}_8\text{F}_3\text{N}_2^+$ $[\text{M}+\text{H}^+]$ 249.0634, Found 249.0642.



2-Phenyl-6-(trifluoromethyl)pyridine (4q). 70%; white solid; $R_f = 0.61$

(hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.44-7.53 (m, 3H), 7.48-7.63 (m, 1H), 7.92 (d, $J = 4.0$ Hz, 2H), 8.07 (dd, $J = 8.3, 1.4$

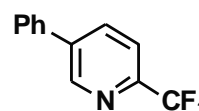
Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 118.6 (q, $J = 3.6$ Hz), 121.7 (q, $J = 274$ Hz), 122.9, 127.2, 129.0, 129.9, 137.9, 138.1, 148.3 (q, $J = 34.6$ Hz), 158.0; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -69.1 (s, 3F); IR (KBr, ν / cm^{-1}) 1597, 1464, 1418, 1346, 1251, 1195, 1133, 1057, 991, 823; HRMS (DART) Calcd for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 224.0682, Found 224.0691.



5-Phenyl-2-(trifluoromethyl)pyridine (4r). 17%; white solid; $R_f = 0.71$

(hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.44-7.56 (m, 3H), 7.61 (d, $J = 7.2$ Hz, 2H), 7.76 (d, $J = 8.2$ Hz, 1H), 8.04 (dd, $J = 8.2,$

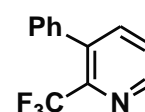
1.7 Hz, 1H), 8.95 (d, $J = 1.7$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 120.6 (q, $J = 2.8$ Hz), 121.8 (q, $J = 274$ Hz), 127.5, 129.2, 129.5, 135.7, 136.5, 139.6, 146.9 (q, $J = 34.8$ Hz), 148.6; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -68.6 (s, 3F).



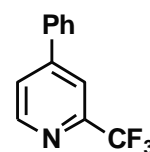
3-Phenyl-2-(trifluoromethyl)pyridine (4r'). 10%; colorless oil; $R_f = 0.56$

(hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 (dd, $J = 6.5,$

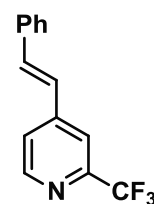
2.9 Hz, 2H), 7.42-7.47 (m, 3H), 7.54 (dd, $J = 7.8, 4.6$ Hz, 1H), 7.73 (dd, $J = 7.8, 1.5$ Hz, 1H), 8.72 (dd, $J = 4.6, 1.5$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 122.0 (q, $J = 276$ Hz), 125.9, 128.3, 128.5, 128.9 (q, $J = 1.8$ Hz), 137.2, 137.4, 140.4, 145.3 (q, $J = 32.3$ Hz), 148.0; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -62.2 (s, 3F); IR (neat, ν / cm^{-1}) 3315, 1627, 1450, 1324, 1182, 1134, 1092, 1055, 789, 763; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 224.0682, Found 224.0675.



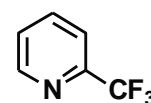
4-Phenyl-2-(trifluoromethyl)pyridine (4s). 43%; pale yellow oil; $R_f = 0.60$ (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46-7.56 (m, 3H), 7.63-7.68 (m, 2H), 7.69 (dd, $J = 4.9, 1.1$ Hz, 1H), 7.89 (d, $J = 1.1$ Hz, 1H), 8.76 (d, $J = 4.9$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 118.6 (q, $J = 2.8$ Hz), 121.8 (q, $J = 274$ Hz), 124.3, 127.2, 129.5, 130.0, 136.9, 148.9 (q, $J = 34.5$ Hz), 150.4, 150.5; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -68.8 (s, 3F).



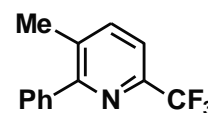
(E)-4-Styryl-2-(trifluoromethyl)pyridine (4t). 43% yield; yellow oil; $R_f = 0.60$ (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CD_3CN) δ 7.24 (d, $J = 16.4$ Hz, 1H), 7.35-7.46 (m, 3H), 7.58 (d, $J = 16.4$ Hz, 1H), 7.64 (d, $J = 7.6$ Hz, 2H), 7.69 (d, $J = 4.9$ Hz, 1H), 7.93 (s, 1H), 8.67 (d, $J = 4.9$ Hz, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 117.5 (q, $J = 2.8$ Hz), 121.8 (q, $J = 275$ Hz), 123.4, 124.8, 127.4, 129.1, 129.5, 135.2, 135.7, 146.7, 149.0 (q, $J = 34.4$ Hz), 150.5; $^{19}\text{F NMR}$ (368 MHz, CD_3CN) δ -69.4 (s, 3F); IR (neat ν / cm^{-1}) 1636, 1604, 1433, 1333, 1180, 1082, 962, 830, 749, 689; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_{11}\text{F}_3\text{N} + [\text{M}+\text{H}^+]$ 250.0838, Found 250.0844.



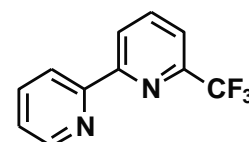
2-(Trifluoromethyl)pyridine (4u). 41% determined by $^{19}\text{F NMR}$ analysis with 1,4-difluorobenzene as a standard; $^{19}\text{F NMR}$ (368 MHz, CD_3CN) δ -68.3 (s, 3F); GC-MS (ED) Calcd for $\text{C}_6\text{H}_4\text{F}_3\text{N}^+ [\text{M}^+]$ 147, Found 147. The spectroscopic data was compared with that of an authentic sample (commercial source).



3-Methyl-2-phenyl-6-(trifluoromethyl)pyridine (4v). 62%; pale yellow oil; $R_f = 0.67$ (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.43 (s, 3H), 7.39-7.50 (m, 3H), 7.53-7.58 (m, 3H), 7.74 (d, $J = 8.1$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 20.3, 118.8 (q, $J = 2.8$ Hz), 121.8 (q, $J = 274$ Hz), 128.4, 128.7, 129.2, 134.6, 139.3, 139.7, 145.7 (q, $J = 34.8$ Hz), 159.3; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -68.4 (s, 3F); IR (neat, ν / cm^{-1}) 3062, 1587, 1466, 1397, 1342, 1212, 1134, 1098, 1054, 862; HRMS (DART) Calcd for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{N}^+ [\text{M}+\text{H}^+]$ 238.0838, Found 238.0850.

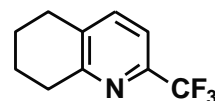


6-(Trifluoromethyl)-2,2'-bipyridine (4w). 59%; white solid; $R_f = 0.47$ (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.32-7.38 (m, 1H), 7.65-7.71 (m, 1H), 7.84 (ddd, $J = 7.7, 7.7, 1.7$ Hz, 1H), 7.98 (dd, $J = 7.7, 7.7$ Hz, 1H), 8.51 (ddd, $J = 8.0, 1.1, 1.1$ Hz, 1H), 8.62 (d, $J = 8.0$ Hz, 1H), 8.66-8.71 (m, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 120.3 (q, $J = 2.8$ Hz), 121.7 (q, $J = 274$ Hz), 121.8, 123.6, 124.6, 137.3, 138.4, 147.8 (q, $J = 34.8$ Hz), 149.3,



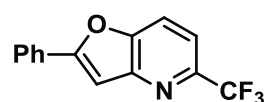
154.8, 156.7; ^{19}F NMR (368 MHz, CDCl_3) δ -68.9 (s, 3F); IR (KBr, ν / cm^{-1}) 1587, 1464, 1438, 1347, 1115, 991, 833, 781, 746, 671; HRMS (DART) Calcd for $\text{C}_{11}\text{H}_8\text{F}_3\text{N}_2^+$ [$\text{M}+\text{H}^+$] 225.0634, Found 225.0642.

2-(Trifluoromethyl)-5,6,7,8-tetrahydroquinoline (4x). 34%; pale yellow oil; R_f = 0.64 (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 1.75-1.98 (m, 4H), 2.83 (t, J = 6.2 Hz, 2H), 2.98 (t, J = 6.2 Hz, 2H),



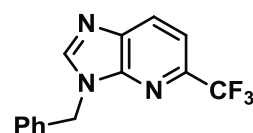
7.39 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 22.4, 22.9, 28.9, 32.6, 117.6 (q, J = 3.2 Hz), 121.9 (q, J = 274 Hz), 136.0, 137.8, 145.3 (q, J = 34.4 Hz), 158.6; ^{19}F NMR (368 MHz, CDCl_3) δ -68.6 (s, 3F); IR (neat, ν / cm^{-1}) 2941, 1585, 1416, 1360, 1333, 1311, 1271, 1140, 1101, 989; HRMS (DART) Calcd for $\text{C}_{10}\text{H}_{11}\text{F}_3\text{N}^+$ [$\text{M}+\text{H}^+$] 202.0838, Found 202.0847.

2-Phenyl-5-(trifluoromethyl)furo[3,2-*b*]pyridine (4y). 34%; white solid; R_f = 0.54 (hexane/ethyl acetate = 5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.28 (s, 1H), 7.43-7.54 (m, 3H), 7.62 (d, J = 8.5 Hz, 1H),



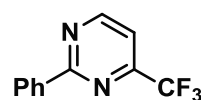
7.88 (d, J = 8.5 Hz, 1H), 7.89-7.94 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 102.3, 115.9 (q, J = 2.7 Hz), 118.4, 122.1 (q, J = 274 Hz), 125.8, 129.1, 129.2, 130.5, 144.6 (q, J = 34.4 Hz), 149.0, 149.6, 162.2; ^{19}F NMR (368 MHz, CDCl_3) δ -67.1 (s, 3F); IR (neat, ν / cm^{-1}) 2359, 1362, 1173, 1119, 1088, 1016, 832, 813, 762, 682; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{NO}^+$ [$\text{M}+\text{H}^+$] 264.0631, Found 264.0637.

3-Benzyl-5-(trifluoromethyl)-3*H*-imidazo[4,5-*b*]pyridine (4z). 28%; yellow oil; R_f = 0.51 (hexane/ethyl acetate = 1/2); ^1H NMR (400 MHz, CDCl_3) δ 5.50 (s, 2H), 7.31-7.38 (m, 5H), 7.66 (d, J = 8.5 Hz, 1H), 8.16 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 47.6, 115.3 (q, J = 2.7 Hz), 122.2 (q, J = 274 Hz), 128.4, 128.7, 128.8, 129.3,



135.3, 137.2, 142.8 (q, J = 34.7 Hz), 146.6, 146.7; ^{19}F NMR (368 MHz, CDCl_3) δ -66.8 (s, 3F); IR (neat, ν / cm^{-1}) 1605, 1504, 1456, 1415, 1365, 1310, 1134, 920, 836, 759; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_{11}\text{F}_3\text{N}_3^+$ [$\text{M}+\text{H}^+$] 278.0900, Found 278.0895.

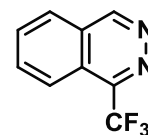
2-Phenyl-4-(trifluoromethyl)pyrimidine (4aa). 45%; white solid; R_f = 0.66 (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.49-7.57 (m, 4H), 8.49-8.55 (m, 2H), 9.04 (d, J = 4.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 114.5 (q, J = 2.7 Hz), 120.7 (q, J = 275 Hz), 128.7, 128.9, 131.9, 136.3,



156.1 (q, J = 36.5 Hz), 159.7, 165.6; ^{19}F NMR (368 MHz, CDCl_3) δ -71.0 (s, 3F); IR (neat,

ν / cm^{-1} 1575, 1462, 1437, 1396, 1342, 1316, 1285, 1213, 1135, 849; HRMS (DART) Calcd for $\text{C}_{11}\text{H}_8\text{F}_3\text{N}_2^+$ $[\text{M}+\text{H}^+]$ 225.0634, Found 225.0640.

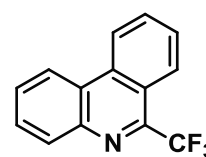
1-(Trifluoromethyl)phthalazine (4ac). 27%; pale yellow solid; $R_f = 0.24$ (hexane/ethyl acetate = 2/1); ^1H NMR (400 MHz, CDCl_3) δ 8.02-8.15 (m, 3H), 8.26-8.32 (m, 1H), 9.67 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 122.1 (q, $J = 277$ Hz), 123.1, 123.9 (q, $J = 2.7$ Hz), 127.45, 127.47, 133.6, 134.2, 147.8 (q, $J = 33.1$ Hz), 154.0; ^{19}F NMR (368 MHz, CDCl_3) δ -64.1 (s, 3F); IR (neat, ν / cm^{-1}) 3043, 1385, 1364, 1221, 1196, 1127, 1002, 977, 803, 761; HRMS (DART) Calcd for $\text{C}_9\text{H}_6\text{F}_3\text{N}_2^+$ $[\text{M}+\text{H}^+]$ 199.0478, Found 199.0483.



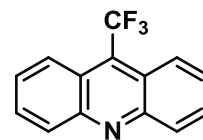
Preparation of 6-(Trifluoromethyl)phenanthridine and 9-(Trifluoromethyl)acridine.

A mixture of CsF (114 mg, 0.750 mmol) and MS4A (25 mg) was flame-dried under vacuum. After cooling to room temperature, difluoro(phenanthridin-5-ium-5-yloxy)(trifluoromethyl)borate (78.3 mg, 0.250 mmol) and ethyl acetate (2.5 mL) were added. To the mixture, Me_3SiCF_3 (111 μL , 0.750 mmol) was added dropwisely with vigorous stirring. After stirring at 25 °C for 1 h, the mixture was heated at 60 °C for 4 h, and then cooled to room temperature. Insoluble solid was filtered off, washed with ethyl acetate, and the solvent was removed under reduced pressure. Methanol (1.0 mL) and conc. HCl (100 μL) was added to the residue. After stirring at 25 °C for 1 h, the mixture was treated with 4.0 M aq. NaOH, extracted with dichloromethane (3 x 4.0 mL), and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{hexane} = 1/2$) to give 6-(trifluoromethyl)phenanthridine (**4m**, 45.7 mg, 74% yield).

6-(Trifluoromethyl)phenanthridine (4m). 74%; white solid; $R_f = 0.59$ (hexane/ethyl acetate = 3/1); ^1H NMR (400 MHz, CDCl_3) δ 7.74-7.84 (m, 3H), 7.92 (dd, $J = 7.6, 7.6$ Hz, 1H), 8.26-8.32 (m, 1H), 8.35-8.42 (m, 1H), 8.57-8.63 (m, 1H), 8.70 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 121.9, 122.1 (q, $J = 278$ Hz), 122.2, 122.7, 125.3, 126.1 (q, $J = 3.6$ Hz), 128.2, 129.4, 129.5, 131.3, 131.5, 134.1, 141.9, 146.7 (q, $J = 33.1$ Hz); ^{19}F NMR (368 MHz, CDCl_3) δ -64.3 (s, 3F); IR (neat, ν / cm^{-1}) 1529, 1446, 1381, 1335, 1312, 1254, 1116, 972, 758, 718; HRMS (DART) Calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{N}^+$ $[\text{M}+\text{H}^+]$ 248.0682, Found 248.0692.



9-(Trifluoromethyl)acridine (4p). 51% yield (0.100 mmol scale); yellow solid; $R_f = 0.31$ (hexane/ethyl acetate = 3/1); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.68 (ddd, $J = 9.1, 6.7, 1.3$ Hz, 2H), 7.83 (ddd, $J = 8.2, 6.7, 1.3$ Hz, 2H), 8.31 (d, $J = 8.2$ Hz, 2H), 8.50 (d, $J = 9.1$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 122.4, 122.9, 124.5 (q, $J = 5.6$ Hz), 125.8 (q, $J = 278$ Hz), 128.3, 129.7 (q, $J = 29.4$ Hz), 130.8, 149.0; $^{19}\text{F NMR}$ (368 MHz, CDCl_3) δ -51.9 (s, 3F).



Preparation of 2-methoxy-3-(trifluoromethyl)quinoxaline.

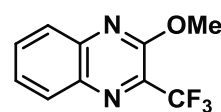
To a mixture of potassium trifluoro(trifluoromethyl)borate (484 mg, 2.75 mmol) in CH_2Cl_2 (5.0 mL) was added $\text{BF}_3\cdot\text{OEt}_2$ (339 μL , 2.75 mmol), and the mixture was stirred at 25 °C for 20 min. Then, 3-methoxyquinoxaline *N*-oxide (440 mg, 2.50 mmol) was added to the reaction mixture, and the mixture was stirred at 25 °C for 18 h. After the reaction mixture was diluted with CH_2Cl_2 /acetone (2:1), insoluble solid was filtered off, washed with CH_2Cl_2 /acetone (2:1), and the solvent was removed under reduced pressure. The obtained solid was washed with hexane/ CH_2Cl_2 (1/1) to give difluoro((3-methoxyquinoxalin-1-ium-1-yl)oxy)(trifluoromethyl)borate (701 mg, 95%).

A mixture of CsF (190 mg, 1.25 mmol) and MS4A (25.0 mg) was flame-dried under vacuum. After cooling to room temperature, the obtained difluoro((3-methoxy-1-quinoxalinium-1-yl)oxy)(trifluoromethyl)borate (73.5 mg, 0.250 mmol) and ethyl acetate (2.50 mL) were added. To the mixture, Me_3SiCF_3 (185 μL , 1.25 mmol) was added dropwisely with vigorous stirring. After stirring at 25 °C for 1 h, the mixture was heated at 60 °C for 24 h, and cooled to room temperature. Insoluble solid was filtered off, washed with ethyl acetate, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to give 2-methoxy-3-(trifluoromethyl)quinoxaline (**4ab**, 23.8 mg, 42% yield).

Technical note for the synthesis of difluoro((3-methoxy-1-quinoxalinium-1-yl)oxy)(trifluoromethyl)borate.

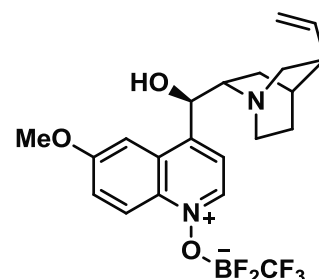
This compound could not be isolated by column chromatography on silica gel due to the decomposition to corresponding *N*-oxide.

2-Methoxy-3-(trifluoromethyl)quinoxaline (4ab). 42%; white solid; $R_f = 0.60$ (hexane/ethyl acetate = 5/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.19 (s, 3H), 7.65 (ddd, $J = 8.5, 7.2, 1.2$ Hz, 1H), 7.77-7.83 (m, 1H), 7.91 (dd, $J = 8.5, 0.9$ Hz, 1H), 8.12 (dd, $J = 8.3, 1.2$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 54.6,



120.7 (q, $J = 275$ Hz), 127.1, 127.8, 129.9, 132.6, 134.9 (q, $J = 36.2$ Hz), 136.9, 142.0, 154.8; ^{19}F NMR (368 MHz, CDCl_3) δ -69.0 (s, 3F); IR (KBr, ν / cm^{-1}) 1588, 1454, 1398, 1335, 1288, 1223, 1179, 1127, 1001, 918; HRMS (DART) Calcd for $\text{C}_{10}\text{H}_8\text{F}_3\text{N}_2\text{O}^+$ [$\text{M}+\text{H}^+$] 229.0583, Found 229.0589.

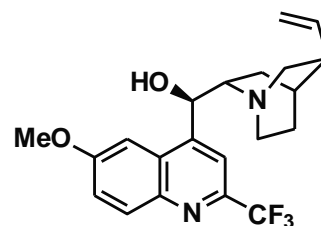
Synthesis of difluoro((4-((1*R*)-hydroxy((2*S*)-5-vinylquinuclidin-2-yl)methyl)-6-methoxyquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (7).



To a mixture of potassium trifluoro(trifluoromethyl)borate (1.03 g, 5.88 mmol, 2.0 equiv) in CH_2Cl_2 (12 mL) was added $\text{BF}_3\cdot\text{OEt}_2$ (726 μL , 5.88 mmol, 2.0 equiv), and the mixture was stirred at 25 °C for 20 min. Then, quinine *N*-oxide^{8b}) (1.00 g, 2.94 mmol) was added to the reaction mixture and the mixture was stirred at 25 °C for 13 h. After the reaction mixture was diluted with CH_2Cl_2 /acetone (1/1), an insoluble solid was filtered off, washed with CH_2Cl_2 /acetone (1/1), and then the solvent was removed under reduced pressure. CH_2Cl_2 /MeOH (20/1) was added followed by the addition of saturated aq. NaHCO_3 . The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 /MeOH (20/1). Combined organic layer was dried over sodium sulfate, filtered, and then the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (CH_2Cl_2 , then CH_2Cl_2 /acetone 2/1, and then CH_2Cl_2 /MeOH = 9/1) to give difluoro((4-((1*R*)-hydroxy((2*S*)-5-vinylquinuclidin-2-yl)methyl)-6-methoxyquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (**7**, 701 mg, 52% yield). white solid; $R_f = 0.67$ (CH_2Cl_2 /MeOH = 5/1); ^1H NMR (400 MHz, CD_3CN) δ 1.45-1.55 (m, 1H), 1.61-1.78 (m, 2H), 1.78-1.88 (m, 2H), 2.22-2.33 (m, 1H), 2.50-2.61 (m, 2H), 2.92 (dd, $J = 13.5, 10.3$ Hz, 1H), 3.12-3.29 (m, 2H), 4.00 (s, 3H), 4.92-5.05 (m, 2H), 5.55 (d, $J = 6.7$ Hz, 1H), 5.89 (ddd, $J = 17.5, 9.9, 7.6$ Hz, 1H), 7.68-7.75 (m, 2H), 7.93 (d, $J = 6.3$ Hz, 1H), 8.45 (d, $J = 10.3$ Hz, 1H), 8.82 (d, $J = 6.3$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3CN) δ 24.5, 28.1, 28.7, 40.7, 43.2, 56.7, 57.3, 62.2, 71.7, 104.4, 114.8, 120.5, 121.4, 127.9, 131.1, 134.8, 140.9, 143.1, 158.0, 161.1; ^{19}F NMR (368 MHz, CD_3CN) δ -160.9~-160.1 (m, 2F), -75.9~-75.3 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.76 (s); IR (KBr, ν / cm^{-1}) 2954, 1619, 1587, 1523, 1475, 1385, 1263, 1076, 1023, 894; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{24}\text{BF}_5\text{N}_2\text{NaO}_3^+$ [$\text{M}+\text{Na}^+$] 481.1692, Found 481.1690.

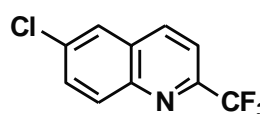
Synthesis of (1*R*)-(6-Methoxy-2-(trifluoromethyl)quinolin-4-yl)((2*S*)-5-vinylquinuclidin-2-yl)methano

1 (**8**). A mixture of CsF (91.1 mg, 0.600 mmol, 3.0 equiv) and MS4A (20.0 mg, 100 mg/mmol) was flame-dried under vacuum. After cooling to room temperature, difluoro((4-((1*R*)-hydroxy((2*S*)-5-vinylquinuclidin-2-yl)methyl)-6-methoxyquinolin-1-ium-1-yl)oxy)(trifluoromethyl)borate (**8**, 91.6 mg, 0.200 mmol) and ethyl acetate (2.0 mL) were



added. To the mixture, Me₃SiCF₃ (88.9 μL, 0.600 mmol, 3.0 equiv) was added dropwisely with vigorous stirring. After stirring at 25 °C for 1 h, the mixture was heated at 60 °C for 24 h, and then cooled to room temperature. An insoluble solid was filtered off, washed with ethyl acetate, and the solvent was removed under reduced pressure. To the residue in MeOH (3.0 mL) was added K₂CO₃ (5.5 mg, 0.20 equiv), and the mixture was heated at 50 °C for 5 h, and then cooled to room temperature. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (ethyl acetate, then ethyl acetate/MeOH = 9/1) to give (1*R*)-(6-Methoxy-2-(trifluoromethyl)quinolin-4-yl)((2*S*)-5-vinylquinuclidin-2-yl)methanol (**8**, 58.9 mg, 2 steps: 75% yield). white solid; R_f = 0.36 (CH₂Cl₂/MeOH = 9/1); ¹H NMR (400 MHz, CDCl₃) δ 1.40-1.64 (m, 2H), 1.75-1.92 (m, 3H), 2.31-2.41 (m, 1H), 2.69-2.82 (m, 2H), 3.09-3.20 (m, 2H), 3.55-3.72 (m, 1H), 3.85 (s, 3H), 4.90-5.01 (m, 2H), 5.68 (ddd, *J* = 17.5, 10.3, 7.2 Hz, 1H), 5.73-5.83 (m, 1H), 7.13 (d, *J* = 2.4 Hz, 1H), 7.34 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.91 (s, 1H), 8.04 (d, *J* = 9.3 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 20.6, 27.0, 27.7, 39.4, 43.4, 55.8, 56.6, 59.9, 70.8, 100.7, 114.3 (m), 115.1, 121.9 (q, *J* = 277 Hz), 123.0, 127.2, 132.2, 141.0, 143.2, 145.1 (q, *J* = 34.4 Hz), 149.8, 159.3; ¹⁹F NMR (368 MHz, CDCl₃) δ -67.9 (s, 3F); IR (KBr, ν / cm⁻¹) 3203, 1623, 1509, 1482, 1270, 1234, 1183, 1135, 1097, 954; HRMS (ESI) Calcd for C₂₁H₂₄F₃N₂O₂⁺ [M+H⁺] 393.1784, Found 393.1780.

Synthesis of 6-chloro-2-(trifluoromethyl)quinoline (4d) by sequential operation without isolation of the intermediates. To a 0 °C solution of 6-chloroquinoline (40.9 mg, 0.250 mmol) in



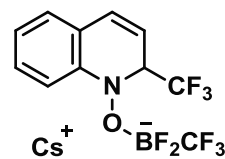
CH₂Cl₂ (0.5 mL) was added *m*-CPBA (77%, 56.0 mg, 0.250 mmol, 1.0 equiv) and the mixture was stirred at 25 °C for 10 h. After the reaction mixture was diluted with CH₂Cl₂, powdered potassium carbonate (51.8 mg, 0.375 mmol, 1.5 equiv) was added to the reaction mixture, and the mixture was stirred for 1 h. Insoluble solid was filtered off through a pad of Celite, washed with CH₂Cl₂, and then the solvent was removed under reduced pressure to give 6-chloroquinoline *N*-oxide (**1d**). To a mixture of potassium trifluoro(trifluoromethyl)borate (48.4 mg, 0.275 mmol, 1.1 equiv) in CH₂Cl₂ (0.50 mL) was added BF₃·OEt₂ (33.9 μL, 0.275 mmol, 1.1 equiv) and the mixture was stirred at

25 °C for 20 min. Then, the obtained **1d** was added to the reaction mixture and the mixture was stirred at 25 °C for 24 h. After the reaction mixture was diluted with CH₂Cl₂/acetone (1:1), insoluble solid was filtered off, washed with CH₂Cl₂/acetone (1:1), and then the solvent was removed under reduced pressure to give ((6-chloroquinolin-1-ium-1-yl)oxy)difluoro(trifluoromethyl)borate (**2d**). A mixture of CsF (114 mg, 0.750 mmol, 3.0 equiv) and MS4A (25.0 mg, 100 mg/mmol) was flame-dried under vacuum. After cooling to room temperature, the obtained **2d** and ethyl acetate (2.50 mL) were added. To the mixture, Me₃SiCF₃ (111 μL, 0.750 mmol, 3.0 equiv) was added dropwisely with vigorous stirring. After stirring at 25 °C for 1 h, the mixture was heated at 60 °C for 5 h, and then cooled to room temperature. Insoluble solid was filtered off, washed with ethyl acetate, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to give 6-chloro-2-(trifluoromethyl)quinoline (**4d**, 39.9 mg, 3 steps: 69% yield).

Reaction mechanism.

Cesium

difluoro(trifluoromethyl)((2-(trifluoromethyl)quinolin-1(2*H*)-yl)oxy)borate (**I**). *R*_f = 0.38 (ethyl acetate); ¹H NMR (400 MHz, CD₃CN) δ 4.84 (qd, *J* = 7.0, 7.0 Hz, 1H), 5.71-5.79 (m, 1H), 6.63 (d, *J* = 9.4 Hz, 1H), 6.63 (td, *J* = 7.2, 1.8 Hz, 1H), 6.94 (d, *J* = 7.4, 1.1 Hz, 1H), 7.06-7.15 (m, 2H); ¹⁹F NMR (368 MHz, CD₃CN) δ -163.1 (q, *J* = 45.5 Hz, 2F), -74.5 (q, *J* = 28.5 Hz, 3F), -72.0 (s, 3F); ¹¹B NMR (125 MHz, CD₃CN) δ 0.61 (m).



Preparation of byproduct 10.

To a mixture of potassium trifluoro(trifluoromethyl)borate (194 mg, 1.10 mmol) in CH₂Cl₂ (2.0 mL) was added BF₃·OEt₂ (136 μL, 1.10 mmol), and the mixture was stirred at 25 °C for 20 min. After insoluble solid was filtered off, washed with CH₂Cl₂, and CsOH·H₂O (185 mg, 1.10 mmol) was added to the filtrate. The mixture was stirred at 25 °C for 8 h, and the solvent was removed under reduced pressure to give the target compound as a major product.

Table 2-4. Comparison of chemical shift of byproduct **10**.

	¹⁹ F NMR shift in CD ₃ CN (ppm)	
	Cs(HO-BF ₂ CF ₃)	Cs(HO-BF ₂ CF ₃)
10 in reaction mixture (Table 2-3, entry 5)	-155.3 (q, <i>J</i> = 45.5 Hz, 2F)	-75.6 (q, <i>J</i> = 28.5 Hz, 2F)
Prepared 10	-152.7 (q, <i>J</i> = 45.5 Hz, 2F)	-75.3 (q, <i>J</i> = 28.5 Hz, 2F)
cf. Na(HO-BF ₃) in water (pH 4.3) ¹⁷⁾	-142.0 (q, <i>J</i> = 14.4 Hz, 3F)	-

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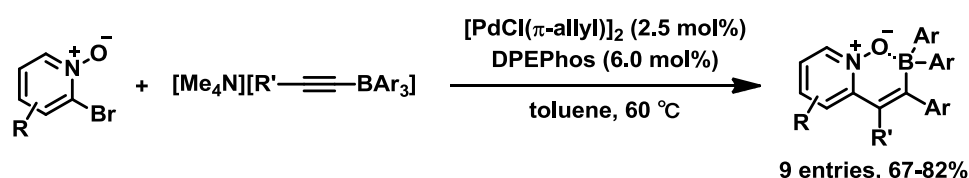
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第3章 ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体の蛍光特性

3-1 背景

有機蛍光色素は生体標識材料、有機エレクトロニクス材料、化学センサーや有機レーザーといった医療から工業まで幅広い分野で活用されており、新たな発光性材料の開発研究が盛んに行われている。ピリジン環、キノリン環、およびその類縁の含窒素ヘテロ芳香環は、天然物や医薬品のみならず、機能性材料の骨格として非常に重要である¹⁾。それらの含窒素ヘテロ芳香環は、他のヘテロ芳香族化合物に比べて電子受容性が高いことが特徴であり、*n*型半導体の構成要素として有用である²⁾。ピリジンやキノリンの *N*-オキシド-ボラン錯体の合成は古くから研究されているが、それらの錯体は溶液中において容易に分解するものが多い³⁾。近年、村上らはピリジン環とボラン部位を炭素鎖で架橋させることにより、分子内でのピリジン *N*-オキシド-ボラン錯体が安定な化合物として得られることを報告しているが、それらは蛍光を示さないことが報告されている(Scheme 3-1)^{3d)}。



Scheme 3-1. Stable pyridine *N*-oxide-borane intramolecular complexes

BODIPY はホウ素を含む蛍光色素として有用であり、種々のイメージングに汎用されている⁴⁾。同様に、 π 電子共役系にボリル基などのホウ素を含む置換基を導入した化合物も、ホウ素を含む π 電子共役系蛍光色素として有用である^{5,6)}。ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体は、ヘテロ芳香環とボラン部位が架橋されていないにもかかわらず安定な化合物として単離、保存することが可能であり、機能性材料としての応用を検討した。

3-2 4-フェニルピリジン誘導体の蛍光特性の比較

4-フェニルピリジン *N*-オキシド-BF₂CF₃ 錯体 **3a** は、溶液および固体状態において紫色の蛍光を示すことがわかった(Table 3-1)。アセトニトリル中における蛍光量子収率を 4-フェニルピリジン *N*-オキシド **2a** と 4-フェニルピリジン **1a** とで比較したところ、**3a** のみが蛍光を示した⁷⁾。

Table 3-1. Photophysical data of 4-phenylpyridine derivatives

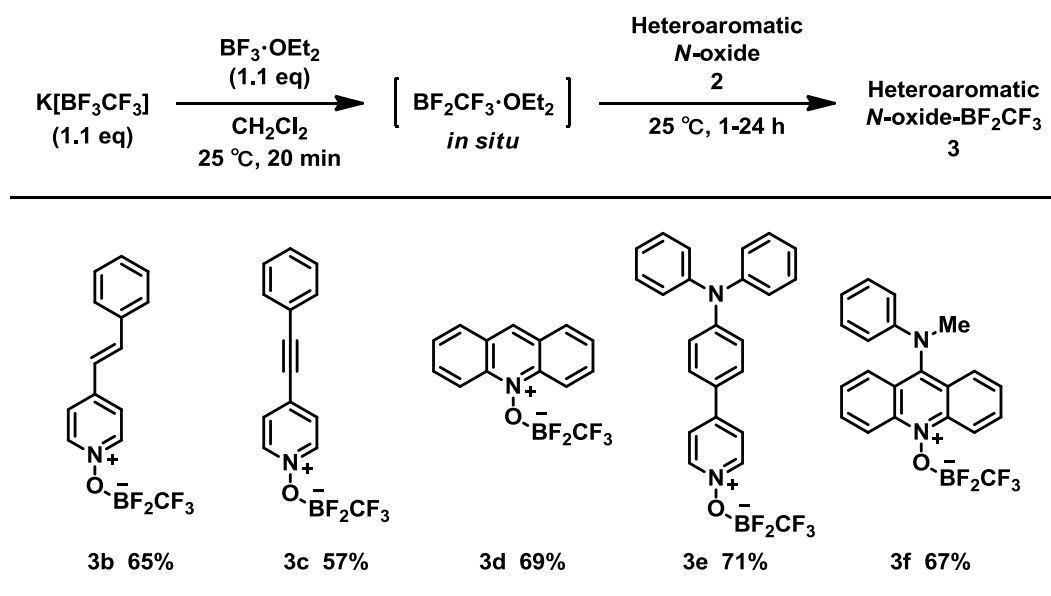
compound	3a	2a	1a
Φ_F (in MeCN) ^a	0.35	<0.005	<0.005
$\lambda_{em, max}$ [nm]	360	342	384

^a Determined using 2-aminopyridine as a standard (excited at 270 nm)⁸⁾

3-3 π 共役系を拡張した誘導体の設計と合成

化合物 **3a** を基に π 共役系を拡張した誘導体、および電子供与性置換基であるアミノ基を導入したドナー・アクセプター型構造を有する誘導体を設計した。定法により種々のヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体(**3b-3f**)が、対応する *N*-オキシドから良好な収率で得られた(Table 3-2)⁹⁾。

Table 3-2. Synthesis of π -extended pyridine *N*-oxide- BF_2CF_3 complexes



3-4 溶液状態における蛍光特性

代表的な化合物のテトラヒドロフラン溶液およびアセトニトリル溶液中における蛍光特性を示す(Table 3-3, Figures 3-1 and 3-2)。紫色の蛍光を示す化合物 **3a** の π 共役系を拡張す

ることにより、化合物 **3c** および **3d** は 365 nm の光照射下において、それぞれ、青色、緑色の蛍光を示した。化合物 **3a** および **3c** の蛍光スペクトルからは大きな溶媒効果は観測されておらず、基底状態と励起状態における双極子モーメントに大きな変化はないと考えられる。化合物 **3a** および **3c** の蛍光量子収率は、溶媒の極性に大きく影響を受けることがわかった。化合物 **3a** はより高極性のアセトニトリル中において高い蛍光量子収率を示すのに対し、化合物 **3c** はより低極性のテトラヒドロフラン溶液中において高い蛍光量子収率を示した。一方、化合物 **3d** は紫外可視吸収スペクトルおよび蛍光スペクトルともに、溶媒の極性による変化はほとんど観測されず、高い量子収率を示した。これは、基底状態と励起状態のいずれにおいても構造が変化しにくい、剛直なアクリジン骨格を有するためであると考えられる。

Table 3-3. Photophysical data of several pyridine *N*-oxide-BF₂CF₃ complexes

compound	solvent	absorption		emission		stokes shift [cm ⁻¹]
		λ_{abs} [nm] ^a	$\epsilon/10^4$ [M ⁻¹ cm ⁻¹]	λ_{em} [nm]	Φ_{F}	
3a	THF	290	2.14	355 ^b	0.0094 ^e	6300
	MeCN	289	2.15	360 ^b	0.35 ^e	6800
3c	THF	330	2.91	439 ^c	0.10 ^f	7500
	MeCN	329	2.93	449 ^c	0.0075 ^f	8100
3d	THF	438	0.25	455 ^d	0.53 ^f	900
	MeCN	438	0.22	456 ^d	0.53 ^f	900

^a The longest wavelength absorption band. ^b Excited at 270 nm. ^c Excited at 290 nm. ^d Excited at 310 nm. ^e Determined using 2-aminopyridine in aq. H₂SO₄ (Φ_{F} = 0.66) as a standard.⁸⁾ ^f Determined using quinine in aq. H₂SO₄ (Φ_{F} = 0.55) as a standard.⁹⁾

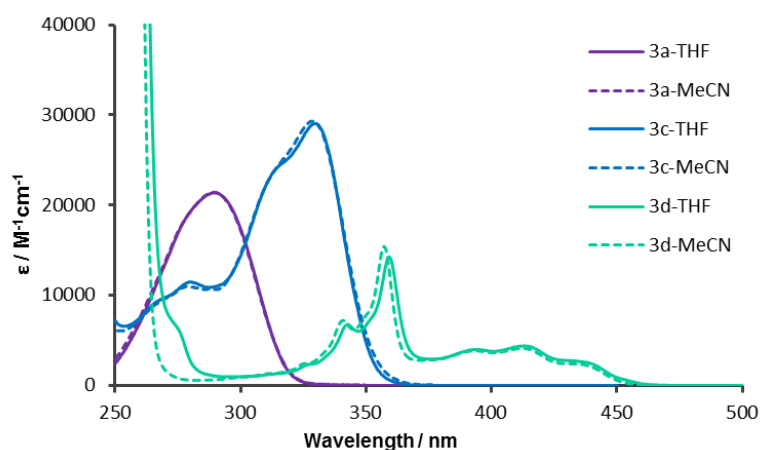


Figure 3-1. UV/Vis absorption spectra of compound **3a**, **3c**, and **3d**

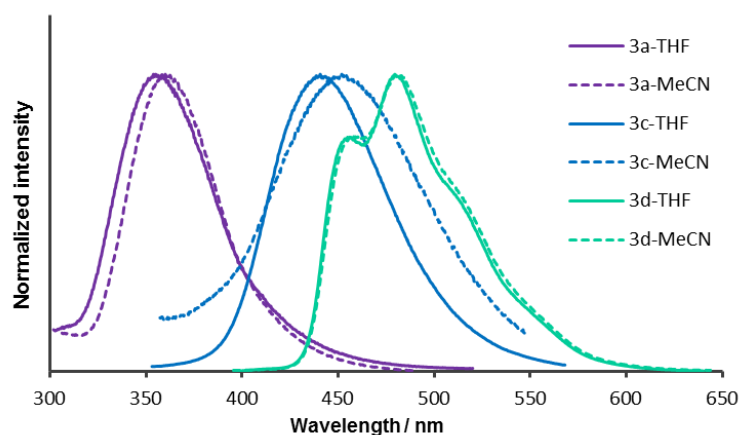


Figure 3-2. Fluorescence spectra of compound **3a**, **3c**, and **3d**

化合物 **3a** はピリジン環上が非常に電子不足であるため、電子供与性置換基であるジフェニルアミノ基を導入することにより、ソルバトクロミズムを示すことが期待された。そこで化合物 **3e** を合成し、各種有機溶媒中での蛍光スペクトルを測定したところ、ソルバトクロミズムを示すことがわかった(**Figure 3-3**)。低極性のシクロヘキサンからジクロロメタンへと極性を高くすることにより、蛍光色が青色からオレンジ色へと **82 nm** の長波長シフトを示した。TD-DFT 計算より、この化合物の LUMO はピリジン部位に、HOMO はジフェニルアミノベンゼン部位に主に局在していることがわかり、HOMO から LUMO への分子内電荷移動型遷移によって生じた励起状態からの蛍光であると考えられる(**Figure 3-4**)。

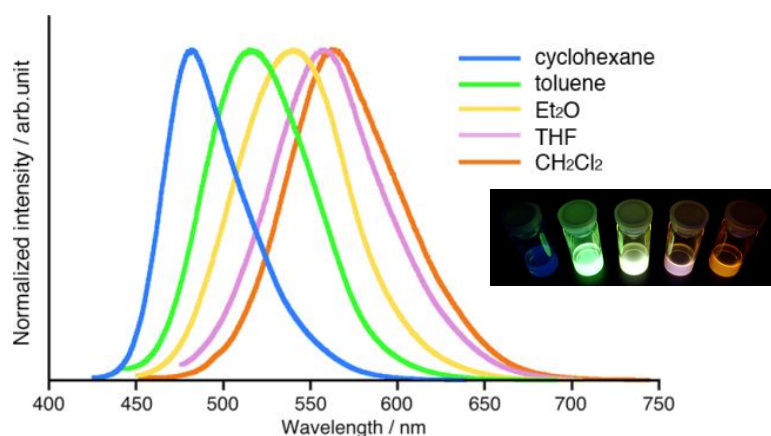


Figure 3-3. Fluorescence spectra of **3e** in various solvents

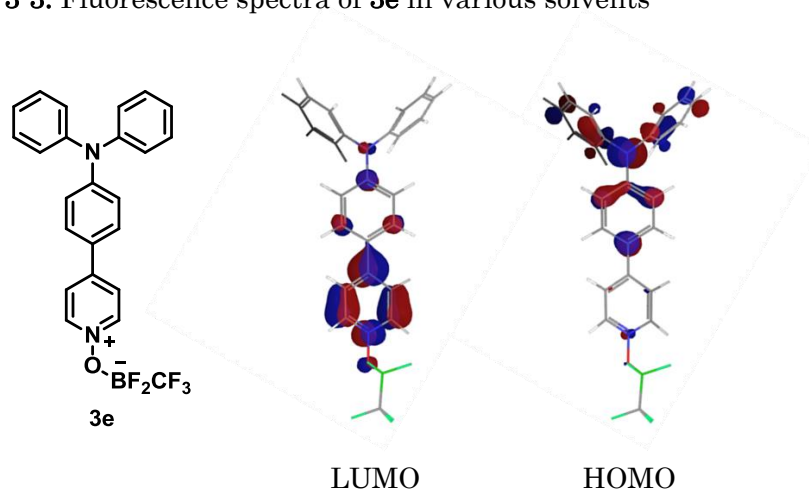


Figure 3-4. Kohn-Sham molecular orbitals of **3e** calculated at the B3LYP/6-31+G* level

3-5 固体状態における蛍光特性

代表化合物の固体状態における蛍光特性を示す(Figure 3-5)。粉末試料を用いた測定の結果、化合物 **3a**、**3c**、**3d**、**3e** の蛍光極大波長はそれぞれ 354、394、497、545 nm であり、365 nm の光照射下において、紫、青、緑、黄色の蛍光を示した。また、蛍光量子収率はそれぞれ 0.51、0.25、0.28、0.11 であった。特に、化合物 **3c** は固体状態における蛍光スペクトルの半値幅が 42 nm と狭いため、高純度の青色蛍光剤として有用であると考えられる。

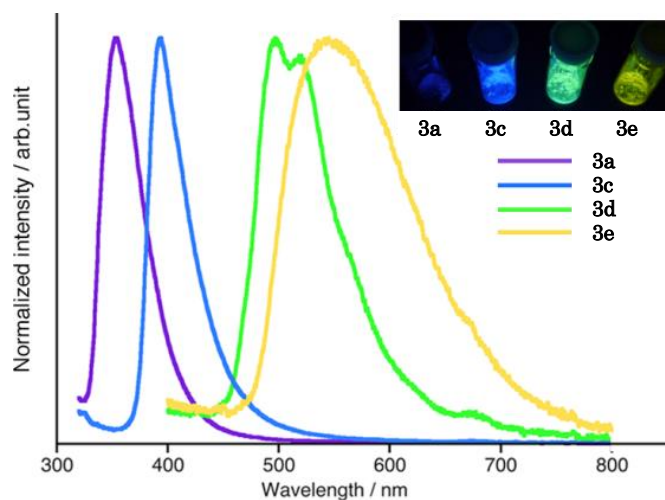


Figure 3-5. Fluorescence spectra of **3a**, **3c**, **3d**, and **3e** in the solid state

3-6 小括

ヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体は、溶液中および固体状態において蛍光を示すことを見出した。 π 共役系の拡張や適切な置換基の導入といったヘテロ芳香環の変換により、蛍光特性が大きく変化することが確認され、溶媒効果の大きいソルバトクロミズムを示す誘導体を得ることができた。ヘテロ芳香族化合物 *N*-オキシド- BF_2CF_3 錯体は、ヘテロ芳香環部位の変換が容易であり、グラムスケールにおいても合成が可能である。本化合物群は空気中での保存が可能なほど安定であり、機能性材料としての応用が期待される。

Experimental

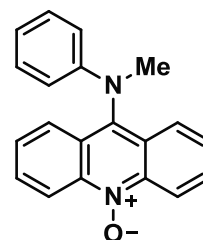
General. All reactions were carried out in a dry solvent under an argon atmosphere. Potassium trifluoro(trifluoromethyl)borate was purchased from Tokyo Chemical Industry Co., Ltd. Known heteroaromatic *N*-oxides **2b**¹¹⁾ and **2e**¹²⁾ were prepared according to the literature methods and identified by comparing these spectroscopic data with those of reported data. Other reagents and heteroaromatic compounds were purchased from commercial sources and used without further purification unless otherwise noted. Column chromatography was performed with silica gel (230-400 mesh ASTM). NMR spectra were recorded on JEOL JNM-ECX500 (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) and JEOL JNM-ECS400 (400 MHz for ^1H NMR, 125 MHz for ^{13}C NMR, 368 MHz for ^{19}F NMR, and 125 MHz for ^{11}B NMR) spectrometers. Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. Fluorine and boron chemical shifts are reported relative to trifluoroacetic acid (δ -76.55 ppm) and $\text{BF}_3\cdot\text{OEt}_2$ (δ 0.00 ppm) as an external reference, respectively. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared

spectrophotometer. ESI-MS spectra and DART-MS spectra were measured on a JEOL JMS-T100LC AccuTOF spectrometer for HRMS. UV/Vis absorption spectra were recorded on a SHIMADZU UV-1800 UV/Vis spectrophotometer using dilute sample solutions in spectral grade solvents in a 1.0 or 0.1 cm quartz cell. Fluorescence spectra were recorded on a SHIMADZU RF-5300PC spectrofluorophotometer in 1.0 cm quartz cell. The measurements of fluorescence spectra and the determination of absolute fluorescence quantum yields in the solid state were conducted with a Hamamatsu C9920-02 calibrated integrating sphere system equipped with multichannel spectrometer (PMA-11). Compounds for the analysis of photophysical properties were purified by recrystallization from hexane/ethyl acetate or hexane/acetone after column chromatography on silica gel.

4-(Phenylethynyl)pyridine 1-oxide (2c). 60% yield; pale yellow solid; $R_f = 0.10$ (ethyl acetate); $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 7.42-7.48 (m, 3H), 7.54-7.61 (m, 4H), 8.23 (d, $J = 6.3$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, $\text{DMSO-}d_6$) δ 86.4, 94.1, 118.5, 121.4, 128.7, 128.9, 129.5, 131.5, 139.1; IR (KBr, ν / cm^{-1}) 3062, 2210, 1496, 1473, 1269, 1173, 1137, 1027, 995, 863; HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{10}\text{NO}^+$ $[\text{M}+\text{H}^+]$ 196.0757, Found 196.0762.



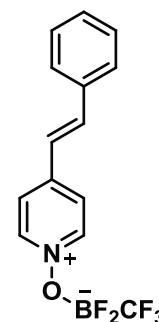
9-(Methyl(phenyl)amino)acridine 10-oxide (2f). 48% yield; orange solid; $R_f = 0.32$ (hexane/ethyl acetate = 1/2); $^1\text{H NMR}$ (400 MHz, acetone- d_6) δ 3.58 (s, 3H), 6.61 (d, $J = 7.3$ Hz, 2H), 6.71 (t, $J = 7.7$ Hz, 1H), 7.14 (dd, $J = 7.7, 7.3$ Hz, 2H), 7.55-7.63 (m, 2H), 7.76-7.84 (m, 2H), 7.93 (d, $J = 9.0$ Hz, 2H), 8.83 (d, $J = 9.0$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, acetone- d_6) δ 39.9, 113.4, 118.4, 121.0, 125.7, 127.5, 128.7, 130.1,



131.2, 137.1, 141.6, 150.5; IR (KBr, ν / cm^{-1}) 3050, 1594, 1572, 1498, 1430, 1384, 1318, 1287, 781, 768; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}^+$ $[\text{M}+\text{H}^+]$ 301.1335, Found 301.1336.

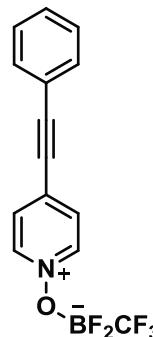
(E)-Difluoro((4-styryl-1-pyridinium-1-yl)oxy)(trifluoromethyl)borate (3b).

65% yield; white solid; $R_f = 0.55$ (hexane/ethyl acetate = 1/1); $^1\text{H NMR}$ (400 MHz, acetone- d_6) δ 7.42-7.51 (m, 3H), 7.55 (d, $J = 16.4$ Hz, 1H), 7.77 (dd, $J = 7.5, 1.6$ Hz, 2H), 7.95 (d, $J = 16.4$ Hz, 1H), 8.20-8.25 (m, 2H), 8.73 (d, $J = 7.2$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, acetone- d_6) δ 123.8, 124.9, 128.9, 129.9, 131.1, 136.3, 141.0, 143.1, 151.6; $^{19}\text{F NMR}$ (368 MHz, acetone- d_6) δ -161.3 (q, $J = 42.8$ Hz, 2F), -75.3 (q, $J = 27.0$ Hz, 3F); $^{11}\text{B NMR}$ (125 MHz, CD_3CN) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3126, 3064, 1619, 1577, 1499, 1460, 1332, 1233,

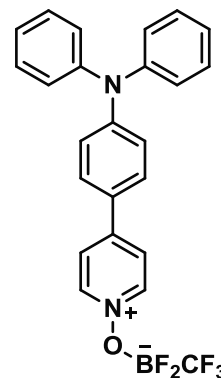


1207, 907; HRMS (ESI) Calcd for $C_{14}H_{11}BF_5NNaO^+$ $[M+Na^+]$ 338.0746, Found 338.0747.

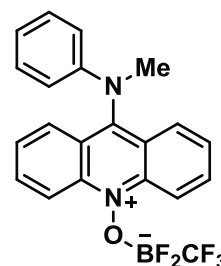
Difluoro((4-(phenylethynyl)-1-pyridinium-1-yl)oxy)(trifluoromethyl)borate (3c). 57% yield; white solid; $R_f = 0.65$ (hexane/ethyl acetate = 1/1); 1H NMR (400 MHz, acetone- d_6) δ 7.47-7.60 (m, 3H), 7.65-7.74 (m, 2H), 8.16-8.23 (m, 2H), 8.87 (d, $J = 6.7$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 85.3, 102.4, 121.2, 129.7, 130.3, 131.6, 133.1, 137.5, 143.3; ^{19}F NMR (368 MHz, acetone- d_6) δ -161.1 (q, $J = 42.8$ Hz, 2F), -75.4 (q, $J = 27.0$ Hz, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3124, 2223, 2186, 1623, 1506, 1482, 1449, 1207, 1079, 899; HRMS (ESI) Calcd for $C_{14}H_9BF_5NNaO^+$ $[M+Na^+]$ 336.0590, Found 336.0581.



((4-(4-(Diphenylamino)phenyl)-1-pyridinium-1-yl)oxy)difluoro(trifluoromethyl)borate (3e). 71% yield; yellow solid; $R_f = 0.59$ (CH_2Cl_2); 1H NMR (400 MHz, CD_3CN) δ 7.02 (d, $J = 9.0$ Hz, 2H), 7.17-7.25 (m, 6H), 7.38 (d, $J = 7.9$ Hz, 2H), 7.40 (d, $J = 7.9$ Hz, 2H), 7.75 (d, $J = 9.0$ Hz, 2H), 8.03 (d, $J = 7.2$ Hz, 2H), 8.52 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ 121.0, 123.9, 125.7, 126.2, 127.2, 130.0, 130.8, 142.7, 147.2, 152.5, 153.3; ^{19}F NMR (368 MHz, CD_3CN) δ -161.5 (q, $J = 34.2$ Hz, 2F), -75.8~-75.3 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 0.61 (m); IR (KBr, ν / cm^{-1}) 3125, 1584, 1485, 1335, 1298, 1213, 1073, 909, 818, 762; HRMS (ESI) Calcd for $C_{24}H_{18}BF_5N_2NaO^+$ $[M+Na^+]$ 479.1325, Found 479.1309.



Difluoro((9-(methyl(phenyl)amino)-10-acridinium-10-yl)oxy)(trifluoromethyl)borate (3f). 67% yield; purple solid; $R_f = 0.71$ (hexane/ethyl acetate = 1/2); 1H NMR (400 MHz, acetone- d_6) δ 3.91 (s, 3H), 6.92-7.00 (m, 3H), 7.28 (dd, $J = 7.6, 7.6$ Hz, 2H), 7.81 (dd, $J = 8.2, 8.0$ Hz, 2H), 8.26 (dd, $J = 8.6, 8.0$ Hz, 2H), 8.30 (d, $J = 8.2$ Hz, 2H), 8.83 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (100 MHz, acetone- d_6) δ 42.8, 116.7, 120.3, 121.8, 126.1, 127.0, 128.5, 130.5, 137.2, 142.9, 150.1, 159.1; ^{19}F NMR (368 MHz, acetone- d_6) δ -156.9 (q, $J = 34.2$ Hz, 2F), -74.8 (m, 3F); ^{11}B NMR (125 MHz, CD_3CN) δ 1.22 (m); IR (KBr, ν / cm^{-1}) 1609, 1573, 1548, 1489, 1439, 1410, 1382, 1071, 893, 763; HRMS (ESI) Calcd for $C_{21}H_{16}BF_5N_2NaO^+$ $[M+Na^+]$ 441.1168, Found 441.1187.



Computational Method. The geometry optimization of **3e** were performed using the B3LYP functional with the 6-31+G(d) basis set, implemented in the Jaguar program¹³, respectively. A stationary point was optimized without any symmetry assumptions and characterized by frequency analysis at the same level of theory (the number of imaginary frequencies, NIMAG, was 0.) The Cartesian coordinates for all calculated compounds are given in Tables 3-4.

Table 3-4. Cartesian Coordinates of **3e**.^a

atom	x	y	z
C1	1.1469520181	-1.1400260173	0.8271161272
C2	0.6317538313	0.0643632712	0.3161030039
C3	-0.6542178061	0.0336272378	-0.2520424158
C4	-1.3916994379	-1.1376334787	-0.3064597965
C5	-0.8745913218	-2.3380795317	0.2170232031
C6	0.4139078757	-2.3149207392	0.7840916253
H7	2.1436105350	-1.1711213397	1.2570095976
H9	-1.0999829768	0.9401026072	-0.6502268732
H10	-2.3779904372	-1.1202839539	-0.7567134012
N10	-1.6258108237	-3.5234431115	0.1768333053
H12	0.8461764122	-3.2219862161	1.1918035794
N12	2.8266830747	3.6743913420	0.5186355857
C13	2.0031395320	3.4774477781	-0.5275762861
C14	1.2914763490	2.3041074578	-0.6178628814
C15	1.4060891811	1.3176129004	0.3803891981
C16	2.2825832408	1.5850197473	1.4491611520
C17	2.9834274923	2.7672852579	1.5007578956
H19	1.9722091877	4.2774316485	-1.2540284929
H20	0.6551537546	2.1547705128	-1.4813367887
H21	2.4096012131	0.8778873681	2.2596118573
H22	3.6731014969	3.0445266496	2.2858638977
O22	3.4734267242	4.8710355595	0.6248694936
B23	4.8427098105	4.8023037779	-0.0548971520
C26	5.5116146894	6.2976608318	0.0857881403
F25	6.7285925640	6.3693849962	-0.5227906829

F26	4.7461662315	7.2829414742	-0.4850435823
F27	5.7164029022	6.6786293249	1.3870009395
F28	4.6527121942	4.4556745388	-1.4063830780
F29	5.6183705359	3.8276127051	0.6014958142
C31	-5.8554766054	-3.4063162026	0.1340257468
C32	-5.1629051949	-4.1704825206	-0.8057111872
C33	-3.7706289247	-4.2066973893	-0.7949007795
C34	-3.0528698824	-3.4786269333	0.1623447081
C35	-3.7522531419	-2.7186698106	1.1096057275
C36	-5.1440614450	-2.6812284173	1.0903813046
H37	-6.9414819560	-3.3787514393	0.1231321957
H38	-5.7072374733	-4.7396008864	-1.5537128539
H39	-3.2353763863	-4.7986912632	-1.5315237611
H40	-3.2026514305	-2.1614440661	1.8628985149
H41	-5.6740777829	-2.0878297920	1.8299419782
C41	0.2596832249	-7.3108420405	0.1169377311
C42	-0.7590984488	-7.0456776737	1.0326761711
C43	-1.3771552621	-5.7979662897	1.0558885780
C44	-0.9821510813	-4.7979695667	0.1579073329
C45	0.0362462437	-5.0704151676	-0.7653801289
C46	0.6545911291	-6.3179482310	-0.7800509374
H47	0.7406560342	-8.2848715922	0.1010655759
H48	-1.0746568009	-7.8121285474	1.7346017853
H49	-2.1667102083	-5.5947217760	1.7734441229
H50	0.3392275277	-4.3043278114	-1.4734962131
H51	1.4430136371	-6.5166177346	-1.5002688678

^a Calculated at the B3LYP/6-31+G(d) level.

Table 3-5. Photophysical data of various pyridine *N*-oxide–BF₂CF₃ complex **3e**

compound	solvent	absorption		emission	stokes
		λ_{abs}	$\varepsilon/10^4$	λ_{em}	shift
		[nm] ^a	[M ⁻¹ cm ⁻¹]	[nm]	[cm ⁻¹]
3e	CH ₂ Cl ₂	426	3.11	564 ^b	5700
	THF	411	2.96	557 ^c	6400
	Et ₂ O	411	3.04	540 ^d	5800
	toluene	416	2.66	515 ^e	4600
	<i>c</i> -Hexane	421	n/a ^f	482 ^e	3000

^a Absorption maximum wavelength of the longest absorption band. ^b Fluorescence maximum wavelength upon excitation at 430 nm. ^c Fluorescence maximum wavelength upon excitation at 400 nm. ^d Fluorescence maximum wavelength upon excitation at 390 nm. ^e Fluorescence maximum wavelength upon excitation at 360 nm. ^f Molar absorption coefficient in cyclohexane could not be determined due to the poor solubility of compound **3e**.

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総論

本論文では、既存の方法によるヘテロ芳香族化合物の活性化に比べ、さらに求電子的な活性化体として、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体を見出し、その特性を活用したヘテロ芳香族化合物の位置選択的トリフルオロメチル化反応の開発、および新規蛍光物質の創出に成功した^{1,2)}。

第 1 章では、既存の方法によるヘテロ芳香族化合物の活性化に比べ、さらに求電子的な活性化体として、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体を見出した。本化合物群は、ヘテロ芳香族化合物 *N*-オキシドから、温和な条件下、高い官能基許容性で得ることが可能であり、分液操作やシリカゲルカラムによる単離精製が可能ほど安定であることがわかった。

第 2 章では、求電子的な活性化体であるヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体の特性を活用し、種々の 6 員環ヘテロ芳香族化合物の位置選択的なトリフルオロメチル化を達成した。本反応は遷移金属触媒を必要とせず、温和な条件下、高い位置選択性、および高い官能基許容性で進行する。既存の求電子的トリフルオロメチルラジカルを用いた方法と相補的な特徴を有しており、二つの方法を使い分けることにより、種々のヘテロ芳香族化合物の位置選択的なトリフルオロメチル化が可能となった。

第 3 章では、ヘテロ芳香族化合物 *N*-オキシド-BF₂CF₃ 錯体が、溶液中および固体状態においても蛍光を示すことを見出した。 π 共役系の拡張や適切な置換基の導入といったヘテロ芳香環の変換により、蛍光特性が大きく変化することが確認され、溶媒効果の大きいソルバトクロミズムを示す誘導体を得ることができた。本化合物群は空気中での保存が可能ほど安定であり、機能性材料としての応用が期待される。

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