Titanocene(III)-catalyzed conversion of *N*-(epoxyalkyl)anilines into indolines

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Dedicated to Prof. Heinz Heimgartner on the occasion of his 70th birthday

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Abstract

Densely substituted indolines and azaindolines can be obtained by the titanocene(III) chloride catalyzed reductive opening of *N*-(oxiran-2-ylmethyl)anilines. The reaction optimization, substrate scope, and limitations are discussed, and a mechanistic pathway for the epoxide-opening rearrangement is proposed.

Keywords: Indoline, titanocene dichloride, *N*-(epoxyalkyl) aniline, radical addition

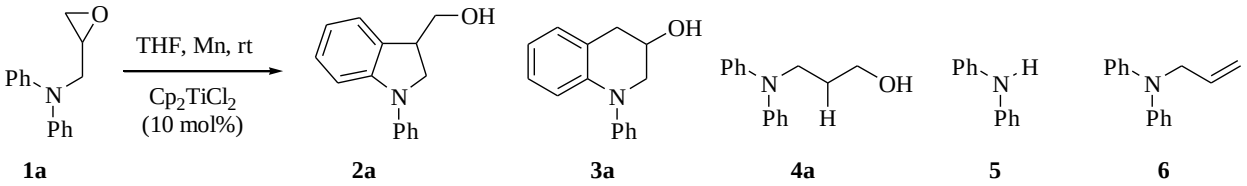
Introduction

The indole scaffold is the third most common aromatic building block present in bioactive molecules.[1] Frequently, indoles are constructed from partially reduced precursors, such as indolines or oxidized derivatives, such as indolinones, and the latter are also often by themselves biologically active.[2] Furthermore, in the pharmaceutical industry, nitrogen replacements of carbon atoms in the indole scaffold are routinely applied for the investigation of structure-activity relationships (SAR), and indazole and azaindole (pyrrolopyridine) subunits are often found in the molecular structure of therapeutic candidates.[3] Therefore, both the discovery of new methods as well as the optimization of the scope of well established protocols for the construction of these heterocycles continues to be a focal point of heterocyclic chemistry. We recently developed a synthesis of 3,3-disubstituted indolines that uses *in situ* generated titanocene(III) chloride[4,5] to promote a new epoxide-opening rearrangement, transforming *N*-(epoxyalkyl)anilines into indolines.[6] Although most one-step protocols to prepare indolines through carbon-carbon bond formation involve an activation of an aryl halide using either a transition metal[7] or a radical initiator,[8] we envisioned exploring a complementary approach toward indoline preparation that uses the reductive opening of an epoxide derived from an allyl

aniline to install a quaternary carbon and the fused pyrrolidine ring in the radical cyclization onto the benzene ring. Herein, we now present a full account of the development, substrate scope, and current limitations of this low-valent titanium catalyzed transformation.

Results and Discussion

The initial methodology development began with studies toward converting epoxide **1a** into indoline **2a** using 10 mol% of *in situ* generated titanocene(III) chloride in the presence of manganese powder as a stoichiometric reducing agent at room temperature in degassed THF (0.1 M). During this process, we detected by GC analysis that in addition to the desired indoline **2a**, the hydroquinoline **3a**, reduced alcohol **4a**, β-bond cleavage product **5**, and deoxygenated product **6** were present in the crude reaction mixtures (Scheme 1). The presence of **4a**, **5**, and **6** suggested that the radical cyclization to form the indoline was slower than other competing reaction pathways, thereby causing the mixture of undesired side products.



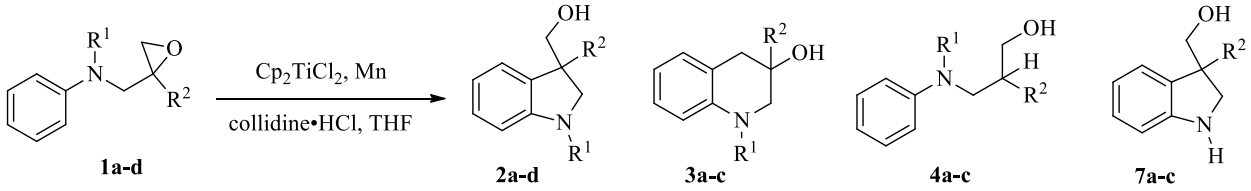
Scheme 1. Product distribution for exposure of *N*-(epoxyalkyl)aniline **1a** to *in situ* generated titanocene(III) chloride.

When lowering the reaction concentration to 0.03 M and using 10 mol% of precatalyst in the presence of 80 mol% of manganese powder under sonication, a 3:1 ratio of indoline **2a** to tetrahydroquinoline **3a** was observed by GC analysis of the crude reaction mixture (Table 1, entry 1). Next, we tested if a methyl substituted alkene substrate would react more selectively and avoid the formation of the undesired mixtures of **2a** and **3a**. Indeed, when epoxide **1b** was treated with *in situ* generated titanocene (III) chloride, indoline **2b** was obtained in 82% yield as a single product (entry 2). It was evident that the additional methyl group on the epoxide improved the selectivity in favor of the desired indoline product. We also observed that sonication provided no additional benefits toward promoting the annulation reaction since **2b** was isolated in nearly identical yield when using conventional magnetic stirring (entry 3). To broaden the scope of the methodology, we screened for a suitable replacement for the *N*-phenyl group. When subjecting the secondary amine (R^1=H) to the cyclization reaction, only a minor amount of reduced amino alcohol was isolated. The benzyloxycarbonyl (Cbz) group was the preferred choice of protecting group among the candidates screened, which included benzyl, *t*-butyloxycarbonyl, *p*-toluenesulfonyl, and trifluoroacetyl. The Cbz protecting group was optimal

since it neither functioned as a radical acceptor nor participated in undesired side reactions with the tethered epoxide during the reaction.

Subjecting carbamate **1c** to catalytic titanocene(III) chloride at room temperature produced a 2:1 mixture of indoline **2c** to alcohol **4c** (Table 1, entry 4). When the precatalyst loading was lowered to 5 mol% and then further to 3 mol%, the product ratio (determined by ^{1}H NMR analysis of the crude reaction mixtures) of **2c**:**4c** increased from 3:1 to 7:1, respectively. However, when using 3 mol% of the precatalyst, **1c** was recovered in 18% yield. In order to drive the reaction further to completion, the mixture was heated at reflux in THF using 3 mol% of the precatalyst. Under these conditions and subsequent hydrogenolysis of the Cbz group, indoline **7c** was isolated in 63% yield over 2 steps (entry 5). Subjecting the ethoxycarbonyl-protected substrate **1d** to the optimized conditions afforded the desired indoline in 65% yield (entry 6). When applied to our model system **1b**, these conditions produced indoline **2b** in 89% yield (entry 7). High yields were also obtained when subjecting epoxide **1a** to 3 mol% of titanocene dichloride and stoichiometric Mn powder in THF at reflux, affording a 3.8:1 mixture of **2a** and **3a** in 87% yield (entry 8).

Table 1. Conditions screened during the optimization of the epoxide-opening rearrangement



entry	epoxide[a,b]	R^1	R^2	Cp_2TiCl_2	Mn (equiv.)	concentration [M]	product(s), yield
1	**1a**	Ph	H	10 mol%	0.80	0.03	**2a**:**3a** (3:1)[c,d]
2	**1b**	Ph	CH_3	10 mol%	0.65	0.03	**2b**, 82%[d]
3	**1b**	Ph	CH_3	10 mol%	0.65	0.03	**2b**, 84%[e]
4	**1c**	Cbz	CH_3	10 mol%	1.5	0.1	**2c**:**4c** (2:1)[f]
5	**1c**	Cbz	CH_3	3 mol%	1.5	0.1	**7c**, 63%[g]
6	**1d**	CO_2Et	CH_3	3 mol%	1.5	0.1	**2d**, 65%
7	**1b**	Ph	CH_3	3 mol%	1.5	0.1	**2b**, 89%
8	**1a**	Ph	H	3 mol%	1.5	0.1	**2a**:**3a** (3.8:1), 87%

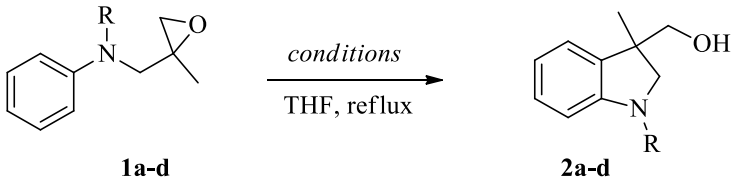
[a]For epoxide preparation, see experimental section. [b]All reactions were performed in degassed THF at reflux unless otherwise noted. [c]Yield was not determined; product ratio was determined by GC analysis of crude reaction mixtures. [d]Reaction was performed in degassed THF at room temperature using sonication. [e]Reaction was performed in degassed THF at room temperature

using magnetic stirring. [f]Reaction was performed at room temperature; yield was not determined; product ratios were obtained by ^{1}H NMR analysis of crude reaction mixtures.
[g]Yield was determined over 2 steps.

We also explored the sensitivity of the reaction to both ambient oxygen and water. When subjecting **1c** to titanocene(III) catalysis in a reaction flask open to ambient air, we observed only a 14% yield of **2c** and recovered 43% of **1c** (Table 2, entry 1). This observation suggested that the desired reaction was inhibited by ambient oxygen. Subjecting **1d** to the titanocene(III) catalyzed epoxide opening using a degassed mixture of distilled THF:H_2O in an equivolume ratio led to the recovery of 89% of the starting material (entry 2). Although some titanocene(III) chloride-mediated processes utilize water as a co-solvent,[9] the desired catalytic process appears to be inhibited by its presence. Additional control experiments using either only 3 mol% of the precatalyst (entry 3) or only 1.5 equiv. of manganese metal (entry 4) under otherwise identical reaction conditions failed to afford indolines. These results indicated that the *in situ* generated reagent was responsible for promoting the annulation. In the presence of a catalytic amount of manganese metal, **2c** was isolated in 35% yield, in addition to 38% of recovered **1c** (entry 5).

For further substrate variation, a series of substituted *N*-(epoxyalkyl) anilines were prepared and subjected to titanocene(III) chloride catalysis to afford the respective indolines (Table 3). The *para*- and *ortho*-methyl substituted substrates **8a** and **8b** (entries 1 and 2, respectively) afforded indolines in good to modest yields. The 5-methoxyindoline **9c** was isolated in low yield (21% yield over 2 steps). In contrast, electron-deficient substrates underwent the epoxide-opening rearrangement to afford indolines in good yields (entries 4 and 5).

Table 2. Control experiments to probe reaction limitations

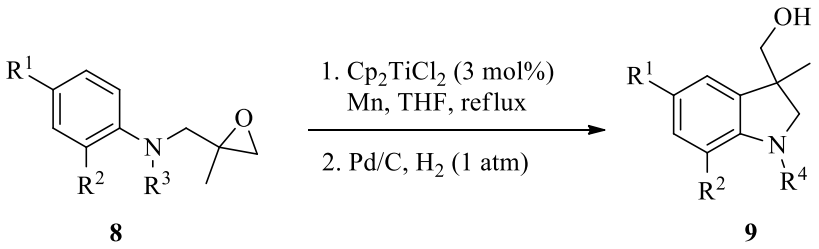


1a-d **2a-d**

entry	epoxide	R	Cp_2TiCl_2 (mol%)	Mn (equiv.)	product(s), yield
1	**1c**	Cbz	3	1.5	**2c**, 14% (recovered **1c**, 43%)[a]
2	**1d**	CO_2Et	3	1.5	**2d**, 0% (recovered **1d**, 89%)[b]
3	**1c**	Cbz	3	0	**2c**, 0%
4	**1c**	Cbz	0	1.5	**2c**, 0%
5	**1c**	Cbz	3	0.15	**2c**, 35% (recovered **1c**, 38%)

[a]Reaction was performed in a flask open to the atmosphere in distilled, non-degassed THF. [b]Reaction was performed in a degassed mixture of distilled THF:H_2O (1:1).

Table 3. Substrates prepared using titanocene(III) chloride catalysis

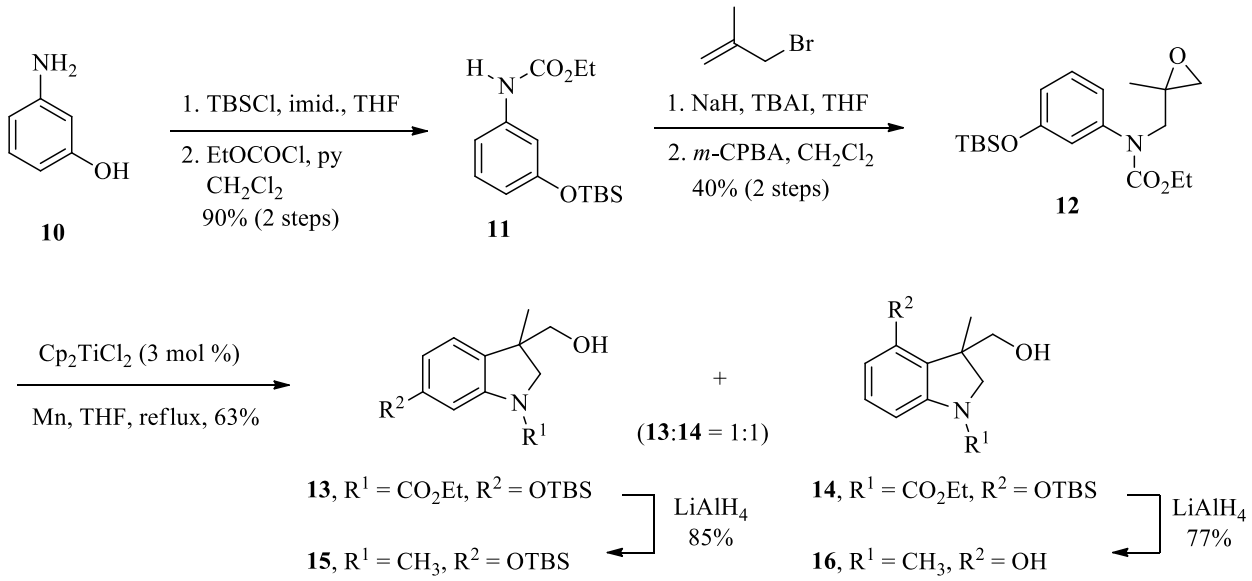


8 **9**

entry	epoxide[a]	R^1	R^2	R^3	R^4	product	yield
1	**8a**	CH_3	H	Cbz	H	**9a**	62%[b]
2	**8b**	H	CH_3	Cbz	H	**9b**	35%[b]
3	**8c**	OCH_3	H	Cbz	H	**9c**	21%[b]
4	**8d**	CO_2CH_3	H	Cbz	H	**9d**	56%[b]
5	**8e**	Cl	H	Cbz	Cbz	**9e**	41%[c]

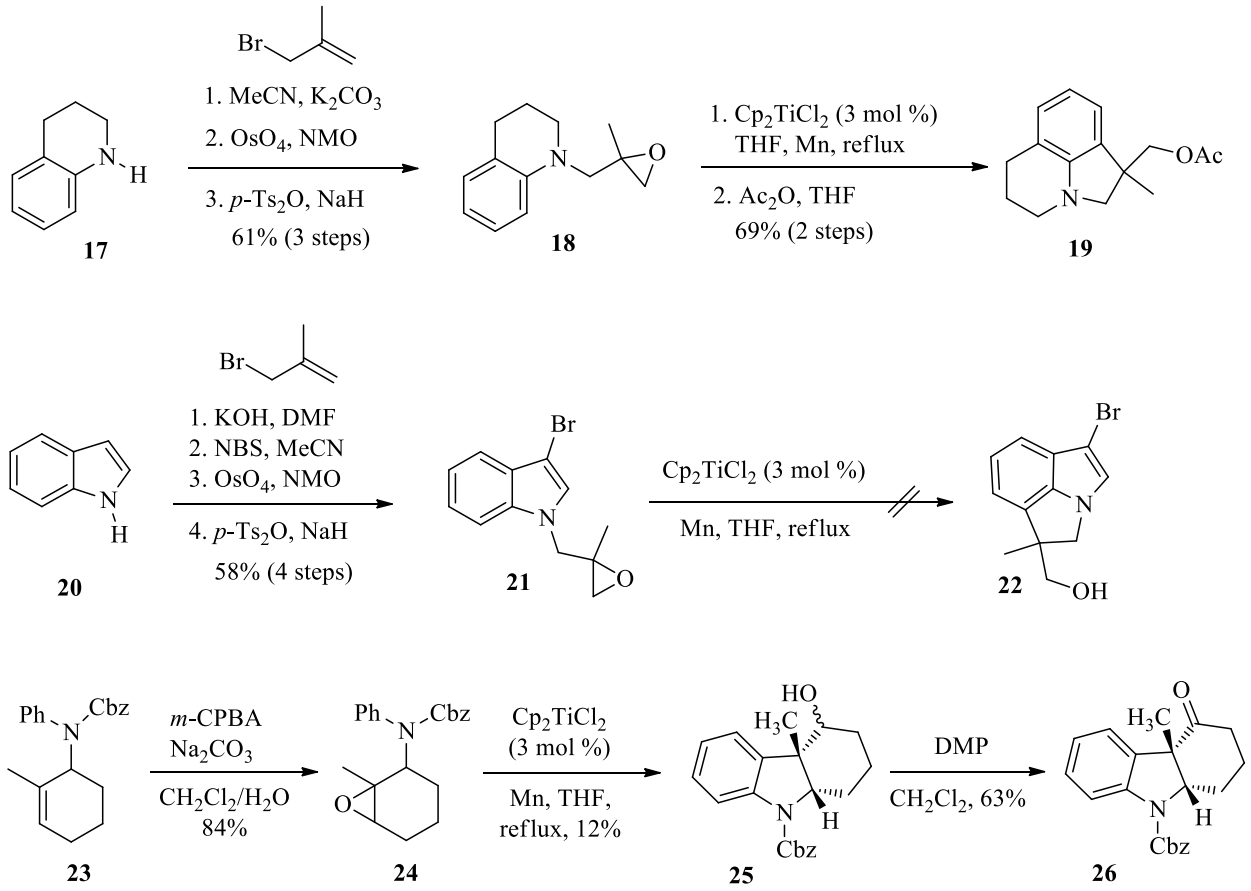
[a]See experimental section for epoxide preparations. [b]Yield was determined over 2 steps. [c]Cbz group was not removed; i.e. step 2 was not performed.

For the study of the regioselectivity of the annulation, epoxide **12** (prepared in 4 steps from aniline **10**) was subjected to the titanocene(III) catalyzed epoxide opening, affording a 1:1 mixture of regioisomers **13** and **14** in a combined yield of 63% (Scheme 2). Subsequent reduction of the ethyl carbamates using lithium aluminum hydride provided *N*-methyl indolines **15** and **16**, respectively.



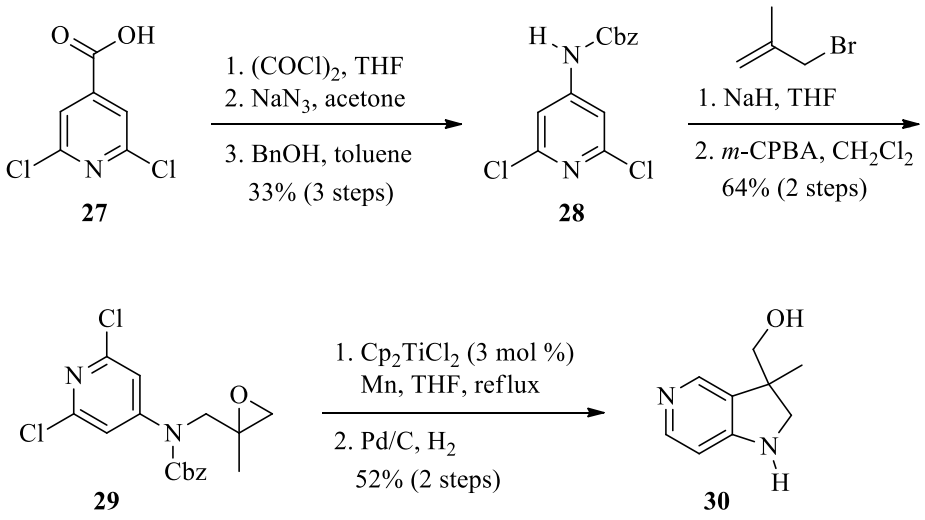
Scheme 2. Regioselectivity of the radical annulation reaction.

We also attempted to prepare heterocycles of higher complexity (Scheme 3). Epoxide **18** was obtained in 61% yield over 3 steps by alkylation of tetrahydroquinoline **17** with 3-bromo-2-methyl propene, followed by OsO_4 oxidation and epoxide formation. Subjecting the epoxide to the titanocene(III) catalyzed annulation and protection of the resulting alcohol as the acetate provided **19** in 69% yield over 2 steps. In contrast, the epoxide **21** (prepared in 4 steps from indole **20**) failed to provide the pyrroloindoline **22**, possibly due to the ring strain in the fused five-membered ring system. The linearly fused tricyclic hydrocarbazole **25** was obtained, albeit in low yield, from cyclohexene oxide **24**. The alcohol function in **25** was converted to the carbonyl group using Dess-Martin periodinane (DMP) in 63% yield. The relative configuration of ketone **26** was assigned to be *syn* based on the strong nOe between the tertiary methyl group and the methine hydrogen observed in the 2D-NOESY NMR.



Scheme 3. Conversions of more highly substituted substrates to tricyclic indolines.

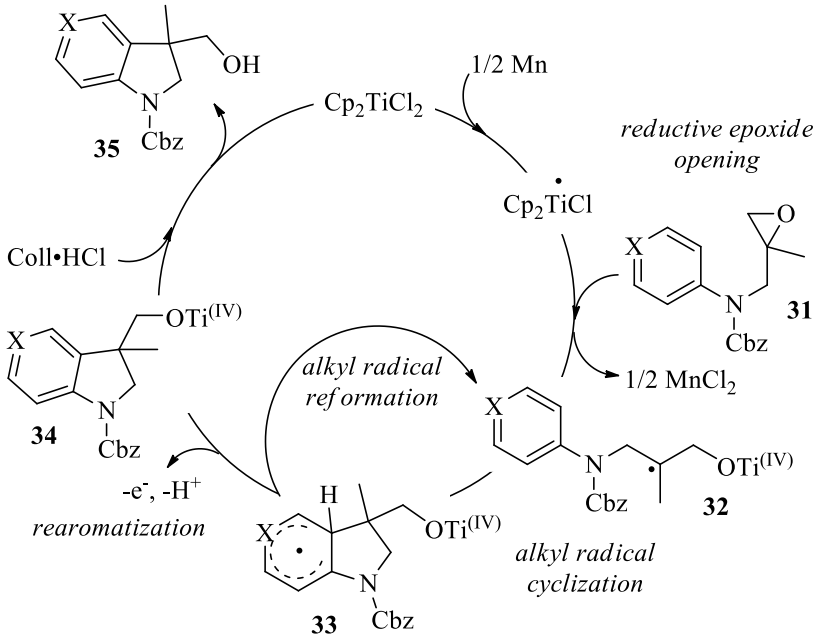
As mentioned previously, azaindolines have found broad applications as bioisosteres of indolines in pharmaceutical research.[10] The use of aminopyridine substrates offered the possibility of applying our methodology toward the preparation of azaindolines.[6,11] Although the chemoselective epoxidation of alkenes in the presence of the pyridine moiety was precedented, attempts to efficiently prepare the epoxide on an unsubstituted aminopyridine substrate were unsuccessful. This negative result was primarily due to the reactivity of the pyridine nitrogen toward either *m*-CPBA or DMDO, i.e. the formation of *N*-oxides.[12] In contrast, the *ortho*-chlorine substitution[13] proved to be sufficient to attenuate the reactivity of the pyridine nitrogen lone pair and prevent this undesired oxidation. A Curtius rearrangement of the known carboxylic acid **27**[14] followed by subsequent trapping of the intermediate isocyanate with benzyl alcohol afforded the Cbz-protected aminopyridine **28** in 33% yield over 3 steps (Scheme 4). Subsequent methallylation and epoxidation using *m*-CPBA led to epoxide **29**, which, when treated with catalytic titanocene(III) chloride in the presence of stoichiometric manganese powder, provided an intermediate 4,6-dichloro-5-azaindoline. Further conversion of this intermediate with Pd/C under an atmosphere of H_2 gave azaindoline **30** in 52% yield over 2 steps.



27 **28** **29** **30**

Scheme 4. Preparation of 5-azaindoline **30**.

Our studies of the mechanism of the titanocene(III)-catalyzed conversion of *N*-(epoxyalkyl)anilines into indolines and azaindolines are still evolving. Based on our current experimental data, we envision that after the *in situ* generation of titanocene(III) chloride, the epoxide **31** is reductively opened to form the β-titanoxy radical **32**. This radical may then undergo an addition onto the aromatic ring forming the cyclohexadienyl radical intermediate **33** (Scheme 5).[15] Oxidation or disproportionation of the cyclohexadienyl radical followed by proton loss affords indoline **34**.[16] It is unlikely that the oxidation of the cyclohexadienyl radical could be occurring through the precatalyst since using 15 mol% of manganese metal in the epoxide-opening rearrangement affords only 35% of the desired indoline (Table 2, entry 5). To complete the catalytic cycle, protodemetallation by collidinium hydrochloride (Coll•HCl) leads to product **35**, and regenerates the titanocene precatalyst. Alternatively, the titanocene (III) chloride catalyst or the manganese chloride byproducts may serve as Lewis acids to promote an epoxide-opening Friedel-Crafts alkylation. However, 5-membered benzene annulations by epoxide opening under typical Friedel-Crafts conditions are quite inefficient.[17] Furthermore, it has been shown that the manganese chloride produced in the reaction is incapable of promoting Lewis acid mediated epoxide-opening rearrangements.[4c]



Scheme 5. Proposed catalytic cycle of the epoxide-opening rearrangement process.

Conclusions

We have developed a new catalytic method to prepare 3,3-disubstituted indolines and azaindolines through an epoxide-opening rearrangement catalyzed by *in situ* generated titanocene(III) chloride. Although the process does not appear to be regioselective, the target heterocycles can be prepared in good to moderate yields from readily available starting materials and do not require halogenation on the aromatic core. Control experiments indicate that the reaction is sensitive to both water and ambient air and requires the presence of both the precatalyst and a stoichiometric amount of manganese metal to promote the annulation.

Experimental Section

General. All moisture-sensitive reactions were performed under an atmosphere of dry nitrogen unless otherwise noted. All glassware was dried in an oven at >140 °C or flame-dried under an atmosphere of dry nitrogen unless otherwise noted. Diethyl ether was dried by distillation over sodium/benzophenone under an argon atmosphere. Tetrahydrofuran was dried either by distillation over sodium/benzophenone under an argon atmosphere or by distillation over $LiAlH_4$ under a nitrogen atmosphere. Dry CH_2Cl_2 and toluene were purified by filtration through an activated alumina column. Unless otherwise stated, solvents and reagents were used as purchased without further purification. Benzyl alcohol was distilled prior to use. Collidine hydrochloride

was recrystallized from absolute ethanol. Manganese and zinc metals were activated through washing with 1 M HCl, followed by rinsing with acetone and drying under vacuum. Titanocene dichloride was recrystallized from chloroform before use. Analytical thin-layer chromatography (TLC) was preformed on pre-coated silica gel 60 F_{254} plates (250 μm layer thickness). Visualization was accomplished by using either a 254 nm UV lamp or by staining with a PMA solution (5 g of phosphomolybdic acid in 100 mL of 95% EtOH), *p*-anisaldehyde solution (2.5 mL of *p*-anisaldehyde, 2 mL of AcOH, and 3.5 mL of conc. H_2SO_4 in 100 mL of 95% EtOH), Vaughn's reagent (4.8 g of $(NH_4)_6Mo_7O_{24}\cdot 4\ H_2O$ and 0.2 g of $Ce(SO_4)_2$ in 100 mL of a 3.5 N H_2SO_4) or a potassium permanganate solution (1.5 g of $KMnO_4$ and 1.5 g of K_2CO_3 in 100 mL of a 0.1% NaOH solution). NMR spectra were recorded at room temperature in $CDCl_3$ at 300 MHz/75MHz ($^1H/^{13}C$ NMR) using a Bruker Avance 300 MHz spectrometer unless stated otherwise. Chemical shifts (δ) are reported in parts per million and referenced from the residual solvent peak or tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (app s = apparent singlet, s = singlet, bs = broad singlet, d = doublet, bd = broad doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, app t = apparent triplet, bt = broad triplet, t = triplet, dt = doublet of triplets, tt = triplet of triplets, q = quartet, app quint = apparent quintet, m = multiplet), integration, and coupling constant(s). IR spectra were recorded on either a Nicolet Avatar 360 FT-IR E.S.P. spectrometer (KBr or neat) or a Smiths Detection IdentifyIR FT-IR spectrometer (ATR). Melting points were uncorrected and determined using a Laboratory Devices Mel-Temp II. Mass spectrometry data were recorded on a VG-70-70 HF instrument. Titanocene-catalyzed radical cyclization reactions were performed under rigorous exclusion of dioxygen under a positive pressure of dry argon. Tetrahydrofuran, in addition to being distilled, was deoxygenated (freeze-pump-thaw) three times and then stored under a positive pressure of dry argon prior to all titanocene(III) catalyzed annulation reactions. Sonication was accomplished with the Sonics Vibracell device (model VCX 130) equipped with a 2 mm microtip.

_N_-Allyl-_N_-phenylaniline (6).[18] General protocol A

According to a modified literature procedure,[18] a solution of 5.07 g (29.9 mmol) of diphenylamine in 45 mL of acetonitrile was treated with 8.28 g (59.9 mmol) of K_2CO_3, 5.2 mL (59.9 mmol) of allyl bromide, and 533 mg (1.49 mmol) of TBAI. This reaction mixture was heated at reflux and the disappearance of starting material was monitored by TLC (hexanes). The solution was cooled to rt, diluted with 100 mL of H_2O and extracted with 3 x 15 mL of EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on SiO_2 (hexanes) to afford 6.24 g (29.8 mmol, quant.) of **6** as a golden oil: ^1H NMR δ 7.30-7.22 (m, 4 H), 7.06-6.91 (m, 6 H), 5.93 (ddt, 1 H, J = 14.7, 9.9, 4.5 Hz), 5.26 (d, 1 H, J = 17.4 Hz) 5.15 (d, 1 H, J = 10.2 Hz), 4.40-4.34 (m, 2 H); ^{13}C NMR δ 148.0, 134.4, 129.4, 121.4, 120.9, 116.6, 54.9.

3-(Diphenylamino)propane-1,2-diol. General protocol B

To a solution of 4.86 g (23.2 mmol) of *N*-allyl-*N*-phenylaniline **6** in 75 mL of a THF/acetone/pH 7.0 phosphate buffer solution (1:1:1) was added 3.53 g (30.1 mmol) of NMO and 700 μL of OsO_4 (1 mol%, 0.33 M in toluene). The reaction mixture was stirred overnight, quenched with a sodium bisulfite solution and extracted with 3 x 20 mL of EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford a white solid which was recrystallized from hexanes/EtOAc to afford 4.85 g (19.9 mmol, 86%) of 3-(diphenylamino)propane-1,2-diol as a white solid: Mp 96-98 ºC; IR (KBr) 3297, 2927, 1589, 1497, 1323, 1070 cm^{-1}; ^{1}H NMR δ 7.28-7.22 (m, 4 H), 7.04-6.94 (m, 6 H), 4.05-3.95 (m, 1 H), 3.85-3.79 (m, 2 H), 3.73 (dd, 1 H, *J* = 10.6, 2.1 Hz), 3.55 (dd, 1 H, *J* = 11.1, 5.4 Hz), 2.62 (bs, 1 H), 2.21 (bs, 1 H); ^{13}C NMR δ 148.5, 129.6, 122.2, 121.6, 69.7, 64.4, 55.1; MS (EI) *m/z* 243 (M^+, 18), 182 (100), 167 (13), 91 (87); HRMS (EI) *m/z* calcd for $C_{15}H_{17}NO_2$ 243.1259, found 243.1260.

***N*-(Oxiran-2-ylmethyl)-*N*-phenylaniline (1a).**[19] According to a modified literature procedure,[19] a solution of 2.39 g (9.82 mmol) of 3-(diphenylamino)propane-1,2-diol in 32 mL of THF was cooled to 0 ºC and treated with 3.84 g (11.7 mmol) of *p*-Ts_2O followed by 545 mg (21.6 mmol) of NaH (95%). The reaction mixture was stirred at 0 ºC for 3 h, and an additional 1.17 g (29.4 mmol) of NaH (60% dispersion in mineral oil) was added. The solution was allowed to stir overnight at rt, cooled to 0 ºC, and quenched with H_2O. The mixture was extracted with 3 x 20 mL of EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes/EtOAc; 6:1) to afford 1.26 g (5.59 mmol, 57%) of **1a** as a colorless oil: IR (neat) 3057, 2995, 2919, 1588, 1493, 1362, 1255, 748 cm^{-1}; ^{1}H NMR δ 7.25-7.19 (m, 4 H), 7.05-7.00 (m, 4 H), 6.93 (tt, 2 H, *J* = 7.2, 0.1 Hz), 3.91 (dd, 1 H, *J* = 15.9, 3.6 Hz), 3.79 (dd, 1 H, *J* = 15.6, 4.8 Hz), 3.19-3.14 (m, 1 H), 2.70 (app t, 1 H, *J* = 4.8 Hz), 2.50 (dd, 1 H, *J* = 5.1, 2.7 Hz); ^{13}C NMR δ 148.0, 129.4, 121.7, 121.1, 53.9, 50.4, 45.9; MS (EI) *m/z* 225 (M^+, 36), 182 (100), 167 (15), 104 (23); HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO$ 225.1153, found 225.1145.

(1-Phenylindolin-3-yl)methanol (2a) and 1-phenyl-1,2,3,4-tetrahydroquinolin-3-ol (3a). General protocol C

To a 3-neck flask was added 273 mg (1.21 mmol) of **1a**, 9.0 mg (0.03 mmol) of Cp_2TiCl_2, 286 mg (1.81 mmol) of collidine hydrochloride, and 99 mg (1.81 mmol) of Mn powder. The vessel was fitted with a reflux condenser, and purged 3 times with Ar. After addition of 12.1 mL of THF (0.1 M), the reaction mixture was heated at reflux for 45 min. The color gradually changed from light orange to deep violet/blue. The mixture was cooled to rt, quenched with satd. NH_4Cl and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), and concentrated *in vacuo.* The residue was purified by chromatography on neutral alumina (hexanes:EtOAc; 3:1 to 1:3) to afford 237 mg (1.05 mmol, 87%) of **2a** and **3a** as a 3.8:1 mixture based on the integration of ^{1}H NMR peaks at 4.10 ppm for **2a** vs 3.15 ppm for **3a**.

2a. ^{1}H NMR δ 7.35-6.93 (m, 9 H), 6.75 (t, 1 H, *J* = 7.2 Hz), 4.10 (app t, 1 H, *J* = 7.8 Hz), 3.87-3.80 (m, 2 H), 3.57-3.48 (m, 1 H), 1.52 (t, 1 H, *J* = 4.2 Hz); ^{13}C NMR δ 147.5, 144.1, 131.2, 129.4, 128.3, 125.0, 121.4, 119.1, 117.9, 108.8, 65.3, 55.4, 43.0.

3a: ^{1}H NMR δ 7.35-6.67 (m, 9 H), 4.38-4.28 (m, 1 H), 3.72 (bd, 1 H, *J* = 11.1 Hz), 3.55 (ddd, 1 H, *J* = 11.7, 4.5, 1.5 Hz), 3.15 (dd, 1 H, *J* = 16.5, 4.2 Hz), 2.88 (dd, 1 H, *J* = 16.5, 4.8 Hz), 2.13 (d, 1 H, *J* = 7.8 Hz); ^{13}C NMR δ 147.4, 143.9, 130.5, 129.6, 126.8, 125.2, 124.5, 120.8, 119.0, 115.0, 64.3, 56.4, 36.2.

***N*-(2-Methylallyl)-*N*-phenylaniline.** According to General Protocol A, 4.20 g (24.8 mmol) of diphenylamine, 6.86 g (49.6 mmol) of K_2CO_3, 4.0 mL (39.7 mmol) of 3-bromo-2-methylpropene, and 1.83 g (4.96 mmol) of TBAI (reaction time 24 h) afforded 3.17 g (14.1 mmol, 57%) of *N*-(2-methylallyl)-*N*-phenylaniline as a colorless oil: IR (neat) 3061, 3035, 2912, 2849, 2358, 1938, 1589, 1495, 1363, 1228, 894, 747 cm^{-1}; ^{1}H NMR δ 7.18 (t, 4 H, *J* = 7.5 Hz), 7.00 (bd, 4 H, *J* = 8.1 Hz), 6.87 (bt, 2 H, *J* = 6.9 Hz), 4.99 (bs, 1 H), 4.86-4.86 (m, 1 H), 4.19 (s, 2 H), 1.70 (s, 3 H); ^{13}C NMR δ 148.2, 141.4, 129.3, 121.3, 120.6, 111.3, 58.4, 20.3; MS (EI) *m/z* 223 (M^+, 75), 208 (19), 182 (100), 168 (57); HRMS (EI) *m/z* calcd for $C_{16}H_{17}N$ 223.1361, found 223.1351.

3-(Diphenylamino)-2-methylpropane-1,2-diol. According to General Protocol B, 1.61 g (7.20 mmol) of *N*-(2-methylallyl)-*N*-phenylaniline, 1.26 g (10.8 mmol) of NMO and 218 μL of OsO_4 (1 mol%, 0.33 M in toluene) produced a brown solid that was recrystallized from chloroform/hexane to afford 1.55 g (6.05 mmol, 84%) of 3-(diphenylamino)-2-methylpropane-1,2-diol as a white solid: Mp 67-68 ºC; IR (KBr) 3445, 3057, 2927, 2873, 1588, 1494, 1363, 1240, 1035, 749 cm^{-1}; ^{1}H NMR (CD_2Cl_2) δ 7.35-7.20 (m, 4 H), 7.14-6.92 (m, 6 H), 3.97, 3.84 (AB, 2 H, *J* = 15.4 Hz), 3.50-3.32 (m, 2 H), 2.27 (bs, 1 H), 1.86 (dd, 1 H, *J* = 6.0, 1.2 Hz), 1.13 (s, 3 H); ^{13}C NMR (CD_2Cl_2) δ 150.1, 129.7, 122.2, 122.0, 74.6, 68.6, 59.8, 23.4; MS (EI) *m/z* 257 (M^+, 10), 182 (100), 169 (15), 104 (16); HRMS (EI) *m/z* calcd for $C_{16}H_{19}NO_2$ 257.1415, found 257.1419.

***N*-((2-Methyloxiran-2-yl)methyl)-*N*-phenylaniline (1b).** To a solution of 430 mg (1.67 mmol) of 3-(diphenylamino)-2-methylpropane-1,2-diol in 16 mL of THF at 0 ºC was added 267 mg (6.68 mmol) of NaH (60% dispersion in mineral oil). The mixture was stirred for 10 min and 597 mg (1.83 mmol) of *p*-Ts_2O dissolved in 3 mL of THF was added dropwise. The disappearance of starting material was monitored by TLC (hexanes:EtOAc; 2:1). The reaction mixture was quenched with H_2O and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes:EtOAc; 10:1) to afford 279 mg (1.16 mmol, 70%) of **1b** as a colorless oil: IR (neat) 3037, 2982, 2924, 1588, 1495, 1362, 1242, 749 cm^{-1}; ^{1}H NMR (CD_2Cl_2) δ 7.31-7.23 (m, 4 H), 7.05-6.93 (m, 6 H), 3.96, 3.90 (AB, 2 H, *J* = 16.0 Hz), 2.68 (d, 1 H, *J* = 4.8 Hz), 2.57 (d, 1 H, *J* = 4.8 Hz), 1.38 (s, 3 H); ^{13}C NMR (CD_2Cl_2) δ 148.9, 129.6, 121.8, 121.3, 57.1, 56.8, 52.4, 19.8; MS (EI) *m/z* 239 (M^+, 30), 182 (100), 167 (15), 104 (23); HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO$ 239.1310, found 239.1311.

(3-Methyl-1-phenylindolin-3-yl)methanol (2b). According to General Protocol C, 71 mg (0.29 mmol) of **1b**, 2.2 mg (0.08 mmol) of Cp_2TiCl_2, 69 mg (0.44 mmol) of collidine hydrochloride and 24 mg (0.44 mmol) of Mn powder provided a mixture (reaction time 25 min) that was purified by chromatography on neutral alumina (hexanes:EtOAc; 6:1 to EtOAc:EtOH; 5:1) to

afford 63 mg (0.26 mmol, 89%) of **2b** as a colorless oil: IR (neat) 3360, 3057, 2959, 2925, 2866, 1591, 1501, 1462, 1385, 1024, 744 cm^{-1}; ^1H NMR δ 7.32 (t, 2 H, *J* = 7.5 Hz), 7.22 (d, 1 H, *J* = 7.6 Hz), 7.15 (dt, 2 H, *J* = 1.2, 6.9 Hz), 7.10 (bt, 2 H, *J* = 6.9 Hz), 6.95 (t, 1 H, *J* = 7.2 Hz), 6.77 (t, 1 H, *J* = 6.9 Hz), 3.91, 3.66 (AB, 2 H, *J* = 9.4 Hz), 3.63 (A of ABX, 1 H, *J* = 6.0, 10.5 Hz), 3.56 (B of ABX, 1 H, *J* = 6.3, 10.5 Hz), 1.70–1.65 (m, 1 H), 1.37 (s, 3 H); ^{13}C NMR δ 146.9, 144.0, 135.6, 129.4, 128.2, 123.4, 121.2, 119.1, 117.8, 108.7, 69.1, 61.8, 45.6, 22.5; MS (EI) *m/z* 239 (M^+, 23), 208 (100), 193 (25), 130 (10); HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO$ 239.1310, found 239.1318.

Benzyl phenylcarbamate.[20] **General protocol D**

According to a modified literature procedure,[20] a solution of 2.04 g (21.9 mmol) of aniline in 50 mL of THF at 0 °C was treated with 2.02 g (24.0 mmol) of $NaHCO_3$ followed by 3.4 mL (24.0 mmol) of benzyl chloroformate. After 15, min the reaction mixture was warmed to rt, quenched with H_2O and extracted with 3 x 20 mL of EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to afford 4.97 g (21.9 mmol, quant.) of benzyl phenylcarbamate as a white solid that was used without further purification: Mp 76-77 °C; ^1H NMR δ 7.40-7.20 (m, 9 H), 7.01 (t, 1 H, *J* = 7.2 Hz), 6.94 (bs, 1 H), 5.13 (s, 2 H); ^{13}C NMR δ 153.6, 138.0, 136.2, 129.1, 128.7, 128.4, 123.6, 118.9, 67.1.

Benzyl (2-methyloxiran-2-yl)methyl(phenyl)carbamate (1c). General protocol E

To a solution of 2.91 g (12.8 mmol) of benzyl phenylcarbamate in 60 mL of THF at 0 °C was added 1.02 g (25.6 mmol) of NaH (60% dispersion in mineral oil). The reaction mixture was warmed to rt over 15 min and 2.6 mL (25.6 mmol) of 3-bromo-2-methylpropene were added. The solution was stirred overnight, quenched with H_2O and extracted with 3 x 20 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in 80 mL of dichloromethane, cooled to 0 °C and 5.67 g (23.0 mmol) of *m*-CPBA (70%) was added portionwise. The reaction mixture was quenched with aq. $Na_2S_2O_3$ solution and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1 with 1% NEt_3) to afford 3.01 g (10.1 mmol, 79%, 2 steps) of **1c** as an orange oil: IR (neat) 3520, 3036, 2934, 2360, 1706, 1597, 1494, 1405, 1273, 1147, 1020 cm^{-1}; ^1H NMR δ 7.38-7.20 (m, 10 H), 5.14 (s, 2 H), 3.95, 3.72 (AB, 2 H, *J* = 14.7 Hz), 2.50, 2.47 (AB, 2 H, *J* = 4.8 Hz), 1.36 (s, 3H); ^{13}C NMR δ 155.6, 142.2, 136.5, 129.0, 128.4, 128.0, 127.6, 127.2, 126.9, 67.5, 55.7, 55.5, 52.5, 19.4; MS (EI) *m/z* 297 (M^+, 23), 196 (71), 132 (47), 91 (100); HRMS (EI) *m/z* calcd for $C_{18}H_{19}NO_3$ 297.1364, found 297.1351.

Benzyl 3-(hydroxymethyl)-3-methylindoline-1-carboxylate (2c). A solution of 85 mg (0.28 mmol) of **1c**, 7.0 mg (0.02 mmol) of Cp_2TiCl_2, 179 mg (1.14 mmol) of collidine hydrochloride, and 23.5 mg (0.42 mmol) of Mn powder in 2.8 mL of THF was stirred for 5 h at rt, quenched with satd. NH_4Cl and extracted with 3 x 5 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to provide a residue containing **2c** and **4c** (~2:1 ratio based

on integration of the crude ^{1}H NMR peaks at 4.15 ppm (**2c**) vs 0.88 ppm (**4c**)). The mixture was partially purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1) to afford 36 mg (0.12 mmol, 42%) of **2c** in addition to 37 mg of an inseparable mixture of **2c** and **4c**.
2c: ^{1}H NMR δ 7.89 (bs, 1 H), 7.49-6.97 (m, 8 H), 5.24 (bs, 2 H), 4.12 (d, 1 H, *J* = 11.8 Hz), 3.68 (d, 1 H, *J* = 11.7 Hz), 3.61, 3.53 (AB, 2 H, *J* = 10.8 Hz), 1.70 (bs, 1 H), 1.34 (s, 3 H); MS (EI) *m/z* 297 (M^+, 28), 222 (55), 130 (40), 91 (100).
4c: ^{1}H NMR δ 7.44-7.41 (m, 10 H), 5.15, 5.11 (AB, 2 H, *J* = 12.7 Hz), 3.96 (dd, 1 H, *J* = 14.4, 9.6 Hz), 3.71-3.30 (m, 3 H), 1.86-1.70 (m, 1 H), 0.89 (d, 3 H, *J* = 6.9 Hz); MS (EI) *m/z* 299 (M^+, 10), 191 (20), 91 (100).

(3-Methylindolin-3-yl)methanol (7c). General protocol F
To a 2-neck flask was added 129 mg (0.43 mmol) of **1c**, 3.2 mg (0.01 mmol) of Cp_2TiCl_2, 102 mg (0.64 mmol) of collidine hydrochloride, and 35.6 mg (0.64 mmol) of Mn powder. The vessel was fitted with a reflux condenser and purged 3 x with argon. After addition of 4.3 mL of THF (0.1 M), the reaction mixture was placed in a preheated oil bath and heated at reflux for 3 h. During this time, the solution gradually changed from light pink to a dark violet color. The mixture was cooled to rt, quenched with satd. NH_4Cl and extracted with 3 x 10 mL of Et_2O. The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in 5 mL of MeOH and treated with 30 mg (25% w/w, 0.01 mmol) of Pd/C. The mixture was stirred at rt under 1 atm of H_2 and the disappearance of starting material was monitored by TLC (hexanes:EtOAc; 1:1). The solution was then quenched with Celite, filtered and purified by chromatography on SiO_2 (hexanes:EtOAc; 1:2) to afford 44 mg (0.26 mmol, 63%, 2 steps) of **7c** as a yellow oil: IR (neat) 3332, 2959, 2926, 2867, 1606, 1487, 1461, 1239, 1030, 747cm^{-1}; ^{1}H NMR δ 7.08-7.02 (m, 2 H), 6.73 (t, 1 H, *J* = 6.6 Hz), 6.62 (d, 1 H, *J* = 7.5 Hz), 3.59, 3.53 (AB, 2 H, *J* = 10.5 Hz), 3.55, 3.26 (AB, 2 H, *J* = 9.0 Hz), 1.31 (s, 3 H); ^{13}C NMR δ 151.7, 133.7, 128.4, 123.2, 118.9, 110.0, 69.4, 57.0, 47.7, 22.4; MS (EI) *m/z* 163 (M^+, 32), 132 (100), 117 (59); HRMS (EI) *m/z* calcd for $C_{10}H_{13}NO$ 163.0997, found 163.0993.
Ethyl phenylcarbamate.[21] According to a modified literature procedure,[21] to a solution of 5.10 g (54.7 mmol) of aniline in 130 mL of THF at 0 ºC was added 3.06 g (76.5 mmol) of NaH (60% dispersion in mineral oil) followed by 6.3 mL (65.7 mmol) of ethyl chloroformate. The reaction mixture was warmed to rt, quenched with H_2O after 3 h and extracted with 3 x 40 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes:EtOAc; 5:1 to 3:1) to afford 8.07 g (48.8 mmol, 89%) of ethyl phenylcarbamate as a brown oil: ^{1}H NMR δ 7.39-7.25 (m, 4 H), 7.05 (t, 1 H, *J* = 6.9 Hz), 6.59 (bs, 1 H), 4.22 (q, 2 H, *J* = 7.2 Hz), 1.31 (t, 3 H, *J* = 7.2 Hz); MS (EI) *m/z* 165 (M^+, 78), 119 (34), 93 (100), 65 (50).
Ethyl (2-methyloxiran-2-yl)methyl(phenyl)carbamate (1d). According to General Procedure E, 2.54 g (15.4 mmol) of ethyl phenylcarbamate, 1.23 g (30.8 mmol) of NaH (60% dispersion in mineral oil), 2.8 mL (27.7 mmol) of 3-bromo-2-methylpropene, and 5.70 g (23.1 mmol) of *m*-CPBA (70%) provided an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc;

4:1) to afford 2.66 g (11.3 mmol, 73%, 2 steps) of **1d** as a golden oil: IR (neat) 3043, 2981, 2933, 1702, 1597, 1536, 1408, 1299, 1023 cm^{-1}; ^1H NMR δ 7.35-7.18 (m, 5 H), 4.14 (q, 2 H, *J* = 6.9 Hz), 3.93 (A of ABX, 1 H, *J* = 14.7, 0.6 Hz), 3.71 (B of ABX, 1 H, *J* = 14.7, 0.9 Hz), 2.51 (bs, 2 H), 1.37 (s, 3 H), 1.19 (t, 3 H, *J* = 6.9 Hz); ^{13}C NMR δ 155.8, 142.4, 128.9, 127.1, 126.6, 61.9, 55.7, 55.3, 52.5, 19.4, 14.5; MS (EI) *m/z* 235 (M^+, 45), 178 (38), 134 (28), 106 (100); HRMS (EI) *m/z* calcd for $C_{13}H_{17}NO_3$ 235.1208, found 235.1219.

Ethyl 3-(hydroxymethyl)-3-methylindoline-1-carboxylate (2d). According to General Protocol C, 125 mg (0.53 mmol) of **1d**, 3.9 mg (0.01 mmol) of Cp_2TiCl_2, 125 mg (0.79 mmol) of collidine hydrochloride, and 43 mg (0.79 mmol) of Mn powder provided a mixture (reaction time 2 h) that was purified by chromatography on SiO_2 (hexanes:EtOAc; 3:1) to afford 81 mg (0.34 mmol, 65%) of **2d** as an oil: IR (neat) 3433, 2976, 2931, 1693, 1600, 1487, 1413, 1051cm^{-1}; ^1H NMR δ 7.85 (bs, 1 H), 7.24 (t, 1 H, *J* = 6.9 Hz), 7.11 (d, 1 H, *J* = 6.9 Hz), 6.98 (t, 1 H, *J* = 7.2 Hz), 4.26 (bs, 2 H), 4.07 (d, 1 H, *J* = 11.4 Hz), 3.64 (d, 1 H, *J* = 11.4 Hz), 3.61 (dd, 1 H, *J* = 11.4, 4.5 Hz), 3.52 (dd, 1 H, *J* = 10.5, 6.6 Hz), 1.97 (bs, 1 H), 1.34 (bs, 6 H); ^{13}C NMR δ 153.6, 142.9, 135.8, 128.6, 123.0, 122.8, 115.1, 69.7, 61.7, 57.7, 45.4, 23.2, 14.8; MS (EI) *m/z* 235 (M^+, 31), 204 (100), 160 (27), 130 (71), 117 (55); HRMS (EI) *m/z* calcd for $C_{13}H_{17}NO_3$ 235.1208, found 235.1202.

Benzyl *p*-tolylcarbamate.[20b] According to General Protocol D, 4.15 g (38.7 mmol) of *p*-toluidine, 3.57 g (42.6 mmol) of $NaHCO_3$, and 6.0 mL (42.6 mmol) of benzyl chloroformate (reaction time 30 min) afforded a solid that was recrystallized from chloroform/hexane to afford 8.12 g (33.6 mmol, 87%) of benzyl *p*-tolylcarbamate as white needles: Mp 82-84 °C; IR (KBr) 3319, 3195, 3032, 2943, 1730, 1707, 1602, 1543, 1406, 1232, 1067, 739 cm^{-1}; ^1H NMR δ 7.39-7.20 (m, 7 H), 7.06 (d, 2 H, *J* = 8.4 Hz), 6.72 (bs, 1 H), 5.15 (s, 2 H), 2.27 (s, 3 H); ^{13}C NMR δ 153.7, 136.3, 135.4, 133.2, 129.7, 128.7, 128.4, 119.1, 67.1, 20.9; MS (EI) *m/z* 241 (M^+, 49), 197 (45), 133 (34), 91 (100), 84 (91); HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO_2$ 241.1102, found 241.1106.

Benzyl (2-methyloxiran-2-yl)methyl(*p*-tolyl)carbamate (8a). According to General Protocol E, 4.42 g (18.3 mmol) of benzyl *p*-tolylcarbamate, 1.46 g (36.6 mmol) of NaH (60% dispersion in mineral oil), 2.8 mL (27.4 mmol) of 3-bromo-2-methylpropene, and 6.76 g (27.4 mmol) of *m*-CPBA (70%) provided an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1) to afford 4.43 g (14.2 mmol, 78%, 2 steps) of **8a** as a red oil: IR (neat) 3583, 3033, 2929, 1702, 1514, 1404, 1271, 1146 cm^{-1}; ^1H NMR δ 7.33-7.24 (m, 5 H), 7.16-7.09 (m, 4 H), 5.14 (bs, 2 H), 3.91, 3.69 (AB, 2 H, *J* = 14.7 Hz), 2.50, 2.47 (AB, 2 H, *J* = 4.6 Hz), 2.33 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR δ 155.9, 139.7, 136.8, 136.7, 129.8, 128.6, 128.1, 127.8, 127.1, 67.6, 55.9, 55.8, 52.7, 21.2, 19.5; MS (EI) *m/z* 311 (M^+, 35), 210 (46), 146 (48), 91 (95), 84 (100); HRMS (EI) *m/z* calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1525.

(3,5-Dimethylindolin-3-yl)methanol (9a). According to General Protocol F, 163 mg (0.52 mmol) of **11**, 3.9 mg (0.01 mmol) of Cp_2TiCl_2, 123 mg (0.78 mmol) of collidine hydrochloride, and 43 mg (0.78 mmol) of Mn powder provided an oil (reaction time 3 h) that was purified first by chromatography on neutral alumina (hexanes:EtOAc; 2:1) and then subjected to 111 mg (70%

w/w, 0.05 mmol) of Pd/C under 1 atm of H_2 (reaction time 2 h) to provide an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 1:1 with 1% NEt_3) to afford 57 mg (0.32 mmol, 62%, 2 steps) of **9a** as an oil: IR (neat) 3327, 2958, 2922, 2864, 1614, 1495, 1463, 1238, 1033, 810 cm^{-1}; ^1H NMR δ 6.87-6.85 (m, 2 H), 6.56-6.53 (m, 1 H), 3.58, 3.51 (AB, 2 H, *J* = 10.6 Hz), 3.53, 3.22 (AB, 2 H, *J* = 9.1 Hz), 2.25 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR δ 149.3, 134.1, 128.7, 128.4, 123.8, 110.1, 69.4, 57.3, 47.7, 22.3, 21.0; MS (EI) *m/z* 177 (M^+, 45), 146 (100), 131 (69), 130 (38); HRMS (EI) *m/z* calcd for $C_{11}H_{15}NO$ 177.1153, found 177.1154.

Benzyl *o*-tolylcarbamate. According to General Protocol D, 3.81 g (35.5 mmol) of *o*-toluidine, 3.28 g (39.1 mmol) of $NaHCO_3$, and 5.5 mL (39.1 mmol) of benzyl chloroformate (reaction time 1 h) provided a solid that was recrystallized from Et_2O to afford 7.41 g (30.7 mmol, 86%) of benzyl *o*-tolylcarbamate as a white solid: Mp 83-84 ºC; IR (KBr) 3297, 3036, 2959, 1695, 1588, 1533, 1454, 1294, 1240, 1064 cm^{-1}; ^1H NMR (DMSO-d_6, 350 K) δ 8.64 (bs, 1 H), 7.47-7.30 (m, 6 H), 7.20-7.09 (m, 3 H), 5.16 (s, 2 H), 2.33 (s, 3 H); ^{13}C NMR (DMSO-d_6, 350 K) δ 153.9, 136.6, 136.0, 131.3, 129.8, 127.9, 127.3, 127.2, 125.5, 124.4, 124.2, 65.3, 17.1; MS (EI) *m/z* 241 (M^+, 13), 197 (13), 133 (18), 104 (16), 91 (100); HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO_2$ 241.1102, found 241.1107.

Benzyl (2-methyloxiran-2-yl)methyl(*o*-tolyl)carbamate (8b). According to General Protocol E, 3.60 g (14.9 mmol) of benzyl *o*-tolylcarbamate, 1.19 g (29.8 mmol) of NaH (60% dispersion in mineral oil), 2.2 mL (22.3 mmol) of 3-bromo-2-methylpropene, and 5.51 g (22.3 mmol) of *m*-CPBA (70%) provided an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1) to afford 3.88 g (12.4 mmol, 84%, 2 steps) of **8b** as an oil: IR (neat) 3033, 2931, 1708, 1583, 1493, 1406, 1299, 1147, 1028 cm^{-1}; ^1H NMR (DMSO-d_6, 350 K) δ 7.34-7.20 (m, 9 H), 5.09 (s, 2 H), 4.10-3.20 (br m, 2 H), 2.50, 2.41 (AB, 2 H, *J* = 4.7 Hz), 2.13 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR (DMSO-d_6, 350 K) δ 154.6, 140.7, 136.3, 134.9, 130.2, 127.9, 127.8, 127.3, 126.9, 126.8, 126.0, 66.3, 54.7, 51.2, 18.9, 16.6; MS (EI) *m/z* 311 (M^+, 15), 210 (8), 118 (25), 91 (100); HRMS (EI) *m/z* calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1527.

(3,7-Dimethylindolin-3-yl)methanol (9b). According to General Protocol F, 230 mg (0.73 mmol) of **13**, 7.3 mg (0.02 mmol) of Cp_2TiCl_2, 174 mg (1.10 mmol) of collidine hydrochloride, and 60 mg (1.10 mmol) of Mn powder (reaction time 5 h) provided an oil that was purified by chromatography on neutral alumina (hexanes:EtOAc; 4:1) and then subjected to 10 mg (10% w/w, 4.6 μmol) of Pd/C under 1 atm of H_2 to provide a mixture that was purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1 with 1% NEt_3) to afford 46 mg (0.25 mmol, 35%, 2 steps) of **9b** as an oil: IR (neat) 3317, 2960, 2926, 2867, 1599, 1478, 1030, 749 cm^{-1}; ^1H NMR δ 6.91 (d, 2 H, *J* = 7.5 Hz), 6.69 (t, 1 H, *J* = 7.5 Hz), 3.61, 3.54 (AB, 2 H, *J* = 10.5 Hz), 3.60 (d, 1 H, *J* = 9.3 Hz), 3.29 (d, 1 H, *J* = 9.3 Hz), 2.12 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR δ 150.1, 133.0, 129.3, 120.6, 119.5, 119.2, 69.4, 56.9, 48.0, 22.6, 16.9; MS (EI) *m/z* 177 (M^+, 14), 146 (100), 131 (35); HRMS (EI) *m/z* calcd for $C_{11}H_{15}NO$ 177.1153, found 177.1154.

Benzyl 4-methoxyphenylcarbamate.[22] According to General Protocol D, 4.08 g (33.1 mmol) of *p*-anisidine, 3.06 g (36.4 mmol) of $NaHCO_3$, and 5.2 mL (36.4 mmol) of benzyl chloroformate (reaction time 30 min) provided a solid that was recrystallized (chloroform/hexane; 1:10) to

afford 7.65 g (29.7 mmol, 90%) of benzyl 4-methoxyphenylcarbamate as a pink solid: Mp 98 ºC; IR (KBr) 3299, 3042, 2842, 1701, 1532, 1415, 1238, 1065, 1029, 825, 743 cm^{-1}; ^1H NMR δ 7.42-7.24 (m, 7 H), 6.86-6.81 (m, 2 H), 6.59 (bs, 1 H), 5.17 (s, 2 H), 3.77 (s, 3 H); ^{13}C NMR δ 156.3, 153.9, 136.4, 131.0, 128.8, 128.5, 121.0, 114.5, 67.1, 55.7; MS (EI) *m/z* 257 (M^+, 11), 213 (7), 122 (32), 91 (100), 65 (50); HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO_3$ 257.1051, found 257.1047.

Benzyl 4-methoxyphenyl((2-methyloxiran-2-yl)methyl)carbamate (8c). According to General Protocol E, 4.21 g (16.3 mmol) of benzyl 4-methoxyphenylcarbamate, 1.30 g (32.7 mmol) of NaH (60% dispersion in mineral oil), 2.5 mL (24.5 mmol) of 3-bromo-2-methylpropene, and 6.04 g (24.5 mmol) of *m*-CPBA (70%) provided an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1) to afford 4.34 g (13.2 mmol, 81%, 2 steps) of **8c** as an oil: IR (neat) 3520, 3037, 2935, 2837, 1701, 1609, 1585, 1512, 1444, 1428, 1294 cm^{-1}; ^1H NMR δ 7.32-7.12 (m, 7 H), 6.83 (d, 2 H, *J* = 12.3 Hz), 5.12 (bs, 2 H), 3.89, 3.65 (AB, 2 H, *J* = 14.7 Hz), 3.74 (s, 3 H), 2.47, 2.45 (AB, 2 H, *J* = 4.3 Hz), 1.34 (s, 3 H); ^{13}C NMR δ 158.2, 155.9, 136.6, 135.0, 128.4, 127.9, 127.5, 114.2, 67.4, 55.8, 55.6, 55.4, 52.4, 19.3; MS (EI) *m/z* 327 (M^+, 23), 192 (15), 146 (23), 91 (81), 84 (100); HRMS (EI) *m/z* calcd for $C_{19}H_{21}NO_4$ 327.1470, found 327.1471.

(5-Methoxy-3-methylindolin-3-yl)methanol (9c). According to General Protocol F, 236 mg (0.72 mmol) of **8c**, 7.1 mg (0.02 mmol) of Cp_2TiCl_2, 170 mg (1.08 mmol) of collidine hydrochloride, and 59 mg (1.08 mmol) of Mn powder afforded an oil (reaction time 3 h) that was subjected to 46 mg (20% w/w, 0.02 mmol) of Pd/C and 1 atm of H_2 to provide an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 1:1) to afford 28 mg (0.14 mmol, 21%, 2 steps) of **9c** as a purple oil: IR (neat) 3339, 2920, 2866, 1596, 1490, 1434, 1280, 1022 cm^{-1}; ^1H NMR δ 6.68-6.57 (m, 3 H), 3.74 (s, 3 H), 3.61, 3.54 (AB, 2 H, *J* = 10.8 Hz), 3.55, 3.25 (AB, 2 H, *J* = 9.3 Hz), 2.64 (bs, 2 H), 1.31 (s, 3 H); ^{13}C NMR δ 154.0, 145.3, 135.8, 113.1, 110.9, 110.2, 69.3, 57.6, 56.2, 48.2, 22.2; MS (EI) *m/z* 193 (M^+, 35), 162 (100), 147 (42), 118 (18); HRMS (EI) *m/z* calcd for $C_{11}H_{15}NO_2$ 193.1102, found 193.1103.

Methyl 4-(benzyloxycarbonylamino)benzoate. According to General Protocol D, 3.80 g (25.1 mmol) of methyl 4-aminobenzoate, 2.32 g (27.6 mmol) of $NaHCO_3$, and 3.9 mL (27.6 mmol) of benzyl chloroformate (reaction time 1 h) provided a solid that was recrystallized (chloroform/hexane; 1:10) to afford 6.47 g (22.6 mmol, 90%) of methyl 4-(benzyloxycarbonylamino)benzoate as a white solid: Mp 137-139 ºC; IR (KBr) 3311, 3117, 2956, 1729, 1694, 1602, 1537, 1451, 1323, 1221, 1042 cm^{-1}; ^1H NMR δ 7.98 (d, 2 H, *J* = 8.7 Hz), 7.45 (d, 2 H, *J* = 8.7 Hz), 7.42-7.31 (m, 5 H), 6.99 (bs, 1 H), 5.20 (s, 2 H), 3.88 (s, 3 H); ^{13}C NMR δ 166.9, 153.1, 142.3, 135.9, 131.1, 128.9, 128.7, 128.6, 125.1, 117.8, 67.5, 52.2; MS (EI) *m/z* 285 (M^+, 38), 241 (43), 177 (77), 146 (88), 91 (100); HRMS (EI) *m/z* calcd for $C_{16}H_{15}NO_4$ 285.1001, found 285.0999.

Methyl 4-((benzyloxycarbonyl)((2-methyloxiran-2-yl)methyl)amino)benzoate (8d). To a solution of 1.96 g (6.87 mmol) of methyl 4-(benzyloxycarbonylamino)benzoate in 20 mL of DMF at rt was added 190 mg (7.55 mmol) of NaH (95% dispersion in mineral oil). The reaction mixture was stirred until H_2 evolution ceased, then 900 μL (8.93 mmol) of 3-bromo-2-

methylpropene was added. The mixture was stirred overnight at rt, quenched with H_2O, poured onto ice and extracted with 3 x 20 mL of dichloromethane. The combined organic layers were washed with 50 mL of H_2O, dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was dissolved in 60 mL of dichloromethane, cooled to 0 ^{0}C and treated batchwise with 2.03 g (8.24 mmol) of *m*-CPBA (70%). The disappearance of starting material was monitored by TLC (hexanes:EtOAc; 2:1). The reaction mixture was quenched with aq. $Na_2S_2O_3$ solution and extracted with 3 x 15 mL of dichloromethane. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes:EtOAc; 5:1 to 3:1) to afford 2.06 g (5.79 mmol, 84%, 2 steps) of **8d** as an oil: IR (neat) 3522, 3033, 2952, 1709, 1605, 1436, 1279, 1109, 1015, 773 cm^{-1}; ^{1}H NMR δ 8.01 (d, 2 H, *J* = 8.7 Hz), 7.37-7.25 (m, 7 H), 5.17 (s, 2 H), 3.92, 3.85 (AB, 2 H, *J* = 14.8 Hz), 3.89 (s, 3 H), 2.51 (appt. s, 2 H), 1.34 (s, 3 H); ^{13}C NMR δ 166.5, 155.2, 146.5, 136.1, 130.5, 128.6, 128.3, 128.2, 128.0, 126.6, 68.0, 55.9, 55.0, 52.3, 52.2, 19.4; MS (EI) *m/z* 355 (M^+, 62), 324 (30), 254 (55), 132 (49), 91 (100); HRMS (EI) *m/z* calcd for $C_{20}H_{21}NO_5$ 355.1419, found 355.1415.

Methyl 3-(hydroxymethyl)-3-methylindoline-5-carboxylate (9d). According to General Protocol F, 206 mg (0.57 mmol) of **8d**, 4.3 mg (0.01 mmol) of Cp_2TiCl_2, 136 mg (0.86 mmol) of collidine hydrochloride, and 47 mg (0.86 mmol) of Mn powder (reaction time 5 h) provided an intermediate that was purified by chromatography on SiO_2 (hexanes:EtOAc; 5:1). The oily intermediate was subjected to 20 mg (10% w/w, 9.3 μmol) of Pd/C and 1 atm of H_2, and the reaction mixture was purified by chromatography on SiO_2 (hexanes:EtOAc; 1:1 with 1% NEt_3) to afford 72 mg (0.32 mmol, 56%, 2 steps) of **9d** as an oil: IR (neat) 3368, 2952, 2868, 1687, 1610, 1502, 1293, 1253, 1110 cm^{-1}; ^{1}H NMR δ 7.78 (dd, 1 H, *J* = 8.4, 1.8 Hz), 7.68 (d, 1 H, *J* = 1.8 Hz), 6.53 (d, 1 H, *J* = 8.4 Hz), 4.21 (bs, 1 H), 3.83 (s, 3 H), 3.69 (d, 1 H, *J* = 9.1 Hz), 3.64, 3.54 (AB, 2 H, *J* = 10.8 Hz), 3.34 (d, 1 H, *J* = 9.1 Hz), 2.02 (bs, 1 H), 1.33 (s, 3 H); ^{13}C NMR δ 167.6, 155.8, 133.2, 131.7, 124.9, 119.6, 107.8, 69.1, 57.0, 51.8, 47.1, 22.8; MS (EI) *m/z* 221 (M^+, 23), 190 (81), 158 (100), 130 (68); HRMS (EI) *m/z* calcd for $C_{12}H_{15}NO_3$ 221.1051, found 221.1053.

Benzyl 4-chlorophenylcarbamate. According to General Protocol D, 3.81 g (29.8 mmol) of *p*-chloroaniline, 2.57 g (32.8 mmol) of $NaHCO_3$, and 4.6 mL (32.8 mmol) of benzyl chloroformate provided a solid that was recrystallized (chloroform:hexanes; 1:10) to afford 6.57 g (25.1 mmol, 84%) of benzyl 4-chlorophenylcarbamate as pink needles: Mp 109-111 ^{0}C; IR (KBr) 3320, 3112, 3037, 2954, 1707, 1594, 1528, 1403, 1237, 1065, 822, 737 cm^{-1}; ^{1}H NMR δ 7.41-7.23 (m, 9 H), 6.70 (bs, 1 H), 5.18 (s, 2 H); ^{13}C NMR δ 153.4, 136.6, 136.0, 129.3, 128.9, 128.8, 128.7, 128.5, 120.1, 67.4; MS (EI) *m/z* 261 (M^+, 20), 217 (15), 153 (79), 91 (100); HRMS (EI) *m/z* calcd for $C_{14}H_{12}ClNO_2$ 261.0556, found 261.0561.

Benzyl 4-chlorophenyl((2-methyloxiran-2-yl)methyl)carbamate (8e). According to General Protocol E, 3.96 g (15.1 mmol) of benzyl 4-chlorophenylcarbamate, 1.21 g (30.2 mmol) of NaH (60% dispersion in mineral oil), 2.3 mL (22.6 mmol) of 3-bromo-2-methylpropene, and 5.58 g (22.6 mmol) of *m*-CPBA (70%) provided an oil that was purified by chromatography on SiO_2 (hexanes:EtOAc; 4:1) to afford 3.96 g (11.9 mmol, 79%, 2 steps) of **8e** as an orange solid: Mp

58-60 °C; IR (KBr) 3319, 3400, 3036, 2968, 2279, 1702, 1412, 1263, 1148, 1090, 1011, 837, 734 cm^{-1}; ^1H NMR δ 7.32-7.16 (m, 9 H), 5.14 (s, 2 H), 3.86, 3.75 (AB, 2 H, *J* = 14.8 Hz), 2.51, 2.50 (AB, 2 H, *J* = 4.9 Hz), 1.34 (s, 3 H); ^{13}C NMR δ 155.5, 140.9, 136.3, 132.5, 129.2, 128.6, 128.5, 128.3, 127.9, 67.8, 55.8, 55.4, 52.3, 19.4; MS (EI) *m/z* 331 (M^+, 33), 230 (46), 111 (42), 91 (100), 84 (94); HRMS (EI) *m/z* calcd for $C_{18}H_{18}ClNO_3$ 331.0975, found 331.0975.

Benzyl 5-chloro-3-(hydroxymethyl)-3-methylindoline-1-carboxylate (9e). According to General Protocol C, 318 mg (0.95 mmol) of **8e**, 7.1 mg (0.02 mmol) of Cp_2TiCl_2, 226 mg (1.43 mmol) of collidine hydrochloride, and 79 mg (1.43 mmol) of Mn powder (reaction time 4 h) provided a mixture that was purified by chromatography on SiO_2 (hexanes:EtOAc; 5:1 to 3:1) to afford 130 mg (0.39 mmol, 41%) of **9e** as an oil: IR (neat) 3435, 2959, 1706, 1597, 1485, 1401, 1334, 1075 cm^{-1}; ^1H NMR (DMSO-*d*$_6$, 350 K) δ 7.64 (d, 1 H, *J* = 8.4 Hz), 7.46-7.29 (m, 5 H), 7.23 (d, 1 H, *J* = 2.1 Hz), 7.19 (dd, 1 H, *J* = 8.7, 2.4 Hz), 5.24 (s, 2 H), 4.71 (bs, 1 H), 4.06 (d, 1 H, *J* = 11.1 Hz), 3.64 (d, 1 H, *J* = 11.1 Hz), 3.45, 3.42 (AB, 2 H, *J* = 10.5 Hz), 1.27 (s, 3 H); ^{13}C NMR (DMSO-*d*$_6$, 350 K) δ 151.9, 140.5, 139.5, 136.0, 127.9, 127.5, 127.2, 126.9, 126.0, 123.1, 114.7, 67.3, 66.3, 57.2, 44.7, 22.6; MS (EI) *m/z* 331 (M^+, 40), 256 (14), 91 (100); HRMS (ESI) *m/z* calcd for $C_{18}H_{18}ClNO_3Na$ (M+Na) 354.0873, found 354.0851.

3-(*tert*-Butyldimethylsilyloxy)aniline. To a solution of 5.78 g (53.0 mmol) of 3-aminophenol (**10**) in 200 mL of THF was added 5.77 g (84.8 mmol) of imidazole, followed by 10.38 g (68.86 mmol) of TBSCl. The reaction mixture was stirred at rt overnight, quenched with 50 mL of satd. NH_4Cl, extracted with 3 x 50 mL of Et_2O, washed with brine, dried ($MgSO_4$), concentrated, and purified on SiO_2 (hexanes:EtOAc; 15:1 to 5:1 gradient) to afford 11.06 g (49.50 mmol, 93%) of 3-(*tert*-butyldimethylsilyloxy)aniline as a tan oil: ^1H NMR (600 MHz) δ 6.99 (t, 1 H, *J* = 8.4 Hz), 6.30 (dd, 1 H, *J* = 7.8 Hz, 1.8 Hz), 6.25 (dd, 1 H, *J* = 7.8 Hz, 1.8 Hz), 6.20 (app t, 1 H, *J* = 1.8 Hz), 3.62 (br s, 2 H), 0.97 (s, 9 H), 0.19 (s, 6 H); ^{13}C NMR (150 MHz) δ 156.9, 147.8, 130.1, 110.7, 108.7, 107.4, 25.9, 18.4, -4.2).

Ethyl 3-(*tert*-butyldimethylsilyloxy)phenylcarbamate (11). To a solution of 6.51 g (29.1 mmol) of 3-(*tert*-butyldimethylsilyloxy)aniline in 150 mL of dichloromethane cooled to 0 °C was added 3.9 mL of pyridine, followed by 2.9 mL (31 mmol) of ethylchloroformate dropwise over 1 h. The reaction mixture was allowed to warm to rt, stirred for 1 h, and then quenched with 60 mL of satd. NH_4Cl, diluted with 60 mL of H_2O, extracted with 2 x 20 mL of dichloromethane, dried ($MgSO_4$), concentrated, and purified on SiO_2 (hexanes:EtOAc; 10:1) to afford 8.34 g (28.22 mmol, 97%) of **11** as a golden oil: IR (ATR) 3321, 2957, 2930, 2859, 1704, 1596, 1540, 1220, 1063 cm^{-1}; ^1H NMR (600 MHz) δ 7.12 (t, 1 H, *J* = 7.8 Hz), 7.04 (br s, 1 H), 6.88 (br d, 1 H, *J* = 7.8 Hz), 6.67 (br s, 1 H), 6.54 (dd, 1 H, *J* = 8.1 Hz, 2.4 Hz), 4.21 (q, 2 H, *J* = 6.6 Hz), 1.29 (t, 3 H, *J* = 7.2 Hz), 0.97 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (150 MHz) δ 156.5, 153.7, 139.3, 129.8, 115.2, 111.7, 110.8, 61.3, 25.9, 18.4, 14.7, -4.3; MS (ESI) *m/z* 318 ($[M+Na]^+$).

Ethyl 3-(*tert*-butyldimethylsilyloxy)phenyl(2-methylallyl)carbamate. To a solution of 6.09 g (20.6 mmol) of **11** in 100 mL of distilled THF cooled to 0 °C was added 380 mg (1.03 mmol) of TBAI, followed by 937 mg (37.1 mmol) of NaH 95% (added piecewise). The reaction mixture was stirred at 0 °C for 20 min when 3.1 mL (31 mmol) of methallyl bromide was added. Upon

addition of the methallyl bromide, the flask was removed from the ice bath and the mixture was stirred for a total of 3 h when TLC (hexanes:EtOAc; 4:1) analysis showed the starting material was consumed. The mixture was then cooled to 0 °C, quenched with 10 mL of H_2O, extracted with 3 x 10 mL of Et_2O, washed with 10 mL of brine, dried (Na_2SO_4), concentrated and purified on SiO_2 (hexanes:EtOAc; 12:1) to afford 4.96 g (14.19 mmol, 69%) of ethyl 3-(*tert*-butyldimethylsilyloxy)phenyl(2-methylallyl)carbamate as a tan oil: IR (ATR) 2931, 1703, 1597, 1488, 1252, 1193 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 7.20 (t, 1 H, *J* = 7.8 Hz), 6.88 (dd, 1 H, *J* = 7.8 Hz, *J* = 1.2 Hz), 6.74 (s, 1 H), 6.68 (dd, 1 H, *J* = 7.8 Hz, *J* = 1.8 Hz), 4.79 (s, 1 H), 4.70 (s, 1 H), 4.18 (s, 1 H), 4.07 (q, 2 H, *J* = 7.2 Hz), 1.66 (s, 3 H), 1.14 (t, 3 H, *J* = 6.6 Hz), 0.93 (s, 9 H), 0.17 (s, 6 H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 155.0, 154.6, 142.8, 141.2, 129.3, 119.0, 118.0, 117.4, 111.6, 61.2, 55.0, 25.5, 19.8, 18.0, 14.4, -4.6; MS (ESI) *m/z* 372 ($[M+Na]^+$).

Ethyl 3-(*tert*-butyldimethylsilyloxy)phenyl((2-methyloxiran-2-yl)methyl)carbamate (12). To a 0 °C solution of 388 mg (1.11 mmol) of ethyl 3-(*tert*-butyldimethylsilyloxy)phenyl(2-methylallyl)carbamate in 5 mL of dichloromethane and 235 mg (2.22 mmol) of Na_2CO_3 in 2 mL of water was added 410 mg (1.67 mmol) of *m*-CPBA (70% purity). The mixture was allowed to warm from 0 °C to 10 °C over 2 h when the flask was removed from the cold bath and allowed to warm to 23 °C. At this time, an additional 273 mg of *m*-CPBA was added. After 30 min, the reaction was determined to be complete by TLC analysis (hexanes:EtOAc; 2:1) and was quenched with 15 mL of $Na_2S_2O_3$ solution, extracted with 3 x 10 mL of $CHCl_3$, dried ($MgSO_4$), concentrated, and purified on SiO_2 (hexanes:EtOAc; 10:1 to 6:1 gradient) to afford 236 mg (0.65 mmol, 58%) of **12** as a light yellow oil: IR (ATR) 2931, 2859, 1703, 1597, 1488, 1260, 954 cm^{-1}; ^1H NMR (600 MHz) δ 7.19 (t, 1 H, *J* = 7.8 Hz), 6.84 (d, 1 H, *J* = 7.8 Hz), 6.74-6.72 (m, 2 H), 4.16 (q, 2 H, *J* = 7.2 Hz), 3.99 (d, 1 H, *J* = 14.4 Hz), 3.61 (d, 1 H, *J* = 14.4 Hz), 2.54 (A of AB, 1 H, *J* = 4.8 Hz), 2.52 (B of AB, 1 H, *J* = 4.8 Hz), 1.38 (s, 3 H), 1.21 (bs, 3 H), 0.98 (s, 9 H), 0.20 (s, 6 H); ^{13}C NMR (150 MHz) δ 156.2, 156.0, 143.5, 129.6, 120.0, 119.5, 118.8, 62.1, 55.9, 55.6, 53.0, 25.9, 19.6, 18.4, 14.8, -4.2; MS (EI) *m/z* 365 (M^+, 77), 280 (55), 238 (67), 220 (100), 192 (97), 178 (65); HRMS (EI) *m/z* calcd for $C_{19}H_{31}NO_4Si$ 365.2022, found 365.2033.

(6-(*tert*-Butyldimethylsilyloxy)-1,3-dimethylindolin-3-yl)methanol (15). A mixture of 178 mg (0.486 mmol) of **12**, 115 mg (0.730 mmol) of coll-HCl, 40 mg (0.73 mmol) of Mn powder, and 3.6 mg (0.015 mmol) of Cp_2TiCl_2 was purged with argon 3 times, dissolved in 5.0 mL of distilled, degassed THF, and heated at reflux. After 4 h, the solution was allowed to cool to room temperature and was quenched with 10 mL of satd. NH_4Cl, extracted with 3 x 10 mL of EtOAc, washed with 10 mL of brine, dried (Na_2SO_4), concentrated, and purified on neutral alumina (hexanes:EtOAc; 10:1 to 1:1 gradient) to afford 53 mg (0.14 mmol, 30%) of **13**. To a solution of 53 mg (0.14 mmol) of **13** in 3 mL of dry THF cooled to 0 °C was added 28 mg (0.72 mmol) of $LiAlH_4$. Upon addition, the mixture was stirred until no gas evolution was observed and then heated at reflux. TLC analysis (hexanes:EtOAc; 1:1) after 50 min showed that the starting material was consumed. The solution was cooled to 0 °C, quenched with MeOH, diluted with 5 mL of H_2O, saturated with potassium sodium tartrate, and diluted with 5 mL of EtOAc. The solution was stirred until biphasic when it was partitioned and extracted with 3 x 5 mL of EtOAc.

The combined organic extracts were washed with 5 mL of brine, dried (Na_2SO_4), concentrated, and purified by chromatography on SiO_2 (hexanes:EtOAc; 2:1) to afford 38 mg (0.12 mmol, 85%) of **15** as a colorless oil: IR (ATR) 3373, 2956, 1612, 1497, 1253, 985 cm^{-1}; ^1H NMR (600 MHz) δ 6.81 (d, 1 H, *J* = 7.8 Hz), 6.15 (dd, 1 H, *J* = 7.8 Hz, 1.8 Hz), 5.98 (d, 1 H, *J* = 1.8 Hz), 3.56 (A of AB, 1 H, *J* = 10.8 Hz), 3.51 (B of AB, 1 H, *J* = 10.8 Hz), 3.40 (d, 1 H, *J* = 9.0 Hz), 2.98 (d, 1 H, *J* = 9.0 Hz), 2.70 (s, 3 H), 1.65 (bs, 1 H), 1.28 (s, 3 H), 0.98 (s, 9 H), 0.19 (s, 6 H); ^{13}C NMR (150 MHz) δ 156.8, 154.6, 127.1, 122.8, 108.8, 100.4, 69.4, 66.0, 45.7, 35.9, 25.9, 22.3, 18.4, -4.2; MS (EI) *m/z* 307 (M^+, 40), 276 (100), 204 (20), 73 (24); HRMS (EI) *m/z* calcd for $C_{17}H_{29}NO_2Si$ 307.1968, found 307.1960.

3-(Hydroxymethyl)-1,3-dimethylindolin-4-ol (16). A mixture of 178 mg (0.486 mmol) of **12**, 115 mg (0.730 mmol) of coll-HCl, 40 mg (0.73 mmol) of Mn powder, and 3.6 mg (0.015 mmol) of Cp_2TiCl_2 was purged with argon 3 times, dissolved in 5.0 mL of distilled, degassed THF, and heated at reflux. After 4 h, the reaction mixture was allowed to cool to room temperature and quenched with 10 mL of satd. NH_4Cl, extracted with 3 x 10 mL of EtOAc, washed with 10 mL of brine, dried (Na_2SO_4), concentrated, and purified by chromatography on neutral alumina (hexanes:EtOAc; 10:1 to 1:1 gradient) to afford 59 mg (0.16 mmol, 33%) of **14**. To a solution of 59 mg (0.16 mmol) of **14** in 3 mL of dry THF cooled to 0 °C was added 31 mg (0.81 mmol) of $LiAlH_4$. Upon addition and after visible gas evolution had ceased, the mixture was heated at reflux. TLC analysis (hexanes:EtOAc; 1:1) after 50 min showed that starting material was consumed. The mixture was cooled to 0 °C and then quenched dropwise with MeOH until no further gas evolution was observed. To this solution was added 2 mL of a satd. potassium sodium tartrate followed by 5 mL of EtOAc. The mixture was extracted with 3 x 5 mL of EtOAc, dried (Na_2SO_4), concentrated and purified by chromatography on SiO_2 (hexanes:EtOAc; 2:1) to afford 24 mg (0.12 mmol, 77%, (25% over 2 steps) of **16** as a tan waxy solid: IR (ATR) 3206, 2959, 1617, 1595, 1477, 1246, 903 cm^{-1}; ^1H NMR (600 MHz) δ 8.33 (bs, 1 H), 7.01 (t, 1 H, *J* = 7.8 Hz), 6.28 (d, 1 H, *J* = 8.4 Hz), 6.07 (d, 1 H, *J* = 7.8 Hz), 3.90 (d, 1 H, *J* = 9.6 Hz), 3.75 (d, 1 H, *J* = 9.6 Hz), 3.09 (d, 1 H, *J* = 9.0 Hz), 2.88 (d, 1 H, *J* = 8.4 Hz), 2.85 (bs, 1 H), 2.73 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (150 MHz) δ 154.1, 153.4, 129.9, 119.2, 107.5, 100.1, 70.1, 65.5, 46.3, 36.0, 21.5; MS (EI) *m/z* 193 (M^+, 26), 162 (100), 147 (29); HRMS (EI) *m/z* calcd for $C_{11}H_{15}NO_2$ 193.1103, found 193.1100.

1-((2-Methyloxiran-2-yl)methyl)-1,2,3,4-tetrahydroquinoline (18). To a solution of 1.48 g (11.1 mmol) of 1,2,3,4-tetrahydroquinoline (**17**) in 40 mL of acetonitrile was added 7.67 g (55.5 mmol) of K_2CO_3 and 1.6 mL (16.6 mmol) of 3-bromo-2-methylpropene at room temperature. The disappearance of starting material was monitored by TLC (hexanes:EtOAc; 4:1). The reaction was quenched with H_2O and extracted with 3 x 20 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated to afford a brown oil that was used without purification. According to General Protocol B, the crude reaction mixture, 1.69 g (14.4 mmol) of NMO and 370 μL of OsO_4 (1 mol%, 0.33 M in toluene) produced a residue which was filtered through a pad of Florisil, purified on SiO_2 (hexanes:EtOAc;1:1) and concentrated *in vacuo*. The diol intermediate was subsequently dissolved in 89 mL of THF and cooled to 0 °C. To this

solution was added 564 mg (22.3 mmol) of NaH (95%). The mixture was stirred for 15 min and 3.50 g (10.7 mmol) of *p*-Ts_2O was added in portions. The disappearance of starting material was monitored by TLC (hexanes:EtOAc; 1:1). The reaction mixture was quenched with H_2O and extracted with 3 x 10 mL of EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexanes:EtOAc; 8:1 with 1% NEt_3) to afford 1.38 g (6.78 mmol, 61%, 3 steps) of **18** as a colorless oil: IR (ATR) 2924, 1660, 1599, 1498, 1455, 1192 cm^{-1}; ^1H NMR δ 7.11 (t, 1 H, *J* = 7.5 H), 7.01 (d, 1 H, *J* = 8.1 Hz), 6.65 (t, 2 H, *J* = 8.1 Hz), 3.53, 3.41 (AB, 2 H, *J* = 15.9 Hz), 3.48-3.31 (m, 2 H), 2.82 (app t, 2 H, *J* = 6.0 Hz), 2.76, 2.66 (AB, 2 H, *J* = 4.8 Hz), 1.99 (app quint, 2 H, *J* = 6.0 Hz), 1.44 (s, 3 H); ^{13}C NMR δ 145.8, 129.2, 127.1, 122.2, 116.1, 111.0, 56.6, 55.9, 51.9, 50.9, 28.3, 22.2, 19.5; MS (EI) *m/z* 203 (M^+, 44), 146 (100), 130 (20); HRMS (EI) *m/z* calcd for $C_{13}H_{17}NO$ 203.1310, found 203.1320.

(1-Methyl-2,4,5,6-tetrahydro-1H-pyrrolo[3,2,1-ij]quinolin-1-yl)methyl acetate (19). According to General Protocol F, 206 mg (1.01 mmol) of **15**, 239 mg (1.52 mmol) of collidine hydrochloride, 7.5 mg (0.03 mmol) of Cp_2TiCl_2, and 111 mg (2.02 mmol) of Mn powder afforded a crude reaction mixture that was subjected to 12 mg (0.10 mmol) of DMAP and 290 uL (3.04 mmol) of acetic anhydride in 10 mL of THF. The mixture was stirred for 5 h at rt until TLC analysis (hexanes:EtOAc; 2:1) showed complete consumption of the alcohol. The reaction was quenched with satd. $NaHCO_3$ and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated, and purified on SiO_2 (hexanes:EtOAc; 12:1) to afford 172 mg (0.70 mmol, 69%, 2 steps) of **19** as an oil: IR (neat) 2936, 2806, 1740, 1599, 1489, 1236, 1034 cm^{-1}; ^1H NMR δ 6.87 (dd, 2 H, *J* = 7.5 Hz, 0.9 Hz), 6.63 (t, 1 H, *J* = 7.5 Hz), 4.14, 4.06 (AB, 2 H, *J* = 10.8 Hz), 3.32 (d, 1 H, *J* = 8.7 Hz), 3.10-3.02 (m, 1 H), 2.93 (d, 1 H, *J* = 8.7 Hz), 2.87 (ddd, 1 H, *J* = 10.5 Hz, 7.2 Hz, 4.8 Hz), 2.68 (appt t, 2 H, *J* = 6.6 Hz), 2.12-2.03 (m, 2 H), 2.08 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR δ 171.4, 149.5, 132.5, 127.4, 120.7, 119.9, 118.8, 69.3, 64.7, 46.9, 44.9, 24.0, 23.1, 22.0, 21.1; MS (EI) *m/z* 245 (M^+, 40), 172 (100), 170 (28), 144 (47); HRMS (EI) *m/z* calcd for $C_{15}H_{19}NO_2$ 245.1416, found 245.1416.

1-(2-Methylallyl)-1*H*-indole.[23] According to a modified literature procedure, a solution of 803 mg (6.85 mmol) of indole (**20**) in 13 mL of DMF and 499 mg (8.90 mmol) of powdered KOH was stirred at 60 °C for 10 min, cooled to rt, and treated with 1.0 mL (10.2 mmol) of 3-bromo-2-methylpropene. The reaction mixture was stirred at 60 °C for 18 h, poured onto ice and diluted with 15 mL of EtOAc. The combined organic layers were washed with H_2O, brine, dried ($MgSO_4$), concentrated *in vacuo* and purified by chromatography on SiO_2 (hexane) to afford 832 mg (4.85 mmol, 71%) of 1-(2-methylallyl)-1*H*-indole as a light green oil: IR (neat) 3054, 2913, 1657, 1612, 1462, 1333, 900, 739 cm^{-1}; ^1H NMR δ 7.61 (d, 1 H, *J* = 7.8 Hz), 7.27 (d, 1 H, *J* = 8.1 Hz), 7.19-7.05 (m, 2 H), 7.02 (d, 1 H, *J* = 3.3 Hz), 6.49 (d, 1 H, *J* = 3.3 Hz), 4.86 (s, 1 H), 4.68 (s, 1 H), 4.57 (s, 2 H), 1.62 (s, 3 H); ^{13}C NMR δ 141.4, 136.5, 128.8, 128.4, 121.7, 121.1, 119.6, 112.8, 109.9, 101.5, 52.7, 20.0; MS (EI) *m/z* 171 (M^+, 88), 156 (70), 130 (100); HRMS (EI) *m/z* calcd for $C_{12}H_{13}N$ 171.1048, found 171.1046.

3-Bromo-1-((2-methyloxiran-2-yl)methyl)-1*H*-indole (21). To a solution of 746 mg (4.35 mmol) of 1-(2-methylallyl)-1*H*-indole in 43 mL of acetonitrile was added 814 mg (4.57 mmol) of NBS. The reaction mixture was stirred overnight, quenched with H_2O and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. According to General Protocol B, the crude oil, 765 mg (6.53 mmol) of NMO and 395 μL of OsO_4 (3 mol%, 0.33 M in toluene) were reacted and the disappearance of starting material was monitored by TLC (hexanes:EtOAc; 2:1). The resulting golden oil was dissolved in 40 mL of THF and cooled to 0 ºC. The solution was treated with 1.04 g (26.1 mmol) of NaH (60% dispersion in mineral oil) and stirred for 15 min. Upon addition of 1.70 g (5.22 mmol) of *p*-Ts_2O, the disappearance of starting material was monitored by TLC (hexanes:EtOAc;, 2:1). After 35 min, the reaction was quenched with H_2O and extracted with 3 x 15 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on SiO_2 (hexanes:EtOAc; 6:1) to afford 947 mg (3.55 mmol, 82%, 3 steps) of **21** as an oil: IR (neat) 3117, 3051, 2985, 2928, 1612, 1457, 1322, 1012 cm^{-1}; ^1H NMR δ 7.56 (d, 1 H, *J* = 8.1 Hz), 7.36 (d, 1 H, *J* = 7.8 Hz), 7.30-7.16 (m, 2 H), 7.15 (s, 1 H), 4.30, 4.09 (AB, 2 H, *J* = 15.0 Hz), 2.65, 2.55 (AB, 2 H, *J* = 4.5 Hz), 1.26 (s, 3 H); ^{13}C NMR δ 136.4, 127.6, 127.5, 123.2, 120.6, 119.6, 110.0, 90.8, 56.4, 52.1, 51.6, 19.0; MS (EI) *m/z* 265 (M^+, 50), 208 (67), 186 (24), 129 (39), 69 (100); HRMS (EI) *m/z* calcd for $C_{12}H_{12}NOBr$ 265.0102, found 265.0103.

Benzyl 2-methylcyclohex-2-enyl(phenyl)carbamate (23). To a solution of 224 mg (2.00 mmol) of 2-methylcyclohex-2-enol in 5 mL of dichloromethane cooled to 0 ºC was added 840 μL (6.03 mmol) of NEt_3 followed by 310 μL (4.01 mmol) of MsCl. Upon addition, the mixture was allowed to warm slowly to 25 ºC overnight. The solution was quenched with 10 mL of H_2O, extracted with 3 x 5 mL of dichloromethane, dried (Na_2SO_4), concentrated, and used without further purification. To a solution of 396 mg (2.40 mmol) of benzyl phenylcarbamate in 10 mL of dry DMF cooled to 0 ºC was added 120 mg (3.00 mmol) of NaH (60%). The reaction mixture was stirred for 15 min at 0 ºC and then the crude mesylate intermediate was added in 1 mL of dry DMF. The resulting yellow mixture was allowed to warm to 25 ºC overnight, quenched with 10 mL of H_2O, extracted with 3 x 10 mL of EtOAc, washed with 10 mL of water and 10 mL of brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography on SiO_2 (hexanes:Et_2O; 10:1) to afford 361 mg (1.12 mmol, 56%, 2 steps) of **23** as a light yellow oil. IR (ATR) 3032, 1697, 1597, 1495, 1453, 1396, 1293, 1120, 1017 cm^{-1}; ^1H NMR (300 MHz, 350 K, DMSO-d_6) δ 7.39-7.22 (m, 8 H), 7.17-7.14 (m, 2 H), 5.57 (bs, 1 H), 5.11, 5.06 (AB, 2 H, *J* = 12.9 Hz), 4.68 (app t, 1 H, *J* = 7.2 Hz), 1.91-1.64 (m, 4 H), 1.76 (s, 3 H), 1.47-1.24 (m, 2 H); ^{13}C NMR (75 MHz, 350K, DMSO-d_6) δ 154.4, 140.1, 136.4, 133.0, 128.1, 127.7, 127.1, 126.7, 126.3, 125.6, 65.9, 57.2, 27.4, 24.0, 19.9, 19.8; MS (ESI) *m/z* 322 ($[M+H]^+$).

(4a*S*,9a*S*)-Benzyl 4a-methyl-4-oxo-2,3,4,4a-tetrahydro-1*H*-carbazole-9(9a*H*)-carboxylate (26). To a solution of 952 mg (2.96 mmol) of **23** in 12 mL of dichloromethane and 691 mg (6.52 mmol) of Na_2CO_3 (dissolved in 12 mL of water) at 0 ºC was added 1.46 g (5.92 mmol) of *m*-CPBA (70%). Upon addition of the oxidant, the mixture was allowed to warm slowly to 25 ºC. After 2 h, the reaction was quenched with 10 mL of a 1 M $Na_2S_2O_3$ solution, diluted with 5 mL

of H_2O, extracted with 3 x 10 mL of dichloromethane, washed with 10 mL of brine, dried ($MgSO_4$), concentrated, and purified by chromatography on SiO_2 (hexanes:EtOAc; 10:1 with 1% NEt_3 to hexanes:EtOAc; 5:1 gradient) to afford 841 mg (2.49 mmol, 84%) of **24** as a colorless oil.

A mixture of 841 mg (2.49 mmol) of **24**, 18.9 mg (0.0759 mmol) of Cp_2TiCl_2, 589 mg (3.73 mmol) of Coll•HCl and 274 mg (4.99 mmol) of Mn powder was then purged 3 times with Ar, diluted with 24 mL of THF and placed in a pre-heated oil bath. After heating at reflux under Ar overnight, the solution was cooled to 25 ºC, quenched with 10 mL of satd. NH_4Cl, extracted with 3 x 10 mL of EtOAc, washed with 10 mL of brine, dried (Na_2SO_4), concentrated, and purified by chromatography on SiO_2 (hexanes:EtOAc; 5:1 with 1% NEt_3 to hexanes:EtOAc; 1:1) to afford 97 mg (0.29 mmol, 12%) of **25** as a light brown oil that was taken on to the Dess-Martin oxidation. To a solution of 97 mg (0.29 mmol) of the alcohol intermediate in 5 mL of dichloromethane was added 366 mg (0.862 mmol) of Dess-Martin periodinane reagent. This mixture was stirred under N_2 at 25 ºC overnight and after 13 h reaction time, TLC analysis (hexanes:EtOAc;4:1) showed that the starting material had been consumed. The mixture was poured over 10 mL of satd. $NaHCO_3$, partitioned, and extracted with 3 x 5 mL of dichloromethane. The combined organic layers were dried (Na_2SO_4), concentrated, and purified by chromatography on SiO_2 (hexanes:EtOAc;6:1) to afford 61 mg (0.18 mmol, 63%, 6% over 3 steps) of **26** as a colorless oil: IR (ATR) 2957, 1700, 1597, 1479, 1401, 1287, 1084 cm^{-1}; ^1H NMR (365 K, DMSO-d_6) δ 7.71 (d, 1 H, J = 8.1 Hz), 7.48-7.33 (m, 5 H), 7.28-7.19 (m, 1 H), 7.04-6.96 (m, 2 H), 5.36-5.29 (m, 2 H), 4.47-4.43 (m, 1 H), 2.44-2.20 (m, 2 H), 2.13-2.00 (m, 1 H), 1.80-1.64 (m, 3 H), 1.33 (s, 3 H); ^{13}C NMR (365 K, DMSO-d_6) δ 207.8, 151.5, 140.4, 135.8, 133.5, 127.9, 127.8, 127.3, 127.1, 122.6, 122.5, 114.4, 68.0, 66.3, 55.1, 37.1, 27.2, 24.5, 17.3; HRMS (TOF MS ES^+) *m/z* calcd for $C_{21}H_{21}NO_3$ 358.1419, found 358.1443.

Methyl 2,6-dichloroisonicotinate. According to a literature procedure,[24] a flask was charged with 9.57 g (61.71 mmol) of citrazinic acid, 7.44 g (67.88 mmol) of Me_4NCl, and 17 mL (188.2 mmol) of $POCl_3$. The reaction mixture was heated to 130 ºC for 18 h, cooled to 0 ºC and quenched with 200 mL of freshly distilled MeOH. The solution was neutralized with powdered $NaHCO_3$, diluted with 200 mL of H_2O and concentrated *in vacuo*. The residue was extracted with 2 x 150 mL of toluene, dried ($MgSO_4$), concentrated and filtered through a plug of SiO_2 (EtOAc:hexanes; 1:9) to afford 8.01 g (38.9 mmol, 63%) of methyl 2,6-dichloroisonicotinate as a pink solid that was used without further purification: Mp 80-81 ºC; ^1H NMR δ 7.82 (s, 2 H), 3.98 (s, 3 H); MS (EI) *m/z* 205 (M^+, 54), 174 (100), 146 (53).

2,6-Dichloroisonicotinic acid (27). According to a literature procedure,[24] a solution of 8.91 g (43.24 mmol) of methyl 2,6-dichloroisonicotinate in 20 mL of THF was treated with 1.24 g (51.89 mmol) of LiOH in 60 mL of H_2O. The reaction mixture was stirred for 20 min at rt and concentrated *in vacuo* to remove the THF. The resulting solution was cooled to 0 ºC and treated with 25 mL of 2 M HCl solution. After 2 h, the solid was filtered and dried to afford 6.05 g (31.5 mmol, 73%) of **27** as a tan solid: Mp 208-210 ºC; ^1H NMR δ 7.86 (s, 2 H); MS (EI) *m/z* 191 (M^+, 100), 174 (61), 156 (43), 85 (56).

Benzyl 2,6-dichloropyridin-4-ylcarbamate (28).[24] To a solution of 1.00 g (5.20 mmol) of **27** in 20 mL of THF was added 540 μL (6.35 mmol) of oxalyl chloride at rt. The reaction mixture was refluxed for 2 h, cooled to rt and concentrated *in vacuo*. The resulting oil was dissolved in 40 mL of freshly distilled acetone, cooled to 0 °C and treated dropwise with a solution of 1.01 g (15.62 mmol) of NaN_3 in 20 mL of H_2O. The mixture was stirred for 90 min, and the temperature was allowed to increase from 0 °C to 10 °C. The mixture was diluted with 15 mL of distilled Et_2O, and the aqueous layer was extracted with 2 x 10 mL of distilled Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated to ~10% volume. After addition of 10 mL of toluene the remaining Et_2O and acetone were removed under reduced pressure. The residue was dissolved in 15 mL of toluene, stirred with $MgSO_4$ and treated with 1.1 mL (10.41 mmol) of benzyl alcohol. The mixture was heated at reflux for 15 h behind a blast shield, cooled to rt, diluted with water and extracted with 2 x 10 mL of EtOAc. The combined organic layers were dried ($MgSO_4$), concentrated and purified on SiO_2 (hexanes:EtOAc; 20:1 to 10:1 gradient) to afford 580 mg (1.95 mmol, 33%, 3 steps) of **28** as a brown oil: IR (ATR) 3302, 3259, 3153, 1699, 1572, 1505, 1250, 1218, 1071 cm^{-1}; ^1H NMR δ 7.37 (bs, 5 H), 7.36 (s, 2 H), 5.21 (s, 2 H); ^{13}C NMR δ 152.4, 151.4, 149.1, 135.1, 129.0, 128.9, 128.7, 111.4, 68.3; MS (EI) *m/z* 296 (M^+, 37), 278 (82), 261 (61), 91 (100); HRMS (EI) *m/z* calcd for $C_{13}H_{10}Cl_2N_2O_2$ 296.0119, found 296.0112.

Benzyl 2,6-dichloropyridin-4-yl(2-methylallyl) carbamate. A solution of 547 mg (1.84 mmol) of **28** in 10 mL of THF at 0 °C was treated with 34 mg (0.09 mmol) of TBAI and 93 mg (3.68 mmol) of NaH (95%). The reaction mixture was stirred for 5 min, treated with 370 μL (3.68 mmol) of 3-bromo-2-methylpropene, warmed to rt and stirred for 16 h. After addition of 160 mg of NaH and 400 μL of 3-bromo-2-methylpropene, the mixture was stirred until starting material was consumed according to TLC (hexanes:EtOAc; 4:1). The solution was then cooled to 0 °C, quenched with water and extracted with 3 x 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified on SiO_2 (hexanes:EtOAc; 15:1 to 10:1 gradient) to afford 497 mg (1.41 mmol, 77%) of benzyl 2,6-dichloropyridin-4-yl(2-methylallyl)carbamate as a colorless oil: IR (ATR) 3280, 1716, 1576, 1367, 1216, 1159 cm^{-1}; ^1H NMR δ 7.38-7.36 (m, 5 H), 7.30 (s, 2 H), 5.25 (s, 2 H), 4.94 (s, 1 H), 4.74 (s, 1 H), 4.26 (s, 2 H), 1.74 (s, 3 H); ^{13}C NMR δ 154.0, 153.4, 151.0, 139.6, 135.4, 128.9, 128.8, 128.4, 116.2, 111.8, 69.0, 54.4, 20.2; MS (EI) *m/z* 350 (M^+, 38), 259 (30), 215 (80), 91 (100); HRMS (EI) *m/z* calcd for $C_{17}H_{16}Cl_2N_2O_2$ 350.0588, found 350.0571.

Benzyl 2,6-dichloropyridin-4-yl((2-methyloxiran-2-yl)methyl)carbamate (29). To a solution of 429 mg (1.22 mmol) of benzyl 2,6-dichloropyridin-4-yl(2-methylallyl)carbamate in 10 mL of dichloromethane at 0 °C was added 451 mg (1.83 mmol) of *m*-CPBA (70%). The reaction mixture was warmed to rt and after 6 h an additional 1 equiv (300 mg) of *m*-CPBA was added. The mixture was stirred for a total of 11 h, cooled to 0 °C, quenched with aq. $Na_2S_2O_3$ solution and extracted with 3 x 10 mL of dichloromethane. The combined organic layers were dried ($MgSO_4$), concentrated and purified on SiO_2 (hexanes:EtOAc; 8:1) to afford 371 mg (1.01 mmol, 83%) of **29** as a colorless oil: IR (ATR) 3089, 1714, 1576, 1535, 1216, 1149, 1088 cm^{-1}; ^1H

NMR δ 7.39 (s, 2 H), 7.39-7.37 (m, 5 H), 5.28, 5.21 (AB, 2 H, *J* = 12.0 Hz), 4.11, 3.78 (AB, 2 H, *J* = 15.6 Hz), 2.60, 2.58 (AB, 2 H, *J* = 4.2 Hz), 1.32 (s, 3 H); ^{13}C NMR δ 154.1, 153.6, 151.0, 135.1, 129.0, 129.0, 128.7, 117.8, 69.1, 56.1, 53.3, 51.7, 19.5; MS (ESI) *m/z* 389 $[M+Na]^+$ (14), 365 (22), 361 (100); HRMS (ESI) *m/z* calcd for $C_{17}H_{16}Cl_2O_3Na$ 389.0436 (M+Na), found 389.0467.

Benzyl 4,6-dichloro-3-(hydroxymethyl)-3-methyl-2,3-dihydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate. According to General Protocol F, 236 mg (0.72 mmol) of **29**, 7.1 mg (0.02 mmol) of Cp_2TiCl_2, 170 mg (1.08 mmol) of collidine hydrochloride, and 59 mg (1.08 mmol) of Mn powder (reaction time 2 h) afforded an oil that was purified on SiO_2 (toluene:acetone; 8:1) to afford 147 mg (0.40 mmol, 55%) of benzyl 4,6-dichloro-3-(hydroxymethyl)-3-methyl-2,3-dihydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate as a waxy solid: IR (ATR) 3397, 2965, 2877, 1718, 1582, 1449, 1380, 1312 cm^{-1}; ^{1}H NMR δ 7.42-7.37 (m, 6 H), 5.30-5.20 (m, 2 H), 4.31 (d, 1 H, *J* = 11.1 Hz), 4.14 (d, 1 H, *J* = 11.1 Hz), 3.74 (d, 1 H, *J* = 11.1 Hz), 3.58 (d, 1 H, *J* = 11.1 Hz), 2.62 (bs, 1 H), 1.41 (s, 3 H); ^{13}C NMR δ 154.6, 152.4, 150.7, 145.0, 135.3, 128.9, 128.6, 127.3, 109.4, 68.5, 66.1, 59.1, 46.3 21.4; MS (EI) *m/z* 368 ($[M+2]^+$, 9), 366 (M^+, 15), 201 (10), 91 (100); HRMS (EI) *m/z* calcd for $C_{17}H_{16}Cl_2N_2O_3$ 366.0538, found 366.0527.

(3-Methyl-2,3-dihydro-1*H*-pyrrolo[3,2-*c*]pyridin-3-yl)methanol (30). To a solution of 78 mg (0.21 mmol) of benzyl 4,6-dichloro-3-(hydroxymethyl)-3-methyl-2,3-dihydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate in 2 mL of MeOH at rt was added 22 mg (0.02 mmol) of Pd/C. The reaction mixture was saturated with 1 atm of H_2, stirred for 21 h, quenched with Celite®, filtered, concentrated and purified on neutral Al_2O_3 (hexanes:EtOAc; 1:1 to 100% EtOH) to afford a white solid. This solid was washed once each (5 mL) with boiling acetone and boiling ethyl acetate. The organic extracts were combined and concentrated *in vacuo* to afford 33 mg (0.20 mmol, 95%) of **30** as a colorless oil: IR (ATR) 3248, 3160, 2925, 2866, 1649, 1608, 1522, 1030 cm^{-1}; ^{1}H NMR (CD_3OD) δ 7.94 (d, 1 H, *J* = 6.3 Hz), 7.90 (s, 1 H) 6.61 (d, 1 H, *J* = 6.3 Hz), 3.77, 3.47 (AB, 2 H, *J* = 10.5 Hz), 3.60, 3.53 (AB, 2 H, *J* = 10.8 Hz), 1.37 (s, 3 H); ^{13}C NMR δ 162.2, 144.3, 137.1, 133.1, 103.9, 69.1, 58.1, 47.0, 23.6; MS (ESI) *m/z* 165 ($[M+H]^+$, 100); HRMS (ESI) *m/z* calcd for $C_9H_{12}N_2O$ (M+H) 165.1028, found 165.1038.

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