Synthesis of *N*-alkylpyridin-4-ones and thiazolo[3,2-*a*]pyridin-5-ones through Pummerer-type reactions

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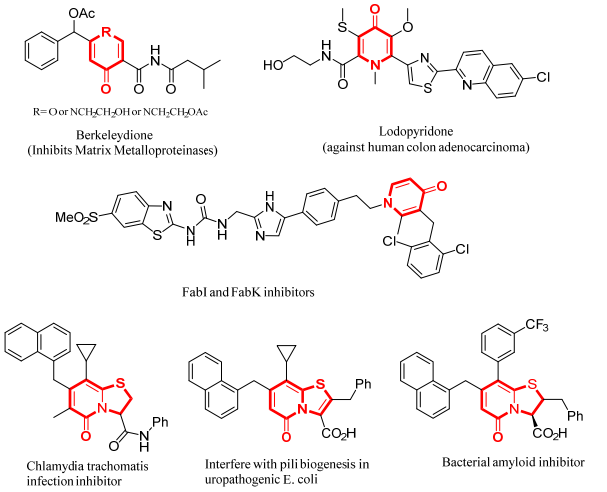
Supporting Information Placeholder

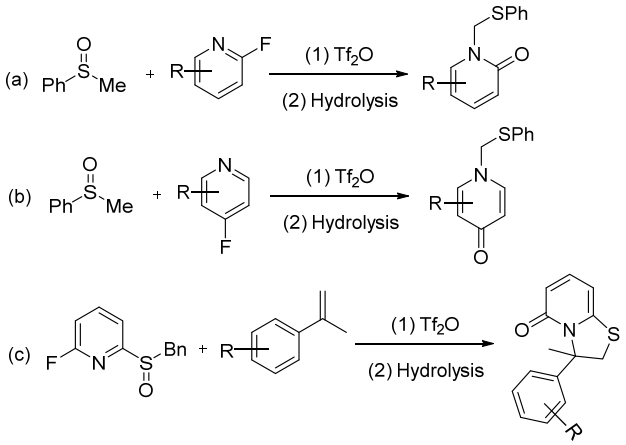
ABSTRACT: *N*-alkylated 4-pyridones were obtained through a one-pot procedure involving either normal or interrupted Pummerer reactions between triflic anhydride activated sulfoxides and 4-fluoropyridine derivatives, followed by hydrolysis. On the other hand, triflic anhydride activated benzyl 6-fluoro-2-pyridyl sulfoxide could react with olefins to afford thiazolo[3,2-*a*]pyridin-5-ones, via the pyridinium salt intermediates.

Pyridones are an important class of heterocyclic compounds.[1-3] For example, a number of *N*-alkylpyridin-4-one or thiazolo[3,2-*a*]pyridin-5-one structures were reported to have interesting pharmaceutical activities (Scheme 1).[4-15]



Scheme 1. Pharmaceutically active pyridin-4-one and thiazolo[3,2-*a*]pyridin-5-one derivatives

For the synthesis of *N*-alkylpyridin-4-one, alkylation of the parent 4-pyridone, or its tautomeric form 4-hydroxypyridine, would afford a mixture of *N*-/*O*-alkylation products,[16-18] namely the *N*-alkylated 4-pyridones or 4-alkoxypyridines. Thus, traditional approach to *N*-alkylated 4-pyridones usually involves the condensation between pyran-4-one and amines,[19-20] oxidation of piperidin-4-one,[21] alkylation of pyridin-4-one,[16-18] as well as other cyclization reactions.[22-28] On the other hand, reports on the synthesis of thiazolo[3,2-*a*]pyridin-5-one structures almost always involves the cyclization reactions to construct the pyridone rings.[29-34] As part of our research program[35-41] on the reactivity of activated sulfoxides,[42-52]



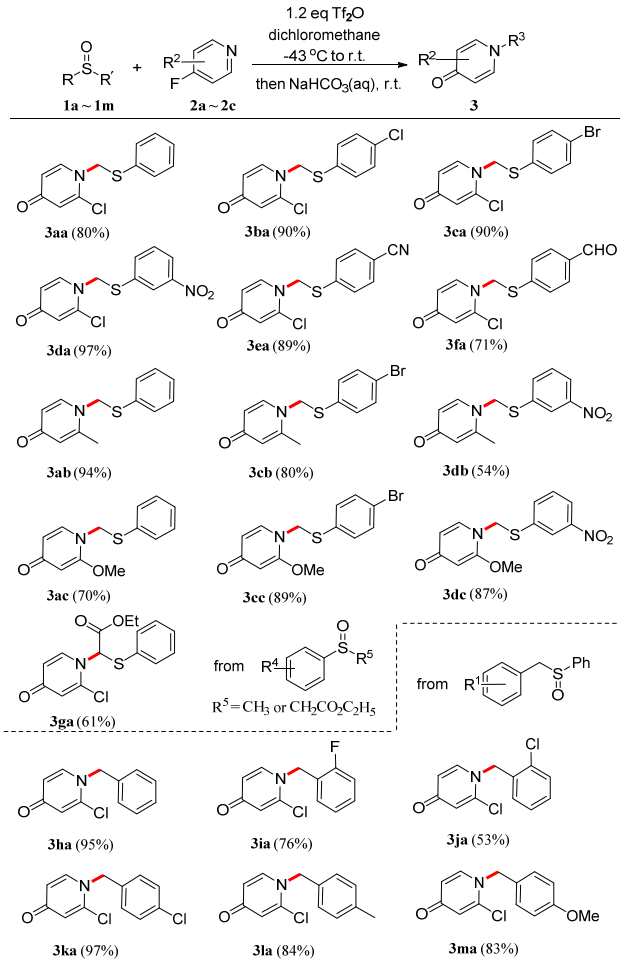
Scheme 2. Pummerer-type reaction approach to access *N*-alkylpyridinones and thiazolo[3,2-*a*]pyridin-5-ones

we report an alternative Pummerer-type reaction approach to access either *N*-alkylpyridin-4-one or thiazolo[3,2-*a*]pyridin-5-one structures from readily available pyridine derivatives.

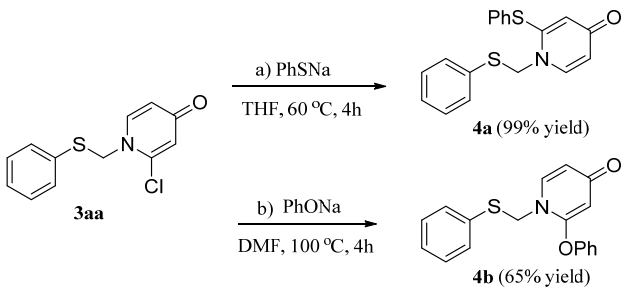
Our group has previously reported the synthesis of *N*-alkylpyridin-2-ones [35] (Scheme 2a) in which 2-fluoropyridines were involved in either normal or interrupted Pummerer reaction with activated sulfoxides. Simple extension for the synthesis of *N*-alkylpyridin-4-one (Scheme 2b) from 4-fluoropyridines worked just as expected. We directly adopted our previous reaction conditions to access a number of 1-(phenylthio)methylpyridin-4-one and 1-benzylpyridin-4-one type products in good to excellent yields (Scheme 3). For product derivatization, we were able to substitute the chloro group in **3aa** with PhSNa to give sulfide **4a**, and with PhONa to give ether **4b** (Scheme 4). Proposed reaction mechanisms for either normal or interrupted Pummerer reaction between 4-fluoropyridines with activated sulfoxides are shown in Scheme 5, which are essentially the same as our previous report for the synthesis of *N*-alkylpyridin-2-ones from 2-fluoropyridines.[35]

It should be noted that, due to their low nucleophilicity, 2-fluoropyridine[53-58] and 2-chloropyridine[59-63] were widely used as acid scavengers in reactions involving triflic anhydride activation of sulfoxides or amides. Therefore, our use of electron-deficient pyridines as nucleophiles in Pummerer-type reactions is still very rare.

Table 1. Synthesis of N-alkylpyridin-4-ones[a]

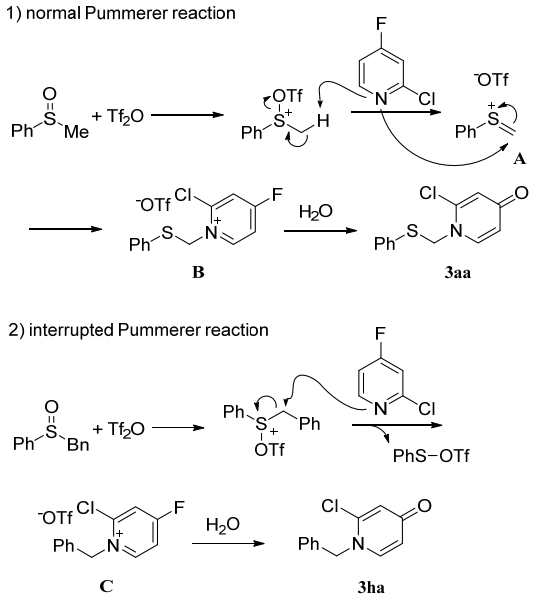


[a]Isolated yields.

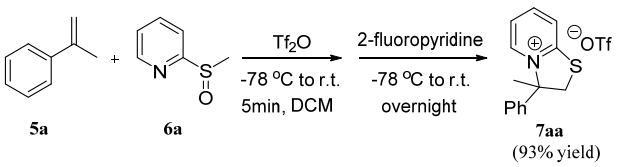


Scheme 3. Product derivatization

Encouraged by the unusual reactivity between either 2-fluoropyridines or 4-fluoropyridines and triflic anhydride activated sulfoxides, we then turned our attention to explore the possibility of using pyridine-containing sulfoxides for Pummerer-type reactions (Scheme 2c). Serendipitously, α-methylstyrene (**5a**) attacked the triflic anhydride activated methyl 2-pyridyl sulfoxide (**6a**) to afford thiazolo[3,2-*a*]pyridin-4-ium triflate **7aa,** as shown in Scheme 5 (see supporting information for the optimization of reaction conditions).



Scheme 4. Proposed reaction mechanisms for the synthesis of *N*-alkylpyridin-4-ones



Scheme 5. Synthesis of thiazolo[3,2-*a*]pyridin-4-ium triflate

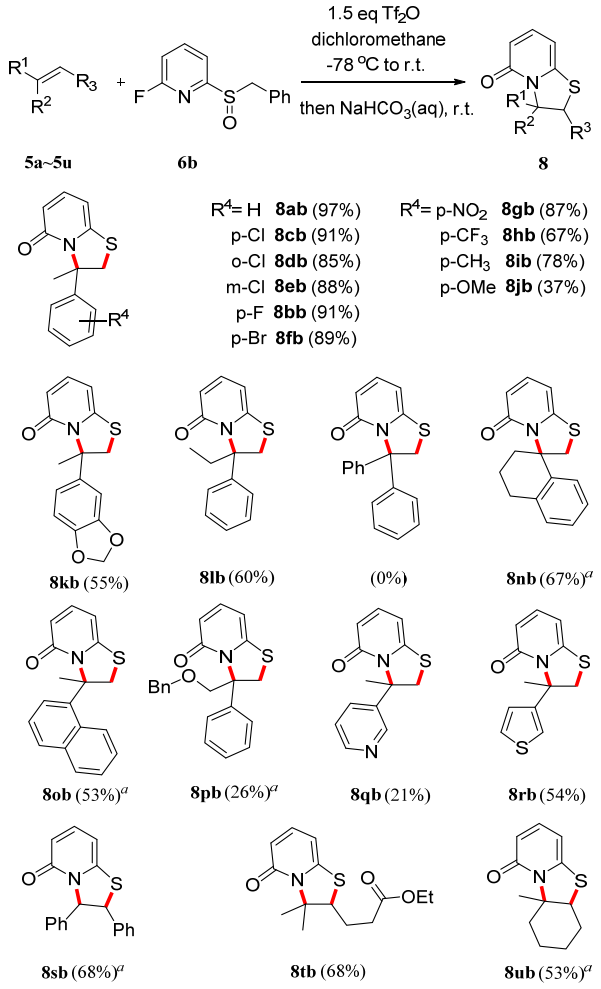
While preparation of thiazolo[3,2-*a*]pyridin-4-ium salts might have its own application in some circumstances, we decided to further explore the conversion of such pyridinium salts into corresponding pyridones. Apparently, the most straightforward means was to switch our substrate to methyl 6-fluoro-2-pyridyl sulfoxide, since the resulting fluoropyridinium intermediates should easily hydrolyzed to give pyridones. Unfortunately, synthesis of this substrate was not successful in our hand.

Considering the substitution reaction of a benzyl group could be as facile as substitution of a methyl group (see our discussion of the proposed reaction mechanism in Scheme 6), we synthesized the related benzyl 6-fluoro-2-pyridyl sulfoxide (**6b**) through a two-step sequence, namely nucleophilic aromatic substitution between 2,6-difluoropyridine with sodium benzylthiolate, followed by controlled oxidation of resulting thioether to give corresponding sulfoxide. Pleasingly, triflic anhydride activated sulfoxide **6b** indeed react with α-methylstyrene **5a** to afford thiazolo[3,2-*a*]pyridin-5-one **8ab**, most likely through same kind of pyridinium salt intermediates as **7aa**.

Then, we explored the substrate scope by using a number of substituted olefins and 6-fluoro-2-pyridyl sulfoxide (Table 2). From various substituted α-methylstyrenes, products **8ab** to **8ib** were obtained in good to excellent yields, while the methoxy containing product **8jb** was obtained in lower yield. Acetal group containing product **8kb** was also

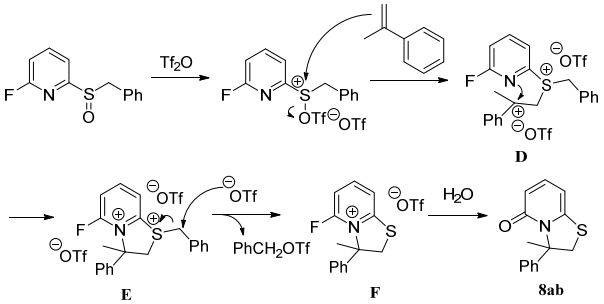
obtained in 55% yield. The use of 1,1-diphenyl ethylene as substrate gave no desire product, probably due to steric effect. Products containing spiro ring (**8nb**) or naphthalene group (**8ob**) were also obtained. Products containing other substituents such as pyridine ring (**8qb**), and thiophene ring (**8rb**), and benzyl ether group (**8pb**) could also be obtained, albeit with lower yields. In addition, 1,2-diphenyl ethylene could react smoothly to obtain product **8sb** in 68% yield. Trisubstituted olefin having an ester group or 1-methylcyclohexene could react with sulfoxide to give corresponding products **8tb** and **8ub** in acceptable yields.

Table 2. Substrate scope for disubstituted and trisubstituted olefins[b]



[a]Use 2.0 eq olefin. [b]Isolated yields.

The proposed mechanism for the reaction between α-methylstyrene and benzyl 6-fluoro-2-pyridyl sulfoxide to form **8ab** is shown in Scheme 6. After the sulfoxide was activated by triflic anhydride, olefin would attack the highly electrophilic sulfur to form intermediate **D**, which then underwent intramolecular ring closure to form dicationic intermediate **E**. Since the dicationic intermediate **E** would be very electrophilic, the benzyl group could then be substituted by the poorly nucleophilic triflate anion, to form intermediate **F**, similar as **7aa** (Scheme 5). And finally, product **8ab** would be formed by hydrolysis of the fluoropyridinium intermediate **F** during aquoues work-up.



Scheme 6. Proposed reaction mechanisms to synthesis thiazolo[3,2-*a*]pyridin-5-ones

In conclusion, novel syntheses of pyridone structures from pyridine derivatives were realized. A one-pot synthesis of *N*-alkylated 4-pyridone products were achieved in good to excellent yields through either normal or interrupted Pummerer reactions between triflic anhydride activated sulfoxides and 4-fluoropyridine derivatives, followed by hydrolysis. Similarly, triflic anhydride activated benzyl 6-fluoro-2-pyridyl sulfoxide can react with olefins to synthesize thiazolo[3,2-*a*]pyridin-5-ones. The use of readily available pyridine derivatives to explore unusual reactivity with different kinds of activated sulfoxide reagents is the key for the development of these chemistry.

Experimental

Unless otherwise noted, all materials were purchased from commercial suppliers. Dichloromethane was refluxed over CaH_2, and freshly distilled prior to use. Flash column chromatography was performed using silica gel (normal phase, 200-300 mesh). Reactions were monitored by thin-layer chromatography on silica gel 60-F254 coated 0.2 mm plates. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer, usually in $CDCl_3$ with TMS as an internal standard, and the chemical shifts (δ) were reported in parts per million (ppm). The IR spectra (KBr pellets, ν [cm^{-1}]) were taken on a FTIR spectrometer. HRMS measurements were carried out on a TOF mass spectrometer. Melting points were obtained on a melting point apparatus and were uncorrected.

A. Preparation of sulfoxide substrates

*Methyl 2-pyridyl sulfoxide (**6a**)*: A 100 mL round bottom flask was charged with 2-mercaptopyridine (1.667 g, 1.0 eq, 15 mmol), 30 mL dry tetrahydrofuran, and 3 mL dry MeCN, Cool to 0 °C. Then DBU (2.2 mL, 1.1 eq, 16.5 mmol) was added, reacted 5 min. CH_3I (1.03 ml, 1.1 eq, 16.5 mmol) was added drop by drop at 0 °C, the mixture was stirred at r.t. for 4 hours. Added 20 mL H_2O, extracted with ethyl acetate (20 ml × 3), dryed over sodium sulfate, purified with flash column chromatography (petroleum ether/ethyl acetate = 20/1), to give 1.713 g thioether product as colorless liquid in 91% yield. 1.71 g (1.0 eq, 13.7 mmol) of the obtained methyl pyridyl sulfide was dissolved in 160 mL of dichloromethane (12 ml/mmol), and after cooling to 0 °C, m-CPBA (3.602 g, 1.3 eq, 17.8 mmol) dissolved in 60 ml dichloromethane was added drop by drop at 0 °C, stirred at room temperature for 16 h, washed with

saturated sodium bicarbonate solution 100 ml × 3, extracted with dichloromethane 100 ml × 3, purified with flash column chromatography (ethyl acetate), to give 658 mg of product **6a**, yield 34%. **6a**: R_f = 0.15 (1:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68−8.55 (m, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.94 (td, J = 7.7, 1.7 Hz, 1H), 7.37 (ddd, J = 7.5, 4.7, 1.2 Hz, 1H), 2.84 (s, 3H).

*Benzyl 6-fluoro-2-pyridyl sulfoxide (**6b**)*: A 100 mL dry round bottom flask was charged with sodium hydride (60%, 306 mg, 1.3 eq, 7.39 mmol), 20 mL of tetrahydrofuran, and benzyl mercaptan (0.9 mL, 1.3 eq, 7.39 mmol) was added at 0 °C. 2,6-difluoropyridine (653 mg, 1.0 eq, 5.68 mmol, dissolved in 8 mL of dry tetrahydrofuran) was added slowly, and react at room temperature for 28 h. After the reaction completed, the tetrahydrofuran was spun dry, added with 30 mL of water, extracted with ethyl acetate 30 mL × 3, dried over anhydrous Na_2SO_4, and evaporated to dryness to give the crude product of 6-fluoropyridylbenzyl thioether. A 100 mL round bottom flask, was added 1.244 g (1.0 eq, 5.68 mmol) of crude thioether, 50 mL of dichloromethane, and m-CPBA (1.154 g, 1.0 eq, 5.68 mmol, 85%, dissolved in 20 mL dichloromethane) was slowly added at 0 °C. The reaction was carried out at room temperature until the starting material was consumed, was washed with saturated sodium bicarbonate solution three times and once with brine. The organic phase was dried over anhydrous sodium sulfateand, purified with flash column chromatography (petroleum ether/ethyl acetate 5:1) to give 927 mg as a white solid of **6b** was obtained in 69% yield. **6b:** R_f = 0.15 (5:1 petroleum ether/ethyl acetate); mp 94-96 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 15.6, 7.6 Hz, 1H), 7.51 (dd, J = 7.4, 1.5 Hz, 1H), 7.35−7.20 (m, 3H), 7.10−7.01 (m, 2H), 6.98 (dd, J = 8.4, 2.4 Hz, 1H), 4.37 (d, J = 13.2 Hz, 1H), 4.06 (d, J = 13.2 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.05 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (d, J = 248.5 Hz), 161.3 (d, J = 12.1 Hz), 142.4 (d, J = 8.1 Hz), 130.2, 128.9, 128.3, 128.3, 118.2 (d, J = 4.0 Hz), 110.7 (d, J = 36.0 Hz), 59.6. IR (KBr) ν (cm^{-1}) 3085, 3031, 2820, 1588, 1496, 1436, 1410, 1264, 1140, 1077, 1055, 991, 891, 801, 764, 699. HRMS(ESI): calculated for $C_{12}H_{10}FNNaOS^+$ $[M+Na]^+$ *m/z*: 258.0359, found: 258.0358.

B. Preparation of olefin substrates

General Procedure 1. To a flame-dried 100 mL round bottom flask, Ph_3PBr (1.2 eq, 4.284 g, 12 mmol) was added. Under nitrogen atmosphere, 40 mL tetrahydrofuran and 5 mL of n-BuLi (2.4 M, 1.2 eq, 12 mmol) was added at 0 °C. After 1 h, ketone (1.0 eq, 10 mmol) was added at room temperature. When the raw materials are exhausted, the reaction is quenched with ammonium chloride solution, extracted with petroleum ether (50 mL × 3), dried over anhydrous sodium sulfate, and then purified with flash column chromatography (petroleum ether).

General Procedure 2. To a flame-dried 100 mL round bottom flask, Ph_3PBr (1.2 eq, 4.284 g, 12 mmol) was added. Under nitrogen atmosphere, 40 mL tetrahydrofuran and 12 mL of t-BuOK (1.0 M, 1.2 eq, 12 mmol) was added at 0 °C. After 1 h, ketone (1.0 eq, 10 mmol) was added at room temperature. When the raw materials are exhausted, the reaction is quenched with ammonium chloride solution, extracted with petroleum ether (50 mL × 3), dried over anhydrous sodium sulfate, and then purified with flash column chromatography (petroleum ether).

*1-Fluoro-4-(prop-1-en-2-yl)benzene (**5b**)* was synthesized according to General Procedure 1 from 1-(4-fluorophenyl)ethan-1-one (1.38 g, 10 mmol), to give 761 mg product **5b** as colorless liquid in 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.41 (m, 2H), 7.08−6.95 (m, 2H), 5.32 (s, 1H), 5.08 (s, 1H), 2.15 (s, 3H).

*1-Chloro-4-(prop-1-en-2-yl)benzene (**5c**)* was synthesized according to General Procedure 1 from 1-(4-chlorophenyl)ethan-1-one (1.54 g, 10 mmol), to give 1.50 g product **5c** as colorless liquid in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 6.8 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 5.38 (s, 1H), 5.12 (s, 1H), 2.15 (s, 3H).

*1-Chloro-2-(prop-1-en-2-yl)benzene (**5d**)* was synthesized according to General Procedure 1 from 1-(2-chlorophenyl)ethan-1-one (1.54 g, 10 mmol), to give 1.145 g product **5d** as colorless liquid in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.35 (m, 1H), 7.25−7.17 (m, 3H), 5.26 (s, 1H), 5.00 (s, 1H), 2.14 (s, 3H).

*1-Chloro-3-(prop-1-en-2-yl)benzene (**5e**)* was synthesized according to General Procedure 1 from 1-(3-chlorophenyl)ethan-1-one (1.54 g, 10 mmol), to give 1.055 g product **5e** as colorless liquid in 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.34−7.30 (m, 1H), 7.25−7.20 (m, 2H), 5.32 (s, 1H), 5.07 (s, 1H), 2.07 (s, 3H).

*1-Bromo-4-(prop-1-en-2-yl)benzene (**5f**)* was synthesized according to General Procedure 1 from 1-(4-bromophenyl)ethan-1-one (1.99 g, 10 mmol), to give 1.055 g product **5f** as colorless liquid in 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 5.37 (s, 1H), 5.11 (s, 1H), 2.14 (s, 3H).

*1-Nitro-4-(prop-1-en-2-yl)benzene (**5g**)* was synthesized according to General Procedure 1 from 1-(4-nitrophenyl) ethan-1-one (1.65 g, 10 mmol), to give 761 mg product **5g** as colorless liquid in 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 9.3 Hz, 2H), 5.52 (s, 1H), 5.29 (s, 1H), 2.19 (s, 3H).

*1-(Prop-1-en-2-yl)-4-(trifluoromethyl)benzene (**5h**)* was synthesized according to General Procedure 1 from 1-(4-(trifluoromethyl)phenyl)ethan-1-one (1.88 g, 10 mmol), to give 767 mg product **5h** as colorless liquid in 41% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 5.45 (s, 1H), 5.21 (s, 1H), 2.18 (s, 3H).

*1-Methyl-4-(prop-1-en-2-yl)benzene (**5i**)* was synthesized according to General Procedure 1 from 1-(p-tolyl)ethan-1-one (1.34 g, 10 mmol), to give 1.415 g product **5i** as colorless liquid in 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.38 (s, 1H), 5.08 (s, 1H), 2.39 (s, 3H), 2.18 (s, 3H).

*1-Methoxy-4-(prop-1-en-2-yl)benzene (**5j**)* was synthesized according to General Procedure 1 from 1-(4-methoxyphenyl)ethan-1-one (1.50 g, 10 mmol), to give 1.416 g product **5j** as colorless liquid in 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 5.34 (s, 1H), 5.04 (s, 1H), 3.84 (s, 3H), 2.18 (s, 3H).

*5-(Prop-1-en-2-yl)benzo[d][1,3]dioxole (**5k**)* was synthesized a ccording to General Procedure 1 from 1-(benzo[d][1,3]dioxol-5-yl)ethan-1-one (1.64 g, 10 mmol), to give 1.37 g product **5k** as colorless liquid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, J = 1.6 Hz, 1H), 6.96 (dd, J = 8.0, 1.6 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 5.96 (s, 2H), 5.28 (s, 1H), 5.01 (s, 1H), 2.12 (s, 3H).

*But-1-en-2-ylbenzene (**5l**)* was synthesized according to General Procedure 1 from propiophenone (1.34 g, 10 mmol), to give 1.145 g product **5l** as colorless liquid in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.33 (m, 2H), 7.27 (t, J = 7.2 Hz, 2H), 7.23−7.18 (m, 1H), 5.22 (s, 1H), 5.01 (s, 1H), 2.46 (q, J = 7.2 Hz, 2H), 1.05 (t, J = 7.2 Hz, 3H).

*Ethene-1,1-diyldibenzene (**5m**)* was synthesized according to General Procedure 1 from benzophenone (1.82 g, 10 mmol), to give 1.69 g product **5m** as colorless liquid in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.29 (m, 10H), 5.51 (s, 2H).

*1-Methylene-1,2,3,4-tetrahydronaphthalene (**5n**)* was synthesized according to General Procedure 2 from 3,4-dihydronaphthalen-1(*2H*)-one (1.46 g, 10 mmol), to give 1.270 g

product **5n** as colorless liquid in 44% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.64 (m, 1H), 7.22−7.09 (m, 3H), 5.50 (s, 1H), 4.98 (s, 1H), 2.87 (t, J = 6.4 Hz, 2H), 2.61−2.53 (m, 2H), 1.91 (q, J = 6.4 Hz, 2H).

*1-(Prop-1-en-2-yl)naphthalene (**5o**)* was synthesized according to General Procedure 1 from 1-(naphthalen-1-yl)ethan-1-one (1.70 g, 10 mmol), to give 1.45 g product **5o** as colorless liquid in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.09 (m, 1H), 7.93−7.87 (m, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.57−7.44 (m, 3H), 7.36 (d, J = 6.8 Hz, 1H), 5.49−5.45 (m, 1H), 5.15−5.10 (m, 1H), 2.27 (s, 3H).

*(3-(Benzyloxy)prop-1-en-2-yl)benzene (**5p**)*: To a dry 100 mL reaction flask, added benzyl alcohol (1.07 g, 1.0 eq, 9.89 mmol), 20 mL dry tetrahydrofuran, sodium hydride (237 mg, 1.0 eq, 9.89 mmol), reacted at room temperature for 30 min. 3-bromo-2-phenyl 1-propene 1.95 g (1.0 eq, 9.89 mmol) was added, heated to reflux until the starting material was consumed. After petroleum ether extraction, purified with flash column chromatography (petroleum ether / ethyl acetate = 20/1) to give 1.38 g of product **5p**, yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.48 (m, 2H), 7.41−7.28 (m, 8H), 5.60 (s, 1H), 5.42 (s, 1H), 4.61 (s, 2H), 4.46 (s, 2H).

*3-(Prop-1-en-2-yl)pyridine (**5q**)* was synthesized according to General Procedure 2 from 1-(pyridin-3-yl)ethan-1-one (1.24 g, 10 mmol), to give 0.843 g product 5**q** as colorless liquid in 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 2.0 Hz, 1H), 8.48 (dd, J = 4.8, 1.6 Hz, 1H), 7.82−7.60 (m, 1H), 7.33−7.12 (m, 1H), 5.40 (s, 1H), 5.16 (s, 1H), 2.15 (s, 3H).

*3-(Prop-1-en-2-yl)thiophene (**5r**)* was synthesized according to General Procedure 1 from 1-(thiophen-3-yl)ethan-1-one (1.26 g, 10 mmol), to give 0.966 g product **5r** as colorless liquid in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.23 (m, 2H), 7.19 (s, 1H), 5.35 (s, 1H), 5.02 (s, 1H), 2.12 (s, 3H).

*Ethyl 5-methylhex-4-enoate (**5t**):* To a 50 mL round bottom flask, added 2-methyl-3-buten-2-ol (2.0 g, 1.0 eq, 23.3 mmol), 1,1,1-triethoxyethane (37.8 g, 10 eq , 233 mmol), cyclohexane-carboxylic acid (297 mg, 0.1 eq, 2.32 mmol), charged with a reflux condenser, refluxed for 3 h in an oil bath. When cooling to room temperature, extracted with ethyl acetate 30 mL × 3, organic phase washed with 10% HCl、saturated Na_2CO_3、saturated NaCl solution，dryed with anhydrous Na_2SO_4. Purified with flash column chromatography (petroleum ether/ethyl acetate = 30/1) to give 1.223 g of product **5t**, yield 34%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (d, J = 0.9 Hz, 1H), 4.09 (dq, J = 7.1, 1.9 Hz, 2H), 2.27 (s, 4H), 1.65 (s, 3H), 1.59 (s, 3H), 1.22 (td, J = 7.0, 1.8 Hz, 3H).

C. Synthesis 4-pyrdinones through Pummerer-type reactions

General Procedure A: To a flame-dried Schlenk tube, sulfoxide (**1**) (1 eq, 0.3 mmol) and 4-fluoropyedine (**2**) (2.4 eq, 0.72 mmol) were added, and then dissolved with dichloromethane (6 mL) before cooling down to -43 ºC. 1.2 eq Tf_2O (60 μL, 0.36 mmol) was added dropwise, and then gradually warming up to room temperature over 10 hours. The reaction was quenched with saturated sodium bicarbonate solution, stir vigorously for about 20 minutes (**3ab**、**3cb** and **3db**、**3ac**、**3cc** and **3dc**, stir vigorously for about 12 hour), diluted with water, extracted with dichloromethane, dried over sodium sulfate, and purified with flash column chromatography (petroleum ether/ethyl acetate/dichloromethane 6:3:1to 3:3:1) to give 61 mg product **3aa** as a solid in 80% yield.

*2-Chloro-1-((phenylthio)methyl)pyridin-4(1H)-one (**3aa**)* was synthesized according to General Procedure A from methyl phenyl sulfoxide (**1a**) (42 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 61 mg product **3aa** as a white solid in 80% yield. **3aa:** R_f = 0.51 (10:1 dichloromethane/methanol) mp 166-168 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.38 (m, 3H), 7.38−7.31 (m, 2H), 6.89 (d, J = 7.6 Hz, 1H), 6.48 (d, J = 2.4 Hz, 1H), 6.14 (dd, J = 7.6, 2.4 Hz, 1H), 5.21 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 140.9, 140.1, 135.3, 130.0, 129.9, 129.7, 119.5, 117.6, 59.9; HRMS[ESI]: calculated for $C_{12}H_{11}ClNOS^+$ $[M+H]^+$: 252.0244, found 252.0244.

*2-Chloro-1-(((4-chlorophenyl)thio)methyl)pyridin-4(1H)-one (**3ba**)* was synthesized according to General Procedure A from 4-chlorophenyl methyl sulfoxide (**1b**) (52 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 77 mg product **3ba** as a colorless liquid in 90% yield. **3ba:** R_f = 0.48 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (q, J = 8.4 Hz, 4H), 7.01 (d, J = 7.6 Hz, 1H), 6.45 (s, 1H), 6.15 (d, J = 7.6 Hz, 1H), 5.23 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 140.7, 140.1, 136.4, 136.3, 129.7, 128.4, 119.4, 117.6, 59.4; IR (neat) ν 3386, 3062, 2958, 1629, 1578, 1458, 1176, 1093 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}Cl_2NOS^+$ $[M+H]^+$: 285.9855, found 285.9857.

*1-(((4-Bromophenyl)thio)methyl)-2-chloropyridin-4(1H)-one (**3ca**)* was synthesized according to General Procedure A from 4-bromophenyl methyl sulfoxide (**1c**) (66 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 90 mg product **3ca** as a light yellow solid in 90% yield. **3ca:** R_f = 0.48 (10:1 dichloromethane/methanol) mp 141-143 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 2.4 Hz, 1H), 6.18 (dd, J = 8.4, 2.4 Hz, 1H), 5.19 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5 , 140.8, 134.0, 136.8, 132.9, 129.1, 124.8, 119.7, 117.9, 59.5; IR (neat) ν 3402, 3066, 2960, 1632, 1574, 1463, 1387, 1175, 1045, 1009, 854, 816 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}BrClNOS^+$ $[M+H]^+$: 329.9355, found 329.9356.

*2-Chloro-1-(((3-nitrophenyl)thio)methyl)pyridin-4(1H)-one (**3da**)* was synthesized according to General Procedure A from 1-(methylsulfinyl)-3-nitrobenzene (**1d**) (56 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 87 mg product **3da** as a light yellow solid in 97% yield. **3da:** R_f = 0.40 (10:1 dichloromethane/methanol) mp 124-126 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.06 (d, J = 7.6 Hz, 1H), 6.45 (s, 1H), 6.18 (d, J = 7.6 Hz, 1H), 5.33 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 148.6, 140.7, 140.6, 139.8, 139.8, 132.7, 130.5, 129.2, 124.6, 119.7, 118.2, 58.8; IR (neat) ν 3422, 3067, 2921, 1637, 1618, 1458, 1350, 1177, 1045 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}ClN_2O_3S^+$ $[M+H]^+$: 297.0095, found 297.0099.

*4-(((2-Chloro-4-oxopyridin-1(4H)-yl)methyl)thio)benzonitrile (**3ea**)* was synthesized according to General Procedure A from 4-(methylsulfinyl)benzonitrile (**1e**) (50 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 75 mg product **3ea** as a white yellow solid in 89% yield. **3ea:** R_f = 0.45 (10:1 dichloromethane/methanol) mp 166-168 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.0 Hz, 1H), 6.45 (d, J = 2.4 Hz, 1H), 6.19 (dd, J = 7.6, 2.4 Hz, 1H), 5.31 (s, 2H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.4, 140.7, 139.7, 136.9, 134.4, 133.0, 119.7, 118.2, 117.7, 113.3, 58.4; IR (neat) ν 3421, 3017, 2226, 1626, 1561, 1463, 1249, 1173, 1046, 829 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{10}ClN_2OS^+$ $[M+H]^+$: 277.0202, found 277.0201.

4-(((2-Chloro-4-oxopyridin-1(4H)-yl)methyl)thio)benzaldehyde ***(3fa)*** was synthesized according to General Procedure A from 4-(methylsulfinyl)benzaldehyde (**1f**) (50 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 59 mg product **3fa** as a colorless liquid in 71% yield. **3fa:** R_f = 0.36 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.44 (s, 1H), 6.14 (d, *J* = 7.6 Hz, 1H), 5.33 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 178.4, 140.8, 139.9, 138.1, 136.4, 134.2, 130.4, 119.6, 118.0, 58.5; IR (neat) ν 3392, 3067, 1698, 1624, 1598, 1462, 1174, 1045, 836, 688 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{11}ClNO_2S^+$ $[M+H]^+$: 280.0199, found 280.0201.

Ethyl 2-(2-chloro-4-oxopyridin-1(4H)-yl)-2-(phenylthio)acetate ***(3ga)*** was synthesized according to General Procedure A from ethyl 2-(phenylsulfinyl)acetate (**1g**) (64 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 59 mg product **3ga** as a colorless liquid in 61% yield. **3ga:** R_f = 0.51 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.44−7.36 (m, 3H), 7.36−7.29 (m, 2H), 6.43 (s, 1H), 6.41 (s, 1H), 6.29 (s, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 165.1, 140.8, 138.8, 134.7, 130.4, 129.8, 128.7, 118.7, 118.4, 63.7, 14.0; IR (neat) ν 3434, 3065, 2981, 1743, 1629, 1585, 1451, 1260, 1182, 1260, 1182, 1021 cm^{-1}; HRMS[ESI]: calculated for $C_{15}H_{15}ClNO_3S^+$ $[M+H]^+$: 324.0456, found 324.0455.

2-Methyl-1-((phenylthio)methyl)pyridin-4(1H)-one ***(3ab)*** was synthesized according to General Procedure A from methyl phenyl sulfoxide (**1a**) (42 mg, 0.3 mmol), 2.4 eq 2-methyl-4-fluoropyedine (**2b**) (80 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 65 mg product **3ab** as a red liquid in 94% yield. **3ab:** R_f = 0.38 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.11 (m, 5H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.14 (s, 1H), 5.99 (d, *J* = 7.6 Hz, 1H), 4.94 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3, 147.4, 140.6, 135.3, 129.9, 129.7, 129.6, 119.4, 116.8, 58.2, 19.2; IR (neat) ν 3421, 3053, 2967, 1637, 1560, 1262, 1180, 1085, 908, 729, 693 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{14}NOS^+$ $[M+H]^+$: 232.0791, found 232.0798.

1-(((4-Bromophenyl)thio)methyl)-2-methylpyridin-4(1H)-one ***(3cb)*** was synthesized according to General Procedure A from 4-bromophenyl methyl sulfoxide (**1c**) (66 mg, 0.3 mmol), 2.4 eq 2-methyl-4-fluoropyedine (**2b**) (80 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 75 mg product **3cb** as a red liquid in 80% yield. **3cb:** R_f = 0.40 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.19 (s, 1H), 6.06 (d, *J* = 6.8 Hz, 1H), 4.96 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4, 147.1, 140.5, 136.8, 132.8, 129.0, 124.6, 119.7, 117.2, 58.0, 19.4; IR (neat) ν 3378, 3047, 3000, 1633, 1564, 1473, 1397, 1260, 1181, 1087, 1009, 860, 816 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}BrNOS^+$ $[M+H]^+$: 309.9896, found 309.9896.

2-Methyl-1-(((3-nitrophenyl)thio)methyl)pyridin-4(1H)-one ***(3db)*** was synthesized according to General Procedure A from 1-(methylsulfinyl)-3-nitrobenzene (**1d**) (56 mg, 0.3 mmol), 2.4 eq 2-methyl-4-fluoropyedine (**2b**) (80 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 45 mg product **3db** as a red liquid in 54% yield. **3db:** R_f = 0.35 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.25 (d, *J* = 7.2 Hz, 1H), 7.73−7.43 (m, 2H), 6.85 (d, *J* = 6.8 Hz, 1H), 6.24 (s, 1H), 6.08 (d, *J* = 5.6 Hz, 1H), 5.11 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4, 148.6, 147.0, 140.8, 140.3, 132.7, 130.5, 129.2, 124.5, 120.1, 117.5, 57.7, 19.5; IR (neat) ν 3365, 2919, 1635, 1565, 1523, 1348, 1181, 1086, 723 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}N_2O_3S^+$ $[M+H]^+$: 277.0641, found 277.0645.

2-Methoxy-1-((phenylthio)methyl)pyridin-4(1H)-one ***(3ac)*** was synthesized according to General Procedure A from methyl phenyl sulfoxide (**1a**) (42 mg, 0.3 mmol), 2.4 eq 4-fluoro-2-methoxypyridine (**2c**) (91 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 52 mg product **3ac** as a colorless liquid in 70% yield. **3ac:** R_f = 0.46 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.11 (m, 5H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.01 (d, *J* = 6.0 Hz, 1H), 5.77 (s, 1H), 5.00 (s, 2H), 3.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.1, 158.50, 137.5, 134.8, 131.1, 129.3, 129.2, 114.5, 96.0, 56.3, 55.0; IR (neat) ν 3053, 2942, 1637, 1570, 1481, 1323, 1181, 1097, 1024, 836 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{14}NO_2S^+$ $[M+H]^+$: 248.0740, found 248.0744.

1-(((4-Bromophenyl)thio)methyl)-2-methoxypyridin-4(1H)-one ***(3cc)*** was synthesized according to General Procedure A from 4-bromophenyl methyl sulfoxide (**1c**) (42 mg, 0.3 mmol), 2.4 eq 4-fluoro-2-methoxypyridine (**2c**) (91 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 87 mg product **3cc** as a colorless liquid in 89% yield. **3cc:** R_f = 0.46 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.01 (d, *J* = 7.2 Hz, 1H), 5.68 (s, 1H), 4.99 (s, 2H), 3.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.0, 158.3, 137.1, 136.4, 132.5, 130.3, 124.0, 114.9, 95.9, 56.2, 54.7; IR (neat) ν 3392, 3018, 1641, 1567, 1538, 1475, 1231, 1181, 1091, 1023, 836, 816 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}BrNO_2S^+$ $[M+H]^+$: 325.9845, found 325.9844.

2-Methoxy-1-(((3-nitrophenyl)thio)methyl)pyridin-4(1H)-one ***(3dc)*** was synthesized according to General Procedure A from 1-(methylsulfinyl)-3-nitrobenzene (**1d**) (42 mg, 0.3 mmol), 2.4 eq 4-fluoro-2-methoxypyridine (**2c**) (91 mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 76 mg product **3dc** as a colorless liquid in 87% yield. **3dc:** R_f = 0.42 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 5.98 (dd, *J* = 7.6, 2.0 Hz, 1H), 5.65 (d, *J* = 1.2 Hz, 1H), 5.17 (s, 2H), 3.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.9, 158.3, 148.4, 139.6, 137.2, 134.3, 130.2, 128.0, 123.7, 115.2, 96.0, 56.4, 53.9; IR (neat) ν 3365, 3069, 1642, 1568, 1537, 1349, 1231, 1181, 1096, 1022, 837 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}N_2O_4S^+$ $[M+H]^+$: 293.0591, found 293.0597.

1-Benzyl-2-chloropyridin-4(1H)-one ***(3ha)*** was synthesized according to General Procedure A from (benzylsulfinyl)benzene (**1h**) (64 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 63 mg product **3ha** as a yellow liquid in 95% yield. **3ha:** R_f = 0.54 (10:1 dichloromethane/methanol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.30 (m, 4H), 7.13 (d, *J* = 6.8 Hz, 2H), 6.51 (d, *J* = 2.4 Hz, 1H), 6.35 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.19 (s, 2H).;^{13}C NMR (101

MHz, $CDCl_3$) δ 141.9, 141.2, 134.5, 129.3, 128.8, 126.8, 119.3, 118.4, 57.4; IR (neat) ν 3391, 3065, 1632, 1567, 1471, 1251, 1179, 1050, 850, 733 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{11}ClNO^+$ $[M+H]^+$: 220.0529, found 220.0528.

2-Chloro-1-(2-fluorobenzyl)pyridin-4(1H)-one ***(3ia)*** was synthesized according to General Procedure A from 1-fluoro-2-((phenylsulfinyl)methyl)benzene (**1i**) (70 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 54 mg product **3ia** as a light yellow solid in 76% yield. **3ia:** R_f = 0.27 (10:1 dichloromethane/methanol) mp = 154-157 °C. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J*=7.7, 1H), 7.38 (dd, *J*=13.7, 6.9, 1H), 7.22−7.15 (m, 1H), 7.15−7.07 (m, 2H), 6.52 (s, 1H), 6.43−6.23 (m, 1H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.5 (s), 161.5 (s), 159.1 (s), 130.8 (d, *J* = 8.3), 129.0 (d, *J* = 3.4), 124.9 (d, *J* = 3.6), 121.7 (d, *J* = 14.2), 118.9 (d, *J* = 96.1), 116.0 (d, *J* = 21.0), 51.5 (d, *J* = 4.3); IR (neat) ν 3400, 3067, 1632, 1573, 1470, 1251, 1193, 1049, 855, 758 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}ClFNO^+$ $[M+H]^+$: 238.0435, found 238.0433.

2-Chloro-1-(2-chlorobenzyl)pyridin-4(1H)-one ***(3ja)*** was synthesized according to General Procedure A from 1-chloro-2-((phenylsulfinyl)methyl)benzene (**1j**) (75 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 40 mg product **3ja** as a light yellow solid in 53% yield. **3ja:** R_f = 0.27 (10:1 dichloromethane/methanol) mp = 108-110 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.6 Hz, 1H), 7.38−7.23 (m, 3H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.57 (s, 1H), 6.43−6.36 (m, 1H), 5.29 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 142.0, 141.0, 132.5, 132.2, 130.1, 129.9, 127.7, 127.6, 55.0; IR (neat) ν 3391, 3065, 2924, 1632, 1573, 1468, 1216, 1050, 854, 752 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}Cl_2NO^+$ $[M+H]^+$: 254.0139, found 254.0140.

2-Chloro-1-(4-chlorobenzyl)pyridin-4(1H)-one ***(3ka)*** was synthesized according to General Procedure A from 1-chloro-4-((phenylsulfinyl)methyl)benzene (**1k**) (75 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 74 mg product **3ka** as a light yellow solid in 97% yield. **3ka:** R_f = 0.38 (10:1 dichloromethane/methanol) mp = 110-112 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.6 Hz, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.53 (s, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 5.16 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 141.6, 140.9, 134.8, 133.0, 129.5, 128.0, 119.5, 118.6, 56.7; IR (neat) ν 3400, 3064, 1627, 1573, 1469, 1395, 1251, 1176, 1048, 855, 811 cm^{-1}; HRMS[ESI]: calculated for $C_{12}H_{10}Cl_2NO^+$ $[M+H]^+$: 254.0139, found 254.0137.

2-Chloro-1-(4-methylbenzyl)pyridin-4(1H)-one ***(3la)*** was synthesized according to General Procedure A from 1-methyl-4-((phenylsulfinyl)methyl)benzene (**1l**) (69 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 59 mg product **3la** as a light yellow solid in 84% yield. **3la:** R_f = 0.40 (10:1 dichloromethane/methanol) mp = 146-148 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.52 (s, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 5.15 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 141.8, 140.8, 138.7, 131.4, 129.9, 126.8, 119.3, 118.4, 57.2, 21.1; IR (neat) ν 3408, 3058, 1627, 1573, 1469, 1177, 1048, 855 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}ClNO^+$ $[M+H]^+$: 234.0686, found 234.0686.

2-Chloro-1-(4-methoxybenzyl)pyridin-4(1H)-one ***(3ma)*** was synthesized according to General Procedure A from 1-methoxy-4-((phenylsulfinyl)methyl)benzene (**1m**) (74 mg, 0.3 mmol), 2-chloro-4-fluoropyridine (**2a**) (2.4 eq, 94mg, 0.72 mmol), eluted by 6:3:1 petroleum ether/ethyl acetate/dichloromethane to 3:3:1 petroleum ether/ethyl acetate/dichloromethane, to give 62 mg product **3ma** as a colorless liquid in 83% yield. **3ma:** R_f = 0.51 (10:1 dichloromethane/methanol). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.50 (d, *J* = 2.4 Hz, 1H), 6.33 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.12 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 159.9, 141.8, 140.8, 128.6, 126.3, 119.3, 118.4, 114.7, 57.0, 55.4; IR (neat) ν 3427, 3066, 2959, 2931, 1624, 1576, 1513, 1466, 1250, 1179, 1030, 854 cm^{-1}; HRMS[ESI]: calculated for $C_{13}H_{13}ClNO_2^+$ $[M+H]^+$: 250.0629, found 250.0630.

2-(Phenylthio)-1-((phenylthio)methyl)pyridin-4(1H)-one ***(4a)*** To a 5 mL flame dried flask, 1.5 eq sodium hydride (60%, 6 mg, 0.15 mmol), 1.5 eq thiophenol (16 mg, 0.15 mmol), and tetrahydrofuran (2.0 mL) were added, and the mixture was stirred at room tempreture for 15 minutes, then added 1eq pyrdin-4-one ***3aa*** (25mg, 0.1 mmol), the mixture was heated to 60 °C and reacted at 60 °C for 4 hours. The mixture was cooled to room temperature, and then extracted by dichloromethane (8 mL × 3). After drying with anhydrous sodium sulfate, it was concentrated and purified with flash column chromatography, eluted by petroleum ether/ethyl acetate (5/1), to give 32 mg product as a viscosity oil in 99% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 - 7.37 (m, 8H), 7.33 (m, 2H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.07 (m, 2H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 150.3, 140.9, 135.2, 134.0, 130.4, 130.1, 129.9, 129.7, 129.6, 128.7, 120.2, 116.7, 59.3; IR (neat) ν 3407, 3055, 2993, 1621, 1573, 1455, 1247, 1177, 1043, 853, 747, 690, 513 cm^{-1}; HRMS[ESI]: calculated for $C_{18}H_{16}NOS_2^+$ $[M+H]^+$: 326.0668, found 326.0669.

*2-Phenoxy-1-((phenylthio)methyl)pyridin-4(1H)-one (****4b****)* To a 5 mL flame dried flask, 1.5 eq sodium hydride (60%, 6 mg, 0.15 mmol), 1.5 eq phenol (14 mg, 0.15 mmol), and *N*,*N*-Dimethyformamide (2.0 mL) were added, and the mixture was stirred at room tempreture for 15 minutes, then added 1eq pyrdin-4-one ***3aa*** (25mg, 0.1 mmol), the mixture was heated to 100 °C and reacted at 100 °C for 4 hours. The mixture was cooled to room temperature, and then extracted by dichloromethane (8 mL × 3). After drying with anhydrous sodium sulfate, it was concentrated and purified with flash column chromatography, eluted by petroleum ether/ethyl acetate (5/1), to give 20 mg product as a viscosity oil in 65% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.2 Hz, 2H), 7.44−7.31 (m, 5H), 7.30−7.22 (m, 1H), 6.90 (dd, *J* = 13.6, 8.0 Hz, 3H), 6.08 (dd, *J* = 7.6, 2.0 Hz, 1H), 5.44 (d, *J* = 2.4 Hz, 1H), 5.23 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.7, 158.3, 151.7, 137.2, 135.0, 130.9, 130.1, 129,6, 129.5, 126.5, 120.9, 115.8, 99.6, 55.2; IR (neat) ν 3421, 3053, 2961, 1647, 1577, 1476, 1261, 1214, 1085, 839, 691 cm^{-1}; HRMS[ESI]: calculated for $C_{18}H_{16}NO_2S^+$ $[M+H]^+$: 310.0896, found 310.0897.

D. Synthesis thiazolo[3,2-*a*]pyridin-5-ones through Pummerer-type reactions

General Procedure B: 10 mL reaction tube flame dried under vacuum. After cooling, 2-benzylsulfinyl-6-fluoropyridine (94 mg, 1.0 eq, 0.4 mmol) was added. Olefin (1.0 eq, 0.4 mmol) or (2.0 eq, 0.8 mmol), 2-fluoropyridine (38 mg, 1.0 eq, 0.4 mmol), 4 mL dry dichloromethane was added under nitrogen atmosphere, then the reaction tube was placed in an ethyl acetate /liquid nitrogen ice bath. 5 min later, trifluoromethanesulfonic anhydride (100 μL, 1.5 eq, 0.6 mmol) was added, naturally warmed to room temperature and allowed to react overnight. Added 6 mL of saturated $NaHCO_3$ solution, stir vigorously for 20 min, extract with dichloromethane 6 mL × 3, dry over anhydrous Na_2SO_4, purified with flash column

chromatography (petroleum ether/ethyl acetate = 5/1 (120 mL) to petroleum ether/ethyl acetate = 3/1).

*3-Methyl-3-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8ab**)* was synthesized according to General Procedure B from prop-1-en-2-ylbenzene (47 mg, 1.0 eq, 0.4 mmol), to give 94 mg product **8ab** as colorless oil liquid in 97% yield; R_f = 0.28 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.30 (m, 2H), 7.29−7.21 (m, 4H), 6.17 (dd, J = 9.2, 0.8 Hz, 1H), 6.12 (dd, J = 7.2, 0.8 Hz, 1H), 3.45 (d, J = 11.6 Hz, 1H), 3.40 (d, J = 11.6 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 148.6, 142.3, 139.7, 128.6, 127.5, 124.6, 116.8, 100.1, 74.7, 44.2, 23.2. IR (KBr) ν (cm^{-1}) 3087, 3027, 2976, 2936, 1652, 1575, 1512, 1446, 1400, 1375, 1247, 1187, 1028, 767, 735, 696. HRMS(ESI): calculated for $C_{14}H_{14}NOS^+$ $[M+H]^+$ *m/z*: 244.0791, found: 244.0796.[1]

*3-(4-Fluorophenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one(**8bb**)* was synthesized according to General Procedure B from 1-fluoro-4-(prop-1-en-2-yl)benzene (54 mg, 1.0 eq, 0.4 mmol), to give 95 mg product **8bb** as yellow oil liquid in 91% yield; R_f = 0.29 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.18 (m, 3H), 7.05−6.96 (m, 2H), 6.16 (d, J = 8.8 Hz, 1H), 6.13 (d, J = 7.2 Hz, 1H), 3.43 (d, J = 12.0 Hz, 1H), 3.40 (d, J = 11.6 Hz, 1H), 2.19 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -115.04. ^{13}C NMR (101 MHz, CDCl3) δ 161.9 (d, J = 247.5 Hz), 162.2, 148.4, 139.8, 138.2 (d, J = 3.0 Hz), 126.5 (d, J = 8.1 Hz), 116.9, 115.5 (d, J = 22.2 Hz), 100.3, 74.2, 44.2, 23.2. IR (KBr) ν (cm^{-1}) 3042, 2977, 2935, 1654, 1602, 1577, 1511, 1445, 1401, 1375, 1230, 1165, 1146, 832, 778. HRMS(ESI): calculated for $C_{14}H_{13}FNOS^+$ $[M+H]^+$ *m/z*: 262.0696, found: 262.0700.

*3-(4-Chlorophenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8cb**)* was synthesized according to General Procedure B from 1-chloro-4-(prop-1-en-2-yl)benzene (61 mg, 1.0 eq, 0.4 mmol), to give 101 mg product **8cb** as yellow oil liquid in 91% yield; R_f = 0.29 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, CDCl3) δ 7.31 (d, J = 8.8 Hz, 2H), 7.24 (dd, J = 9.2 Hz, 7.6 Hz, 1H), 7.18 (d, J = 8.8 Hz, 2H), 6.16 (d, J = 8.8 Hz, 1H), 6.13 (d, J = 6.8 Hz, 1H), 3.42 (d, J = 11.6 Hz, 1H), 3.38 (d, J = 11.6 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 162.1, 148.3, 141.0, 139.8, 133.4, 128.8, 126.1, 116.9, 100.3, 74.1, 44.0, 22.9. IR (KBr) ν (cm^{-1}) 3085, 3032, 2976, 2935, 1654, 1578, 1508, 1443, 1400, 1375, 1224, 1146, 1094, 1011, 823, 778, 733. HRMS(ESI): calculated for $C_{14}H_{13}ClNOS^+$ $[M+H]^+$ *m/z*: 278.0401, found: 278.0407.

*3-(2-Chlorophenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8db**)* was synthesized according to General Procedure B from 1-chloro-2-(prop-1-en-2-yl)benzene (61 mg, 1.0 eq, 0.4 mmol), to give 94 mg product **8db** as yellow oil liquid in 85% yield; R_f = 0.27 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, CDCl3) δ 7.57 (d, J = 7.6, 1H), 7.38−7.28 (m, 2H), 7.25−7.22 (m, 1H), 7.20 (dd, J = 8.8, 7.2, 1H), 6.11 (d, J = 7.2, 1H), 6.07 (d, J = 9.2, 1H), 4.00 (d, J = 11.2, 1H), 3.11 (d, J = 11.2, 1H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 161.6, 148.0, 139.8, 138.6, 131.7, 131.4, 129.2, 128.2, 127.0, 115.8, 100.1, 73.6, 40.5, 22.4. IR (KBr) ν (cm^{-1}) 3080, 2978, 1654, 1576, 1510, 1439, 1372, 1280, 1223, 1144, 1036, 1025, 766, 747 . HRMS(ESI): calculated for $C_{14}H_{13}ClNOS^+$ $[M+H]^+$ *m/z*: 278.0401, found: 278.0404.

*3-(3-Chlorophenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8eb**)* was synthesized according to General Procedure B from 1-chloro-3-(prop-1-en-2-yl)benzene (61 mg, 1.0 eq, 0.4 mmol), to give 98 mg product **8eb** as yellow oil liquid in 88% yield; R_f = 0.29 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, CDCl3) δ 7.33−7.20 (m, 4H), 7.14−7.06 (m, 1H), 6.17 (d, J = 8.8, 1H), 6.13 (d, J = 6.8, 1H), 3.43 (d, J = 11.6, 1H), 3.38 (d, J = 11.6, 1H), 2.18 (s,3 H). ^{13}C NMR (101 MHz, CDCl3) δ 162.1, 148.3, 144.6, 139.9, 134.6, 129.9, 127.7, 125.0, 122.9, 116.9, 100.3, 77.3, 77.0, 76.7, 74.1, 44.0, 22.9. IR (KBr) ν (cm^{-1}) 3082, 2977, 2937, 1654, 1577, 1512, 1374, 1268, 1225, 1145, 1029, 878, 777, 736, 692. HRMS(ESI): calculated for $C_{14}H_{13}ClNOS^+$ $[M+H]^+$ *m/z*: 278.0401, found: 278.0405.

*3-(4-Bromophenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8fb**)* was synthesized according to General Procedure B from 1-bromo-4-(prop-1-en-2-yl)benzene (79 mg, 1.0 eq, 0.4 mmol), to give 115 mg product **8fb** as yellow oil liquid in 89% yield; R_f = 0.28 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.6 Hz, 2H), 7.30−7.20 (m, 1H), 7.12 (d, J = 8.0 Hz, 2H), 6.23−6.05 (m, 2H), 3.54−3.24 (m, 2H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 148.3, 141.5, 139.8, 131.6, 126.4, 121.5, 116.8, 100.2, 74.1, 43.9, 22.8. IR (KBr) ν (cm^{-1}) 2980, 2920, 2849, 1713, 1524, 1489, 1444, 1377, 1267, 1187, 1074, 1011, 840, 824, 749,695. HRMS(ESI): calculated for $C_{14}H_{13}BrNOS^+$ $[M+H]^+$ *m/z*: 321.9896, found: 321.9897.

*3-Methyl-3-(4-nitrophenyl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8gb**)* was synthesized according to General Procedure B from 1-nitro-4-(prop-1-en-2-yl)benzene (65 mg, 1.0 eq, 0.4 mmol), to give 100 mg product **8gb** as yellow oil liquid in 87% yield; R_f = 0.26 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.36−7.22 (m, 1H), 6.18 (d, J = 8.0 Hz, 2H), 3.46 (d, J = 11.6 Hz, 1H), 3.41 (d, J = 11.6 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 149.8, 148.0, 147.1, 140.2, 125.8, 124.0, 116.9, 100.6, 74.0, 43.7, 22.4. IR (KBr) ν (cm^{-1}) 3081, 2980, 2938, 2852, 1655, 1577, 1511, 1454, 1347, 1277, 1147, 1110, 1029, 851, 781, 737. HRMS(ESI): calculated for $C_{14}H_{13}N_2O_3S^+$ $[M+H]^+$ *m/z* : 289.0641, found: 289.0643.

*3-Methyl-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-on (**8hb**)* was synthesized according to General Procedure B from 1-(prop-1-en-2-yl)-4-(trifluoromethyl) benzene (74 mg, 1.0 eq, 0.4 mmol), to give 83 mg product **8hb** as yellow oil liquid in 67% yield; R_f = 0.28 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.27 (dd, J = 9.2, 7.2 Hz, 1H), 6.17 (dd, J = 11.6, 9.6 Hz, 2H), 3.57−3.33 (m, 2H), 2.22 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.59. ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 148.4, 146.5, 140.1, 129.8 (q, J = 32.7 Hz), 125.8 (d, J = 3.5 Hz), 125.2, 122.6 (q, J = 273.7 Hz), 117.0, 100.5, 74.3, 44.0, 22.9. IR (KBr) ν (cm^{-1}) 2978, 2921, 1655, 1577, 1511, 1325, 1117, 1076, 1014, 776.HRMS(ESI): calculated for $C_{15}H_{13}F_3NOS^+$ $[M+H]^+$ *m/z*: 312.0664, found: 312.0667.

*3-Methyl-3-(p-tolyl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8ib**)* was synthesized according to General Procedure B from 1-methyl-4-(prop-1-en-2-yl)benzene (53 mg, 1.0 eq, 0.4 mmol), to give 80 mg product **8ib** as yellow oil liquid in 78% yield; R_f = 0.28 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, J = 8.8, 7.2 Hz, 1H), 7.18−7.07 (m, 4H), 6.16 (d, J = 8.8 Hz, 1H), 6.11 (d, J = 6.8 Hz, 1H), 3.45 (d, J = 11.6 Hz, 1H), 3.38 (d, J = 11.6 Hz, 1H), 2.31 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 148.6, 139.7, 139.5, 137.3, 129.4, 124.6, 117.0, 100.2, 74.7, 44.3, 23.2, 21.0. IR (KBr) ν (cm^{-1}) 3024, 2974, 2922, 1660, 1579, 1514, 1443, 1400, 1375, 1273, 1225, 1145, 1029, 814, 777. HRMS(ESI): calculated for $C_{15}H_{16}NOS^+$ $[M+H]^+$ *m/z*: 258.0947, found: 258.0948.

*3-(4-Methoxyphenyl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one (**8jb**)* was synthesized according to General Procedure B from 1-methoxy-4-(prop-1-en-2-yl)benzene (59 mg, 1.0 eq, 0.4 mmol), to give 40 mg product **3jb** as colorless oil liquid in 37% yield; R_f = 0.16 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, J = 8.8, 7.2 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.16 (d, J = 8.8 Hz, 1H),

6.11 (d, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 3.44 (d, *J* = 11.6 Hz, 1H), 3.39 (d, *J* = 11.2 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.3, 158.8, 148.5, 139.6, 134.4, 125.9, 116.9, 113.9, 100.1, 74.4, 55.2, 44.2, 23.3. IR (KBr) *ν* (cm^{-1}) 2921, 2849, 1657, 1577, 1512, 1458, 1250, 1180, 1142, 1075, 1029, 826, 777. HRMS(ESI): calculated for $C_{15}H_{16}NO_2S^+$ $[M+H]^+$ *m/z*: 274.0896, found: 274.0895.

3-(Benzo[d][1,3]dioxol-5-yl)-3-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8kb)*** was synthesized according to General Procedure B from 5-(prop-1-en-2-yl)benzo[d][1,3]dioxole (65 mg, 1.0 eq, 0.4 mmol), to give 63 mg product **8kb** as yellow oil liquid in 55% yield; R_f = 0.16 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.23 (dd, *J* = 8.8, 7.2 Hz, 1H), 6.79−6.67 (m, 3H), 6.17 (d, *J* = 8.8 Hz, 1H), 6.12 (d, *J* = 7.2 Hz, 1H), 5.93 (d, *J* = 1.3 Hz, 2H), 3.44 (d, *J* = 11.2 Hz, 1H), 3.37 (d, *J* = 11.6 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.2, 148.4, 148.0, 146.9, 139.7, 136.5, 118.1, 116.9, 108.1, 105.6, 101.2, 100.2, 74.6, 44.2, 23.3. IR (KBr) *ν* (cm^{-1}) 2922, 1658, 1577, 1513, 1487, 1435, 1245, 1145, 1036, 933, 778. HRMS(ESI): calculated for $C_{15}H_{14}NO_3S^+$ $[M+H]^+$ *m/z*: 288.0689, found: 288.0691.

3-Ethyl-3-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8lb)*** was synthesized according to General Procedure B from but-1-en-2-ylbenzene (53 mg, 1.0 eq, 0.4 mmol), to give 62 mg product **8lb** as colorless oil liquid in 60% yield; R_f = 0.22 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.35−7.30 (m, 2H), 7.29−7.24 (m, 2H), 7.18 (d, *J* = 7.6 Hz, 2H), 6.18 (d, *J* = 8.8 Hz, 1H), 6.11 (d, *J* = 7.2 Hz, 1H), 3.68 (d, *J* = 11.6 Hz, 1H), 3.31 - 3.19 (m, 2H), 2.33 (dq, *J* = 14.4, 7.2 Hz, 1H), 1.00 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.4, 150.0, 143.1, 139.9, 128.6, 127.5, 124.4, 116.2, 99.7, 78.4, 40.4, 29.9, 8.3. IR (KBr) *ν* (cm^{-1}) 2919, 2840, 1657, 1576, 1511, 1450, 1144, 870, 824, 737. HRMS(ESI): calculated for $C_{15}H_{16}NOS^+$ $[M+H]^+$ *m/z*: 258.0947, found: 258.0946.

3,4-Dihydro-2H,2'H,5'H-spiro[naphthalene-1,3'-thiazolo[3,2-a]pyridin]-5'-one ***(8nb)*** was synthesized according to General Procedure B from 1-methylene-1,2,3,4-tetrahydronaphthalene (116 mg, 2.0 eq, 0.8 mmol), to give 72 mg product **8nb** as colorless oil liquid in 67% yield; R_f = 0.35 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.20 (dd, *J* = 8.8, 7.2 Hz, 1H), 7.16−7.11 (m, 3H), 7.06−7.00 (m, 1H), 6.16− 6.07 (m, 2H), 3.58 (dd, *J* = 12.0, 1.6 Hz, 1H), 3.45 (d, *J* = 12.0 Hz, 1H), 3.13−2.98 (m, 1H), 2.88−2.74 (m, 1H), 2.59 (t, *J* = 12.8 Hz, 1H), 2.35 (d, *J* = 12.8 Hz, 1H), 2.15−2.00 (m, 1H), 1.89−1.70 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 161.4, 148.2, 139.3, 138.5, 137.1, 128.9, 127.1, 126.7, 125.1, 117.0, 99.9, 74.3, 42.0, 29.3, 28.7, 21.3. IR (KBr) *ν* (cm^{-1}) 3019, 2927, 2863, 1651, 1574, 1513, 1446, 1400, 1351, 1220,1124, 1144, 1109, 1040, 1025, 966, 837, 764, 742. HRMS(ESI): calculated for $C_{16}H_{16}NOS^+$ $[M+H]^+$ *m/z*: 270.0947, found: 270.0945.

3-Methyl-3-(naphthalen-1-yl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8ob)*** was synthesized according to General Procedure B from 1-(prop-1-en-2-yl) naphthalene (134 mg, 2.0 eq, 0.8 mmol), to give 62 mg product **8ob** as colorless oil liquid in 53% yield; R_f = 0.33 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.88 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.47−7.20 (m, 3H), 7.20 (dd, *J* = 7.2, 6.8 Hz, 1H), 6.23 (dd, *J* = 7.2, 0.8 Hz, 1H), 5.96 (d, *J* = 9.2, 1H), 4.11 (d, *J* = 11.6 Hz, 1H), 3.20 (d, *J* = 11.2 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 161.6, 147.3, 139.7, 137.2, 134.9, 130.2, 129.6, 126.4, 125.2（d）, 125.1, 122.8, 116.5, 100.5, 74.8, 41.3, 23.4. IR (KBr) *ν* (cm^{-1}) 3084, 3050, 2978, 2876, 1654, 1577, 1508, 1458, 1400, 1375, 1261, 1198, 1177, 1141, 1092, 1032, 794, 742. HRMS(ESI): calculated for $C_{18}H_{16}NOS^+$ $[M+H]^+$ *m/z*: 294.0947, found: 294.0944.

3-((Benzyloxy)methyl)-3-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8pb)*** was synthesized according to General Procedure B from (3-(benzyloxy)prop-1-en-2-yl)benzene (180 mg, 2.0 eq, 0.8 mmol), to give 36 mg product **8pb** as colorless oil liquid in 26% yield; R_f = 0.40 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.38−7.15 (m, 10H), 6.20 (dd, *J* = 9.2, 0.8 Hz, 1H), 6.12 (dd, *J* = 7.2, 1.2 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 9.6 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.11 (d, *J* = 11.2 Hz), 3.30 (d, *J* = 11.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.8, 149.8, 139.9, 139.6, 137.9, 128.6, 128.4, 128.0, 127.7, 125.0, 116.4, 100.3, 77.8, 73.4, 72.3, 39.7. IR (KBr) *ν* (cm^{-1}) 3029, 2865, 1651, 1574, 1504, 1402, 1265, 1147, 1027, 850, 696. HRMS(ESI): calculated for $C_{21}H_{20}NO_2S^+$ $[M+H]^+$ *m/z*: 350.1209, found: 350.1206.

3-Methyl-3-(pyridin-3-yl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8qb)*** was synthesized according to General Procedure B from 3-(prop-1-en-2-yl)pyridine (48 mg, 1.0 eq, 0.4 mmol), to give 21 mg product **8qb** as yellow oil liquid in 21% yield; R_f = 0.10 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.60 (d, *J* = 2.0 Hz, 1H), 8.54 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.57−7.50 (m, 1H), 7.35−7.20 (m, 2H), 6.20−6.11 (m, 2H), 3.47 (d, *J* = 11.6 Hz, 1H), 3.43 (d, *J* = 11.6 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.1, 148.8, 148.1, 146.4, 140.0, 137.9, 132.5, 123.3, 116.9, 100.5, 73.1, 44.0, 22.8. IR (KBr) *ν* (cm^{-1}) 3038, 2977, 2936, 1654, 1577, 1508, 1419, 1400, 1376, 1278, 1227, 1147, 1103, 1021, 780, 711. HRMS(ESI): calculated for $C_{13}H_{13}N_2OS^+$ $[M+H]^+$ *m/z*: 245.0743, found: 245.0745.

3-Methyl-3-(thiophen-3-yl)-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8rb)*** was synthesized according to General Procedure B from 3-(prop-1-en-2-yl)thiophene (50 mg, 1.0 eq, 0.4 mmol), to give 54 mg product **8rb** as yellow oil liquid in 54% yield; R_f = 0.30 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.27 (dd, *J* = 4.8, 2.8 Hz, 1H), 7.20 (dd, *J* = 8.8, 6.8 Hz, 1H), 7.14 (dd, *J* = 2.8, 1.2 Hz, 1H), 6.99 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.16 (d, *J* = 8.8 Hz, 1H), 6.09 (d, *J* = 7.2 Hz, 1H), 3.46 (d, *J* = 11.6 Hz, 1H), 3.39 (d, *J* = 11.6 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.4, 148.1, 143.4, 139.6, 126.3, 125.1, 120.8, 116.9, 100.2, 72.4, 43.2, 24.0. IR (KBr) *ν* (cm^{-1}) 3088, 3046, 2975, 2933, 1654, 1578, 1511, 1440, 1400, 1375, 1267, 1146, 1114, 1029, 777, 737, 663. HRMS(ESI): calculated for $C_{12}H_{12}NOS_2^+$ $[M+H]^+$ *m/z*: 250.0355, found: 250.0357.

2,3-Diphenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-5-one ***(8sb)*** was synthesized according to General Procedure B from ethyl 1,2-diphenylethene (144 mg, 2.0 eq, 0.8 mmol), to give 83 mg product **8sb** as colorless oil liquid in 68% yield; R_f = 0.36 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.45 −7.21 (m, 11H), 6.29 (d, *J* = 9.2 Hz, 1H), 6.26 (d, *J* = 5.2 Hz, 1H), 6.24 (s, 1 H), 4.60 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 161.7, 148.0, 141.2, 140.4, 138.1, 129.3, 128.9, 128.6, 128.5, 126.3, 125.6, 115.6, 99.9, 72.7, 56.2. IR (KBr) *ν* (cm^{-1}) 3060, 3031, 2958, 1653, 1576, 1511, 1452, 1406, 1266, 1220, 1141, 1078, 1031, 779, 734, 696. HRMS(ESI): calculated for $C_{19}H_{15}NNaOS^+$ $[M+H]^+$ *m/z*: 328.0767, found: 328.0769.

Ethyl3-(3,3-dimethyl-5-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyridin-2-yl)propanoate ***(8tb)*** was synthesized according to General Procedure B from ethyl 5-methylhex-4-enoate (62 mg, 1.0 eq, 0.4 mmol), to give 76 mg product **8tb** as colorless oil liquid in 68% yield; R_f = 0.30 (2:1 petroleum ether/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.12 (dd, *J* = 9.2, 7.2 Hz, 1H), 6.18 (d, *J* = 8.8 Hz, 1H), 6.00 (dd, *J* = 7.2, 0.8 Hz, 1H), 4.17 (q, *J* = 7.2, 2H), 3.57 (dd, *J* = 12.0, 2.8 Hz, 1H), 2.55−2.45 (m, 1H), 2.44− 2.30 (m, 1H), 2.29−2.10 (m, 1H), 1.86 (s, 3H), 1.90−1.78 (m, 1H), 1.55 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 172.0, 163.1, 146.5, 138.9, 117.2, 100.5, 72.7, 60.9, 55.5, 32.9, 25.3, 24.4,

17.8, 14.2. IR (KBr) ν (cm^{-1}) 2977, 2933, 1733, 1655, 1579, 1517, 1442, 1385, 1247, 1181, 1091, 1038, 778. HRMS(ESI): calculated for $C_{14}H_{20}NO_3S^+$ $[M+H]^+$ *m/z*: 282.1158, found: 282.1161.

*9A-methyl-5a,6,7,8,9,9a-hexahydro-1H-benzo[4,5]thiazolo[3,2-a]pyridin-1-one (**8ub**)* was synthesized according to General Procedure B from 1-methylcyclohex-1-ene (126 mg, 2.0 eq, 0.8 mmol), to give (44 mg product **8ub** as colorless oil liquid in 53% yield; R_f = 0.36 (2:1 petroleum ether/ethyl acetate). ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, J = 8.8 Hz, 1H), 6.14 (d, J = 8.8 Hz, 1H), 6.02 (d, J = 6.8 Hz, 1H), 3.65− 3.50 (m, 1H), 2.40−2.25 (m, 1H), 2.24−2.10 (m, 1H), 2.07−1.93 (m, 1H), 1.90−1.75 (m, 4H), 1.68−1.46 (m, 3H), 1.45−1.30 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 147.8, 138.8, 116.8, 101.1, 71.8, 51.0, 30.9, 26.5, 23.2, 21.2, 21.0. IR (KBr) ν (cm^{-1}) 2933, 2859, 1656, 1578, 1515, 1441, 1376, 1177, 1144, 1035, 775. HRMS(ESI): calculated for $C_{12}H_{16}NOS^+$ $[M+H]^+$ *m/z*: 222.0947, found 222.0950.

*3-Methyl-3-phenyl-2,3-dihydrothiazolo[3,2-a]pyridin-4-ium trifluoromethanesulfonate (**7aa**):* 10 mL reaction tube flame dried under vacuum. After cooling, methyl 2-pyridyl sulfoxide (56 mg, 1.0 eq, 0.4 mmol), α-methylstyrene (1.0 eq, 0.4 mmol), 2-fluoropyridine (38 mg, 1.0 eq, 0.4 mmol), 4 mL dry dichloromethane was added under nitrogen atmosphere, then the reaction tube was placed in an ethyl acetate /liquid nitrogen ice bath. 5 min later, trifluoromethanesulfonic anhydride (100 μL, 1.5 eq, 0.6 mmol) was added., naturally warmed to room temperature and allowed to react overnight. Extract with dichloromethane 6 mL × 3, dry over anhydrous Na_2SO_4, purified with flash column chromatography (ethyl acetate to dichloromethane/Methanol = 30/1), to give 140 mg product **7aa** as colorless oil liquid in 93% yield. **7aa:** R_f = 0.36 (10:1 dichloromethane/ methyl alcohol). ^1H NMR (400 MHz, Acetone) δ 8.69 (d, J = 6.4 Hz, 1H), 8.60 - 8.46 (m, 1H), 8.31 (d, J = 8.4 Hz, 1H), 7.92−7.87 (m, 1H), 7.54−7.48 (m, 3H), 7.48−7.43 (m, 2H), 4.29 (s, 2H), 2.39 (s, 3H). ^{19}F NMR (376 MHz, Acetone) δ 98.74. ^{13}C NMR (101 MHz, Acetone) δ 161.5, 146.2, 141.9, 139.9, 130.5, 130.2, 127.2, 125.0, 124.7, 82.9, 44.9, 25.1. IR (KBr) ν (cm^{-1}) 3111, 1610, 1560, 1470, 1450, 1258, 1170, 1028, 767, 698. HRMS(ESI): calculated for $C_{14}H_{14}NS^+$ $[M+H]^+$ *m/z*: 228.0841, found: 228.0845.

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