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Preparation of functionalized 3,4-pyridynes via 2-magnesiated diaryl sulfonates

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Abstract—The preparation of functionalized 3,4-pyridynes of type **1** as highly reactive intermediates has been achieved by the controlled elimination of readily generated 2-magnesiated diaryl sulfonates of type **2** obtained by a low temperature I/Mg- or Br/Mg-exchange starting from the corresponding halides of type **3**. After trapping with furan, moderate to good yields of the desired functionalized cycloadducts of type **4** are obtained. The addition of a magnesium arylthiolate or magnesium phenylselenide to 3,4-pyridyne followed by quenching with an electrophile is also described.

1. Introduction

3,4-Pyridyne (**1a**, see Table 1) is a highly reactive intermediate,[1] which can react with a broad range of reagents (nucleophiles in addition reactions and alkenes in cycloadditions). Whereas several methods for the generation of 3,4-pyridyne have been developed,[2] the preparation of functionalized 3,4-pyridyne is often incompatible with the harsh basic conditions, which are necessary for their syntheses.

Recently, we have developed a new method allowing the generation of polyfunctional arylmagnesium compounds using an I/Mg- or Br/Mg-exchange.[3] We have also found a new preparation of polyfunctionalized arynes via the elimination of 2-magnesiated diaryl sulfonates, and the resulting reactive immediates arynes can be trapped efficiently with furan or various nucleophiles in good yields.[4] Herein, we wish to apply the same strategy to the preparation of a broad range of functionalized 3,4-pyridynes of type **1** using 4-chlorobenzenesulfonate as a leaving group (see Scheme 1). The reactive intermediates functionalized 3,4-pyridynes **1** were trapped by furan furnishing Diels–Alder cycloadducts of type **4** (Scheme 1 and Table 1).

2. Results and discussion

The precursors **3a–e** for the 3,4-pyridyne generation were prepared via iodination[5] or bromination[6] of corresponding 3-hydroxypyridine derivatives followed by reacting with 4-chlorobenzenesulfonyl chloride in the presence of Et_3N in CH_2Cl_2 at 25 °C for 12 h. When treating the diiodo-pyridine **3c** with *i*-PrMgCl in THF at −78 °C, the I/Mg-exchange was completed in 30 min. The corresponding Grignard reagent was reacted with 1,2-dibromotetrafluoroethane (1.5 equiv) followed by slowly warming to 25 °C during 6 h, and finally led to 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) in 67% yield (Scheme 2).

4-Bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) did undergo a selective I/Mg-exchange (*i*-PrMgCl, −78 °C, 30 min) giving rise to the corresponding Grignard reagent **6** as the major product. The intermediate Grignard reagent **6** was reacted with *S*-phenyl arenethiosulfonates (1.2 equiv) leading to the products **3f** and **3g** in 45–63% yields. In addition, **6** was reacted with an allyl bromide (2.0 equiv) in the presence of CuCN·2LiCl (1.0 equiv) furnishing the product **3h** in 55% yield. After transmetallation with $ZnBr_2$ (1.1 equiv), the resulting zinc reagent was reacted with ethyl 4-iodobenzoate (1.5 equiv) in the presence of $Pd(dba)_2$ (5 mol %) and tri-(2-furyl)phosphine (10 mol %) at 50 °C for 3.5 days affording the product **3i** in 54% yield (Scheme 3).

Compounds **3a–i** were treated with *i*-PrMgCl or *i*-PrMgCl·LiCl at −78 °C within 0.5–6 h leading to the corresponding Grignard reagents **2a–i**. After warming to 25 °C within 1–16 h, functionalized 3,4-pyridynes **1a–i** were formed and trapped with furan leading to **4a–i** in 32–88% yields (Table 1). Various functionalities like an iodine (or bromine or chlorine) (Table 1, entries 2–5), a methoxy group (entry 5), an aryl sulfide (entries 6 and 7), an allyl group (entry 8) and an ester (entry 9) were readily tolerated on the pyridyne

Keywords: Magnesium; Functionalized organomagnesium reagents; Cycloaddition; Functionalized 3,4-pyridyne; Halogen–magnesium exchange.
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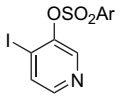
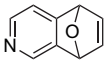
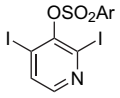
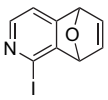
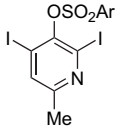
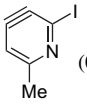
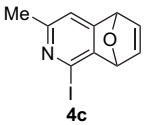
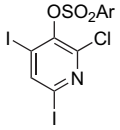
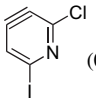
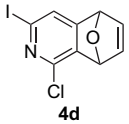
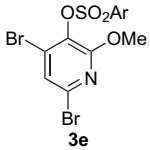
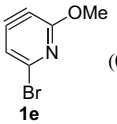
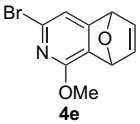
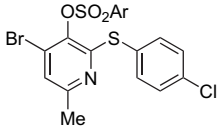
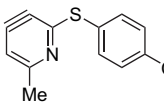
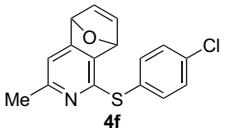
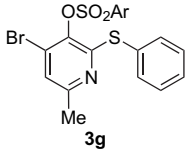
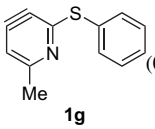
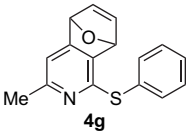
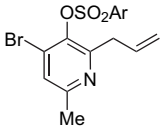
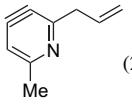
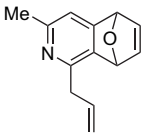
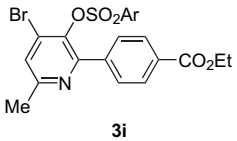
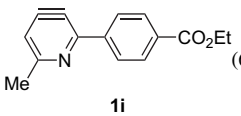
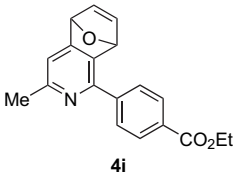
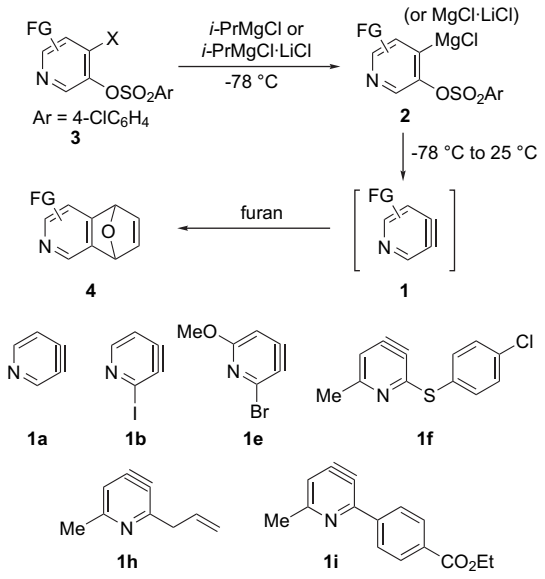
Table 1. Generation of functionalized 3,4-pyridynes of type **1** and their trapping with furan

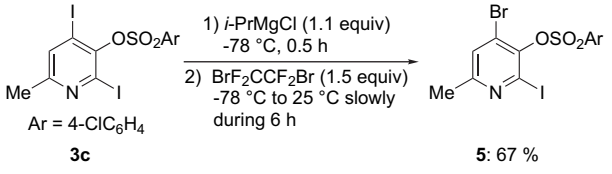
Entry	Precursor of type **3**	3,4-Pyridyne of type **1**	Product of type **4**	Yield[a] (%)
1	 **3a**	 (0.5 h[b]; 2.5 h[c]) **1a**	 **4a**	54
2	 **3b**	 (0.5 h[b]; 1.5 h[c]) **1b**	 **4b**	45
3	 **3c**	 (0.5 h[b]; 6 h[c]) **1c**	 **4c**	75
4	 **3d**	 (0.5 h[b]; 16 h[c]) **1d**	 **4d**	32
5	 **3e**	 (0.5 h[d]; 4 h[c]) **1e**	 **4e**	78
6	 **3f**	 (0.5 h[d]; 1 h[c]) **1f**	 **4f**	88
7	 **3g**	 (0.5 h[d]; 1 h[c]) **1g**	 **4g**	85
8	 **3h**	 (2 h[d]; 1 h[c]) **1h**	 **4h**	57
9	 **3i**	 (6 h[d]; 1 h[c]) **1i**	 **4i**	76

[a] Isolated yield of analytically pure product.
[b] Reaction time for the I/Mg-exchange using *i*-PrMgCl at −78 °C.
[c] Reaction time for the formation of functionalized 3,4-pyridyne at room temperature using furan (5.0 equiv) as a trapping reagent.
[d] Reaction time for the Br/Mg-exchange using *i*-PrMgCl·LiCl at −78 °C.

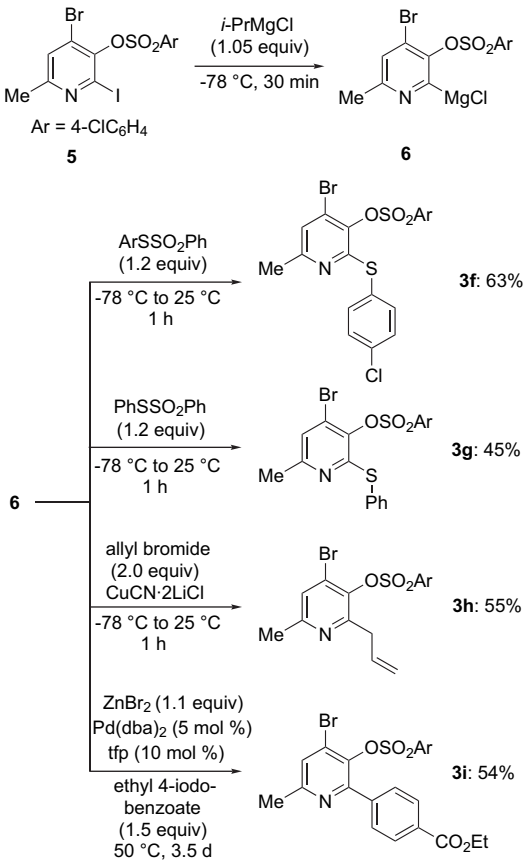
intermediates. We also observed that more than one halogen substituent on the pyridyne changed its reactivity and complicated its subsequent quenching reaction. When there was only one halogen substituent on pyridynes such as **1b**,**1c** and **1e**, their Diels–Alder reactions with furan went smoothly giving rise to **4b**,**4c** and **4e** in 45–78% yields (entries 2, 3 and 5). However, with two halogen substituents on a pyridyne like for **1d**, its reaction with furan only led to the



Scheme 1. Preparation of functionalized 3,4-pyridynes of type **1**.



Scheme 2. Preparation of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**).

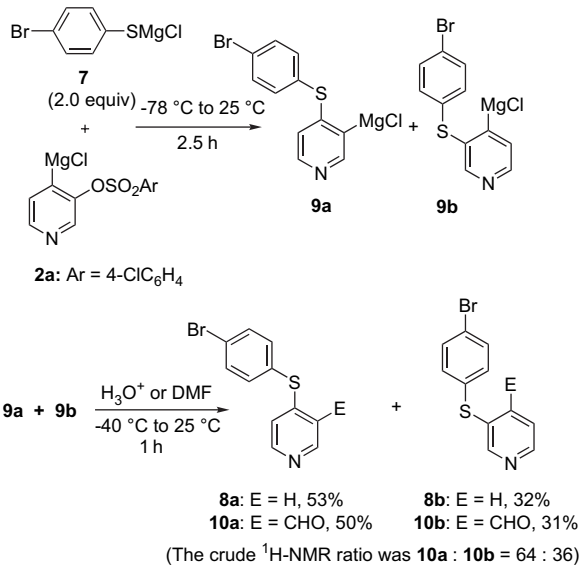


Scheme 3. Preparation of **3f–i** from **6** via an I/Mg-exchange with *i*-PrMgCl followed by quenching with an electrophile.

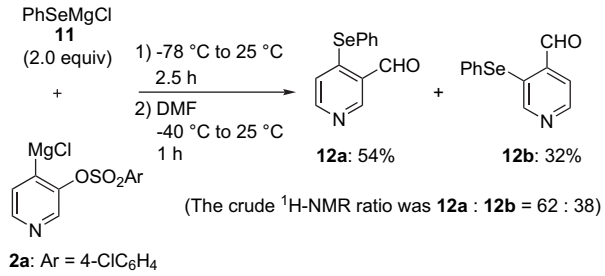
cycloadduct **4d** in 32% yield and the reaction did not go further to completion even after 16 h at 25 °C (entry 4). Also, a functionalized 3,4-pyridyne with one substituent on 6-position led to an increase yield, and the additional steric hindrance near the nitrogen atom gave rise to cleaner reactions with furan. For instance, **1c** was reacted with furan leading to **4c** in 75% yield, while **1b** was trapped with furan giving rise to **4b** in 45% yield probably due to further nucleophilic addition of the pyridine nitrogen atom of **1b** (entries 2 and 3). The stabilization of 3,4-pyridynes by an alkoxy group or a sulfide function in 2-position was essential to afford the Diels–Alder cycloaddition products **4e–g** in good yields (78–88%) after trapping the reactive intermediates in situ **1e–g** with furan (entries 5–7). Alkyl groups have little electron-donating ability for stabilizing the functionalized 3,4-pyridyne **1h**. Therefore, the reaction of **1h** with furan furnished the product **4h** in 57% yield (entry 8). Finally, a 3,4-pyridyne with an aryl group bearing an ester function, such as **1i**, was trapped with furan in situ giving rise to **4i** in 76% yield (entry 9).

Interestingly, the magnesium arylthiolate **7** (2.0 equiv) added successfully to 3,4-pyridyne (**1a**) followed by quenching with saturated aqueous NH_4Cl solution lead to **8a** and **8b** in 53% and 32% yields, respectively. The resulting Grignard reagents **9a** and **9b** could be formylated with DMF (3.0 equiv) furnishing **10a** and **10b** in 50% and 31% yields, respectively (The crude ^{1}H NMR ratio was **10a/10b**=64:36) (Scheme 4). In addition, magnesium phenylselenide (**11**) was also a good nucleophile for the addition reaction of 3,4-pyridyne (**1a**) followed by quenching with DMF (3.0 equiv) giving rise to **12a** and **12b** in 54% and 32% yields, respectively (The crude ^{1}H NMR ratio was **12a/12b**=62:38) (Scheme 5).

The magnesium arylthiolate **7** (2.0 equiv) also added to the functionalized 3,4-pyridyne **3f** followed by quenching with

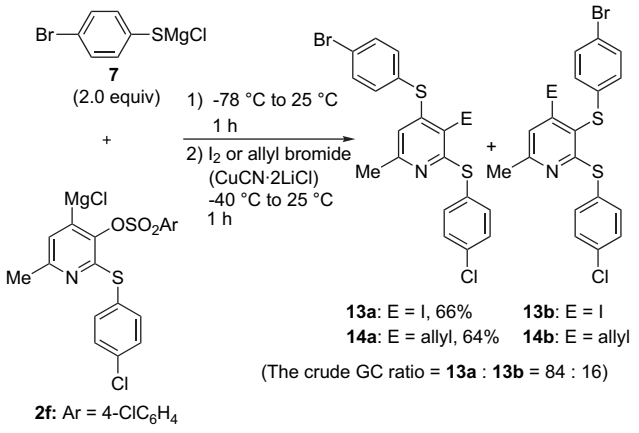


Scheme 4. The addition of magnesium arylthiolate **7** to 3,4-pyridyne (**1a**).



Scheme 5. The addition of magnesium phenylselenide (**11**) to 3,4-pyridyne (**1a**).

iodine lead to **13a** as the major product in 66% isolated yield. (The crude GC ratio was **13a/13b**=84:16.) The corresponding Grignard reagents underwent allylation with allyl bromide (4.0 equiv) in the presence of CuCN·2LiCl (0.5 equiv) affording **14a** as the major product in 64% isolated yield (Scheme 6).



Scheme 6. The addition of magnesium arylthiolate **7** to the functionalized 3,4-pyridyne **3f**.

3. Conclusion

In conclusion, we have developed a new and general preparation of functionalized 3,4-pyridynes using the easily tunable elimination of 2-magnesium arylsulfonates. In addition, we have showed a procedure allowing the thio- and seleno-magnesiation of 3,4-pyridynes. The resulting arylmagnesium species can be trapped with electrophiles in contrast to most previously reported addition reactions. Further applications of this convenient preparation of fuctionalized arynes are underway in our laboratories.

4. Experimental

4.1. General methods

Unless otherwise indicated, all reactions were carried out under an argon atmosphere. THF and Et_2O were distilled from sodium/benzophenone. CH_2Cl_2 and DMF were distilled from CaH_2. Reactions were monitored by gas chromatography (GC) analysis of worked up reaction aliquots. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel 60 F_{254} plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 F_{254} (70–230 mesh). NMR data were recorded on a 600, 400 or 300 MHz NMR spectrometer. The ionization method used was electron impact ionization (EI, 70 eV). Melting points are uncorrected.

4.2. Preparation of the reagent *i*-PrMgCl

A dry three-necked flask equipped with an argon inlet, a dropping funnel and a thermometer was charged with magnesium turnings (110 mmol). A small amount of THF was added to cover the magnesium, and a solution of isopropyl chloride (100 mmol) in THF (50 mL) was added dropwise, keeping the temperature of the mixture below 30 °C (water bath). After the addition was completed, the reaction mixture was stirred for 12 h at room temperature. The grey solution of *i*-PrMgCl was cannulated to another flask under argon and removed in this way from excess of magnesium. An yield of ca. 95–98% of *i*-PrMgCl was obtained and the *i*-PrMgCl-solution was titrated prior to use according to the reported literature.[8]

4.3. Preparation of the reagent *i*-PrMgCl·LiCl

Magnesium turnings (110 mmol) and anhydrous LiCl (100 mmol) were placed in an argon-flushed flask, and THF (50 mL) was added. A solution of *i*-PrCl (100 mmol) in THF (50 mL) was slowly added at room temperature. The reaction starts within a few minutes. After addition, the reaction mixture was stirred for 12 h at room temperature. The grey solution of *i*-PrMgCl·LiCl was cannulated to another flask under argon and removed in this way from excess of magnesium. An yield of ca. 95–98% of *i*-PrMgCl·LiCl was obtained and the *i*-PrMgCl·LiCl solution is titrated prior to use according to the reported literature.[8]

4.4. Starting materials

The following starting materials were prepared according to the procedures of literature: **3a**,[5a,b] **3b**,[5] **3c**,**d**,[5c] **3e**,[6] benzenethiosulfonic acid *S*-(4-chloro-phenyl) ester,[7] 2-methoxypyridin-3-ol[6a] and 3-hydroxy-4-iodopyridine.[5b]

4.5. Typical procedure for the formation of arylsulfonates 3a–e from the corresponding phenols (TP 1)

A dry 250-mL round-bottomed flask, equipped with a magnetic stirrer and a septum, was charged with a solution of corresponding 3-hydroxypyridine derivative (50 mmol) in dry CH_2Cl_2 (100 mL). After cooling to 0 °C, Et_3N (20.9 mL, 150 mmol) was added, and then 4-chlorobenzenesulfonyl chloride (12.7 g, 60 mmol) was added portionwise. After the addition was completed, the reaction mixture was stirred at 25 °C overnight. Then this mixture was diluted with 100 mL CH_2Cl_2. Saturated aqueous NH_4Cl solution (100 mL) was then added, and then the resulting mixture was extracted with CH_2Cl_2 (2×100 mL). The organic extracts were dried over anhydrous Na_2SO_4 and concentrated. Purification by flash chromatography furnished the desired products (**3a–e**).

4.5.1. 4-Iodopyridin-3-yl 4-chlorobenzenesulfonate (3a). Prepared according to TP 1 from 3-hydroxy-4-iodopyridine

(11.1 g, 50.0 mmol), triethylamine (20.9 mL, 150 mmol) and 4-chlorobenzenesulfonyl chloride (12.7 g, 60.0 mmol). Recrystallization from ethanol yielded **3a** as a yellow solid (16.1 g, 81%). Mp: 135.3–136.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.40 (s, 1H), 8.10 (d, ^3J=5.1 Hz, 1H), 7.89–7.83 (m, 2H), 7.74 (d, ^3J=5.1 Hz, 1H), 7.58–7.51 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 148.7, 148.1, 144.3, 142.3, 135.3, 134.2, 131.0, 130.6, 102.2. MS (70 eV, EI) *m*/*z* (%): 395 (56) [M$^+$], 192 (4), 175 (100), 165 (12), 111 (65), 93 (14). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3103 (m), 3044 (w), 1586 (m), 1562 (s), 1478 (m), 1393 (vs), 1200 (s), 1174 (vs), 1087 (s), 864 (s), 767 (vs), 718 (s), 618 (s), 565 (s), 484 (m). HRMS (EI) for $C_{11}H_7{}^{35}ClINO_3S$ (394.8880): found 394.8846.

4.5.2. 2,4-Diiodo-pyridin-3-ol. To a solution of 3-hydroxy-4-iodo-pyridine (2.21 g, 10 mmol) and Na_2CO_3 (2.22 g, 21 mmol) in water was added iodine (2.54 g, 10 mmol) with stirring at 20 °C for 2 h. Then $HCl_{(aq)}$ is added carefully until approximate pH 4. The solid is filtered off and dried to give 3-hydroxy-2,4-diiodo-pyridine as a brown solid (2.78 g, 80%). Mp: 179.0–180.3 °C. ^{1}H NMR (300 MHz, CD_3SOCD_3, 25 °C) δ/ppm: 10.22 (s, 1H), 7.75 (d, ^3J=4.5 Hz, 1H), 7.54 (d, ^3J=4.5 Hz, 1H). ^{13}C NMR (75 MHz, CD_3SOCD_3, 25 °C) δ/ppm: 153.5, 143.3, 133.7, 112.1, 97.1. MS (70 eV, EI) *m*/*z* (%): 347 (100) [M$^+$], 221 (19), 220 (64), 165 (11), 127 (14), 93 (30), 66 (12), 65 (11), 64 (20). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3437 (br s), 1628 (w), 1524 (m), 1446 (m), 1409 (w), 1265 (w), 1149 (m), 1079 (w), 1061 (w), 812 (w), 706 (m). HRMS (EI) for $C_5H_3ONI_2$ (346.8304): found 346.8304.

4.5.3. 2,4-Diiodo-pyridin-3-yl 4-chlorobenzenesulfonate (3b). Prepared according to TP 1 from 2,4-diiodo-pyridin-3-ol (2.08 g, 6.0 mmol), 4-chlorobenzenesulfonyl chloride (1.52 g, 7.2 mmol) and triethylamine (1.26 mL, 9.0 mmol). Purification by flash chromatography (*n*-pentane/ether=10:1) yielded **3b** as a white solid (2.354 g, 75%). Mp: 145.4–146.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.01–7.96 (m, 2H), 7.85 (d, ^3J=4.9 Hz, 1H), 7.73 (d, ^3J=4.9 Hz, 1H), 7.63–7.58 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 150.1, 148.4, 141.9, 136.1, 134.9, 130.5, 129.8, 114.3, 101.8. MS (70 eV, EI) *m*/*z* (%): 523 (18), 521 (50) [M$^+$], 219 (25), 177 (34), 175 (100), 113 (12), 111 (40), 75 (11), 64 (14). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3096 (w), 1537 (m), 1520 (w), 1478 (w), 1425 (w), 1401 (m), 1382 (vs), 1353 (s), 1223 (m), 1200 (m), 1189 (s), 1178 (s), 1088 (m), 1078 (w), 1061 (w), 1015 (w), 850 (m), 830 (m), 762 (s), 718 (s), 690 (s), 617 (s), 566 (s), 481 (w). HRMS (EI) for $C_{11}H_6O_3NIS^{35}Cl_2$ (520.7846): found 520.7827.

4.5.4. 2,4-Diiodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (3c). To a solution of 3-hydroxy-6-methylpyridine (11.0 g, 100 mmol) and Na_2CO_3 (22.3 g, 210 mmol) in water was added iodine (25.4 g, 100 mmol) with stirring at 20 °C. After 1 h, the iodine colour has disappeared. Then $HCl_{(aq)}$ is added carefully until approximate pH 3. The solid is filtered off and dried to give 2-iodo-3-hydroxy-6-methylpyridine as a crude product (a yellow solid). To a solution of 2-iodo-3-hydroxy-6-methylpyridine (without further purification) and Na_2CO_3 (22.3 g, 210 mmol) in water was added iodine (25.4 g, 100 mmol) with stirring at 20 °C overnight. Then $HCl_{(aq)}$ is added carefully until approximate pH 6. Water was evaporated and 2,4-diiodo-3-hydroxy-6-methylpyridine was obtained as a crude product (a brown solid).

2,4-Diiodo-3-hydroxy-6-methylpyridine: mp: 109.2–110.6 °C. ^{1}H NMR (300 MHz, CD_3SOCD_3, 25 °C) δ/ppm: 7.61 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, CD_3SOCD_3, 25 °C) δ/ppm: 152.0, 151.2, 132.7, 111.0, 98.5, 21.5. MS (70 eV, EI) *m*/*z* (%): 361 (100) [M$^+$], 235 (59), 234 (60), 108 (17), 107 (59), 79 (11), 78 (14), 52 (21), 51 (19). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3416 (br s), 1606 (w), 1562 (w), 1510 (w), 1430 (w), 1240 (w), 1211 (w), 714 (w). HRMS (EI) for $C_6H_5ONI_2$ (360.8461): found 360.8447.

A dry 250-mL round-bottomed flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 2,4-diiodo-3-hydroxy-6-methylpyridine (crude product) in dry CH_2Cl_2 (100 mL). After cooling to 0 °C, Et_3N (18.8 mL, 135 mmol) was added, and then 4-chlorobenzenesulfonyl chloride (23.5 g, 108 mmol) was added portionwise. After addition was completed, the reaction mixture was stirred at room temperature overnight. Then this mixture was diluted with 100 mL CH_2Cl_2. Saturated aqueous NH_4Cl solution (100 mL) was then added, and then the resulting mixture was extracted with CH_2Cl_2 (2×100 mL). The organic extracts were dried over anhydrous Na_2SO_4, and concentrated. Purification by flash chromatography (*n*-pentane/ether=40:1) yielded **3c** (30.05 g, 55%; the total yield over three steps) as a brown solid. Mp: 119.4–121.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.00–7.95 (m, 2H), 7.61–7.56 (m, 3H), 2.48 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 158.8, 147.9, 141.8, 136.1, 134.4, 130.5, 129.8, 112.9, 101.7, 22.9. MS (70 eV, EI) *m*/*z* (%): 537 (37), 535 (100) [M$^+$], 360 (85), 332 (19), 233 (90), 177 (28), 175 (77), 159 (20), 111 (38), 78 (26), 51 (19). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3086 (w), 1546 (m), 1504 (m), 1476 (w), 1402 (m), 1380 (s), 1320 (m), 1242 (m), 1200 (m), 1185 (s), 1176 (vs), 1088 (m), 1061 (m), 1015 (w), 870 (w), 846 (w), 814 (s), 759 (s), 742 (m), 703 (m), 683 (s), 624 (m), 617 (m). HRMS (EI) for $C_{12}H_8O_3NI_2S^{35}Cl$ (534.8003): found 534.7997.

4.5.5. 4-Chloro-benzenesulfonic acid 2-chloro-4,6-diiodo-pyridin-3-yl ester (3d). To a solution of 2-chloro-3-hydroxypyridine (2.60 g, 20 mmol) and Na_2CO_3 (4.45 g, 42 mmol) in water was added iodine (5.33 g, 21 mmol) with stirring at 20 °C overnight. Then $HCl_{(aq)}$ is added carefully until approximate pH 3. The solid is filtered off and dried to give 2-chloro-3-hydroxy-6-iodopyridine as a crude product (a yellow solid). To a solution of 2-chloro-3-hydroxy-6-iodopyridine (without further purification) and Na_2CO_3 (4.45 g, 42 mmol) in water was added iodine (5.33 g, 21 mmol) with stirring at 20 °C overnight. Then $HCl_{(aq)}$ is added carefully until approximate pH 6. Water was evaporated and 4,6-diiodo-3-hydroxy-6-methylpyridine was obtained as a crude product (a brown solid). A dry 250-mL round-bottomed flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4,6-diiodo-3-hydroxy-6-methylpyridine (crude product) in dry CH_2Cl_2 (100 mL). After cooling to 0 °C, Et_3N (4.18 mL, 30 mmol) was added, and then 4-chlorobenzenesulfonyl chloride (4.35 g, 20 mmol) was added portionwise. After addition was completed, the reaction mixture was stirred at room temperature overnight. Then this mixture was diluted with 100 mL CH_2Cl_2. Saturated aqueous NH_4Cl solution

(100 mL) was then added, and then the resulting mixture was extracted with CH_2Cl_2 (2×100 mL). The organic extracts were dried over anhydrous Na_2SO_4, and concentrated. Purification by flash chromatography (*n*-pentane/ether=80:1) yielded **3d** (6.45 g, 57%; the total yield over three steps) as a yellow solid. Mp: 141.7–142.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.13 (s, 1H), 7.98–7.93 (m, 2H), 7.61–7.56 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 145.7, 144.4, 144.3, 141.9, 135.4, 130.0, 129.8, 112.0, 105.8. MS (70 eV, EI) *m*/*z* (%): 557 (13) [M^+], 555 (21), 380 (10), 253 (16), 177 (37), 175 (100), 113 (13), 111 (42), 75 (12). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3085 (w), 1587 (w), 1527 (s), 1512 (s), 1395 (vs), 1381 (vs), 1309 (s), 1282 (w), 1231 (w), 1210 (m), 1187 (s), 1170 (m), 1086 (m), 1072 (m), 1014 (w), 867 (s), 823 (w), 779 (s), 758 (s), 728 (s), 656 (w), 625 (s), 580 (m), 481 (m). HRMS (EI) for $C_{11}H_5O_3NI_2S^{35}Cl_2$ (554.7457): found 554.7453.

4.5.6. 4-Chloro-benzenesulfonic acid 4,6-dibromo-2-methoxy-pyridin-3-yl ester (3e). A 100-mL round-bottomed flask, equipped with a magnetic stirring bar was charged with 2-methoxy-pyridin-3-ol (2.50 g, 20 mmol) and dissolved in CCl_4 (100 mL). *N*-Bromosuccinimide (7.48 g, 42 mmol) was added portionwise and the reaction mixture was stirred at room temperature for 72 h in darkness. The progress of the reaction was followed by GC and GC–MS spectroscopies. After the reaction was complete, the solvent was evaporated, diluted with CH_2Cl_2 (50 mL), washed with water (30 mL), extracted with CH_2Cl_2 (50 mL×3) and ether (50 mL×3) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo to obtain the crude product (4,6-dibromo-2-methoxy-pyridin-3-ol) for the next step. The compound **3e** was prepared according to TP 1 from the crude 4,6-dibromo-2-methoxy-pyridin-3-ol, 4-chlorobenzenesulfonyl chloride (16.2 g, 74 mmol) and triethylamine (12.9 mL, 93 mmol). Filtration and then purification by flash chromatography (*n*-pentane/ether=250:1) yielded **3e** as a white solid (1.83 g, 20% for two steps). Mp: 115.0–117.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.95–7.90 (m, 2H), 7.59–7.54 (m, 2H), 7.30 (s, 1H), 3.77 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C) δ/ppm: 157.0, 141.2, 135.6, 135.5, 132.2, 129.9, 129.8, 129.3, 124.5, 54.9. MS (70 eV, EI) *m*/*z* (%): 459 (9), 457 (12), 455 (5) [M^+], 284 (46), 283 (7), 282 (100), 280 (48), 213 (9), 211 (6), 177 (5), 175 (14), 160 (5), 159 (9), 158 (5), 113 (6), 111 (19), 75 (9). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3088 (w), 1570 (m), 1473 (m), 1390 (m), 1321 (vs), 1283 (m), 1141 (s), 1090 (s), 1071 (s), 1009 (m), 830 (m), 820 (m), 752 (m), 745 (m), 702 (w). HRMS (EI) for $C_{12}H_8O_4N^{79}Br_2{}^{35}ClS$ (454.8229): found 454.8204.

4.5.7. Synthesis of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (5). A dry and argon-flushed 250-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 2,4-diiodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate **3c** (16.1 g, 30 mmol) in dry THF (60 mL). *i*-PrMgCl (0.87 M/THF, 37.9 mL, 1.1 equiv) was then added dropwise at −78 °C. After 30 min, 1,2-dibromotetrafluoroethane (13.3 g, 50 mmol) was added slowly at −78 °C, and the resulting mixture was warmed up slowly to room temperature during 6 h. Thereafter, the reaction was quenched with saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2 (3×100 mL). The organic fractions were dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (*n*-pentane/ether=50:1) yielded **5** (9.82 g, 67%) as a yellow solid. Mp: 112.6–113.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.99–7.94 (m, 2H), 7.60–7.55 (m, 2H), 7.34 (s, 1H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 159.1, 144.8, 141.7, 135.9, 130.3, 129.7, 128.1, 127.1, 114.4, 23.3. MS (70 eV, EI) *m*/*z* (%): 491 (13), 489 (40), 487 (33) [M^+], 314 (29), 312 (28), 286 (17), 284 (17), 177 (41), 175 (100), 159 (14), 113 (12), 111 (41), 78 (19), 75 (14), 51 (16). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1558 (m), 1513 (w), 1473 (w), 1390 (vs), 1325 (m), 1283 (w), 1244 (m), 1202 (w), 1183 (s), 1092 (m), 1064 (m), 1012 (w), 878 (w), 826 (m), 820 (s), 760 (m), 741 (w), 728 (m), 701 (m), 680 (m), 620 (m). HRMS (EI) for $C_{12}H_8O_3NIS^{79}Br^{35}Cl$ (486.8141): found 486.8141.

4.5.8. 4-Chloro-benzenesulfonic acid 4-bromo-2-(4-chloro-phenylsulfanyl)-6-methylpyridin-3-yl ester (3f). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) (2.41 g, 4.0 mmol) in dry THF (8.0 mL). *i*-PrMgCl (0.87 M/THF, 4.71 mL, 4.1 mmol) was then added dropwise at −78 °C. After 30 min, benzenethiosulfonic acid *S*-(4-chloro-phenyl) ester (1.25 g, 4.4 mmol) in dry THF (3 mL) was added slowly at −78 °C, and the resulting mixture was warmed to room temperature and stirred for 1 h. Thereafter, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3×60 mL). The organic fractions were dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (*n*-pentane/ether=50:1) yielded **3f** (1.28 g, 63%) as a white solid. Mp: 109.3–111.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.03–7.97 (m, 2H), 7.60–7.54 (m, 2H), 7.36–7.28 (m, 4H), 7.15 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 157.5, 153.8, 141.5, 139.6, 135.9, 135.5, 135.0, 130.1, 129.5, 129.0, 128.2, 127.6, 125.3, 23.5. MS (70 eV, EI) *m*/*z* (%): 505 (10), 503 (6) [M^+], 443 (20), 442 (11), 441 (41), 440 (9), 439 (24), 332 (16), 331 (16), 330 (53), 329 (12), 328 (39), 296 (16), 295 (100), 294 (15), 293 (100), 267 (12), 265 (12), 251 (11), 249 (24), 248 (9), 186 (10), 111 (13), 108 (9), 51 (15). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3104 (w), 1572 (w), 1557 (w), 1537 (m), 1476 (m), 1414 (m), 1380 (vs), 1334 (m), 1262 (m), 1200 (w), 1177 (s), 1090 (s), 1071 (m), 1015 (w), 828 (s), 818 (m), 758 (s), 746 (m), 702 (m), 680 (m), 636 (m). HRMS (EI) for $C_{18}H_{12}O_3{}^{79}Br^{35}Cl_2S_2$ (502.8819): found 502.8816.

4.5.9. 4-Chloro-benzenesulfonic acid 4-bromo-6-methyl-2-phenylsulfanyl-pyridin-3-yl ester (3g). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) (1.466 g, 3.0 mmol) in dry THF (9.0 mL). *i*-PrMgCl (0.87 M/THF, 3.57 mL, 3.1 mmol) was then added dropwise at −78 °C. After 30 min, *S*-phenyl benzenethiosulfonate (875 mg, 3.5 mmol) in dry THF (3 mL) was added slowly at −78 °C, and the resulting mixture was warmed to room temperature and stirred for 1 h. Thereafter, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2

(3×50 mL). The organic fractions were dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (*n*-pentane/ether=50:1) and recrystallization (ethanol/acetone=1:1) yielded **3g** (636 mg, 45%) as a white solid. Mp: 86.7–89.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.04–7.98 (m, 2H), 7.59–7.53 (m, 2H), 7.41–7.30 (m, 5H), 7.15 (s, 1H), 2.30 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 157.4, 154.1, 141.3, 139.7, 135.6, 134.4, 130.1, 129.8, 129.5, 128.8, 128.6, 127.6, 125.1, 23.5. MS (70 eV, EI) *m*/*z* (%): 471 (3), 469 (2) [M^+], 407 (20), 405 (15), 297 (35), 296 (100), 295 (35), 294 (94), 280 (14), 278 (15), 216 (11), 215 (21), 214 (13), 187 (18), 186 (21), 111 (10), 109 (11), 77 (12), 51 (21). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3098 (w), 1553 (m), 1538 (m), 1474 (m), 1442 (w), 1410 (m), 1383 (vs), 1330 (m), 1284 (w), 1262 (m), 1198 (w), 1180 (s), 1168 (s), 1093 (m), 1070 (m), 832 (s), 759 (s), 747 (m), 704 (m), 682 (s), 629 (m). HRMS (EI) for $C_{18}H_{13}O_3{}^{79}Br^{35}ClS_2$ (468.9209): found 468.9223.

4.5.10. 2-Allyl-4-bromo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (3h). A dry and argon-flushed 50-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) (1.466 g, 3.0 mmol) in dry THF (6.0 mL). *i*-PrMgCl (0.87 M in THF, 3.79 mL, 1.1 equiv) was then added dropwise at −78 °C. After 30 min, CuCN·2LiCl (1.0 M in THF, 1.50 mL, 0.5 equiv) was added slowly at −78 °C, and the resulting mixture was stirred at this temperature for 10 min. Then allyl bromide (0.43 mL, 5.0 mmol, 1.7 equiv) was added at −78 °C, and the resulting mixture was warmed to room temperature and stirred for 1 h. Thereafter, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3× 40 mL). The organic fractions were dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (*n*-pentane/ether=30:1) yielded **3h** (0.665 g, 55%) as a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.96–7.93 (m, 2H), 7.57–7.54 (m, 2H), 7.22 (s, 1H), 6.03–5.95 (m, 1H), 5.13–5.07 (m, 2H), 3.65–3.62 (m, 2H), 2.48 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C) δ/ppm: 157.4, 155.4, 141.4, 140.7, 135.1, 133.9, 129.9, 129.6, 127.4, 126.3, 117.1, 38.1, 23.7. MS (70 eV, EI) *m*/*z* (%): 403 (10) [M^+], 402 (18), 400 (14), 229 (19), 228 (99), 227 (27), 226 (100), 175 (12), 148 (11), 147 (22), 146 (15), 144 (12), 119 (23), 118 (22), 111 (24), 75 (12), 51 (20). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 1586 (w), 1562 (s), 1476 (w), 1431 (m), 1373 (s), 1277 (w), 1205 (m), 1186 (vs), 1089 (s), 1014 (w), 910 (m), 844 (s), 806 (s), 758 (s), 730 (s), 706 (m), 676 (m), 645 (m). HRMS (EI) for $C_{15}H_{13}ClBrNO_3S$ (402.9488): found 402.9402.

4.5.11. 4-[4-Bromo-3-(4-chloro-benzenesulfonyloxy)-6-methylpyridin-2-yl]-benzoic acid ethyl ester (3i). A dry and argon-flushed 250-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromo-2-iodo-6-methylpyridin-3-yl 4-chlorobenzenesulfonate (**5**) (4.89 g, 10.0 mmol) in dry THF (20 mL). *i*-PrMgCl (0.87 M/THF, 12.65 mL, 1.1 equiv) was then added dropwise at −78 °C and stirred for 30 min. $ZnBr_2$ (1.0 M/THF, 11.0 mL, 1.1 equiv) was added to the magnesiated arene at −78 °C. Another dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with $Pd(dba)_2$ (290 mg, 5 mol %) and tris-*o*-furylphosphine (250 mg, 10 mol %) in dry THF (8 mL). The initial red colour disappeared after 2 min leading to yellow solution and ethyl 4-iodobenzoate (4.27 g, 15.0 mmol) was added. This solution was added, via cannula after 10 min stirring, to the reaction mixture at −78 °C. The reaction mixture was stirred at 50 °C for 4 days. Thereafter, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3×100 mL). The organic fractions were dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (*n*-pentane/ether=50:1) yielded **3i** (2.759 g, 54%) as a white solid. Mp: 130.0–131.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.87–7.82 (m, 2H), 7.56–7.51 (m, 2H), 7.47 (s, 1H), 7.43–7.38 (m, 2H), 7.19–7.14 (m, 2H), 4.41 (q, ^3J=7.1 Hz, 2H), 2.58 (s, 3H), 1.44 (t, ^3J=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 165.9, 157.9, 152.0, 141.0, 141.0, 140.5, 134.9, 130.8, 130.0, 129.2, 129.2, 129.2, 127.8, 61.2, 23.9, 14.3. MS (70 eV, EI) *m*/*z* (%): 511 (20), 509 (14) [M^+], 336 (24), 334 (24), 308 (25), 306 (25), 292 (45), 291 (27), 290 (53), 289 (21), 264 (93), 263 (21), 262 (98), 211 (50), 184 (14), 183 (100), 182 (42), 154 (23), 133 (20), 131 (20), 113 (14), 111 (32), 75 (19), 52 (18), 51 (41). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 2984 (w), 1711 (vs), 1576 (w), 1556 (m), 1474 (w), 1431 (w), 1390 (s), 1271 (s), 1209 (m), 1184 (s), 1157 (m), 1107 (m), 1090 (m), 1062 (m), 1016 (w), 826 (s), 783 (m), 757 (m), 701 (m), 676 (m), 632 (m). HRMS (EI) for $C_{21}H_{18}O_5N^{79}Br^{35}ClS$, [$M^+$+H] (509.9778): found 509.9771.

4.6. Typical procedure for the generation and trapping of functionalized 3,4-pyridynes 4 with furan (TP 2): 4-(5-methyl-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraen-3-yl)-benzoic acid ethyl ester (4i)

A dry and argon-flushed 10-mL Schlenk-tube, equipped with a magnetic stirrer and a septum, was charged with a solution of the corresponding arylsulfonate of type **3i** (255 mg, 0.5 mmol) in dry THF (2 mL). *i*-PrMgCl·LiCl (0.51 mL, 0.51 mmol, 1.00 M in THF) was then added dropwise at −78 °C. After 6 h, furan (170 mg, 2.5 mmol) was added slowly at −78 °C, and the resulting mixture was warmed to 25 °C and stirred for 1 h. Saturated aqueous NH_4Cl solution (50 mL) was then added, and then the resulting mixture was extracted with CH_2Cl_2 (3×40 mL). The organic extracts were dried over anhydrous Na_2SO_4 and concentrated. Purification by flash chromatography (pentane/diethyl ether= 10:1) furnished the product **4i** as a pale yellow solid (117 mg, 76%). Mp: 148.6–150.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.18–8.13 (m, 2H), 7.74–7.69 (m, 2H), 7.20 (dd, ^3J=5.6 Hz, ^3J=1.8 Hz, 1H), 7.13 (s, 1H), 7.06 (dd, ^3J=5.6 Hz, ^3J=1.9 Hz, 1H), 5.93–5.91 (m, 1H), 5.74–5.72 (m, 1H), 4.41 (q, ^3J=7.1 Hz, 2H), 2.59 (s, 3H), 1.42 (t, ^3J=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 166.3, 160.0, 156.4, 147.3, 143.1, 142.8, 142.1, 139.2, 130.3, 129.9, 127.8, 115.6, 81.7, 81.3, 61.0, 24.7, 14.3. MS (70 eV, EI) *m*/*z* (%): 307 (14) [M^+], 291 (13), 281 (35), 280 (23), 279 (100), 278 (17), 262 (27), 253 (14), 252 (12), 251 (96), 250 (24), 234 (17), 225 (13), 218 (20), 206 (22), 205 (17), 204 (24), 178 (11), 165 (14), 164 (11). IR (neat) $\tilde{\nu}$ (cm^{-1}): 2983 (w), 1708 (vs), 1610

(m), 1584 (w), 1404 (w), 1369 (w), 1278 (s), 1222 (w), 1108 (m), 1078 (w), 1016 (m), 862 (m), 843 (m), 816 (w), 761 (m), 718 (w), 704 (m), 650 (w). HRMS (EI) for $C_{19}H_{17}O_3N$ (307.1208): found 307.1222.

4.6.1. 11-Oxa-4-aza-tricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraene (4a). Prepared according to TP 2 from 4-iodo-pyridin-3-yl 4-chlorobenzenesulfonate (**3a**) (396 mg, 1.0 mmol), *i*-PrMgCl (1.21 mL, 1.05 mmol, 0.87 M in THF) and furan (340 mg, 5.0 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 2.5 h. Purification by flash chromatography (*n*-pentane/diethyl ether=2:1) yielded **4a** as a yellow oil (79 mg, 54%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.40 (s, 1H), 8.23 (d, ^3J=4.6 Hz, 1H), 7.18 (d, ^3J=4.6 Hz, 1H), 6.99 (dd, ^3J=5.6 Hz, ^3J=1.8 Hz, 1H), 6.93 (dd, ^3J=5.6 Hz, ^3J=1.8 Hz, 1H), 5.77–5.75 (m, 1H), 5.68–5.66 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 158.8, 147.2, 144.1, 143.3, 141.8, 139.6, 116.0, 81.5, 80.4. MS (70 eV, EI) *m*/*z* (%): 145 (8) [M$^+$], 119 (21), 118 (9), 117 (100), 116 (20), 91 (8), 90 (39), 89 (40), 64 (7), 63 (18). IR (film) $\tilde{\nu}$ (cm^{-1}): 1584 (w), 1414 (w), 1282 (w), 1126 (w), 1019 (w), 995 (w), 876 (w), 850 (s), 836 (m), 705 (m), 645 (w), 592 (w). HRMS (EI) for C_9H_7ON (145.0528): found 145.0525.

4.6.2. 3-Iodo-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraene (4b). Prepared according to TP 2 from 2,4-diiodo-pyridin-3-yl 4-chlorobenzenesulfonate (**3b**) (522 mg, 1.0 mmol), *i*-PrMgCl (1.21 mL, 1.05 mmol, 0.87 M in THF) and furan (340 mg, 5.0 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 1.5 h. Purification by flash chromatography (*n*-pentane/diethyl ether=10:1) yielded **4b** as a white solid (123 mg, 45%). Mp: 91.8–93.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.03 (d, ^3J=4.7 Hz, 1H), 7.16 (d, ^3J=4.7 Hz, 1H), 7.14 (dd, ^3J=5.6 Hz, ^3J=1.8 Hz, 1H), 7.03 (dd, ^3J=5.6 Hz, ^3J=1.8 Hz, 1H), 5.85–5.82 (m, 1H), 5.61–5.58 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 160.4, 152.0, 148.8, 143.0, 142.5, 115.7, 107.1, 84.0, 83.0. MS (70 eV, EI) *m*/*z* (%): 271 (22) [M$^+$], 245 (11), 243 (29), 144 (14), 118 (20), 117 (10), 116 (100), 115 (35), 89 (28), 63 (11). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 1560, 1410, 1396, 1270, 1116, 856, 832, 731, 654. HRMS (EI) for C_9H_6ONI (270.9494): found 270.9507.

4.6.3. 3-Iodo-5-methyl-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]-undeca-2(7),3,5,9-tetraene (4c). Prepared according to TP 2 from 2,4-diiodo-6-methylpyridin-3-yl 4-chlorobenzene-sulfonate (**3c**) (536 mg, 1.0 mmol), *i*-PrMgCl (1.21 mL, 1.05 mmol, 0.87 M in THF) and furan (340 mg, 5.0 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 6 h. Purification by flash chromatography (*n*-pentane/diethyl ether=2:1) yielded **4c** as a yellow oil (214 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.09 (dd, ^3J= 5.6 Hz, ^3J=1.9 Hz, 1H), 7.00 (s, 1H), 6.96 (dd, ^3J=5.6 Hz, ^3J=1.9 Hz, 1H), 5.77–5.75 (m, 1H), 5.54–5.52 (m, 1H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 160.6, 158.6, 148.7, 143.0, 142.0, 115.8, 105.8, 83.8, 82.9, 24.2. MS (70 eV, EI) *m*/*z* (%): 285 (12) [M$^+$], 257 (20), 132 (14), 130 (100), 129 (28), 103 (35), 77 (13). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1613 (w), 1549 (s), 1428 (m), 1322 (m), 1280 (m), 1180 (s), 1080 (s), 1004 (w), 910 (w), 865 (w), 851 (vs), 838 (s), 795 (m), 727 (m), 702 (s), 646 (m). HRMS (EI) for $C_{10}H_8ONI$ (284.9651): found 284.9633.

4.6.4. 3-Chloro-5-iodo-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]-undeca-2(7),3,5,9-tetraene (4d). Prepared according to TP 2 from 4-chloro-benzenesulfonic acid 2-chloro-4,6-diiodo-pyridin-3-yl ester (**3d**) (556 mg, 1.0 mmol), *i*-PrMgCl (1.21 mL, 1.05 mmol, 0.87 M in THF) and furan (340 mg, 5.0 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 16 h. Purification by flash chromatography (*n*-pentane/diethyl ether=30:1) yielded **4d** as a white solid (98 mg, 32%). Mp: 123.1–124.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.59 (s, 1H), 7.12 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 6.99 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 5.80–5.77 (m, 1H), 5.73–5.70 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 164.2, 143.9, 142.9, 141.9, 140.7, 126.6, 113.0, 81.9, 80.5. MS (70 eV, EI) *m*/*z* (%): 307 (6), 305 (20) [M$^+$], 281 (7), 279 (23), 277 (12), 241 (9), 152 (44), 151 (13), 150 (100), 149 (12), 123 (12), 115 (7), 114 (25). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 1598, 1553, 1402, 1300, 1284, 1204, 1134, 1054, 853, 814, 805, 728, 642. HRMS (EI) for $C_9H_5ON^{35}ClI$ (304.9104): found 304.9087.

4.6.5. 5-Bromo-3-methoxy-11-oxa-4-aza-tricyclo-[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraene (4e). Prepared according to TP 2 from 4-chloro-benzenesulfonic acid 4,6-dibromo-2-methoxy-pyridin-3-yl ester (**3e**) (229 mg, 0.5 mmol), *i*-PrMgCl·LiCl (0.51 mL, 0.51 mmol, 1.00 M in THF) and furan (170 mg, 2.5 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 4 h. Purification by flash chromatography (*n*-pentane/diethyl ether=100:1) yielded **4e** as a colourless oil (100 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.12–7.08 (m, 2H), 6.97 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 5.84–5.81 (m, 1H), 5.67–5.64 (m, 1H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 166.2, 155.9, 143.6, 141.7, 135.7, 129.3, 115.0, 81.9, 79.3, 54.1. MS (70 eV, EI) *m*/*z* (%): 255 (15), 253 (17) [M$^+$], 229 (29), 227 (52), 226 (99), 225 (34), 224 (100), 212 (15), 210 (17), 198 (29), 197 (18), 196 (23), 195 (13), 185 (29), 183 (27), 148 (26), 146 (20), 145 (19), 131 (21), 130 (41), 116 (19), 115 (17), 103 (15), 102 (13), 76 (19). IR (neat) $\tilde{\nu}$ (cm^{-1}): 2950 (w), 1600 (m), 1572 (s), 1458 (m), 1411 (w), 1354 (vs), 1279 (m), 1079 (m), 1060 (m), 994 (m), 864 (m), 842 (m), 728 (w), 649 (w). HRMS (EI) for $C_{10}H_8O_2N^{79}Br$ (252.9738): found 252.9716.

4.6.6. 3-(4-Chloro-phenylsulfanyl)-5-methyl-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraene (4f). Prepared according to TP 2 from 4-chloro-benzenesulfonic acid 4-bromo-2-(4-chloro-phenylsulfanyl)-6-methylpyridin-3-yl ester (**3f**) (253 mg, 0.5 mmol), *i*-PrMgCl·LiCl (0.51 mL, 0.51 mmol, 1.00 M in THF) and furan (170 mg, 2.5 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/diethyl ether=3:1) yielded **4f** as a yellow solid (134 mg, 88%). Mp: 98.1–101.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.29–7.20 (m, 4H), 6.92 (s, 1H), 6.82 (dd, ^3J= 5.5 Hz, ^3J=1.9 Hz, 1H), 6.57 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 5.57–5.54 (m, 1H), 5.34–5.31 (m, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 160.7, 157.2, 146.4, 143.0, 142.7, 141.7, 133.8, 133.1, 132.4, 129.4, 114.9, 81.7, 80.5, 24.5. MS (70 eV, EI) *m*/*z* (%): 303 (35), 302 (23), 301 (88) [M$^+$], 300 (20), 275 (43), 274 (63), 273 (70), 272 (100), 257 (24), 247 (29), 240 (34), 237 (31), 236 (23), 108 (29), 103 (31), 77 (42), 63 (20). IR (neat) $\tilde{\nu}$ (cm^{-1}): 3077 (w), 2612 (w), 1558 (m), 1476 (s), 1443

(w), 1428 (m), 1390 (m), 1326 (w), 1282 (m), 1201 (m), 1086 (vs), 1007 (m), 860 (m), 848 (s), 826 (s), 810 (m), 750 (m), 709 (s), 649 (m). HRMS (EI) for $C_{16}H_{12}ON^{35}ClS$ (301.0328): found 301.0339.

4.6.7. 5-Methyl-3-phenylsulfanyl-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5,9-tetraene (4g). Prepared according to TP 2 from 4-chloro-benzenesulfonic acid 4-bromo-6-methyl-2-phenylsulfanyl-pyridin-3-yl ester (**3f**) (235 mg, 0.5 mmol), *i*-PrMgCl·LiCl (0.51 mL, 0.51 mmol, 1.00 M in THF) and furan (170 mg, 2.5 mmol). Reaction condition: −78 °C, 0.5 h; 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/diethyl ether=8:1) yielded **4g** as a yellow oil (114 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.46–7.40 (m, 2H), 7.37–7.29 (m, 3H), 6.95 (s, 1H), 6.83 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 6.47 (dd, ^3J=5.5 Hz, ^3J=1.9 Hz, 1H), 5.58 (dd, ^3J=1.9 Hz, ^4J=0.9 Hz, 1H), 5.19 (dd, ^3J=1.9 Hz, ^4J=0.9 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 160.6, 156.7, 147.8, 142.8, 142.6, 141.4, 133.6, 132.4, 129.3, 127.9, 114.5, 81.5, 80.4, 24.4. MS (70 eV, EI) *m*/*z* (%): 267 (81) [M$^+$], 266 (23), 250 (37), 246 (30), 245 (25), 241 (20), 240 (35), 239 (57), 238 (100), 231 (27), 223 (36), 213 (25), 77 (25), 57 (24). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1612 (w), 1555 (s), 1477 (m), 1440 (m), 1424 (s), 1324 (m), 1280 (m), 1204 (m), 1186 (w), 1086 (m), 1024 (w), 1007 (w), 890 (w), 845 (vs), 812 (m), 730 (s), 703 (s), 689 (s), 650 (s). HRMS (EI) for $C_{16}H_{13}ONS$ (267.0718): found 267.0694.

4.6.8. 3-Allyl-5-methyl-11-oxa-4-aza-tricyclo[6.2.1.0^{2,7}]-undeca-2(7),3,5,9-tetraene (4h). Prepared according to TP 2 from 2-allyl-4-bromo-6-methylpyridin-3-yl 4-chloro-benzenesulfonate (**3h**) (403 mg, 1.0 mmol), *i*-PrMgCl·LiCl (1.02 mL, 1.02 mmol, 1.00 M in THF) and furan (340 mg, 5.0 mmol). Reaction condition: −78 °C, 2 h; 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/diethyl ether=5:1) yielded **4h** as a yellow oil (114 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ/ppm: 6.98 (dd, ^3J=5.6 Hz, ^3J=1.9 Hz, 1H), 6.97 (s, 1H), 6.91 (dd, ^3J=5.6 Hz, ^3J=1.9 Hz, 1H), 6.03–5.92 (m, 1H), 5.82–5.81 (m, 1H), 5.64–5.63 (m, 1H), 5.11–5.01 (m, 2H), 3.62–3.46 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ/ppm: 159.6, 155.8, 148.7, 143.0, 141.6, 139.4, 135.7, 116.4, 114.4, 81.6, 80.3, 40.4, 24.5. MS (70 eV, EI) *m*/*z* (%): 199 (55) [M$^+$], 198 (100), 173 (37), 172 (53), 171 (70), 170 (70), 169 (19), 168 (22), 155 (16), 154 (14), 145 (14), 144 (20), 130 (12), 128 (14), 115 (13), 103 (11), 77 (21), 63 (10), 51 (12). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1616 (w), 1587 (m), 1433 (m), 1367 (w), 1280 (w), 845 (s), 700 (m), 647 (m). HRMS (EI) for $C_{13}H_{13}ON$ (199.0997): found 199.0967.

4.6.9. 4-(4-Bromo-phenylsulfanyl)-pyridine (8a). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromothiophenol (380 mg, 2.0 mmol) in dry THF (5 mL). After cooling to −78 °C, *i*-PrMgCl (2.81 mL, 3.0 equiv, 1.07 M in THF) was then added dropwise and stirred for 10 min. 4-Chloro-benzenesulfonic acid 4-iodo-pyridin-3-yl ester (**3a**) (395 mg, 1.0 mmol) dissolved in dry THF (2 mL) was added and stirred vigorously for 30 min at the same temperature. Thereafter the resulting mixture was warmed to 25 °C and stirred for 2.5 h. The reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×40 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (*n*-pentane/diethyl ether=10:1) yielded **8a** as a yellow solid (141 mg, 53%) and **8b** as a yellow oil (85 mg, 32%). Mp: 70.5–71.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.34 (d, ^3J=5.3 Hz, 2H), 7.60–7.52 (m, 2H), 7.44–7.34 (m, 2H), 6.99–6.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 149.5, 149.4, 136.4, 133.1, 128.7, 124.2, 120.9. MS (70 eV, EI) *m*/*z* (%): 265 (100) [M$^+$], 186 (60), 154 (5), 115 (14), 93 (10), 78 (7), 51 (4). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3044 (w), 1567 (m), 1472 (m), 1405 (m), 1386 (m), 1189 (w), 1086 (m), 1008 (m), 814 (m), 705 (m), 618 (m). HRMS (EI) for $C_{11}H_8{}^{79}BrNS$ (264.9561): found 264.9586.

4.6.10. 3-(4-Bromo-phenylsulfanyl)-pyridine (8b). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.58 (d, ^4J=1.9 Hz, 1H), 8.51 (dd, ^3J=4.9 Hz, ^4J=1.3 Hz, 1H), 7.66–7.59 (m, 1H), 7.51–7.42 (m, 2H), 7.29–7.20 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 151.2, 148.1, 138.4, 133.4, 132.8, 132.5, 124.0, 121.9. MS (70 eV, EI) *m*/*z* (%): 265 (100) [M$^+$], 240 (4), 186 (50), 154 (4), 115 (7), 93 (6). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3045 (w), 1630 (w), 1552 (vs), 1467 (s), 1404 (s), 1382 (m), 1087 (m), 1067 (m), 1008 (s), 818 (s), 805 (s), 699 (m), 528 (m), 491 (s). HRMS (EI) for $C_{11}H_8{}^{79}BrNS$ (264.9561): found 264.9568.

4.6.11. 4-(4-Bromo-phenylsulfanyl)-pyridine-3-carbaldehyde (10a). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromothiophenol (380 mg, 2.0 mmol) in dry THF (5 mL). After cooling to −78 °C, *i*-PrMgCl (2.81 mL, 3.0 equiv, 1.07 M in THF) was then added dropwise and stirred for 10 min. 4-Chloro-benzenesulfonic acid 4-iodopyridin-3-yl ester (**3a**) (395 mg, 1.00 mmol) dissolved in dry THF (2 mL) was added and stirred vigorously for 30 min at the same temperature. Thereafter the resulting mixture was warmed to 25 °C and stirred for 2.5 h. The reaction mixture was cooled to −78 °C, added with DMF (219 mg, 3.00 mmol), warmed to 25 °C and stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×40 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (*n*-pentane/diethyl ether=5:1) yielded **10a** as a pale yellow solid (147 mg, 50%) and **10b** as a yellow solid (91 mg, 31%). Mp: 89.8–91.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 10.22 (s, 1H), 8.90 (s, 1H), 8.37 (d, ^3J=5.8 Hz, 1H), 7.68–7.61 (m, 2H), 7.47–7.39 (m, 2H), 6.67 (d, ^3J(H,H)=5.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 190.3, 154.9, 154.4, 152.1, 137.3, 133.6, 127.6, 125.4, 120.4, 112.6. MS (70 eV, EI) *m*/*z* (%): 295 (76) [M$^+$], 266 (6), 185 (24), 137 (100), 105 (18), 77 (6), 50 (4). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3081 (w), 2849 (w), 2760 (w), 1684 (vs), 1576 (s), 1523 (s), 1466 (s), 1358 (s), 1256 (m), 1183 (s), 1066 (s), 1008 (vs), 816 (vs), 730 (m), 685 (m), 479 (m). HRMS (EI) for $C_{12}H_8{}^{79}BrNOS$ (294.9510): found 294.9511.

4.6.12. 3-(4-Bromo-phenylsulfanyl)-pyridine-4-carbaldehyde (10b). Mp: 85.7–87.3 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 10.39 (s, 1H), 8.65 (d, ^3J=4.9 Hz,

1H), 8.43 (s, 1H), 7.66 (d, ^3J=4.9 Hz, 1H), 7.55–7.48 (m, 2H), 7.33–7.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 190.6, 152.1, 148.3, 138.9, 134.2, 133.1, 131.2, 123.3, 123.1, 112.6. MS (70 eV, EI) *m/z* (%): 265 (100) [M$^+$], 266 (25), 214 (30), 185 (54), 137 (18), 109 (9). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3080 (w), 2843 (w), 2752 (w), 1925 (w), 1691 (vs), 1467 (s), 1387 (s), 1387 (m), 1204 (m), 1138 (m), 1067 (m), 1009 (s), 826 (s), 729 (m), 658 (m), 525 (m), 480 (m). HRMS (EI) for $C_{12}H_8{}^{79}BrNOS$ (294.9510): found 294.9471.

4.6.13. 4-Phenylselanyl-pyridine-3-carbaldehyde (12a). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of phenylselenol (305 mg, 2.0 mmol) in dry THF (5 mL). After cooling to −78 °C, *i*-PrMgCl (2.81 mL, 3.0 equiv, 1.07 M in THF) was then added dropwise and stirred for 10 min. 4-Chloro-benzenesulfonic acid 4-iodo-pyridin-3-yl ester (**3a**) (395 mg, 1.0 mmol) dissolved in dry THF (2 mL) was added and stirred vigorously for 30 min at the same temperature. Thereafter the resulting mixture was warmed to 25 °C and stirred for 2.5 h. The reaction mixture was cooled to −78 °C, added with DMF (219 mg, 3.00 mmol), warmed to 25 °C and stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×40 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (*n*-pentane/diethyl ether=5:1) yielded **12a** as a pale yellow solid (142 mg, 54%) and **12b** as a yellow solid (84 mg, 32%). Mp: 94.7–98.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 10.18 (s, 1H), 8.84 (s, 1H), 8.23 (d, ^3J=5.5 Hz, 1H), 7.67–7.60 (m, 2H), 7.53–7.40 (m, 3H), 6.81 (d, ^3J=5.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 191.1, 155.7, 152.5, 151.9, 137.2, 130.1, 130.0, 129.3, 126.0, 123.3. MS (70 eV, EI) *m/z* (%): 263 (100) [M$^+$], 234 (17), 185 (58), 157 (16), 127 (6), 115 (9), 105 (15), 77 (19), 51 (16). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3068 (w), 2838 (w), 2745 (w), 1709 (m), 1683 (vs), 1571 (vs), 1524 (m), 1461 (m), 1389 (m), 1255 (m), 1188 (m), 1067 (m), 914 (w), 851 (s), 748 (m), 690 (m), 660 (m), 523 (w), 480 (w). HRMS (EI) for $C_{12}H_9NOSe$ (262.9849): found 262.9846.

4.6.14. 3-Phenylselanyl-pyridine-4-carbaldehyde (12b). Mp: 38.8–41.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 10.24 (s, 1H), 8.59 (d, ^3J=4.9 Hz, 1H), 8.31 (s, 1H), 7.68–7.59 (m, 3H), 7.46–7.33 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 191.9, 151.6, 147.2, 138.5, 136.1, 133.1, 130.0, 129.4, 126.7, 125.6. MS (70 eV, EI) *m/z* (%): 263 (100) [M$^+$], 234 (32), 185 (24), 155 (32), 127 (6), 115 (7), 105 (6), 77 (16), 51 (9). IR (KBr) $\tilde{\nu}$ (cm^{-1}): 3068 (w), 2820 (w), 1686 (s), 1568 (w), 1466 (m), 1438 (m), 1404 (m), 1276 (m), 1229 (m), 1206 (m), 1156 (m), 1093 (m), 1020 (m), 916 (w), 856 (m), 818 (m), 744 (m), 693 (m), 657 (m), 513 (w), 480 (m). HRMS (EI) for $C_{12}H_9NOSe$ (262.9849): found 262.9859.

4.6.15. 4-(4-Bromo-phenylsulfanyl)-2-(4-chloro-phenylsulfanyl)-3-iodo-6-methylpyridine (13a). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromothiophenol (190 mg, 1.0 mmol) in dry THF (1 mL). After cooling to −78 °C, *i*-PrMgCl·LiCl (1.41 mL, 3.0 equiv, 1.07 M in THF) was then added dropwise and stirred for 10 min. 4-Chloro-benzenesulfonic acid 4-bromo-2-(4-chloro-phenylsulfanyl)-6-methylpyridin-3-yl ester (**3f**) (253 mg, 0.5 mmol) dissolved in dry THF (2 mL) was added and stirred vigorously for 30 min at the same temperature. Thereafter the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was cooled to −78 °C, added with iodine (508 mg, 2.0 mmol), warmed to 25 °C and stirred for 1 h. The reaction was quenched with 5% aqueous $Na_2S_2O_3$ and saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×40 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (*n*-pentane/diethyl ether=50:1) yielded **13a** as a white solid (182 mg, 66%). Mp: 216.1–217.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.63–7.58 (m, 2H), 7.47–7.38 (m, 4H), 7.37–7.32 (m, 2H), 6.02 (s, 1H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 161.3, 157.7, 155.4, 137.4, 136.5, 135.2, 133.8, 131.6, 130.1, 129.4, 125.2, 117.0, 89.7, 24.3. MS (70 eV, EI) *m/z* (%): 551 (27), 550 (27), 549 (83) [M$^+$], 548 (44), 547 (56), 546 (23), 424 (25), 423 (30), 422 (83), 421 (52), 420 (100), 419 (29), 418 (39), 386 (17), 342 (19), 341 (16), 340 (38), 257 (22), 256 (22), 229 (20), 196 (22), 171 (21), 153 (29), 152 (17), 108 (31). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1538 (m), 1502 (m), 1468 (m), 1434 (w), 1384 (m), 1309 (m), 1091 (m), 1084 (w), 1066 (w), 1010 (m), 992 (m), 817 (s), 786 (m), 745 (m), 730 (m), 718 (w). HRMS (EI) for $C_{18}H_{12}{}^{79}Br^{35}ClINS_2$ (546.8328): found 546.8322.

4.6.16. 3-Allyl-4-(4-bromo-phenylsulfanyl)-2-(4-chloro-phenylsulfanyl)-6-methylpyridine (14a). A dry and argon-flushed 25-mL Schlenk-flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 4-bromothiophenol (190 mg, 1.0 mmol) in dry THF (1 mL). After cooling to −78 °C, *i*-PrMgCl·LiCl (1.41 mL, 3.0 equiv, 1.07 M in THF) was then added dropwise and stirred for 10 min. 4-Chloro-benzenesulfonic acid 4-bromo-2-(4-chloro-phenylsulfanyl)-6-methylpyridin-3-yl ester (**3f**) (253 mg, 0.5 mmol) dissolved in dry THF (2 mL) was added and stirred vigorously for 30 min at the same temperature. Thereafter the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was cooled to −78 °C, and then CuCN·2LiCl (1.0 M in THF, 0.5 mL, 0.5 equiv) was added and stirred for 20 min. Allyl bromide (0.17 mL, 2.0 mmol, 4.0 equiv) was added at −78 °C, and the solution was allowed to warm to 25 °C and kept stirring for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×40 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (*n*-pentane/diethyl ether=200:1) yielded **14a** as a white solid (149 mg, 64%). Mp: 163.2–164.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ/ppm: 7.58–7.53 (m, 2H), 7.42–7.27 (m, 6H), 6.36 (s, 1H), 6.01–5.87 (m, 1H), 5.16–5.07 (m, 2H), 3.74–3.69 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ/ppm: 156.4, 156.1, 149.0, 136.1, 134.6, 133.7, 133.2, 133.0, 131.1, 130.1, 128.8, 127.8, 123.8, 118.8, 116.8, 34.0, 24.0. MS (70 eV, EI) *m/z* (%): 463 (9) [M$^+$], 462 (7), 461 (6), 450 (33), 449 (23), 448 (100), 447 (17), 446 (69), 368 (14), 97 (18), 95 (12), 85 (13), 83 (16), 71 (19), 69 (18), 57 (28), 55 (19), 43 (20). IR (neat) $\tilde{\nu}$ (cm^{-1}): 1557 (m), 1518 (m), 1471 (m), 1416 (m), 1385 (w), 1335 (m),

1174 (w), 1090 (s), 1167 (m), 1008 (s), 914 (m), 820 (vs), 802 (s), 777 (s), 746 (m), 730 (m). HRMS (EI) for $C_{21}H_{17}{}^{79}Br^{35}ClNS_2$ (460.9674): found 460.9680.

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