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Brønsted Acid Catalyzed Monoalkylation of Anilines with Trichloroacetimidates

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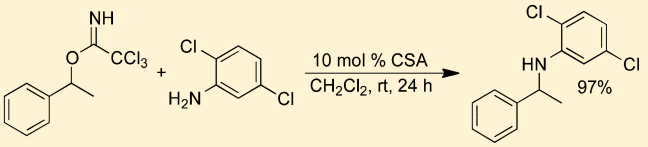
Supporting Information

ABSTRACT: Trichloroacetimidates are useful alkylating agents for aromatic amines, requiring only a catalytic amount of a Brønsted acid to facilitate the reaction. Monoalkylation predominates under these conditions. Electron-poor anilines provide superior yields, with electron-rich anilines sometimes showing competitive Friedel–Crafts alkylation. A single flask protocol with formation of the imidate *in situ* is demonstrated, providing a convenient method for the direct substitution of alcohols with anilines. Reaction with a chiral imidate favors a mechanism that proceeds through a carbocation intermediate.



Our recent findings on the spontaneous reaction of trichloroacetimidates with carboxylic acids[1] led us to speculate about the reactivity of these alkylating agents with other functional groups, including anilines. Substituted anilines are a common structural unit often found in natural products and other bioactive compounds (Figure 1). For example, a

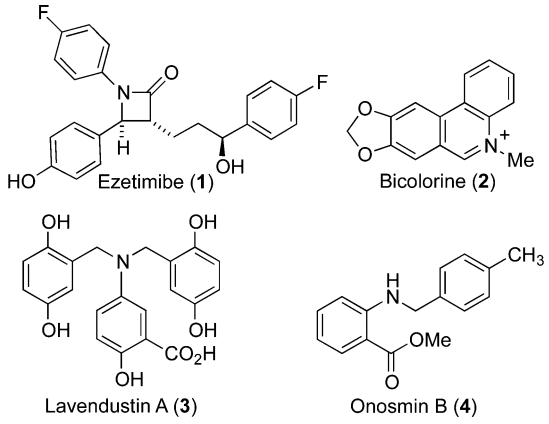


Figure 1. Aniline-based pharmaceuticals and natural products.

substituted aniline core is found in the cholesterol lowering drug ezetimibe (**1**).[2] Biologically active natural products also commonly contain substituted anilines, like the topoisomerase inhibitor bicolorine (**2**),[3] the tyrosine kinase inhibitor lavendustin A (**3**),[4] and the lipoxygenase inhibitor onosmin B (**4**).[5] Substituted anilines also frequently appear in molecules used in sensor applications and other synthetic receptors.[6] Given the ubiquity of *N*-alkyl anilines, new methods for their formation from readily available precursors like trichloroacetimidates are in high demand.

A search of the literature revealed that *tert*-butyl-2,2,2-trichloroacetimidate has been occasionally used for the alkylation of anilines, typically with $BF_3{\cdot}OEt_2$ as the catalyst or promoter.[7] More recently, copper(II) triflate in nitromethane was reported to provide improved conversions for this transformation.[8] Additionally, allylic trichloroacetimidates have been used as substrates for transition-metal-catalyzed allylic amination with aniline nucleophiles. These reactions[9] employ catalysts based on rhodium,[10] iridium,[11] or palladium.[12] Fewer studies have evaluated protic acids in these N-substitution reactions, although $(PhO)_2PO_2H$ was recently used with aniline and a highly reactive isatin derived trichloroacetimidate[13] and TsOH was evaluated in the alkylation of anilines with *tert*-butyl-2,2,2-trichloroacetimidate.[8]

As previous studies have generally focused on specific imidates, we set out to find more general conditions that could be applied to a greater variety of reaction partners. Initial experiments were performed with imidate **5**[14] and 2,5-dichloroaniline **6** (Table 1). No reaction between the imidate and the aniline was observed in control experiments performed without an acid catalyst (entries 1 and 2). The use of $BF_3{\cdot}OEt_2$ as a catalyst provided a 33% yield of monoalkylated aniline **7a**. This reaction also gave a number of side products including dialkylation of the aniline nitrogen, which made isolation and purification of the desired monoalkylation product difficult. Repeating the $BF_3{\cdot}OEt_2$ reaction with an excess of aniline to suppress dialkylation of the nitrogen did provide an improved yield, but dialkylation and other products were still apparent in the crude ^1H NMR spectra. These polyalkylation products may be less problematic with the more sterically hindered *tert*-butyl-2,2,2-trichloroacetimidate, but this side product formation seems to be a significant issue with less encumbered imidates. The switch was then made to less powerful Brønsted acid catalysts in the hope of improving the selectivity for monoalkylation of the aniline nitrogen. The use of diphenylphosphoric acid provided a 31% yield of the desired N-substituted aniline **7a**. Promisingly, only unreacted starting materials and N-alkylation product **7a** were observed in the

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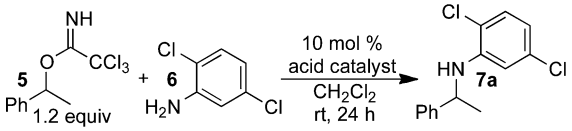
Table 1. Optimization of the Reaction of Imidate 5 with 2,5-Dichloroaniline 6



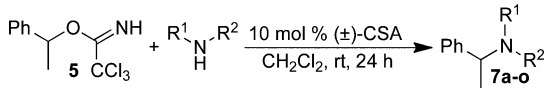
entry	catalyst	% yield
1	none	0
2[a]	none	0
3	$BF_3{\cdot}OEt_2$	33 (68[b])
4	$(PhO)_2PO_2H$	31
5	$(BnO)_2PO_2H$	0
6	*p*-TsOH	59
7	(±)-CSA	97
8	DNBSA[e]	83
9[c]	(±)-CSA	82
10[d]	(±)-CSA	22

[a]Heated to reflux in toluene for 24 h. [b]1.1 equiv of aniline **6** was used. [c]2.4 equiv of imidate was used. [d]5 mol % catalyst was used. [e]DNBSA = 2,4-dinitrobenzenesulfonic acid.

reaction mixture, with no polyalkylation products being observed. Building on this result, a number of Brønsted acid catalysts were screened in the N-substitution reaction. (±)-Camphorsulfonic acid (CSA) provided the highest yield of the monoalkylation product. Interestingly, only a mono-alkylation product was obtained even when excess imidate was used (entry 9). Given the selectivity of this protocol for monoalkylation, these conditions were chosen for evaluation in further studies.

Next, a number of aniline nucleophiles were evaluated for their reactivity (Table 2). Electron-poor anilines proved to be the best substrates for the substitution reaction. This is notable and quite useful, as electron-deficient anilines are typically difficult substrates for reductive aminations, and even with the addition of molecular sieves and Lewis acids to facilitate imine formation, yields are often moderate.[15] More electron-rich aniline nucleophiles gave lower isolated yields of monoalkylated products (like **7h** and **7i**), and often the crude reaction mixtures appeared to be contaminated with side products from Friedel–Crafts reactions that led to difficult purifications (trichloroacetimidates have been shown to participate in Friedel–Crafts alkylations[16]). In some cases where the yields were moderate (Table 2, entries 4 and 9), heating the reaction to reflux in toluene provided a higher yield of the desired product. Sterics also appeared to play a significant role in the yield of the N-alkylation reaction. While one ortho substituent was well tolerated on the aniline, the incorporation of two ortho substituents effectively stopped all alkylation (Table 2, entry 14). *N*-Alkyl anilines readily participated in the reaction, with *N*-methylaniline and indoline providing good yields of alkylated products **7n** and **7o**, respectively. With the alkylation of the anilines performing well, we attempted to expand the scope to the more basic alkyl amines using morpholine as the nucleophile. No N-alkylation products were observed with morpholine (Table 2, entry 17), even when heated in toluene with CSA, only unreacted starting materials were observed in the reaction mixture.

Table 2. Reaction of Amines with Imidate 5



entry	amine	% yield 7
1	2,5-dichloroaniline	97 (**7a**)
2	aniline	76 (**7b**)
3	4-chloroaniline	89 (**7c**)
4	4-bromoaniline	56 (70[a]) (**7d**)
5	2-bromoaniline	70 (**7e**)
6	3,5-bis(trifluoromethyl)aniline	98 (**7f**)
7	2-nitroaniline	94 (**7g**)
8	4-(methylthio)aniline	70 (**7h**)
9	4-ethylaniline	47 (65[a]) (**7i**)
10	2-fluoro-4-methylaniline	80 (**7j**)
11	2-chloro-5-(trifluoromethyl)aniline	98 (**7k**)
12	2-chloro-4-fluoroaniline	99 (**7l**)
13	2-chloro-4-methylaniline	94 (**7m**)
14	2,4,6-tribromoaniline	0
15	*N*-methylaniline	84 (**7n**)
16	indoline	74 (**7o**)
17	morpholine	0

[a]Reaction performed in toluene at reflux.

Evaluation of the substrate scope with respect to imidate electrophile was also undertaken (Table 3). Most unhindered benzylic imidates were effective in the alkylation reaction. Only the electron-poor 4-cyanobenzyl imidate **14** (entry 4) gave poor conversion. In this case, the reaction had to be heated to reflux in toluene to obtain product **15**, as no reaction was observed at room temperature in CH_2Cl_2. Allylic trichloro-acetimidates **20** and **22** also provided good yields of product (Table 3, entries 8 and 9), providing the mono-*N*-Alkylated products in excellent yield. The tertiary benzylic imidate **24** gave moderate yield of *N*-alkyl product **25** as this reaction is slowed by the steric encumbrance of the hindered imidate. The *tert*-butyl-2,2,2-trichloroacetimidate **26** gave only a low yield of the corresponding *tert*-butyl aniline **27**. Evidently, the Brønsted acid catalyzed conditions are more mild than the Lewis acid catalyzed conditions typically employed for this imidate[7] and, combined with the greater steric requirements of 2,5-dichloroaniline compared to aniline, resulted in a reduced yield (most reactions with *tert*-butyl-2,2,2-trichloroacetimidate **26** and aniline also require a large excess (2–5 equiv) of the imidate for good conversion). These results are consistent with the recent report on the copper triflate catalyzed alkylation of anilines with imidate **26** where special conditions and excess imidate are needed to obtain high yields.[8] No alkylation product was observed in the reaction of the ethyl imidate (entry 12), even under forcing conditions (toluene, reflux, 24 h). Alternatively, the phthalimidomethyl imidate **30** (entry 13) gave *N*-alkylated product **31** in excellent yield. One interesting facet of these alkylations was the preference for substitution over elimination in benzylic systems like **7a** and **19**. In order to further investigate the preference for substitution, the doubly unsaturated imidate **32** that is more prone to elimination was explored as a reaction partner (entry 14). This substitution provided the desired *N*-alkyl aniline **33** in 63% yield but required 72 h to proceed to completion. Some elimination side products were observed in this reaction, but given the simplicity of the reaction conditions, the selectivity for substitution over elimination is impressive. In the cases where some elimination was observed in the crude NMR (Table 3, entries 6, 7, 10, and 14), the signals for the minor alkene byproducts in the ^1H

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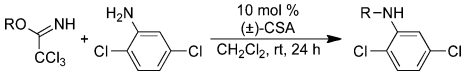
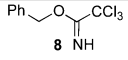
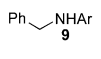
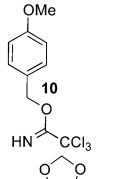
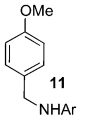
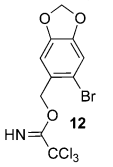
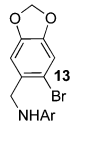
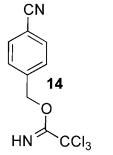
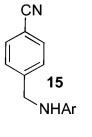
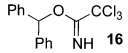
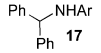
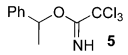
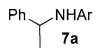
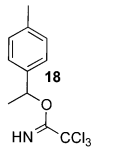
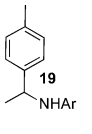
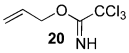
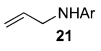
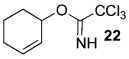
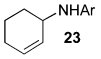
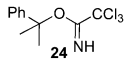
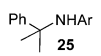
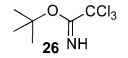
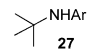
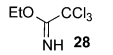
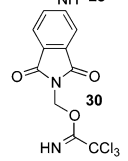
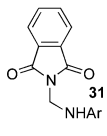
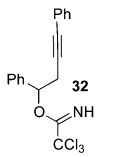
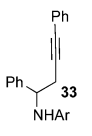
Table 3. Reaction of Imidates with 2,5-Dichloroaniline 6



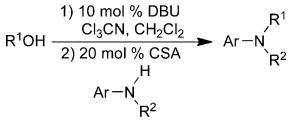
Entry	Imidate	Product[d]	Yield (%)
1			92
2			91
3			80
4			0 (43[a])
5			87
6			97
7			68
8			77
9			79
10			42
11			5 (21[b])
12		EtNHAr 29	0
13			74
14			63[c]

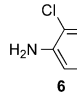
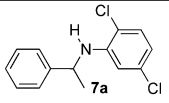
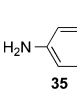
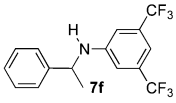
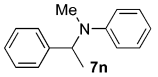
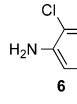
[a]Reaction performed in toluene at reflux. [b]Reaction performed with $BF_3{\cdot}OEt_2$ (10 mol %) [c]Reaction was performed at room temperature for 72 h [d]Ar = 2,5-dichlorophenyl.

NMR were contaminated with other impurities that made quantification difficult. Attempts to isolate and quantify these side-products were thwarted by the presence of other nonpolar impurities and the volatility of the alkenes.

A single flask method for the conversion of alcohols to substituted anilines was then developed. The use of alcohols as alkylating agents for anilines typically requires a transition-metal catalyst and high temperatures.[17] In contrast, a direct procedure through the imidate intermediate would avoid the use of transition metals and proceed at room temperature. Taking the desired alcohol and forming the imidate in dichloromethane with 10 mol % DBU catalyst, followed by addition of the aniline and 20 mol % (±)-CSA, proved to be a useful protocol for the synthesis of substituted anilines (Table 4), with yields for the single flask protocol often surpassing the

Table 4. Single Flask Synthesis of Monosubstituted Anilines



Entry	Alcohol	Aniline	Product	Yield (%)
1				90
2				99
3				82
4				88
5				81
6				85

two-step procedure. In addition to the synthesis of several alkylated anilines, the synthesis of the natural product onosmin B **4** was performed using the methodology. This provided the lipoxygenase inhibitor in 85% yield from the corresponding alcohol. Additionally, the alkylated piperonal derivative **39** was synthesized, which represents a formal synthesis of 5,6-dihydrobicolorine, as this system has been cyclized previously to the natural product in a single step.[18]

The propensity of the N-substitution reaction to displace an enantiomerically enriched imidate was also investigated with the use of phenethyl imidate (*R*)-**5**. The ability to generate a chiral amine directly from the chiral alcohol via the trichloroacetimidate would be quite useful, but substitution reactions of similar enantiomerically pure imidates with oxygen nucleophiles are challenging and typically provide mixtures of enantiomers as products.[19] Reaction of imidate (*R*)-**5** with 4-chloroaniline **42** (Scheme 1) provided the substituted aniline

Scheme 1

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product **7c** in excellent conversion. Evaluation of the enantiomeric purity of the reaction product revealed that both enantiomers of the aniline **7c** were formed in the reaction, as the product was shown to be a 35:65 mixture of the *R* and *S* enantiomers.

These results and the inability to alkylate ethyl trichloroacetimidate (Table 3, entry 12) are consistent with a carbocation intermediate in the reaction, which precludes high levels of stereocontrol (scalemic mixtures often result from cationic processes due to ion pairing[20]). A proposed mechanism is shown in Figure 2 below. Protonation of the

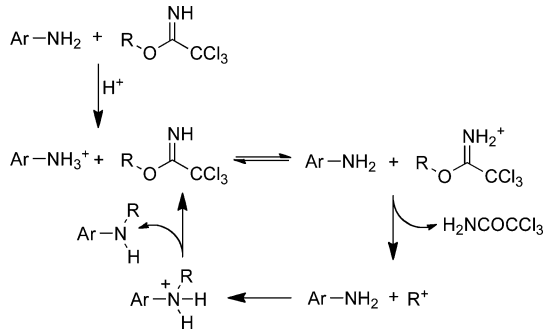

Figure 2. Proposed mechanism.

aniline and imidate is reversible, but protonation of the imidate eventually leads to the formation of a carbocation and loss of trichloroacetamide. Capture of the carbocation by the aniline, followed by proton transfer to another equivalent of aniline, provides the observed alkylated product and regenerates the protonated aniline to turnover the catalytic cycle. More basic amines (like morpholine) are not acidic enough to protonate the imidate, explaining their low reactivity under these conditions.

In summary, a method for alkylating anilines using trichloroacetimidate electrophiles under Brønsted acid catalyzed conditions has been described. Monoalkylation of anilines is primarily observed under these conditions. While most anilines react well, electron-rich anilines provide more moderate yields, often forming side products due to competing Friedel−Crafts alkylations. The more basic alkylamines fail to react under these conditions, as the amine salt formed from their reaction with the catalyst is less acidic and, therefore, not capable of catalyzing the reaction. A range of imidates proved compatible, although the structures must be benzylic, allylic, or tertiary, implicating a mechanism that proceeds through a carbocation intermediate. This new method appears to favor substitution over elimination in sensitive systems such as **33**. A one-step protocol where the imidate is formed *in situ* and then displaced by the aniline nucleophile was also demonstrated as a useful method for the alkylation of aromatic amines with alcohols. The utility of this protocol has been demonstrated in the synthesis of the lipoxygenase inhibitor onosmin and a formal synthesis of 5,6-dihydrobicolorine.

EXPERIMENTAL SECTION

General. All anhydrous reactions were run under a positive pressure of argon or nitrogen. Dichloromethane and THF were dried by passage through an alumina column following the method of Grubbs.[21] Column chromatography was performed using silica gel 60 (230−400 mesh). Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$, with residual chloroform or TMS used as the internal reference.

Representative procedures for the aniline substitution reactions:

Representative Procedure A: Reaction of Imidate 5 with 2,5-Dichloroaniline 6. 1-Phenethyl imidate **5** (0.30 g, 1.13 mmol) and 2,5-dichloroaniline **6** (0.15 g, 0.94 mmol) were added to a flame-dried round-bottom flask under argon. Dry dichloromethane (4 mL) was added, followed by camphorsulfonic acid (0.03 g, 0.11 mmol). The reaction was stirred at room temperature for 24 h. After triethylamine (0.5 mL) was added, the reaction mixture was preadsorbed on silica gel and purified by silica gel chromatography using 19% dichloromethane/80% hexanes/1% triethylamine to give 0.24 g (97%) of substituted aniline **7a** as a yellow oil.

Representative Procedure B: Single Flask Synthesis of Monosubstituted Aniline 7a. Phenethyl alcohol **34** (0.33 g, 2.73 mmol) and trichloroacetonitrile (0.33 mL, 3.27 mmol) were added to a flame-dried round-bottom flask under argon. Dry dichloromethane (4 mL) was added, followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (0.04 g, 0.27 mmol). The reaction was stirred at room temperature and monitored for disappearance of the alcohol by TLC (4 h). 2,5-Dichloroaniline **6** (0.37 g, 2.28 mmol) was added, followed by camphorsulfonic acid (0.13 g, 0.54 mmol). The reaction was allowed to stir at room temperature for 24 h. Triethylamine (0.5 mL) was then added, and the reaction mixture was preadsorbed on silica gel and purified by silica gel chromatography using 19% dichloromethane/80% hexanes/1% triethylamine to provide 0.55 g (90%) of substituted aniline **7a** as a yellow oil.

*2,5-Dichloro-N-(1-phenylethyl)aniline (**7a**).*[22] Prepared using procedure **A** (0.24 g, 97%) from 2,5-dichloroaniline **6** and the known imidate **5**[14] or procedure **B** (0.55 g, 90%) from 1-phenethyl alcohol, purified using silica gel chromatography (4% ethyl acetate/95% hexanes/1% triethylamine). Yellow oil (0.24 g, 97%); TLC R_f = 0.71 (19% dichloromethane/80% hexanes/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H), 7.14 (d, J = 8.4 Hz, 1H), 6.54 (dd, J = 8.4, 2.4 Hz, 1H), 6.38 (d, J = 2.4 Hz, 1H), 4.49 (q, J = 6.6 Hz, 1H), 1.57 (d, J =6.6 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 144.0, 133.6, 129.8, 129.1, 128.5, 127.6, 125.9, 117.3, 117.2, 112.4, 53.5, 25.1.

*N-(1-Phenylethyl)aniline (**7b**).*[22] Prepared using procedure **A** from aniline and the known imidate **5**,[14] purified using silica gel chromatography (95% hexanes/4% ethyl acetate/1% triethylamine). Yellow oil (0.14 g, 76%); TLC R_f = 0.59 (95% hexanes/4% ethyl acetate/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.28 (m, 4H), 7.25−7.24 (m, 1H), 7.12−7.06 (m, 2H), 6.66 (t, J = 7.8 Hz, 1H), 6.54 (d, J = 7.5 Hz, 2H), 4.48 (q, J = 6.9 Hz, 1H), 1.53 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 145.4, 129.4, 128.9, 127.1, 126.1, 117.5, 113.6, 53.7, 25.3.

*4-Chloro-N-(1-phenylethyl)aniline (**7c**).*[23] Prepared using procedure **A** from 4-chloroaniline and the known imidate **5**,[14] purified using silica gel chromatography (4% ethyl acetate/95% hexanes/1% triethylamine). Reddish crystals (0.19 g, 89%); mp = 58−60 °C; TLC R_f = 0.43 (5% ethyl acetate/95% hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.19 (m, 5H), 7.00 (dt, J = 9.9, 3.0 Hz, 2H), 6.40 (dt, J = 10.2, 3.3 Hz, 2H), 4.42 (q, J = 6.9 Hz, 1H), 4.04 (br s, 1H), 1.49 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 144.7, 128.9, 128.7, 127.1, 125.8, 121.9, 114.4, 53.6, 25.0. When (*R*)-**5** (>98:2 er) was used, an 85% yield (0.061 g) of reddish crystals was obtained as a 35:65 ratio of *R*:*S* enantiomers. Chiral HPLC analysis: Chiralcel OD (heptane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm, 25 °C): t_{minor} = 7.52 min, t_{major} = 9.75 min, 35:65 ratio, 30% ee.

*4-Bromo-N-(1-phenylethyl)aniline (**7d**).*[24] Prepared using procedure **A** from 4-bromoaniline and the known imidate **5**,[14] purified using silica gel chromatography (49% dichloromethane/50% hexanes/1% triethylamine). Off-white solid (0.18 g, 70%); mp = 68−71 °C; TLC R_f = 0.71 (49% dichloromethane/50% hexanes/1% triethylamine); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.28 (m, 4H), 7.24−7.21 (m, 1H), 7.14 (dt, J = 9.6, 3.2 Hz, 2H), 6.36 (dt, J = 10.0, 2.4 Hz, 2H), 4.43 (q, J = 6.8 Hz, 1H), 4.06 (br s, 1H) 1.50 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.3, 144.7, 132.0, 128.9, 127.2, 125.9, 115.0, 109.0, 53.6, 25.1.

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*2-Bromo-N-(1-phenylethyl)aniline (**7e**).*[25] Prepared using procedure **A** from 2-bromoaniline and the known imidate **5**,[14] purified using silica gel (19% dichloromethane/80% hexanes/1% triethylamine). Clear colorless oil (0.18 g, 70%); TLC R_f = 0.50 (19% dichloromethane/80% hexanes/1% triethylamine); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.0, 1.6 Hz, 1H), 7.44−7.38 (m, 4H), 7.33−7.29 (m, 1H), 7.07 (ddd, J = 8.0, 7.2 1.2 Hz, 1H), 6.58 (ddd, J = 7.6, 7.2 1.6 Hz, 1H), 6.48 (dd, J = 8.4, 1.2 Hz, 1H), 4.81 (br d, J = 3.6 Hz, 1H), 4.60 (p, J = 6.8 Hz, 1H), 1.65 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 144.1, 132.3, 128.9, 128.4, 127.1, 125.8, 117.9, 112.8, 109.7, 53.6, 25.3.

*N-(1-Phenylethyl)-3,5-bis(trifluoromethyl)aniline (**7f**).*[26] Prepared using procedure **A** (0.29 g, 98%) from 3,5-bis(trifluoromethyl)aniline and the known imidate **5**,[14] or procedure **B** (0.75 g, 99%) from 1-phenethyl alcohol **34**, purified using silica gel chromatography (19% dichloromethane/80% hexanes/1% triethylamine). White solid (0.29 g, 98%); mp = 56−57 °C; TLC R_f = 0.47 (19% dichloromethane/80% hexanes/1% triethylamine); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.37 (m, 4H), 7.32−7.29 (m, 1H), 7.15 (s, 1H), 6.91 (s, 2H), 4.57 (q, J = 6.8 Hz, 1H), 4.51 (br s, 1H), 1.59 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 143.6, 132.2 (q, J = 33.0 Hz), 129.2, 127.7, 125.6, 123.8 (q, J = 271.0 Hz), 112.6 (q, J = 3.0 Hz), 110.2 (sep, J = 3.0 Hz), 53.6, 24.6.

*2-Nitro-N-(1-phenylethyl)aniline (**7g**).* Prepared using procedure **A** from 2-nitroaniline and the known imidate **5**,[14] purified using silica gel chromatography (49% dichloromethane/50% hexanes/1% triethylamine). Yellow oil (0.24 g, 94%); TLC R_f = 0.31 (50% dichloromethane/50% hexanes); IR (thin film) 3380, 3086, 3029, 2972, 2929, 2873, 1618 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (br s, 1H), 8.17 (dd, J = 8.4, 1.5 Hz, 1H), 7.35−7.25 (m, 6H), 6.64−6.57 (m, 2H), 4.69 (p, J = 6.6 Hz, 1H), 1.65 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 143.7, 136.1, 132.3, 129.1, 127.5, 126.8, 125.7, 115.7, 115.3, 53.3, 25.1. Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.15; H, 5.90; N, 11.16.

*4-(Methylthio)-N-(1-phenylethyl)aniline (**7h**).*[27] Prepared using procedure **A** from 4-(methylthio)aniline and the known imidate **5**,[14] purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Orange oil (0.17g, 70%); TLC R_f = 0.31 (5% ethyl acetate/94% hexanes/1% triethylamine); IR (thin film) 3411, 3082, 3061, 3026, 2979, 2919, 2867, 1598 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 4H), 7.24−7.23 (m, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.46 (br d, J = 7.6 Hz, 2H), 4.46 (q, J = 6.8 Hz, 1H), 2.36 (s, 3H), 1.51 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.2, 145.0, 131.4, 128.8, 127.1, 125.9, 124.2, 114.0, 53.6, 25.0, 19.1.

*4-Ethyl-N-(1-phenylethyl)aniline (**7i**).*[28] Prepared using procedure **A** from 4-ethylaniline and the known imidate **5**,[14] purified using silica gel chromatography (1% dichloromethane/98% hexanes/1% triethylamine). Orange oil (0.10 g, 47%); TLC R_f = 0.74 (1% dichloromethane/98% hexanes/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.22 (m, 5H), 6.94−6.92 (m, 2H), 6.47 (dt, J = 9.0, 2.4 Hz, 2H), 4.45 (q, J = 6.9 Hz, 1H), 2.49 (q, J = 7.5 Hz, 2H), 1.51 (d, J = 6.6 Hz, 3H), 1.15 (t, J = 7.5, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 145.5, 133.3, 128.9, 128.7, 127.1, 126.1, 113.6, 54.0, 28.1, 25.3, 16.2.

*2-Fluoro-4-methyl-N-(1-phenylethyl)aniline (**7j**).* Prepared using procedure **A** from 2-fluoro-4-methylaniline and the known imidate **5**,[14] purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Clear colorless oil (0.17g, 80%); TLC R_f = 0.59 (5% ethyl acetate/94% hexanes/1% triethylamine); IR (thin film) 3431, 3061, 3031, 2968, 2925, 1658 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.28 (m, 4H), 7.25−7.19 (m, 1H), 6.79 (dd, J = 12.3, 1.5 Hz, 1H), 6.64−6.61 (m, 1H), 6.40 (br s, 1H), 4.48 (q, J = 6.6 Hz, 1H), 2.18 (s, 3H), 1.57 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6 (d, J = 236.6 Hz), 145.2, 133.4 (d, J = 11.8 Hz), 128.9, 127.2, 126.7 (d, J = 6.6 Hz), 126.0, 124.9 (d, J = 3.1 Hz), 115.3 (d, J = 18.2 Hz), 113.5 (d, J = 3.4 Hz), 53.8, 25.3, 20.6 (d, J = 1.1 Hz). Anal. Calcd for $C_{15}H_{16}FN$: C, 78.57; H, 7.03; N, 6.11. Found: C, 78.31; H, 7.27; N, 5.76.

*2-Chloro-N-(1-phenylethyl)-5-(trifluoromethyl)aniline (**7k**).* Prepared using procedure **A** from 2-chloro-5-(trifluoromethyl)aniline and the known imidate **5**,[14] purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Yellow oil (0.28 g, 98%); TLC R_f = 0.57 (5% ethyl acetate/94% hexanes/1% triethylamine); IR (thin film) 3428, 3087, 3066, 3031, 2974, 2930, 2873, 1603 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.25 (m, 6H), 6.80 (ddd, J = 8.1, 2.1, 0.6 Hz, 1H), 6.64 (d, J = 1.8 Hz, 1H), 4.55 (q, J = 6.6 Hz, 1H), 1.60 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 143.3, 130.1 (q, J = 32.0 Hz), 129.3, 129.0, 127.5, 125.7, 124.0 (q, J = 271.0 Hz), 122.2, 113.7 (q, J = 4.0 Hz), 108.8 (q, J = 4.0 Hz), 53.4, 24.7. Anal. Calcd for $C_{15}H_{13}ClF_3N$: C, 60.11; H, 4.37; N, 4.67. Found: C, 60.27; H, 4.36; N, 4.55.

*2-Chloro-4-fluoro-N-(1-phenylethyl)aniline (**7l**).* Prepared using procedure **A** from 2-chloro-4-fluoroaniline and the known imidate **5**,[14] purified using silica gel chromatography (19% dichloromethane/80% hexanes/1% triethylamine). Dark oil (0.27 g, 99%); TLC R_f = 0.52 (19% dichloromethane/80% hexanes/1% triethylamine); IR (thin film) 3424, 3064, 3029, 2971, 2929, 2871, 1599 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.28 (m, 4H), 7.25−7.22 (m, 1H), 7.03 (dd, J = 8.4, 3.0 Hz, 1H), 6.69 (ddd, J = 9.0, 8.1, 2.7 Hz, 1H), 6.32 (dd, J = 9.0, 5.7 Hz, 1H), 4.52 (br s, 1H), 4.47 (q, J = 6.9 Hz, 1H), 1.57 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4 (d, J = 236.4 Hz) 144.5, 139.9 (d, J = 2.2 Hz), 128.9, 127.2, 125.8, 118.8 (d, J = 10.3 Hz), 116.3 (d, J = 25.8 Hz), 114.3 (d, J = 21.5 Hz), 112.8 (d, J = 8.0 Hz), 53.9, 25.3. Anal. Calcd for $C_{14}H_{13}ClFN$: C, 67.34; H, 5.25; N, 5.61. Found: C, 67.39; H, 4.97; N, 5.53.

*2-Chloro-4-methyl-N-(1-phenylethyl)aniline (**7m**).*[29] Prepared using procedure **A** from 2-chloro-4-methylaniline and the known imidate **5**,[14] purified using silica gel chromatography (5% dichloromethane/94% hexanes/1% triethylamine). Yellow oil (0.22 g, 94%); TLC R_f = 0.56 (5% dichloromethane/94% hexanes/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.19 (m, 5H), 7.07 (dd, J = 2.1, 0.9 Hz, 1H), 6.76 (dd, J = 8.1, 1.8, 0.6 Hz, 1H), 6.35 (d, J = 8.1 Hz, 1H), 4.51 (q, J = 6.6 Hz, 1H), 2.16 (s, 3H), 1.58 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 140.8, 129.6, 128.9, 128.4, 127.2, 127.0, 126.0, 119.0, 112.9, 53.8, 25.4, 20.3.

*N-Methyl-N-(1-phenylethyl)aniline (**7n**).*[30] Prepared using procedure **A** (0.17 g, 84%) from *N*-methylaniline and the known imidate **5**,[14] or procedure **B** (0.36 g, 82%) from 1-phenethyl alcohol, purified using silica gel chromatography (4% ethyl acetate/95% hexanes/1% triethylamine). Yellow oil (0.17 g, 84%); TLC R_f = 0.32 (2% ethyl acetate/97% hexane/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.22 (m, 7H), 6.84 (d, J = 8.1 Hz, 2H), 6.73 (t, J = 7.2 Hz, 1H), 5.13 (q, J = 6.9 Hz, 1H), 2.68 (s, 3H), 1.55 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 143.0, 129.4, 128.6, 127.1, 127.0, 116.9, 113.3, 56.7, 32.0, 16.5.

*1-(1-Phenylethyl)indoline (**7o**).*[31] Prepared using procedure **A** from indoline and the known imidate **5**,[14] purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Dark oil (0.18 g, 74%); TLC R_f = 0.52 (5% ethyl acetate/94% hexanes/1% triethylamine); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5H), 7.05 (dd, J = 7.2, 0.9 Hz, 1H), 6.98 (t, J = 7.5 Hz, 1H), 6.60 (t, J = 6.9 Hz, 1H), 6.35 (d, J = 7.5 Hz, 1H), 4.71 (q, J = 7.2 Hz, 1H), 3.44−3.28 (m, 2H), 2.94 (t, J = 8.7 Hz, 2H), 1.53 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 143.2, 130.5, 128.7, 127.5, 127.4, 127.2, 124.7, 117.3, 107.6, 54.9, 48.3, 28.5, 16.9.

*N-Benzyl-2,5-dichloroaniline (**9**).* Prepared using procedure **A** (0.23 g, 92%) from 2,5-dichloroaniline **6** and the commercially available benzyl-2,2,2-trichloroacetimidate **8** or procedure **B** (0.37 g, 64%) from benzyl alcohol, purified using silica gel chromatography (19% dichloromethane/80% hexanes/1% triethylamine). Clear colorless oil (0.23 g, 92%); TLC R_f = 0.50 (20% dichloromethane/80% hexanes); IR (thin film) 3422, 3064, 3030, 2852, 1595 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.29 (m, 5H), 7.18−7.15 (m, 1H), 6.62−6.59 (m, 2H), 4.76 (br s, 1H), 4.36 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 138.1, 133.8, 129.9, 129.1, 127.8, 127.6, 117.5, 117.4, 111.5, 48.0. Anal. Calcd for $C_{13}H_{11}Cl_2N$: C, 61.93; H, 4.40; N, 5.56. Found: C, 62.26; H, 4.26; N, 5.51.

*2,5-Dichloro-N-(4-methoxybenzyl)aniline (**11**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the commercially available

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J. Org. Chem. 2015, 80, 1993−2000

4-methoxybenzyl-2,2,2-trichloroacetimidate **10**, purified with silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Yellow oil (0.22 g, 91%); TLC R_f = 0.42 (2% ethyl acetate/97% hexanes/1% triethylamine); IR (thin film) 3422, 3071, 3003, 2958, 2836, 1595 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.62−6.58 (m, 2H), 4.66 (br s, 1H), 4.27 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 144.9, 133.8, 130.1, 129.9, 128.9, 117.4, 117.2, 114.4, 111.5, 55.5, 47.5. Anal. Calcd for $C_{14}H_{13}Cl_2NO$: C, 59.59; H, 4.64; N, 4.96. Found: C, 59.61; H, 4.94; N, 4.84.

*N-((6-Bromobenzo[d][1,3]dioxol-5-yl)methyl)-2,5-dichloroaniline (**13**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **12**,[32] purified using silica gel chromatography (19% dichloromethane/80% hexanes/1% triethylamine). Yellow oil (0.20 g, 80%); TLC R_f = 0.29 (20% dichloromethane/80% hexanes); IR (thin film) 3436, 3107, 3078, 3010, 2915, 1593 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.17 (d, J = 8.4 Hz, 1H), 7.04 (s, 1H), 6.82 (s, 1H), 6.62 (dd, J = 8.4, 2.4 Hz, 1H), 6.51 (d, J = 2.1 Hz, 1H), 5.97 (s, 2H), 4.84 (t, J = 5.4 Hz, 1H), 4.33 (d, J = 5.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 147.82, 147.76, 144.2, 133.7, 130.0, 129.8, 117.5, 117.4, 113.5, 113.0, 111.4, 108.7, 101.9, 47.8. Anal. Calcd for $C_{14}H_{10}O_2NBrCl_2$: C, 44.83; H, 2.69; N, 3.73. Found: C, 45.10; H, 2.74; N, 3.94.

*4-(((2,5-Dichlorophenyl)amino)methyl)benzonitrile (**15**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **14**,[16] purified using silica gel chromatography (9% ethyl acetate/90% hexanes/1% triethylamine). White solid (0.11 g, 43%); mp = 114−115 °C; TLC R_f = 0.59 (50% dichloromethane/50% hexanes); IR (thin film) 3409, 2916, 2224, 1595, 1567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 6.4, 1.6 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.8 Hz, 1H), 6.63 (dd, J = 8.4, 2.0 Hz, 1H), 6.45 (d, J = 2.0 Hz, 1H), 4.92 (t, J = 5.6 Hz, 1H), 4.47 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 143.7, 133.7, 132.7, 130.0, 127.6, 118.7, 117.8, 117.5, 111.4, 111.3, 47.2. Anal. Calcd for $C_{14}H_{10}Cl_2N_2$: C, 60.67; H, 3.64; N, 10.11. Found: C, 60.32; H, 3.58; N, 9.80.

*N-Benzhydryl-2,5-dichloroaniline (**17**).* Prepared using procedure **A** (0.28 g, 87%) from 2,5-dichloroaniline **6** and the known imidate **16**[33] and procedure **B** (0.39 g, 88%) from diphenylmethanol, purified using silica gel chromatography (10% dichloromethane/89% hexanes/1% triethylamine). Clear colorless oil (0.28 g, 87%); TLC R_f = 0.59 (10% dichloromethane/89% hexanes/1% triethylamine); IR (thin film) 3417, 3031, 2925, 1656, 1596 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.25 (m, 10H), 7.16 (d, J = 8.4 Hz, 1H), 6.59 (dd J = 8.4, 2.4 Hz, 1H), 6.44 (d, J = 2.1 Hz, 1H), 5.52 (s,1H), 4.95 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 141.9, 133.7, 129.9, 129.2, 128.7, 128.0, 127.6 117.7, 112.7, 62.7. Anal. Calcd for $C_{19}H_{15}Cl_2N$: C, 69.52; H, 4.61; N, 4.27. Found: C, 69.75; H, 4.62; N, 4.60.

*2,5-Dichloro-N-(1-(p-tolyl)ethyl)aniline (**19**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **18**,[34] purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Clear colorless oil (0.17 g, 68%); TLC R_f = 0.81 (5% ethyl acetate/95% hexanes); IR (thin film) 3422, 2968, 2923, 2867, 1594 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.23−7.20 (m, 2H), 7.16−7.12 (m, 3H), 6.53 (dd, J = 8.4, 2.4 Hz, 1H), 6.40 (d, J = 2.1 Hz, 1H), 4.72 (br s, 1H), 4.46 (q, J = 6.6 Hz, 1H), 2.33 (s, 3H), 1.55 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 140.8, 136.9, 133.4, 129.6, 125.6, 117.1, 116.9, 112.2, 53.0, 24.9, 21.1 (one signal in the aromatic region was not resolved). Anal. Calcd for $C_{15}H_{15}Cl_2N$: C, 64.30; H, 5.40; N, 5.00. Found: C, 64.52; H, 5.20; N, 4.74.

*N-Allyl-2,5-dichloroaniline (**21**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the commercially available *O*-allyl 2,2,2-trichloroacetimidate **20**, purified using silica gel chromatography (4% dichloromethane/94% hexanes/1% triethylamine). Clear colorless oil (0.19 g, 77%); TLC R_f = 0.24 (5% dichloromethane/95% hexanes); IR(thin film) 3426, 3086, 3013, 2985, 2926, 2850, 1645, 1595 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.16−7.13 (m, 1H), 6.61−6.58 (m, 2H), 5.94−5.87 (m, 1H), 5.32−5.20 (m, 2H), 4.52 (br s, 1H), 3.82 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 134.0, 133.6, 129.7, 117.3, 117.0, 116.8, 111.3, 45.9; Anal. Calcd for $C_9H_9Cl_2N$: C, 53.49; H, 4.49; N, 6.69. Found: C, 53.40; H, 4.89; N, 6.69.

*2,5-Dichloro-N-(cyclohex-2-en-1-yl)aniline (**23**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **22**,[35] purified using silica gel chromatography (2% ethyl acetate/97% hexanes/1% triethylamine). Orange oil (0.19 g, 79%); TLC R_f = 0.60 (5% ethyl acetate/95% hexanes); IR (thin film) 3418, 3026, 2938, 2862, 1593 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 8.4 Hz, 1H), 6.66 (d, J = 2.4 Hz, 1H), 6.57 (dd, J = 8.4, 2.4 Hz, 1H), 5.94- 5.88 (m, 1H), 5.75−5.70 (m, 1H), 4.36 (br d, J = 7.8 Hz, 1H), 3.98 (br s, 1H), 2.09−2.05 (m, 2H), 1.96−1.89 (m, 1H), 1.77−1.63 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 133.6, 131.2, 129.9, 127.4, 117.3, 116.5, 111.3, 47.7, 28.6, 25.1, 19.5; Anal. Calcd for $C_{12}H_{13}Cl_2N$: C, 59.52; H, 5.41; N, 5.78. Found: C, 59.38; H, 5.27; N, 5.45.

*2,5-Dichloro-N-(2-phenylpropan-2-yl)aniline (**25**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **24**,[36] purified using silica gel chromatography (9% dichloromethane/90% hexanes/1% triethylamine). Clear colorless oil (0.22 g, 42%); TLC R_f = 0.58 (10% dichloromethane/90% hexanes); IR (thin film) 3419, 3042, 3011, 2857, 1578 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.42 (m, 2H), 7.34 (tt, J = 6.8, 1.6 Hz, 2H), 7.25 (tt, J = 6.8, 1.6 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 6.48 (dd, J = 8.0, 2.4 Hz, 1H), 6.06 (d, J = 2.4 Hz, 1H), 4.84 (br s, 1H), 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 142.7, 132.7, 129.6, 128.9, 126.9, 125.4, 118.0, 116.8, 114.4, 56.1, 30.5. Anal. Calcd for $C_{15}H_{15}Cl_2N$: C, 64.30; H, 5.40; N, 5.00. Found: C, 63.95; H, 5.71; N, 4.70.

*N-(tert-Butyl)-2,5-dichloroaniline (**27**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the commercially available *tert*-butyl 2,2,2-trichloroacetimidate **26**, purified using silica gel chromatography (19% dichloromethane/80% hexanes/1% triethylamine). Clear colorless oil (0.01 g, 5%); TLC R_f = 0.45 (20% dichloromethane/80% hexanes); IR (thin film) 3416, 3086, 3060, 2981, 1592, 1504 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 2.4 Hz, 1H), 6.56 (dd, J = 8.4, 2.4 Hz, 1H), 4.38 (br s, 1H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 132.9, 129.8, 118.6, 116.6, 113.8, 51.4, 29.6. Anal. Calcd for $C_{10}H_{13}Cl_2N$: C, 55.06; H, 6.01; N, 6.42. Found: C, 55.13; H, 6.35; N, 6.13.

*2-(((2,5-Dichlorophenyl)amino)methyl)isoindoline-1,3-dione (**31**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **30**,[37] purified using silica gel chromatography (20% ethyl acetate/79% hexanes/1% triethylamine). White powder (0.24 g, 74%); mp = 200−201 °C; TLC R_f = 0.83 (20% ethyl acetate/79% hexanes/1% triethylamine); IR (KBr) 3397, 3067, 1718, 1657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88−7.86 (m, 2H), 7.74−7.72 (m, 2H), 7.26 (s, 1H), 7.13 (d, J = 8.4 Hz, 1H), 6.66 (dd, J = 8.4, 2.4 Hz, 1H), 5.47 (t, J = 7.6 Hz, 1H), 5.19 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 142.0, 134.4, 133.8, 131.8, 130.1, 123.7, 119.0, 118.0, 112.4, 46.6. Anal. Calcd for $C_{15}H_{10}Cl_2N_2O_2$: C, 56.10; H, 3.14; N, 8.72. Found: C, 56.06; H, 3.33; N, 8.51.

*2,5-Dichloro-N-(1,4-diphenylbut-3-yn-1-yl)aniline (**33**).* Prepared using procedure **A** from 2,5-dichloroaniline **6** and the known imidate **32**,[38] purified using silica gel chromatography (4% dichloromethane/95% hexanes/1% triethylamine). Yellow solid (50 mg, 63%); mp = 86−88 °C; TLC R_f = 0.54 (10% ethyl acetate/90% hexanes); IR (KBr) 3380, 3114, 2989, 1594, 1504 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.27 (m, 10H), 7.15 (d, J = 8.4 Hz, 1H), 6.57 (dd, J = 8.4, 2.4 Hz, 1H), 6.40 (d, J = 2.0 Hz, 1H), 5.33 (d, J = 5.2 Hz, 1H), 4.61 (q, J = 5.6 Hz, 1H), 3.05 (dd, J = 16.8, 5.2 Hz, 1H), 2.91 (dd, J = 16.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 141.1, 133.4, 131.6, 129.7, 128.9, 128.3, 128.1, 127.9, 126.2, 123.0, 117.7, 117.5, 112.6, 84.8, 84.2, 56.5, 29.3. Anal. Calcd for $C_{22}H_{17}Cl_2N$: C, 72.14; H, 4.68; N, 3.82. Found: C, 72.35; H, 4.63; N, 3.82.

*N-((6-Bromobenzo[d][1,3]dioxol-5-yl)methyl)-N-methylaniline (**39**).* Prepared using procedure **B** from the known 6-bromo-1,3-benzodioxole-5-methanol **38**[39] and *N*-methylaniline **36**, purified using silica gel chromatography (49% dichloromethane/50% hexanes/1% triethylamine). Yellow solid (0.81 g, 81%); mp = 72−74 °C; TLC R_f = 0.37 (50% dichloromethane/50% hexanes); IR (KBr) 3436, 3093, 3064, 2893, 2827, 2565, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24−7.20 (m, 2H), 7.04 (s, 1H), 6.73 (dt, J = 7.2, 0.8 Hz, 1H), 6.73−

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J. Org. Chem. 2015, 80, 1993−2000

6.65 (m, 3H), 5.93 (s, 2H), 4.44 (s, 2H), 3.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 149.2, 147.8, 147.3, 131.0, 129.3, 116.8, 113.0, 112.6, 112.1, 108.0, 101.7, 57.4, 38.8. Anal. Calcd for $C_{15}H_{14}O_2NBr$: C, 56.27; H, 4.41; N, 4.37. Found: C, 56.43; H, 4.28; N, 4.36.

Onosmin B (4).[5] Prepared using procedure **B** with 4-methylbenzyl alcohol **40** and 2-aminomethylbenzoate **41**, purified using silica gel chromatography (29% dichloromethane/70% hexanes/1% triethylamine). Clear colorless oil (0.26 g, 85%); TLC R_f = 0.55 (10% ethyl acetate/90% hexanes); IR (thin film) 3368, 3078, 3020, 2949, 2921, 2847, 1681 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.92 (dd, J = 8.0, 1.6 Hz, 1H), 7.29 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.26–7.23 (m, 2H), 7.14 (d, J = 7.6 Hz, 2H), 6.65 (dd, J = 8.0, 0.8 Hz, 1H), 6.59 (ddd, J = 8.0, 7.2, 1.2 Hz, 1H), 4.41 (s, 2H), 3.86, (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 169.1, 150.9, 136.8, 135.7, 134.6, 131.6, 129.4, 127.1, 114.8, 111.7, 110.2, 51.5, 46.8, 21.1. Anal. Calcd for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.54; H, 6.67; N, 5.83.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra of new compounds as well as chiral HPLC data for compounds **5** and **7c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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