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Iridium-Catalyzed *Ortho*-C(sp^2)–H Amidation of Benzaldehydes with Organic Azides

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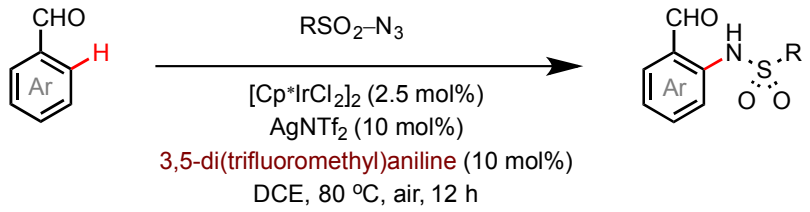
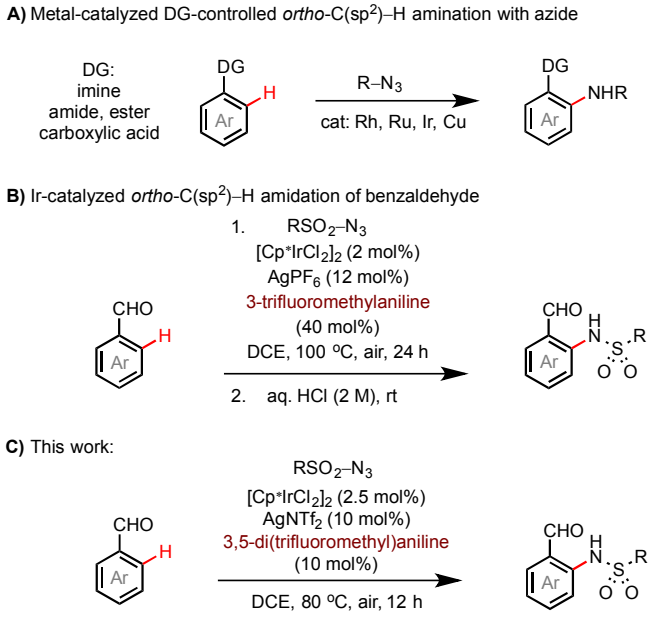


Abstract

An iridium-catalyzed *ortho*-C(sp^2)–H amidation reaction of benzaldehydes with organic azides has been developed. A catalytic amount of 3,5-di(trifluoromethyl)aniline was used to promote the Ir-catalyzed directed C-H amination reaction through a transient aldimine intermediate. This reaction tolerates a broad scope of benzaldehyde substrates and works well with a range of aryl- and alkylsulfonyl azides.

Ortho-aminobenzaldehydes are useful building blocks for the synthesis of natural products, pharmaceuticals, and organic materials.[1] Reactions based on metal-catalyzed coupling of prefunctionalized arenes with amine partners, such as Buchwald-Hartwig amination, have provided powerful methods to form the C(sp^2)–N bond of *ortho*-aminobenzaldehydes.[2] Over the past several years, metal-catalyzed directing group-controlled *ortho*-C(sp^2)–H amination of arenes with organic azides, pioneered by Chang and others, has come to offer an efficient alternative for appending *ortho* amide or sulfonamide groups.[3-6] A range of functional groups including imine, ketone, ester, carboxylic acid and amide have successfully facilitated the desired *ortho*-C(sp^2)–H amination reactions under various metal catalyzed reaction manifolds (Scheme 1A). However, the direct *ortho*-C-H amination of benzaldehydes is still challenging, probably due to the relatively weak coordinating ability and instability of the aldehyde group.[7,8] Recently, Shi reported an iridium-catalyzed *ortho*-C(sp^2)–H amidation reaction of benzaldehydes with arylsulfonyl azides using preformed imines or sub-stoichiometric amounts of aniline derivatives as transient directing groups (Scheme 1B).[9] Herein, we report an efficient and broadly applicable protocol for the synthesis of 2-sulfonylaminobenzaldehydes via the Ir-catalyzed *ortho*-C(sp^2)–H amidation of benzaldehydes with aryl- and alkylsulfonyl azides using a catalytic amount of 3,5-di(trifluoromethyl)aniline (Scheme 1C). [10-15]



Scheme 1. Metal-catalyzed *ortho*-C(sp^2)-H amination of arenes with organic azide

We commenced our study by evaluating catalytic amine promoters for the reaction of 2-methylbenzaldehyde **1** with *p*-toluenesulfonyl azide **2** under reported Ir-catalyzed amidation conditions, with 2.5 mol% of $[Cp^*IrCl_2]_2$ catalyst and 10 mol% of $AgNTf_2$ in dichloroethane (DCE) solvent (Table 1).[5e] The desired C-H amidated product **3** was obtained in 19% NMR yield in the absence of any amine additive. We were pleased to see that the addition of 10 mol% of aniline derivative significantly improved the C-H amidation reaction. In comparison, the use of aliphatic amines and amino acid derivatives gave less than 20% yield of **3** (see Supporting Information for details). In general, electron deficient anilines (e.g. **L4**, and **L5**) gave much better results than electron rich ones (e.g. **L2**, **L3**). *Ortho*-substituted anilines were less effective than *para*-substituted ones (see **L5** vs **L7**). 3,5-di(trifluoromethyl)aniline **L8** stood out among the aniline derivatives tested, providing product **3** in 90% isolated yield. As shown in Table 2, a number of optimizations were necessary to achieve efficient *ortho*-C-H amination of **1** with **L8**. We found that $AgNTf_2$ was the best chloride scavenger for generating the active cationic iridium species (entry 2-5). Chlorobenzene and DCE were the best solvents; other solvents tested gave significantly lower yield (entries 6-10). Other metal catalysts tested showed little reactivity (entries 11-14).

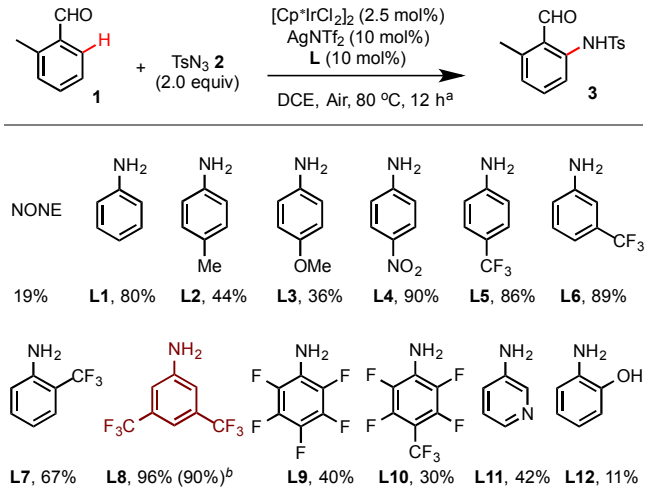
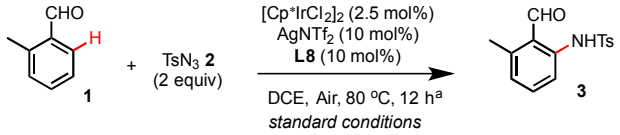


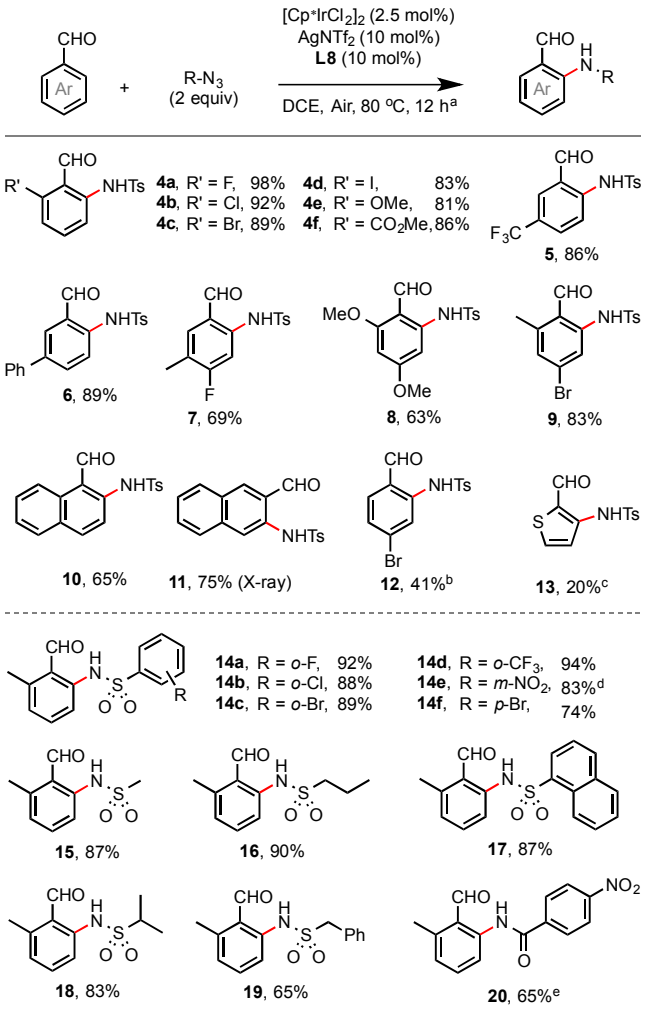
Table 1. Evaluation of aniline promoters for *ortho*-C-H amidation of 2-methylbenzaldehyde **1** with *p*-toluenesulfonyl azide **2**. a) Yields are based on ^{1}H-NMR analysis on a 0.2 mmol scale using 1,1,2,2-tetrachloroethane as internal standard. b) Isolated yield.



entry	variation from the "standard conditions"	Yield (%)[b]
1	None	96 (90)[c]
2	$AgSbF_6$ instead of $AgNTf_2$	87
3	$AgPF_6$ instead of $AgNTf_2$	79
4	$AgBF_4$ instead of $AgNTf_2$	63
5	Ag_2CO_3 instead of $AgNTf_2$	<5
6	Dioxane instead of DCE	<5
7	MeCN instead of DCE	<5
8	*t*AmylOH instead of DCE	<5
9	Toluene instead of DCE	10
10	Chlorobenzene instead of DCE	86
11	$IrCl_3$ instead of $[Cp^*IrCl_2]_2$	ND
12	$Pd(OAc)_2$ instead of $[Cp^*IrCl_2]_2$	ND
13	$[Cp^*RhCl_2]_2$ instead of $[Cp^*IrCl_2]_2$	5
14	$[Ru(p\text{-cymene})Cl_2]_2$ instead of $[Cp^*IrCl_2]_2$	<5

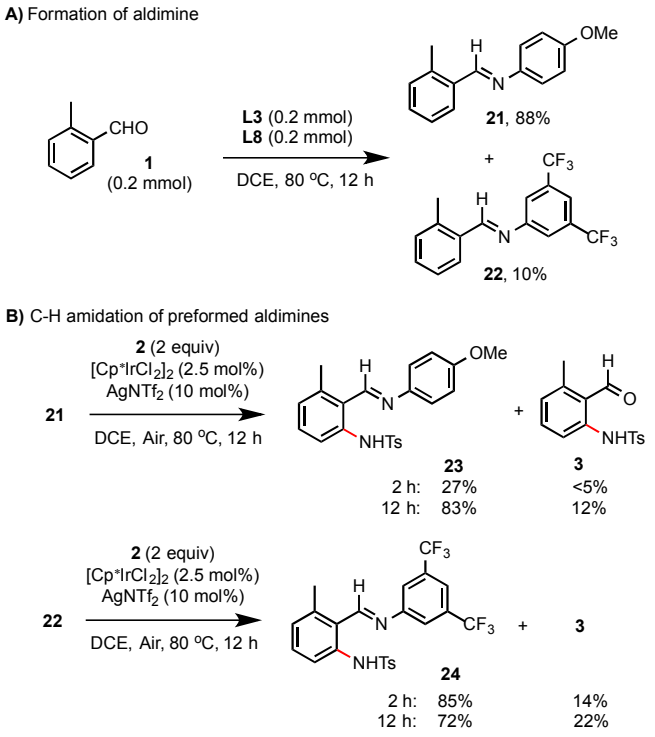
Table 2. Optimization of amidation reaction conditions. a) All the reactions were run on a 0.2 mmol scale at 0.1 M concentration. b) NMR yield using 1,1,2,2-tetrachloroethane as internal standard. c) Isolated yield. See Supporting Information for more evaluation conditions.

With the optimized conditions in hand, we next explored the substrate scope of benzaldehydes with *p*-toluenesulfonyl azide **2** (Scheme 2). The amidation of benzaldehydes carrying either electron donating or withdrawing groups proceeded well under the standard conditions (see **5**, **8**). A variety of functional groups including esters, ethers, and halides were tolerated. For *meta*-substituted benzaldehydes, C-H amidation took place selectively at the less sterically hindered position (see **5**-**7**). The reactions of 1-naphthaldehyde and 2-naphthaldehyde gave products **10** and **11,** respectively, in good yield and with excellent selectivity. The amidation of *para*-substituted benzaldehydes proceeds with lower conversion (see **12**) for reasons that are not clear. Reactions of heteroarenes gave notably lower yield (see **13**). As seen in compounds **14**-**19**, the reaction of 2-methylbenzaldehyde with various aryl- or alkylsulfonyl azides also proceeded smoothly. Furthermore, the reaction of 2-methylbenzaldehyde with 4-nitrobenzoyl azide gave amidation product **20** in good yield under modified conditions.

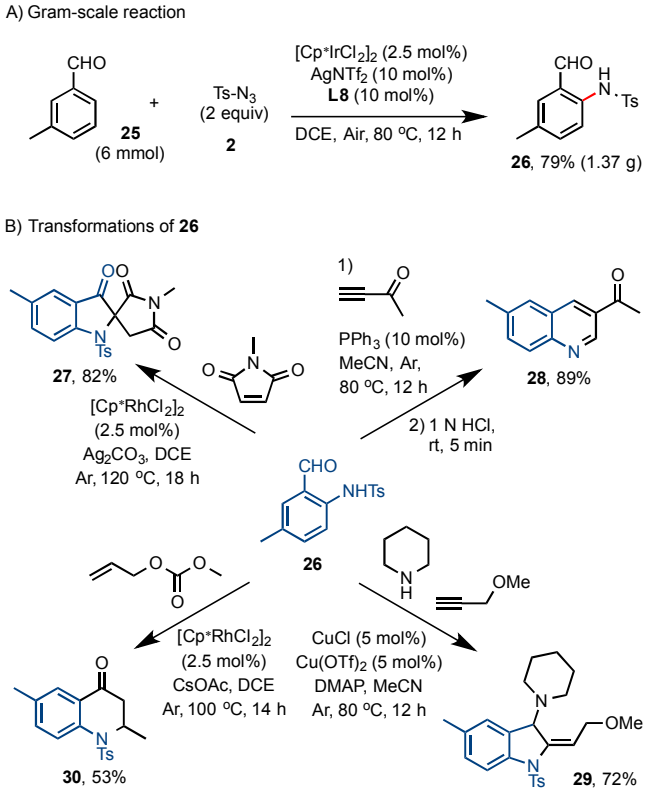


Scheme 2. Substrate scope of Ir-catalyzed *ortho*-C-H amination of benzaldehydes with organic azides. a) Isolated yield on a 0.2 mmol scale. b) $[Cp^*IrCl_2]_2$ (5.0 mol%), **L8** (20 mol%), $AgNTf_2$ (20 mol%), 90 °C. c) $[Cp^*IrCl_2]_2$ (5.0 mol%), **L8** (20 mol%), $AgNTf_2$ (20 mol%), 110 °C. d) 100 °C. e) $[Cp^*IrCl_2]_2$ (5.0 mol%), **L8** (20 mol%), $AgNTf_2$ (20 mol%). See the X-ray structure of compound **4e**, **4f**, and **11** in Supporting Information (**Figure S1-Figure S3)**.

We carried out experiments to investigate the unique effectiveness of 3,5-di(trifluoromethyl)aniline in this Ir-catalyzed *ortho*-C-H amidation reaction. As shown in Scheme 3A, aldimine **21** was the major product of a competitive condensation reaction with equal amount of 2-methylbenzaldehyde, 4-methoxylaniline (**L3**), and 3,5-di(trifluoromethyl)aniline (**L8**) in DCE at 80 °C. Aldimine **21** and **22** were then separately subjected to the standard Ir-catalyzed C-H amidation reaction conditions with **2** (Scheme 3B). The reaction of **22** gave 85% of **24** along with 14% of **3** in 2 hours. In comparison, the amidation of **21** gave 27% of **23** and a trace amount of **3** in 2 hours. After 12 hours, 83% yield of **23** and 12% yield of **3** was obtained, while 72% yield of **24** and 22% yield of **3** was obtained from the parallel reaction of **22**. These results suggest that aldimine **22** is slower to form than **21**, but is more reactive to Ir-catalyzed *ortho*-C-H amidation.



Scheme 3. Mechanistic studies. NMR yield on a 0.2 mmol scale using 1,1,2,2-tetrachloroethane as internal standard



Scheme 4. Synthetic applications

In order to demonstrate the applicability of this amidation reaction, a large scale reaction and post transformations of the amidated product were carried out. As shown in Scheme 4A, Ir-catalyzed *ortho*-C-H amidation of **25** gave **26** in 79% yield on a 6 mmol scale. As shown in Scheme 4B, compound **26** were successfully transformed to a wide variety of N-heterocyclic products including spiroketone **27**[16a], quinoline **28**[16b], indoline **29**[16c], and hydroquinolone **30**[16d] in good yield following reported procedures.

In summary, we have developed a new protocol for the Ir-catalyzed *ortho*-C-H amidation of benzaldehydes with organic azides using a catalytic amount of 3,5-di(trifluoromethyl)aniline promoter. 3,5-di(trifluoromethyl)aniline facilitates the Ir-catalyzed directed C-H amination reaction through formation of a transient aldimine intermediate. This protocol tolerates a broad scope of both benzaldehydes and sulfonyl azides, and offers a convenient method for the synthesis of various 2-sulfonylaminobenzaldehydes.

EXPERIMENTAL SECTION

General Method and Materials. All commercial materials were used as received unless otherwise noted. TLC were performed on silica gel Huanghai HSGF254 plates and visualization of the developed chromatogram was performed by fluorescence quenching (λ_{max} = 254 nm). Flash chromatography was performed using Silica gel (200-300 mesh) purchased from Qingdao Haiyang Chemical Co., China. $[Cp^*IrCl_2]_2$ (> 94%) was purchased from TCI. $AgNTf_2$ (99.3%) was purchased from Boka Chemical Co., China. DCE (> 99.5%) was purchased from TCI, other solvents were purchased from J&K. Organic azides were prepared according to the literature method.[17] NMR spectra were recorded on Bruker AVANCE AV 400 instruments and all NMR experiments were reported in units, parts per million (ppm), using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet. High resolution ESI mass experiments were operated on a Waters Xevo G2-Xs QTof instrument. IR spectra were recorded on a Bruker Tensor 27 instrument and are reported in wavenumbers (cm^{-1}). X-ray crystallography was recorded on Rigaku 007 Saturn 70 or Bruker SMART APEX CCD instruments.

General procedure of *ortho* amidation of benzaldehydes with organic azides. To a 12 mL glass vial was added benzaldehyde (0.2 mmol, 1.0 equiv), organic azide (0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (4.0 mg, 0.005 mmol, 2.5 mol%), $AgNTf_2$ (7.8 mg, 0.02 mmol, 10 mol%) and **L8** (4.6 mg, 0.02 mmol, 10 mol%) at room temperature. DCE (2 mL) was then added and the vial was sealed with PTFE cap. The mixture was stirred at 80 ^oC for 12 hours. After been cooled to room temperature, the reaction mixture was di-

luted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to give the amidated product.

2-Tolylsulfonylamino-6-methyl-benzaldehyde (**3**).[8b] Yellow solid, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 52.0 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H), 10.32 (s, 1H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 7.4 Hz, 1H), 2.59 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 144.2, 143.8, 140.9, 136.5, 136.1, 129.8, 127.3, 125.8, 119.4, 116.1, 21.6, 19.0.

2-Tolylsulfonylamino-6-fluoro-benzaldehyde (**4a**).[8b] Yellow solid, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 57.3 mg, 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (s, 1H), 10.26 (s, 1H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.51-7.44 (m, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 6.79-6.74 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4 (d, *J* = 12.2 Hz), 166.0 (d, *J* = 260.6 Hz), 144.6, 141.4 (d, *J* = 20.2 Hz), 137.8 (d, *J* = 11.7 Hz), 136.1, 129.9, 127.4, 113.3 (d, *J* = 3.6 Hz), 110.8 (d, *J* = 9.4 Hz), 109.5 (d, *J* = 21.0 Hz), 21.6.

2-Tolylsulfonylamino-6-chloro-benzaldehyde (**4b**).[9] Pale yellow solid, R_f = 0.7 (Hexanes/EtOAc = 4/1). Yield: 57.0 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.35 (s, 1H), 10.44 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 144.6, 142.3, 140.4, 136.5, 136.2, 130.0, 127.4, 124.6, 117.6, 116.6, 21.6.

2-Tolylsulfonylamino-6-bromo-benzaldehyde (**4c**).[9] Yellow solid, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 63.2 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.37 (s, 1H), 10.34 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 6.6 Hz, 1H), 7.30-7.25 (m, 4H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 144.6, 142.3, 136.5, 136.1, 130.1, 130.0, 128.1, 127.3, 118.3, 117.4, 21.6.

2-Tolylsulfonylamino-6-iodo-benzaldehyde (**4d**).[9] Brown solid, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 66.9 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.38 (s, 1H), 10.06 (s, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.09 (t, *J* = 8.2 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 144.6, 141.7, 136.5, 136.2, 135.4, 130.0, 127.4, 119.2, 118.5, 105.0, 21.7.

2-Tolylsulfonylamino-6-methoxy-benzaldehyde (**4e**).[8b] Pale yellow solid, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 49.4 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.53 (s, 1H), 10.36 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 8.4 Hz, 1H), 7.24-7.18 (m, 3H), 6.55 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 2.36 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 163.4, 144.2, 141.6, 137.6, 136.5, 129.8, 127.3, 110.9, 109.5, 105.1, 56.0, 21.6.

2-Tolylsulfonylamino-6-methoxycarbonyl-benzaldehyde (**4f**).[9] Pale yellow solid, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 57.6 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1H), 10.29 (s, 1H), 7.89 (d, *J* = 7.3 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.56-7.51 (m, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 3.94 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6, 166.4, 144.5, 140.4, 136.2, 135.7, 134.7, 129.9, 127.3, 125.1, 122.3, 121.1, 53.3, 21.7.

2-Tolylsulfonylamino-5-trifluoromethyl-benzaldehyde (**5**). Pale yellow solid, mp 137-139 ^{o}C, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 59.0 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.01 (s, 1H), 9.90 (s, 1H), 7.87 (s, 1H), 7.82-7.79 (m, 3H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 145.0, 142.8, 135.9, 133.1 (q, *J* = 3.4 Hz), 132.3 (q, *J* = 3.3 Hz), 130.1, 127.3, 124.9 (q, *J* = 34.1 Hz), 123.3 (q, *J* = 272.7 Hz), 121.0, 117.5, 21.6; HRMS calcd for $C_{15}H_{13}F_3NO_3S$ [M+H$^+$]: 344.0563, found: 344.0565; IR (KBr) 3167, 2856, 2755, 2360, 2341, 1680, 1623, 1588, 1508, 1442, 1398, 1163, 874 cm^{-1}.

2-Tolylsulfonylamino-5-phenyl-benzaldehyde (**6**). Brown solid, mp 112-114 ^{o}C, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 62.5 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (s, 1H), 9.89 (s, 1H), 7.81-7.71 (m, 5H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.1 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 144.4, 139.0, 138.7, 136.5, 136.2, 134.5, 134.3, 129.9, 129.2, 128.0, 127.4, 126.7, 122.3, 118.4, 21.7; HRMS calcd for $C_{20}H_{17}NNaO_3S$ [M+Na$^+$]: 374.0821, found: 374.0825; IR (KBr) 3210, 2958, 2869, 2360, 2341, 1670, 1653, 1507, 1486,1382, 1158, 869 cm^{-1}.

2-Tolylsulfonylamino-4-fluoro-5-methyl-benzaldehyde (**7**). Pale yellow solid, mp 143-145 ^{o}C, R_f = 0.4 (Hexanes/EtOAc = 4/1). Yield: 42.5 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.87 (s, 1H), 9.73 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.43-7.36 (m, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 165.5 (d, *J* = 258.2 Hz), 144.5, 140.2 (d, *J* = 12.8 Hz), 139.5 (d, *J* = 9.0 Hz), 136.1, 130.0, 127.3, 120.3 (d, *J* = 19.0 Hz), 118.6, 105.2 (d, *J* = 29.1 Hz), 21.6, 13.8 (d, *J* = 2.8 Hz); HRMS calcd for $C_{15}H_{14}FNNaO_3S$ [M+Na$^+$]: 330.0571, found: 330.0575; IR (KBr) 3126, 2926, 2864, 2360, 2341, 1668, 1653, 1583, 1507, 1405, 1320, 1157, 845 cm^{-1}.

2-Tolylsulfonylamino-4,6-dimethoxy-benzaldehyde (**8**). White solid, mp 200-201 ^{o}C, R_f = 0.4 (Hexanes/EtOAc = 4/1). Yield: 42.3 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 10.16 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.77 (s, 1H), 6.02 (s, 1H), 3.82 (s, 6H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 167.0, 164.9, 144.2, 144.1, 136.7, 129.9, 127.5, 105.8, 94.0, 92.9,

56.0, 55.9, 21.7; HRMS calcd for $C_{16}H_{18}NO_5S$ [M+H$^+$]: 336.0900, found: 336.0903; IR (KBr) 3060, 2983, 2892, 2360, 2341, 1652, 1614, 1576, 1494, 1432, 1396, 1341, 1283, 1155, 843 cm^{-1}.

2-Tolylsulfonylamino-4-bromo-6-methyl-benzaldehyde (**9**). Yellow solid, mp 183-185 ^{o}C, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 61.4 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (s, 1H), 10.26 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 2H), 7.72 (s, 1H). 7.27 (d, *J* = 7.8 Hz, 2H), 7.01 (s, 1H), 2.56 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 145.1, 144.5, 141.7, 136.2, 131.3, 130.0, 128.7, 127.4, 119.0, 117.9, 21.7, 18.9; HRMS calcd for $C_{15}H_{15}BrNO_3S$ [M+H$^+$]: 367.9951, found: 367.9949; IR (KBr) 3051, 2902, 2803, 2360, 2341, 1654, 1586, 1559, 1488, 1416, 1372, 1162, 868 cm^{-1}.

2-Tolylsulfonylamino-1-naphthaldehyde (**10**).[9] Yellow solid, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 42.3 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.16 (s, 1H), 10.88 (s, 1H), 8.35 (d, *J* = 8.3 Hz, 1H), 7.96-7.90 (m, 2H), 7.80 (t, *J* = 7.6 Hz, 3H), 7.61 (t, *J* = 7.0 Hz, 1H), 7.46 (t, *J* = 7.0 Hz, 1H), 7.23 (d, *J* = 7.3 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 144.4, 141.6, 137.7, 136.6, 133.6, 129.9, 129.51, 129.46, 129.36, 127.3, 125.5, 119.7, 116.8, 112.8, 21.6.

3-Tolylsulfonylamino-2-naphthaldehyde (**11**). Yellow solid, mp 157-159 ^{o}C, R_f = 0.2 (Hexanes/EtOAc = 4/1). Yield: 49.1 mg, 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 9.93 (s, 1H), 8.10 (s, 1H), 8.00 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 3H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.0, 144.1, 140.4, 136.5, 136.3, 134.6, 130.7, 129.7, 129.2, 128.9, 127.6, 127.3, 126.2, 122.9, 115.8, 21.6; HRMS calcd for $C_{18}H_{15}NNaO_3S$ [M+Na$^+$]: 348.0665, found: 348.0670; IR (KBr) 3203, 2844, 2759, 2360, 2342, 1668, 1597, 1558, 1508, 1473, 1404, 1375, 1156, 870 cm^{-1}.

2-Tolylsulfonylamino-4-bromo-benzaldehyde (**12**).[8b] To a 12 mL glass vial was added 4-bromo-benzaldehyde (37.0 mg, 0.2 mmol, 1.0 equiv), *p*-toluenesulfonyl azide **2** (78.9 mg, 0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (8.0 mg, 0.01 mmol, 5 mol%), $AgNTf_2$ (15.6 mg, 0.04 mmol, 20 mol%) and **L8** (9.2 mg, 0.04 mmol, 20 mol%) at room temperature. DCE (2 mL) was then added and the vial was sealed with PTFE cap. The mixture was stirred at 90 ^{o}C for 12 hours. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to give compound **12** in 41% yield (29.1 mg). Pale yellow solid, R_f = 0.3 (Hexanes/EtOAc = 4/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.84 (s, 1H), 9.78 (s, 1H), 7.89 (s, 1H), 7.79 (d, *J* = 7.0 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 6.7 Hz, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 144.7, 141.0, 137.1, 136.2, 131.6, 130.1, 127.4, 126.4, 120.9, 120.5, 21.7.

3-Tolylsulfonylamino-thiophene-2-carbaldehyde (**13**).[8b] To a 12 mL glass vial was added thiophene-2-carbaldehyde (22.4 mg, 0.2 mmol, 1.0 equiv), *p*-toluenesulfonyl azide **2** (78.9 mg, 0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (8.0 mg, 0.01 mmol, 5 mol%), $AgNTf_2$ (15.6 mg, 0.04 mmol, 20 mol%) and **L8** (9.2 mg, 0.04 mmol, 20 mol%) at room temperature. DCE (2 mL) was then added and the vial was sealed with PTFE cap. The mixture was stirred at 110 ^oC for 12 hours. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to give compound **13** in 20% yield (11.2 mg). Pale yellow solid, R_f = 0.3 (Hexanes/EtOAc = 4/1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 9.60 (s, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 5.3 Hz, 1H), 7.43 (d, *J* = 5.3 Hz, 1H), 7.28-7.26 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.0, 144.6, 143.8, 136.5, 136.4, 130.0, 127.2, 121.0, 120.7, 21.7.

2-(2-Fluorobenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14a**). Brown solid, mp 132-135 ^oC, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 54.2 mg, 92%. ^1H NMR (400 MHz, $CDCl_3$) δ 11.79 (s, 1H), 10.39 (s, 1H), 7.99 (t, *J* = 7.0 Hz, 1H), 7.55 (d, *J* = 5.2 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.34-7.25 (m, 2H), 7.12 (t, *J* = 9.1 Hz, 1H), 6.87 (d, *J* = 7.3 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 158.9 (d, *J* = 258.2 Hz), 143.9, 140.2, 136.1, 135.8 (d, *J* = 8.5 Hz), 130.9, 127.2 (d, *J* = 13.2 Hz), 126.0, 124.4 (d, *J* = 3.9 Hz), 119.2, 117.4 (d, *J* = 20.9 Hz), 115.3, 19.0; HRMS calcd for $C_{14}H_{13}FNO_3S$ $[M+H^+]$: 294.0595, found: 294.0596; IR (KBr) 3089, 2925, 2786, 2360, 2341, 1664, 1599, 1579, 1488, 1385, 1157, 763 cm^{-1}.

2-(2-Chlorobenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14b**). Pale yellow solid, mp 138-140 ^oC, R_f = 0.4 (Hexanes/EtOAc = 4/1). Yield: 54.5 mg, 88%. ^1H NMR (400 MHz, $CDCl_3$) δ 11.97 (s, 1H), 10.39 (s, 1H), 8.22 (d, *J* = 7.5 Hz, 1H), 7.50-7.47 (m, 1H), 7.44-7.40 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 7.4 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 144.0, 140.1, 136.4, 136.1, 134.4, 132.2, 132.1, 132.1, 127.0, 125.7, 118.9, 114.6, 19.1; HRMS calcd for $C_{14}H_{13}ClNO_3S$ $[M+H^+]$: 310.0299, found: 310.0300; IR (KBr) 3090, 2902, 2361, 2341, 1666, 1599, 1577, 1489, 1472, 1386, 1162, 758 cm^{-1}.

2-(2-Bromobenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14c**). Pale yellow solid, mp 158-160 ^oC, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 63.0 mg, 89%. ^1H NMR (400 MHz, $CDCl_3$) δ 12.02 (s, 1H), 10.40 (s, 1H), 8.28 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.41-7.37 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.30-7.26 (m, 1H), 6.84 (d, *J* = 7.3 Hz, 1H), 2.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.7, 144.0, 140.2, 138.3, 136.1, 135.7, 134.4, 132.4, 127.6, 125.6, 120.5, 118.9, 114.6, 19.2; HRMS calcd for $C_{14}H_{13}BrNO_3S$ $[M+H^+]$: 353.9794, found: 353.9792; IR (KBr) 3091, 2360, 1652, 1598, 1575, 1558, 1471, 1448, 1380, 1165, 732 cm^{-1}.

2-(2-Trifluoromethylbenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14d**). Pale yellow solid, mp 121-123 °C, R_f = 0.4 (Hexanes/EtOAc = 4/1). Yield: 64.5 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 10.38 (s, 1H), 8.31-8.29 (m, 1H), 7.86-7.84 (m, 1H), 7.70-7.68 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 144.1, 140.2, 137.9, 136.2, 133.4, 132.4, 131.9, 128.9, 128.8 (q, *J* = 6.2 Hz), 128.1 (q, *J* = 33.3 Hz), 125.9, 122.7 (q, *J* = 275.4 Hz), 119.1, 114.9, 19.1; HRMS calcd for $C_{15}H_{12}F_3NNaO_3S$ [M+Na$^+$]: 366.0382, found: 366.0388; IR (KBr) 3118, 2920, 2360, 1636, 1597, 1576, 1507, 1456, 1388, 1168, 770 cm^{-1}.

2-(3-Nitrobenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14e**). To a 12 mL glass vial was added 2-methylbenzaldehyde **1** (24.0 mg, 0.2 mmol, 1.0 equiv), 3-nitrobenzenesulfonyl azide (91.3 mg, 0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (4.0 mg, 0.005 mmol, 2.5 mol%), $AgNTf_2$ (7.8 mg, 0.02 mmol, 10 mol%) and **L8** (4.6 mg, 0.02 mmol, 10 mol%) at room temperature. DCE (2 mL) was then added and the vial was sealed with PTFE cap. The mixture was stirred at 100 °C for 12 hours. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to give compound **14e** in 83% yield (53.2 mg). Brown solid, mp 157-159 °C, R_f = 0.2 (Hexanes/EtOAc = 4/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 10.34 (s, 1H), 8.69 (s, 1H), 8.38 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.3, 148.3, 144.3, 141.7, 140.0, 136.5, 132.8, 130.8, 127.8, 126.9, 122.6, 119.8, 116.4, 19.1; HRMS calcd for $C_{14}H_{13}N_2O_5S$ [M+H$^+$]: 321.0540, found: 321.0537; IR (KBr) 3084, 2360, 1646, 1602, 1576, 1472, 1457, 1385, 1169, 791, 733 cm^{-1}.

2-(4-Bromobenzenesulfonyl)-amino-6-methyl-benzaldehyde (**14f**). Brown solid, mp 158-160 °C, R_f = 0.5 (Hexanes/EtOAc = 4/1). Yield: 52.7 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.44 (s, 1H), 10.32 (s, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 144.0, 140.4, 138.6, 136.2, 132.5, 128.9, 128.3, 126.3, 119.6, 116.3, 19.0; HRMS calcd for $C_{14}H_{13}BrNO_3S$ [M+H$^+$]: 353.9794, found: 353.9789; IR (KBr) 3093, 2903, 2360, 1645, 1598, 1575, 1470, 1456, 1390, 1168, 863 cm^{-1}.

2-Methylsulfonyl-amino-6-methyl-benzaldehyde (**15**).[8b] Yellow solid, R_f = 0.5 (Hexanes/EtOAc = 4/1). Yield: 37.3 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.18 (s, 1H), 10.41 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 3.07 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 144.2, 141.2, 136.5, 125.9, 119.2, 115.4, 40.3, 19.1.

2-Propanylsulfonyl-amino-6-methyl-benzaldehyde (**16**). Brown solid, mp 57-59 ^{o}C, R_f = 0.6 (Hexanes/EtOAc = 4/1). Yield: 43.4 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1H), 10.41 (s, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 3.14-3.11 (m, 2H), 2.67 (s, 3H), 1.85-1.75 (m, 2H), 0.99 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 144.2, 141.4, 136.5, 125.6, 119.0, 115.3, 54.0, 19.2, 17.3, 12.9; HRMS calcd for $C_{11}H_{16}NO_3S$ [M+H$^+$]: 242.0845, found: 242.0848; IR (KBr) 3117, 2972, 2876, 2360, 1652, 1600, 1576, 1507, 1457,1375 cm^{-1}.

2-(1-Naphthylsulfonyl)-amino-6-methyl-benzaldehyde (**17**). Pale yellow solid, mp 167-169 ^{o}C, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 56.5 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1H), 10.25 (s, 1H), 8.69 (d, *J* = 8.6 Hz, 1H), 8.38 (d, *J* = 7.2 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.58-7.49 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 7.3 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 143.8, 140.8, 136.1, 135.0, 134.2, 134.0, 130.5, 129.1, 128.7, 127.9, 127.1, 125.4, 124.2, 123.9, 118.8, 115.1, 18.9; HRMS calcd for $C_{18}H_{15}NNaO_3S$ [M+Na$^+$]: 348.0665, found: 348.0670; IR (KBr) 3057, 2915, 2342, 1646, 1601, 1577, 1506, 1468, 1376, 1159 cm^{-1}.

2-Isopropanylsulfonyl-amino-6-methyl-benzaldehyde (**18**). Brown solid, mp 78-80 ^{o}C, R_f = 0.3 (Hexanes/EtOAc = 4/1). Yield: 40.0 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (s, 1H), 10.41 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 3.37-3.30 (m, 1H), 2.66 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 144.1, 141.9, 136.5, 125.5, 119.0, 115.6, 53.3, 19.2, 16.5; HRMS calcd for $C_{11}H_{16}NO_3S$ [M+H$^+$]: 242.0845, found: 242.0843; IR (KBr) 3099, 2979, 2936, 2360, 1636, 1600, 1576, 1507, 1456, 1380, 1142 cm^{-1}.

2-Benzylsulfonyl-amino-6-methyl-benzaldehyde (**19**). Brown oil, R_f = 0.5 (Hexanes/EtOAc = 4/1). Yield: 37.6 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.04 (s, 1H), 10.27 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.33-7.25 (m, 3H), 7.18 (d, *J* = 7.0 Hz, 2H), 6.92 (d, *J* = 7.4 Hz, 1H), 4.41 (s, 2H), 2.64 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 143.9, 141.5, 136.3, 130.7, 129.1, 128.8, 128.2, 125.7, 119.0, 115.5, 58.7, 19.1; HRMS calcd for $C_{15}H_{15}NNaO_3S$ [M+Na$^+$]: 312.0665, found: 312.0670; IR (KBr) 3066, 2917, 2360, 1652, 1576, 1540, 1507, 1488, 1362, 1154, 763, 693 cm^{-1}.

2-(4-Nitrobenzoyl)-amino-6-methyl-benzaldehyde (**20**). To a 12 mL glass vial was added 2-methylbenzaldehyde **1** (24.0 mg, 0.2 mmol, 1.0 equiv), *p*-nitrobenzoyl azide (76.8 mg, 0.4 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (8.0 mg, 0.01 mmol, 5 mol%), $AgNTf_2$ (15.6 mg, 0.04 mmol, 20 mol%) and **L8** (9.2 mg, 0.04 mmol, 20 mol%) at room temperature. DCE (2 mL) was then added and the vial was sealed with PTFE cap. The mixture was stirred at 80 ^{o}C for 12 hours. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate

was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to give compound **20** in 62% yield (35.3 mg). Yellow solid, mp 212-214 ^{o}C, R_f = 0.5 (Hexanes/EtOAc = 4/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.74 (s, 1H), 10.54 (s, 1H), 8.79 (d, *J* = 8.5 Hz, 1H), 8.38 (d, *J* = 8.8 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 164.1, 150.1, 143.8, 141.6, 140.3, 137.0, 128.9, 126.9, 124.2, 119.9, 118.8, 19.3; HRMS calcd for $C_{15}H_{13}N_2O_4$ [M+H$^+$]: 285.0870, found: 285.0870; IR (KBr) 3108, 2923, 2793, 2360, 1653, 1609, 1576, 1508, 1458, 1396, 1197, 802 cm^{-1}.

(E)-N-(4-methoxyphenyl)-1-(o-tolyl)methanimine (**21**). To a solution of 2-methylbenzaldehyde **1** (1.20 g, 10 mmol, 1.0 equiv) and 4-methoxyaniline **L3** (1.23 g, 10 mmol, 1.0 equiv) in DCM (20 mL) was added $MgSO_4$ (2.4 g). The mixture was stirred at room temperature overnight, then filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel to afford compound **21** as yellow solid (mp 56-57 ^{o}C, R_f = 0.6, Hexanes/EtOAc = 10/1) in 98% yield (2.2 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.34-7.26 (m, 2H), 7.21 (dd, *J* = 7.2, 5.0 Hz, 3H), 6.92 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 157.2, 145.6, 138.4, 134.4, 131.0, 130.8, 127.6, 126.4, 122.3, 114.5, 55.6, 19.5; HRMS calcd for $C_{15}H_{16}NO$ [M+H$^+$]: 226.1226, found: 226.1223; IR (KBr) 1652, 1616, 1558, 1506, 1456, 1436, 1246, 856 cm^{-1}.

(E)-N-(3,5-bis(trifluoromethyl)phenyl)-1-(o-tolyl)methanimine (**22**). To a solution of 2-methylbenzaldehyde **1** (1.0 g, 8.3 mmol, 1.0 equiv) in toluene (5 mL) was added **L8** (1.91 g, 8.3 mmol, 1.0 equiv) and 4-methylbenzenesulfonic acid (30 mg, 0.17 mmol, 2 mol%). The mixture was stirred at 110 ^{o}C for 12 h. After been cooled to room temperature, the reaction mixture was diluted with hexanes (20 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, the crude residue was recrystallized with hexanes/DCM (50/1) to afford the compound **22** as colorless solid (mp 52-53 ^{o}C, R_f = 0.8, Hexanes/EtOAc = 10/1) in 89% yield (2.4 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.72 (s, 1H), 7.58 (s, 2H), 7.43-7.37 (m, 1H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 154.1, 139.5, 133.4, 133.2, 132.9, 132.5, 132.2, 131.5, 128.8, 126.7, 123.4 (q, *J* = 273.9 Hz), 121.2, 119.1 (m), 19.7; HRMS calcd for $C_{16}H_{12}F_6N$ [M+H$^+$]: 332.0868, found: 332.0873; IR (KBr) 1634, 1576, 1540, 1507, 1457, 1376, 760 cm^{-1}.

Competitive reaction for aldimine formation. A mixture of 2-methylbenzaldehyde **1** (24.0 mg, 0.2 mmol, 1.0 equiv), **L3** (24.6 mg, 0.2 mmol, 1.0 equiv), and **L8** (45.8 mg, 0.2 mmol, 1.0 equiv) in DCE (2 mL) was heated at 80 ^{o}C for 12 h. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*,

and the crude residue was dissolved in 1 mL of deuterated chloroform for ^{1}H-NMR analysis. 1,1,2,2-tetrachloroethane (33.6 mg, 0.2 mmol, 1.0 equiv, a singlet peak around 5.92 ppm was set as 1.00) was added as an internal standard. By analysis of crude ^{1}H-NMR, 88% of compound **21** and 10% of compound **22** were formed.

Competitive reaction for C-H amidation. Compound **21** and **22** (0.2 mmol, 1.0 equiv) were applied into the standard amidation conditions for 2 hour and 12 hour respectively. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (3 mL), and filtered through a pad of celite. The filtrate was concentrated in *vacuo*, the resulting crude residue was dissolved in 1 mL of deuterated chloroform for ^{1}H-NMR analysis. 1,1,2,2-tetrachloroethane (33.6 mg, 0.2 mmol, 1.0 equiv, a singlet peak around 5.92 ppm was set as 1.00) was added as internal standard.

(E)-N-(2-(((4-methoxyphenyl)imino)methyl)-3-methylphenyl)-4-methylbenzenesulfonamide (**23**). Yellow solid, mp 158-160 ^{o}C, R_f = 0.1 (Hexanes/EtOAc = 10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.78 (s, 1H), 8.91 (s, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.35-7.31 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 3H), 7.02 (d, *J* = 8.3 Hz, 2H), 6.89 (d, *J* = 7.4 Hz, 1H), 3.91 (s, 3H), 2.54 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 156.9, 143.5, 142.3, 140.4, 140.1, 137.4, 132.0, 129.6, 127.3, 125.4, 122.6, 119.1, 116.7, 114.8, 55.7, 21.6, 20.1; HRMS calcd for $C_{22}H_{23}N_2O_3S$ [M+H$^+$]: 395.1424, found: 395.1421; IR (KBr) 2959, 2311, 1575, 1506, 1456, 1253, 1161, 808 cm^{-1}.

(E)-N-(2-(((3,5-bis(trifluoromethyl)phenyl)imino)methyl)-3-methylphenyl)-4-methylbenzenesulfonamide (**24**). Pale yellow solid, mp 162-164 ^{o}C, R_f = 0.1 (Hexanes/EtOAc = 10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.57 (s, 1H), 8.81 (s, 1H), 7.81 (s, 1H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.55 (s, 3H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 7.3 Hz, 1H), 2.53 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 151.5, 144.0, 141.7, 140.4, 137.2, 133.8, 133.1 (q, *J* = 34.0 Hz), 129.8, 127.3, 125.8, 123.2 (q, *J* = 274.0 Hz), 121.5, 120.2 (m), 118.6, 117.3, 21.6, 20.2; HRMS calcd for $C_{23}H_{19}F_6N_2O_2S$ [M+H$^+$]: 501.1066, found: 501.1063; IR (KBr) 3079, 2930, 1598, 1571, 1468, 1376, 1152, 784 cm^{-1}.

2-Tolylsulfonyl-amino-5-methyl-benzaldehyde (**26**). To a 250 mL flask were added 3-methylbenzaldehyde **25** (0.72 g, 6 mmol, 1.0 equiv), *p*-toluenesulfonyl azide (TsN_3) **2** (2.37 g, 12 mmol, 2.0 equiv), $[Cp^*IrCl_2]_2$ (119.5 mg, 0.15 mmol, 2.5 mol%), $AgNTf_2$ (232.8 mg, 0.6 mmol, 10 mol%) and **L8** (137.4 mg, 0.06 mmol, 10 mol%) at room temperature. DCE (60 mL) was then added under air atmosphere and the mixture was stirred at 80 ^{o}C for 12 h. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (100 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to afford compound **26** as pale yellow solid (mp 107-109 ^{o}C, R_f = 0.3, Hexanes/EtOAc = 4/1) in 79% yield

(1.37g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 9.76 (s, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 2.35 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 144.1, 137.4, 136.7, 136.4, 133.0, 129.8, 127.3, 122.1, 118.2, 21.6, 20.4; HRMS calcd for $C_{15}H_{16}NO_3S$ [M+H$^+$]: 290.0845, found: 290.0846; IR (KBr) 3131, 2924, 2856, 2361, 2341, 1664, 1585, 1497, 1405, 1308, 1154, 901 cm^{-1}.

1',5-dimethyl-1-[(4-methylphenyl)sulfonyl]-Spiro-[2H-indole-2,3'-pyrrolidine]-2',3,5'(1H)-trione (**27**).[16a] Compound **26** (57.9 mg, 0.2 mmol, 1.0 equiv), *N*-Methyl maleimide (44 mg, 0.4 mmol, 2.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), Ag_2CO_3 (55.2 mg, 0.2 mmol, 1.0 equiv) and DCE (2 mL) were added to a 12 mL glass vial at room temperature. The vial was purged with argon for 1 min and then sealed with PTFE cap. The reaction mixture was stirred at 120 °C for 18 h. After been cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the compound **27** as pale yellow liquid (R_f = 0.3, Hexanes/EtOAc = 4/1) in 82% yield (65.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.50 (s, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.35 (t, *J* = 8.5 Hz, 3H), 3.49 (d, *J* = 17.8 Hz, 1H), 3.16 (s, 3H), 3.11 (d, *J* = 17.8 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 173.1, 170.9, 151.5, 145.7, 139.6, 135.6, 134.3, 130.2, 128.2, 125.4, 121.4, 113.8, 73.9, 39.2, 26.1, 21.8, 20.7.

3-acetyl-6-methyl-quinoline (**28**). Compound **26** (57.9 mg, 0.2 mmol, 1.0 equiv), acetylacetylene (20.4 mg, 0.3 mmol, 1.5 equiv), PPh_3 (5.2 mg, 0.02 mmol, 10 mol%), and MeCN (1 mL) were added to a 12 mL glass vial at room temperature. The vial was purged with argon for 1 min and then sealed with PTFE cap. The reaction mixture was stirred at 80 °C for 12 h. After been cooled to room temperature, 1M aqueous solution of HCl (1 mL) was added, and the mixture was stirred for 5 min before quenched with aqueous $NaHCO_3$ (1 mL). The mixture was extracted with EtOAc for three times and the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel to afford compound **28** as yellow solid (mp 83-85 ^{o}C, R_f = 0.3, Hexanes/EtOAc = 4/1) in 89% yield (33.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.58 (s, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.66-7.62 (m, 2H), 2.70 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.9, 148.4, 148.3, 137.7, 136.8, 134.5, 129.1, 128.2, 26.9, 21.6; HRMS calcd for $C_{12}H_{12}NO$ [M+H$^+$]: 186.0913, found: 186.0915; IR (KBr) 1574, 1419 cm^{-1}.

(Z)-2-(2-methoxyethylidene)-5-methyl-3-(piperidin-1-yl)-1-tosylindoline (**29**). Compound **26** (57.9 mg, 0.2 mmol, 1.0 equiv), piperidine (17.0 mg, 0.2 mmol, 1.0 equiv), 3-methoxyprop-1-yne (21.0 mg, 0.3 mmol, 1.5 equiv), CuCl (1.0 mg, 0.01 mmol, 5 mol%), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol, 5 mol%), DMAP (24.4 mg, 0.2 mmol, 1.0 equiv), and MeCN (2 mL) were added to a 12 mL glass vial at room temperature. The vial was purged with argon for 1 min and then sealed with PTFE cap. The reaction mixture

was stirred at 80 °C for 12 h. After been cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford compound **29** as yellow oil (R_f = 0.6, Hexanes/EtOAc = 10/1) in 72% yield (61.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.08-7.05 (m, 3H), 6.95 (s, 1H), 5.86-5.82 (m, 1H), 4.54-4.48 (m, 1H), 4.44-4.39 (m, 1H), 3.81 (s, 1H), 3.36 (s, 3H), 2.58-2.54 (m, 2H), 2.36-2.32 (m, 5H), 2.30 (s, 3H), 1.44-1.42 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 140.5, 139.8, 135.4, 134.1, 133.6, 129.2, 129.0, 128.0, 125.8, 121.3, 119.7, 70.1, 68.5, 58.2, 50.4, 26.8, 24.6, 21.7, 21.4; HRMS calcd for $C_{24}H_{31}N_2O_3S$ [M+H$^+$]: 427.2050, found: 427.2053; IR (KBr) 1575, 1437, 1364, 1171, 816 cm^{-1}.

2,3-dihydro-2,6-dimethyl-1-[(4-methylphenyl)sulfonyl]-4(1H)-Quinolinone (**30**).[16d] Compound **26** (57.9 mg, 0.2 mmol, 1.0 equiv), allyl methyl carbonate (69.6 mg, 0.6 mmol, 3.0 equiv), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), CsOAc (57.6 mg, 0.3 mmol, 1.5 equiv), and DCE (2 mL) were added to a 12 mL glass vial at room temperature. The vial was purged with argon for 1 min and then sealed with PTFE cap. The reaction mixture was stirred at 100 °C for 14 h. After been cooled to room temperature, the reaction mixture was diluted with EtOAc (2 mL), and filtered through a pad of celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography on silica gel to afford compound **30** as yellow solid (R_f = 0.2, Hexanes/EtOAc = 4/1) in 53% yield (35.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 1H), 7.72 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 2H), 4.87-4.84 (m, 1H), 2.41-2.29 (m, 7H), 2.18 (d, *J* = 17.8 Hz, 1H), 1.27 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 144.4, 137.3, 136.7, 136.0, 135.8, 130.1, 127.2, 126.97, 126.62, 125.3, 51.9, 41.9, 21.7, 20.9, 19.8.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXXXX.

Detailed optimization of reaction conditions, crystal structure of compounds **4e**, **4f**, **11** and copy of ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

X-ray crystallographic data of compounds **4e**, **4f** and **11** (CIF)

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