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Direct Dehydrative *N*-Pyridinylation of Amides

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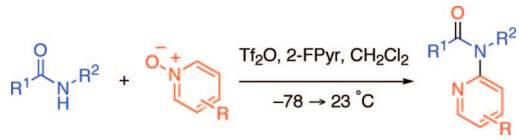
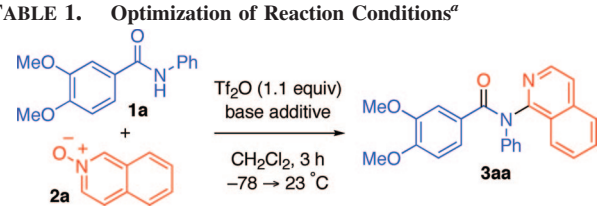


Electrophilic activation of secondary amides with trifluoromethanesulfonic anhydride in the presence of 2-fluoropyridine followed by introduction of a pyridine *N*-oxide derivative and warming affords the corresponding *N*-pyridinyl tertiary amide derivatives. A mechanism supported by in situ monitoring and deuterium labeling experiments is discussed.

Pyridinylated, isoquinolinylated, and quinolinylated amides are key structural motifs in a wide variety of pharmaceutical compounds and natural products.[1] Abramovitch and co-workers reported a fascinating methodology for the synthesis of *N*-pyridinyl amide derivatives via the nucleophilic addition of heteroaromatic *N*-oxides to imidoyl chlorides followed by a thermal rearrangement.[2] Recently, alternative conditions have been reported for the in situ activation of primary[3] and secondary[4] amides for nucleophilic addition of *N*-oxides to furnish the *N*-pyridinylated amides. The development of mild reaction conditions and expansion of the substrate scope for this transformation is of interest given the importance of the products. Herein we describe the *N*-pyridinylation, *N*-isoquinolinylation, and *N*-quinolinylation of various secondary amides and discuss a plausible mechanism supported by deuterium labeling and in situ monitoring experiments.

We have reported the use of 2-chloropyridine (2-ClPyr) with trifluoromethanesulfonic anhydride[6] (Tf_2O) as a versatile reagent combination for the synthesis of pyrimidine[7] and pyridine derivatives.[8] These methodologies provide the desired azaheterocycles via electrophilic activation of secondary *N*-aryl or *N*-vinyl amides to enable nucleophilic addition and annulation. We envisioned that these conditions would serve well for a modified Abramovitch reaction. Amide **1a** and isoquinoline *N*-oxide (**2a**) served as substrates for our early exploration of this chemistry (Table 1). Interestingly, the use of 2-fluoropyridine (2-FPyr, 1.2 equiv) as a base additive afforded a significant improvement in the reaction yield as compared to 2-ClPyr, furnishing amide **3aa** in 99% yield (compare entries 1 and 11, Table 1). More nucleophilic and stronger base additives generally gave poorer yields as compared to base additives with attenuated nucleophilicity and basicity. These observations suggest that optimal conditions provide a balance between the need for a base additive to promote electrophilic activation of the amide substrate while avoiding nucleophilic inhibition of this reaction. Consistent with our earlier findings,[7,8] the presence of the optimal base additive in excess or its absence led to a marked decrease in the yield of the desired product (entries 3, 12, and 13, Table 1). The use of the Hendrickson reagent ($(Ph_3P^+)_2O\cdot 2TfO^-$)[5] as the activating agent for this dehydrative *N*-pyridinylation reaction proved less effective as compared to the optimal conditions described above (entry 16, Table 1). The overall yield can be improved by use of excess **2a** due to competitive *N*-oxide decomposition (entry 2, Table 1, vide infra).

TABLE 1. Optimization of Reaction Conditions[a]



entry	base additive	base equiv	*N*-oxide *x* equiv	yield (%)[b]
1	2-Cl-pyridine	1.2	1.1	77
2	2-Cl-pyridine	1.2	2.0	81
3	none		1.1	16
4	pyridine	1.2	1.1	10
5	Et_3N	1.2	1.1	0
6	2-Br-pyridine	1.2	1.1	58
7	3-Cl-pyridine	1.2	1.1	74
8	ethyl nicotinate	1.2	1.1	73
9	3-Br-pyridine	1.2	1.1	72
10	2,6-lutidine	1.2	1.1	55
11	***2-F-pyridine***	**1.2**	**1.1**	***99***
12	2-F-pyridine	2.0	1.1	88
13	2-F-pyridine	5.0	1.1	76
14	DIPEA	1.2	1.1	48
15	2,6-dichloropyridine	1.2	1.1	15
16	Hendrickson reagent[c]	1.5	1.1	72

[a] Conditions: Amide **1a**, Tf_2O (1.1 equiv), base additive, CH_2Cl_2, −78→0 °C; isoquinoline *N*-oxide, 0→23 °C, 3 h. [b] Isolated yield. [c] Hendrickson reagent ($(Ph_3P^+)_2O\cdot 2TfO^-$) was prepared (ref 5) and used in place of Tf_2O without base additive.

(1) (a) Jones, G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., McKillop, A., Eds.; Pergamon: Oxford, 1996; Vol. 5, p 245. (b) Henry, G. D. *Tetrahedron* **2004**, *60*, 6043.

(2) (a) Abramovitch, R. A.; Singer, G. M. *J. Am. Chem. Soc.* **1969**, *91*, 5672. (b) Abramovitch, R. A.; Singer, G. M. *J. Org. Chem.* **1974**, *39*, 1795. (c) Abramovitch, R. A.; Rogers, R. B. *J. Org. Chem.* **1974**, *39*, 1802. (d) Abramovitch, R. A.; Rogers, R. B.; Singer, G. M. *J. Org. Chem.* **1975**, *40*, 41. (e) Abramovitch, R. A.; Rogers, R. B. *Tetrahedron Lett.* **1971**, *22*, 1951.

(3) Couturier, M.; Caron, L.; Tumidajksi, S.; Jones, K.; White, T. D. *Org. Lett.* **2006**, *8*, 1929.

(4) Manley, P. J.; Bilodeau, M. T. *Org. Lett.* **2002**, *4*, 3127.

(5) Hendrickson, J. B.; Hussoin, M. D. *J. Org. Chem.* **1987**, *52*, 4137.

(6) For elegant prior studies on amide activation, see: (a) Charette, A. B.; Grenon, M. *Can. J. Chem.* **2001**, *79*, 1694. Review: (b) Baraznenok, I. L.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **2000**, *56*, 3077. For 2-chloropyridine as a base additive, see: (c) Myers, A. G.; Tom, N. J.; Fraley, M. E.; Cohen, S. B.; Madar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 6072.

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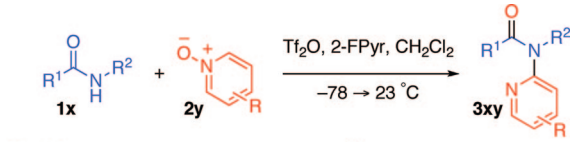
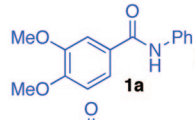
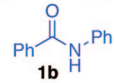
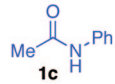
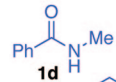
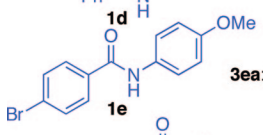
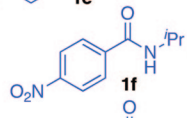
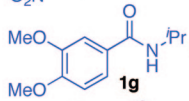
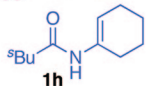
TABLE 2. Direct Dehydrative *N*-Pyridinylation of Amides[a]



N-oxide: 2a 2b 2c

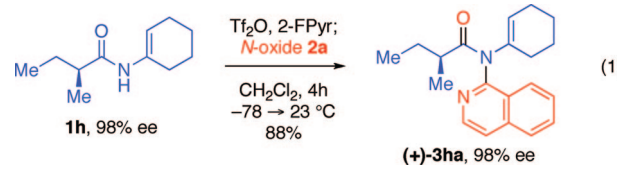
amide	*N*-(isoquinolin-1-yl) product 3	*N*-(quinolin-2-yl) product 3	*N*-(pyridin-2-yl) product 3
 1a	**3aa**: 99%[b]	**3ab**: 0%[c]	**3ac**: 41%
 1b	**3ba**: 72%	**3bb**: 36%	**3bc**: 40%
 1c	**3ca**: 97%	**3cb**: 35%	**3cc**: 66%[d]
 1d	**3da**: 100%	**3db**: 60%	**3dc**: 67%[d]
 1e	**3ea**: 74%	**3eb**: 42%	**3ec**: 37%
 1f	**3fa**: 92%	**3fb**: 13%	**3fc**: 74%
 1g	**3ga**: 94%	**3gb**: 25%	**3gc**: 48%
 1h	**3ha**: 91%	**3hb**: 78%	**3hc**: 39%[d,e]

[a] Isolated yields of products **3xy**. Average of two experiments. Conditions: Amide **1x** (1 equiv), Tf_2O (1.1 equiv), 2-FPyr (1.2 equiv), CH_2Cl_2, −78→0 °C; *N*-oxide **2y** (2.0 equiv), 0→23 °C, 4 h. [b] *N*-Oxide **2a** (1.1 equiv), 3 h. [c] Decomposition of **1a** observed over 4 h. [d] 2,6-Lutidine used as base. [e] Low yield due to product decomposition.

We next examined the optimal conditions with a range of amide substrates with three representative heteroaromatic *N*-oxides (Table 2). Isoquinolinylation of amides under our conditions is highly efficient, giving good to excellent yields in all cases examined. Isoquinolinylation of *N*-alkyl benzamides (**3da**, **3fa**, and **3ga**, Table 2), in addition to *N*-aryl and *N*-vinyl amides (**3ca** and **3ha**, Table 2), was achieved in high yields under our standard reaction conditions. Electron-rich benzamides notwithstanding (**3aa**, Table 2), the least efficient substrates in this series were *N*-aryl benzamides (**3ba** and **3ea**, Table 2). In all cases, completely regioselective isoquinolinylations proceeded at the 1-position of the isoquinoline ring.[2−4]

The use of quinoline *N*-oxide (**2b**, Table 2) and pyridine *N*-oxide (**2c**) as substrates also gave completely regioselective acylamination, however, with reduced overall efficiency for the formation of the desired products. This is due in part to the faster decomposition[2b,e,9] of *N*-oxides **2b** and **2c** (as compared to **2a**) under the electrophilic activation reaction conditions.[10] Interestingly, in reactions employing *N*-oxide **2c**, amides that exhibited high reactivity in isoquinolinylation reactions gave higher yields when 2,6-lutidine[4] was used in place of 2-FPyr as the base additive (products **3cc**, **3dc**, and **3hc**, Table 2), likely owing to slight suppression of *N*-oxide decomposition. However, the use of 2,6-lutidine in place of 2-fluoropyridine with less reactive *N*-aryl benzamides (**1b** and **1e**, Table 2) resulted in significantly lower yields of the desired products.

Attempts to *N*-quinolinylate amide **1a** under our standard conditions gave no detectable amount of the desired product **3ab**. This is consistent with poor nucleophilic addition of **2b** to the activated intermediate, allowing a competitive decomposition of amide **1a**.[11] Given that nucleophilic base additives inhibit the desired reaction (Table 1), we conjectured that the *N*-pyridinylated products formed may also play an inhibitory role. Activation of amide **1f** followed by sequential addition of *N*-pyridinylated amide **3fc** (1.00 equiv) and pyridine *N*-oxide (**2c**) gave a low 33% yield of the desired amide **3fc**,[12] which is less than half the expected yield. This suggests that product inhibition can be significant in these pyridinylation reactions. However, activation of amide **1f** under optimized conditions, followed by sequential addition of product **3fa** (1.00 equiv) and isoquinoline *N*-oxide (**2a**), gave 92% yield of the desired *N*-isoquinolinylated amide **3fa**,[12] indicating no significant product inhibition in this reaction. Furthermore, sequential



(1)

activation of an enantiomerically enriched amide **1h**[8] under optimized conditions followed by introduction of isoquinoline *N*-oxide (**2a**) provided the optically active *N*-isoquinolinylated amide (+)-**3ha** without erosion of optical activity (eq 1). Interestingly, while *N*-pyridinylation of amides was generally less efficient as compared to *N*-isoquinolinylation, the use of both electron-rich and electron-poor 4-substituted pyridine *N*-oxides **2d** and **2e**, respectively, gave modest yield of the desired products (eqs 2 and 3). The successful *N*-pyridinylation of amide **1d** with 4-nitropyridine *N*-oxide (**2e**) is notable, as its use as a nucleophile for the Abramovitch reaction was previously reported to be unsuccessful,[2a,b] suggesting greater electrophilicity of the intermediate under the conditions described here.

(2)

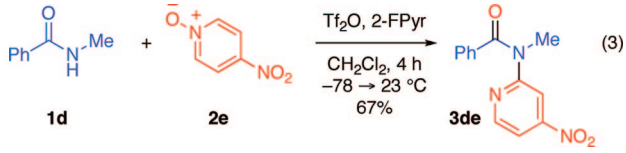
To gain better understanding of the intermediates involved in this transformation, a series of in situ IR and NMR monitoring

(9) Yin, J.; Xiang, B.; Huffman, M. A.; Raab, C. E.; Davies, I. W. *J. Org. Chem.* **2007**, *72*, 4554.

(10) This observation is supported by control experiments involving the exposure of *N*-oxides **2a**−**c** to trifluoromethanesulfonic anhydride and 2-fluoropyridine under standard reaction conditions.

(11) Control experiments revealed that activation of amide **1a** in the absence of a competent nucleophile led to decomposition.

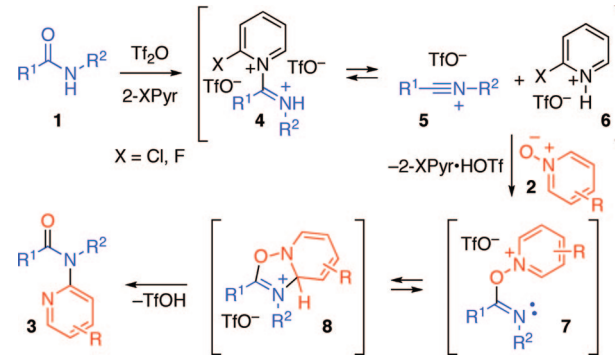
(12) Please see the Supporting Information for details.



experiments were performed. The conversion of amide **1d** to *N*-isoquinolinylated amide **3da** under optimized conditions was monitored by in situ IR analysis. Addition of Tf_2O to a mixture of amide **1d** and 2-FPyr resulted in complete consumption of the amide absorption band (1668 cm^{-1}) and appearance of a persistent absorption at 2370 cm^{-1}, suggestive of a nitrilium ion intermediate.[2b,13] Addition of isoquinoline *N*-oxide (**2a**) resulted in immediate disappearance of the absorption at 2370 cm^{-1} and appearance of a persistent absorption at 1691 cm^{-1}, which was due to the protonated product **3da**. Interestingly, the activation of *N*-(4-methoxyphenyl)benzamide (**1i**) with the reagent combination of 2-ClPyr and Tf_2O did not lead to an observable absorption corresponding to a nitrilium ion, but instead gave rise to a persistent absorption at 1600 cm^{-1}, suggestive of an amidinium intermediate.[8] These observations suggest that while electrophilic activation of **1d** using 2-FPyr results in **5d** (Scheme 1), similar activation of **1i** using 2-ClPyr leads to predominant formation of **4i** rather than **5i**.

To determine the degree to which the formation of a nitrilium ion depends on the nature of the base additive and the amide structure itself, a series of in situ IR monitoring experiments were carried out.[12] For comparison, while activation of *N*-alkyl benzamide **1d** under optimal conditions resulted in an absorption suggesting a nitrilium ion (2370 cm^{-1}),[14] the activation of *N*-aryl benzamides **1b** and **1i** under the same conditions led to no detection of an IR absorption consistent with a nitrilium ion, but instead resulted in the appearance of an IR absorption suggesting an amidinium ion (1621 cm^{-1} in both cases).[8] However, Tf_2O activation of the electron-rich *N*-aryl benzamide **1a** in the presence of either 2-FPyr or 2-ClPyr (1.2 equiv) indeed resulted in an absorption at 2312 cm^{-1}, suggesting a persistent nitrilium ion intermediate. Interestingly, addition of extra equivalents of 2-ClPyr resulted in complete disappearance of this absorption band and appearance of a persistent absorption at 1594 cm^{-1}, consistent with the formation of the previously observed amidinium ion.[8] Even the electron-poor *N*-alkyl benzamide **1f** resulted in a lasting nitrilium ion (2354 cm^{-1}) upon electrophilic activation in the presence of either 2-FPyr or 2-ClPyr (1.2 equiv), although the presence of excess 2-ClPyr resulted in disappearance of the absorption at 2354 cm^{-1} and the appearance of an absorption at 1609 cm^{-1}.[15] These observations suggest that activation of *N*-alkyl amides under these conditions more readily results in persistent nitrilium ion formation, while *N*-aryl amides show reluctance to form the corresponding nitrilium ion, likely owing to the inductive effect of the nitrogen substituent.[16] Only the particularly electron-rich *N*-aryl benzamide **1a** resulted in any observable nitrilium ion, perhaps due to greater stabilization by resonance contribution.

SCHEME 1



These differences in amide reactivity were further substantiated by in situ ^1H NMR monitoring of the electrophilic activation step. Interestingly, amides that demonstrated the least propensity to form a nitrilium ion upon activation under the optimal reaction conditions also gave the lowest yields in reactions with isoquinoline *N*-oxide (e.g., entry **3ba**, Table 2). Furthermore, reduced yield of the desired product upon addition of excess base additive (or use of nucleophilic bases, Table 1) is consistent with the observed disappearance of the nitrilium species during in situ monitoring experiments.

Additional mechanistic insight was obtained using deuterated substrates **2a**-d_2, **2c**-d_2, and **2c**-d_1 (eqs 4 and 5). Electrophilic activation of *N*-alkyl benzamide **1f** under optimal conditions followed by introduction of excess[17] isoquinoline *N*-oxide (**2a**) and 1,3-dideuteroisoquinoline *N*-oxide (**2a**-d_2) provided a mixture of *N*-isoquinolinylated products **3fa** and **3fa**-d_1 corresponding to $k_H/k_D = 1.0$ in 86% combined yield (eq 4).[12] The same outcome was observed in a similar experiment using excess **2c**-d_2 and **2c**, resulting in a mixture of the *N*-pyridinylated products **3fc** and **3fc**-d_1 corresponding to $k_H/k_D = 1.0$ in a combined yield of 59% (eq 4). As another mechanistic probe, activation of **1f** under optimal conditions and the use of excess 2-deuteropyridine *N*-oxide (**2a**-d_1) provided the expected *N*-pyridinylated amide **3fc** as a mixture of nondeuterated and monodeuterated derivatives (eq 5).[12] Importantly, the ratio of **3fc**-d_0 and **3fc**-d_1 was found to be 1.0:2.0, reflecting an observable primary kinetic isotope effect ($k_H/k_D = 2.0$).[18] These observations suggest that addition[19] of the imidate nitrogen onto the pyridinium ring is reversible, whereas nucleophilic addition of the *N*-oxide **2** to the nitrilium ion **5** (or another electrophilic variant) is irreversible (Scheme 1).

We describe a direct method for the dehydrative *N*-pyridinylation of amides under electrophilic activation by the reagent

(13) For IR characterization of isolated nitrilium salts, see: (a) Booth, B. L.; Jibodu, K. O.; Proença, M. F. *J. Chem. Soc., Chem. Commun.* **1980**, 1151. (b) Carrier, A. M.; Davidson, J. G.; Barefield, E. K.; Van Derveer, D. G. *Organometallics* **1987**, *6*, 454.

(14) Addition of either 2-FPyr or 2-ClPyr resulted in an increase in the intensity of this absorption band.

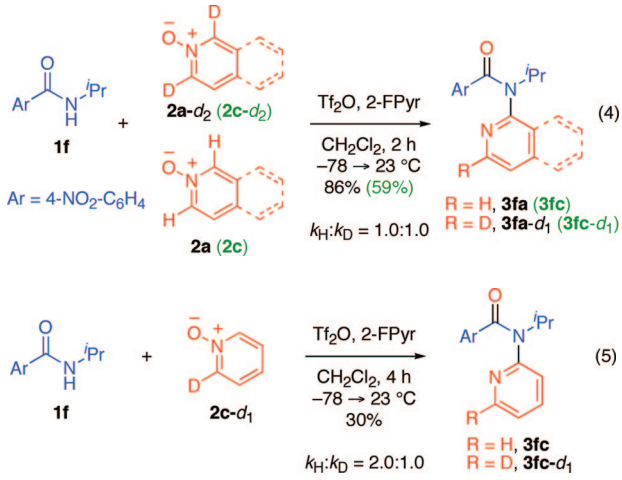
(15) When these conditions (excess of 2-ClPyr) were used for the transformation of amide **1f** to amide **3fa** and **3fc**, a significant decrease in the yields (70 and 23%, respectively) was observed.

(16) Ugar, I.; Beck, F.; Fetzer, U. *Chem. Ber.* **1962**, *95*, 126.

(17) Excess *N*-oxides were used to minimize any effect due to change in concentration during the reaction. Deuterated pyridine *N*-oxides were particularly prone to decomposition as compared to deuterated isoquinoline *N*-oxide derivatives.

(18) (a) Zollinger, H. In *Advances in Physcial Organic Chemistry*; Gold, V., Ed.; Academic Press: London, 1964; Vol. 2, pp 163−196. (b) Berliner, E. In *Progress in Physical Organic Chemistry*; Cohen, S. G., Streitweiser, A., Taft, R. W., Eds.; Interscience: New York, 1964; Vol. 2, pp 253−321. (c) Jackson, A. H.; Lynch, P. P. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1483. (d) Maresh, J. J.; Giddings, L.-A.; Friedrich, A.; Loris, E. A.; Panjikar, S.; Trout, B. L.; Stöckigt, J.; Peters, B.; O'Connor, S. E. *J. Am. Chem. Soc.* **2008**, *130*, 710.

(19) Scheme 1 only depicts an intramolecular pathway in the conversion of **7** to **3**. Given the range of reactivity observed, we do not rule out an intermolecular C−N bond forming step. For representative related studies, see: (a) Pachter, I. J. *J. Am. Chem. Soc.* **1953**, *75*, 3026. (b) Vozza, J. F. *J. Org. Chem.* **1962**, *27*, 3856. (c) Oae, S.; Kitao, T.; Kitaoka, Y. *J. Am. Chem. Soc.* **1962**, *84*, 3359. (d) Oae, S.; Kitaoka, Y.; Kitao, T. *Tetrahedron* **1964**, *20*, 2685. (e) Bodalski, R.; Katritzky, A. R. *Tetrahedron Lett.* **1968**, 257. (f) Kozuka, S.; Tamagoki, S.; Negoro, T.; Oae, S. *Tetrahedron Lett.* **1968**, 923.



combination of Tf_2O and 2-FPyr. This methodology allows for a highly effective activation of a variety of amide substrates, including *N*-aryl amides,[4] without requiring the isolation of sensitive intermediates or the use of heavy metal Lewis acid additives, and proceeds in shortened reaction times without the need for elevated temperatures.[2] Our in situ monitoring experiments suggest greater propensity for the formation of persistent nitrilium ion intermediates when *N*-alkyl amide substrates are used as compared to *N*-aryl amides. Our studies with deuterated *N*-oxide substrates suggest an irreversible nucleophilic addition step and a plausible interconversion of intermediates **7** and **8** based on the observed kinetic isotope effect. The activation conditions described here allow the trapping of highly electrophilic intermediates with weakly nucleophilic *N*-oxides.

Experimental Section

***N*-(Isoquinolin-1-yl)-*N*-methylbenzamide (3da, Table 2):** Trifluoromethanesulfonic anhydride (55.7 μL, 0.331 mmol, 1.10 equiv) was added via gastight syringe to a solution of *N*-methylbenzamide (**1d**, 40.7 mg, 0.301 mmol, 1 equiv) and 2-fluoropyridine (31.0 μL, 0.361 mmol, 1.20 equiv) in dichloromethane (1.5 mL) at −78 °C. After 2 min, the reaction mixture was allowed to warm to 0 °C. After 5 min, isoquinoline *N*-oxide (**2a**, 87.4 mg, 0.602 mmol, 2.00 equiv) was added as a solid under an argon atmosphere. After 5 min, the resulting mixture was allowed to warm to 23 °C. After 4 h, triethylamine (100 μL) was added to quench the trifluoromethanesulfonate salts, and the mixture was diluted by the addition of dichloromethane (10 mL). The reaction mixture was washed with brine (10 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (30 → 50% ethyl acetate in hexanes) to afford the amide **3da** (79.0 mg, 100%): ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C) δ 8.31 (d, 1H, J = 5.5 Hz), 7.99 (d, 1H, J = 8.5 Hz), 7.78 (d, 1H, J = 8.5 Hz), 7.65−7.50 (m, 3H), 7.40−7.20 (m, 2 H), 7.15−6.90 (m, 3H), 3.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C) δ 171.8, 155.9, 141.5, 138.2, 136.2, 130.8, 130.0, 128.4, 128.1, 127.8, 127.3, 125.0, 124.5, 121.0, 37.2; FTIR (neat) cm^{-1} 3058 (m), 2936 (w), 1651 (s), 1560 (s), 1363 (s); HRMS (ESI) calcd for $C_{17}H_{15}N_2O$ $[M + H]^+$ 263.1179, found 263.1179; TLC (50% ethyl acetate in hexanes), R_f 0.33 (UV).

***N*-(4-Methoxypyridin-2-yl)-*N*-methylbenzamide (3dd, eq 2):** Trifluoromethanesulfonic anhydride (46.0 μL, 0.273 mmol, 1.10 equiv) was added via syringe to a solution of *N*-methylbenzamide (**1d**, 33.6 mg, 0.249 mmol, 1 equiv) and 2-fluoropyridine (25.6 μL, 0.298 mmol, 1.20 equiv) in dichloromethane (1.5 mL) at −78 °C. After 2 min, the reaction mixture was allowed to warm to 0 °C. After 5 min, 4-methoxypyridine *N*-oxide (62.2 mg, 0.497 mmol, 2.00 equiv) was added as a solid under an argon atmosphere. After 5 min, the resulting mixture was allowed to warm to 23 °C. After 4 h, triethylamine (100 μL) was added to quench the trifluoromethanesulfonate salts, and the mixture was diluted by the addition of dichloromethane (10 mL). The reaction mixture was washed with brine (10 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on alumina gel (10 → 20% ethyl acetate in hexanes) to afford the amide **3dd** (44.9 mg, 75%): ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C) δ 8.22 (d, 1H, J = 6.0 Hz), 7.38−7.28 (m, 3H), 7.26−7.20 (m, 2H), 6.57 (dd, 1H, J = 6.0, 2.5 Hz), 6.28 (d, 1H, J = 2.5 Hz), 3.56 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C) δ 171.2, 166.6, 158.4, 149.6, 136.3, 130.3, 128.5, 128.2, 108.4, 107.3, 55.4, 36.1; FTIR (neat) cm^{-1} 3061 (w), 2941 (w), 1652 (s), 1595 (s), 1362 (s); HRMS (ESI) calcd for $C_{14}H_{15}N_2O_2$ $[M + H]^+$ 243.1128, found 243.1133; TLC (50% ethyl acetate in hexanes), R_f 0.28 (UV).

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Supporting Information Available: Experimental procedures, spectroscopic data for products. This material is available free of charge via the Internet at http://pubs.acs.org.

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