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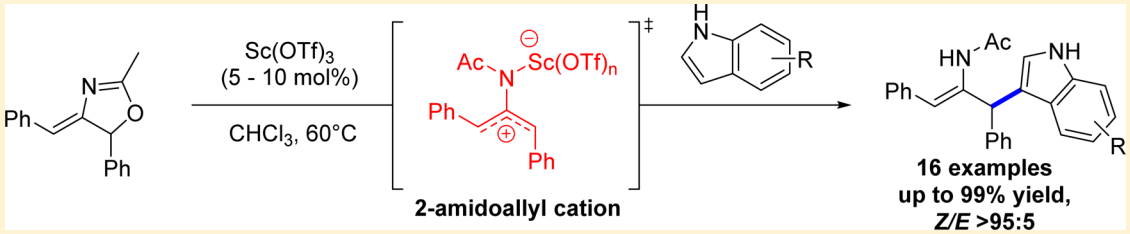
Lewis Acid-Catalyzed Nucleophilic Addition of Indoles to in Situ-Generated 2-Amidoallyl Cations

Marcel Schlegel and Christoph Schneider*

Institut für Organische Chemie, University of Leipzig, Johannisallee 29, D-04103 Leipzig, Germany

Supporting Information



ABSTRACT: We report herein the first Lewis acid-catalyzed generation of 2-amidoallyl cations through ring-opening of 4-benzylidene-2-oxazolines with $Sc(OTf)_3$. Upon nucleophilic addition of indoles, indolylenamides were obtained with yields of 60−99% and excellent (*Z*)-selectivity. In addition, the novel strategy was also successfully applied to pyrroles and naphthols as π-nucleophiles. A Brønsted acid-catalyzed process using TfOH formed in situ was ruled out by control experiments.

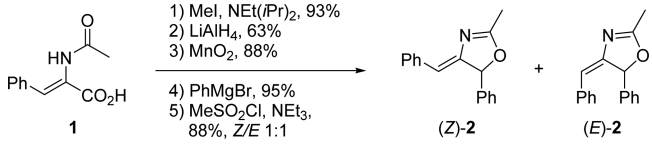
Oxyallyl cations have emerged as highly reactive intermediates in C−C-bond forming processes due to their unique electrophilic character. These species are known to easily undergo (4 + 3)[1]- and (3 + 2)-cycloadditions,[2] and therefore, many synthetic applications have been developed for the construction of complex molecules. More recently, the nucleophilic capture of oxyallyl cations has become a versatile method for synthesizing highly functionalized ketones that are otherwise not accessible by classical strategies.[3−10] For example, Kartika et al. demonstrated the first Brønsted acid-catalyzed, regioselective addition of π- and σ-nucleophiles to introduce α-quaternary centers in ketone-derived compounds.[3] Moreover, the group of MacMillan has very recently developed the first enantioselective, nucleophilic addition of *N*-protected indoles to oxyallyl cations generated in situ using a Jørgensen−Hayashi-type catalyst.[10]

Despite their enormous potential as templates in organic synthesis, 2-amino- and 2-amidoallyl cations are less well-studied because methods for their generation are limited. Typical procedures comprise ionization of rather unstable α-chloroenamines or α-chloroimines with stoichiometric amounts of silver(I) salts as Lewis acids followed by (4 + 3)-cycloaddition with furan or dienes.[11] Shipman and co-workers reported a $BF_3{\cdot}OEt_2$-promoted or $Sc(OTf)_3$-catalyzed intramolecular (4 + 3)-cycloaddition of 2-aminoallyl cations, which are formed in situ by the release of ring strain from 2-methyleneaziridines.[12,13] Blakey and Stoll developed a Rh-catalyzed allene amination that affords cyclopropaneimines via 2-amidoallyl cation species.[14] These intermediates were also described in (4 + 3)-,[15] (3 + 3)-,[16] and (3 + 2)-cycloadditions[14] as well as addition reactions with nucleophiles.[17]

We envisioned 4-alkylidene-substituted 2-oxazolines as suitable precursors in the generation of 2-amidoallyl cations. Although 2-oxazolines are particularly known to undergo cationic polymerization reactions by Lewis acid-catalyzed ring opening,[18] the addition of π-nucleophiles to trap the resulting cations has never been achieved in an effective and catalytic manner.[19] Hence, we decided to install the 4-alkylidene group to stabilize the cation more efficiently by resonance effects, which would allow the attack of a nucleophile under mild conditions. We now report our results on the first Lewis acid-catalyzed nucleophilic capture of in situ-generated 2-amidoallyl cations with indole.

Commercially available α-acetamidocinnamic acid **1** was converted into 4-benzylidene-2-oxazoline **2** in a 5-step prodecure. Esterification of the carboxylic acid and reduction with $LiAlH_4$ afforded the allyl alcohol as a single double bond isomer. Selective oxidation was achieved with high yields by treating with MnO_2. The addition of phenyl magnesium bromide delivered the secondary alcohol, which was then dehydrated through methanesulfonyl chloride and NEt_3 to give rise to oxazoline **2**. The resulting (*Z*)- and (*E*)-isomers of **2** were separated by column chromatography, and their relative configuration was determined by NOE experiments (Scheme 1).

Scheme 1. Synthesis of Oxazoline 2



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Scheme 2. Synthesis of 3a with DPP and $Sc(OTf)_3$ under Optimized Conditions

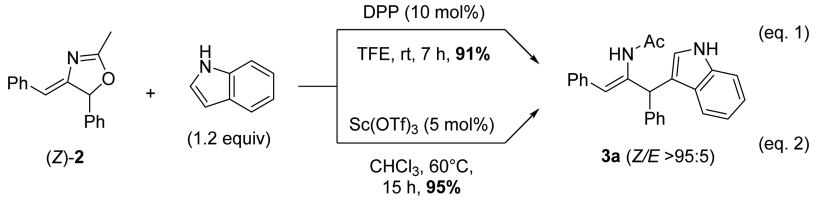
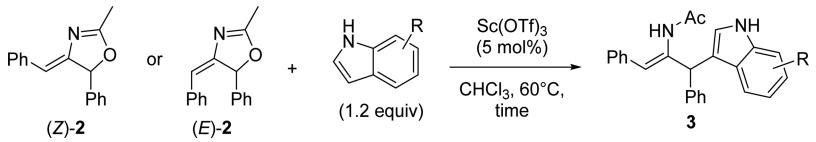


Table 1. Substrate Scope with Indoles toward Indolylenamides 3[a]



entry	product	2	R	time [h]	yield [%][b]	Z/E[c]
1	**3a**	*Z*	H	15	95	>95:5
2	**3a**	*E*	H	39	91	>95:5
3	**3b**	*E*	1-CH_3	96	82	>95:5
4	**3c**	*E*	2-CH_3	96[d,e]	72	>95:5
5	**3d**	*Z*	5-CH_3	21	92	>95:5
6	**3e**	*Z*	7-CH_3	20	97	>95:5
7	**3f**	*E*	5-OCH_3	22	89	94:6
8	**3g**	*E*	7-OCH_3	69[d]	80	>95:5
9	**3h**	*Z*	4,5-$(OCH_2)_2$	44	72	94:6
10	**3i**	*Z*	2-Ph	15	99	>95:5
11	**3j**	*Z*	4-Br	96[d,e]	82	85:15
12	**3k**	*E*	6-Cl	64	93	94:6
13	**3l**	*Z*	5-F	18	90	92:8
14	**3m**	*Z*	5-CO_2Me	48[d]	95	>95:5
15	**3n**	*Z*	6-CO_2Me	69[d]	92	>95:5
16	**3o**	*Z*	5-CN	96[d,f]	62	>95:5
17	**3p**	*Z*	5-NO_2	96[d,f]	60	>95:5

[a]Reaction conditions: oxazoline **2** (0.20 mmol), indole (0.24 mmol), $Sc(OTf)_3$ (5 mol %) in 0.5 mL of $CHCl_3$ at 60 °C. [b]Isolated yield after column chromatography. [c]*Z*/*E* ratio determined by ^1H NMR spectroscopy after column chromatography. [d]Catalyst loading increased to 10 mol % $Sc(OTf)_3$ after 40 h. [e]Added 0.8 additional equivalents of the corresponding indole after 40 h. [f]Incomplete conversion of starting material.

We initially started our investigation with the Brønsted acid-catalyzed activation of (*Z*)-**2** with diphenylphosphate (DPP) followed by the reaction with indole. It turned out that conventional solvents (CH_2Cl_2, CH_3CN, THF, toluene) failed to yield the desired addition product even under refluxing conditions. On the basis of procedures in which oxyallyl cations were generally formed in protic solvents,[5−9] we decided to employ trifluoroethanol (TFE), which successfully gave rise to the formation of indolylenamide **3a** with 91% yield and high (*Z*)-selectivity (Scheme 2, eq 1). The (*Z*)-configuration of the enamide double bond, which was rigorously determined by X-ray crystal structure analysis (see Figure S1), is favored to minimize 1,3-allylic strain. No reaction was observed without DPP in TFE.

In addition to Brønsted acid catalysis, we decided to study the ring-opening of oxazoline **2** with Lewis acids in nonprotic organic solvents mainly for two reasons: (1) During our investigations, we occasionally observed the addition of TFE to the intermediate 2-amidoallyl cations in competition with other nucleophiles, a side reaction that is also described in the nucleophilic capture of oxyallyl cations.[5,9] (2) We wanted to exclude the potential hydrolysis of the enamide moiety in the presence of the Brønsted acid and the protic solvent. After extensive optimization studies (see Table S1), we eventually settled on 5 mol % of $Sc(OTf)_3$, providing **3a** in 95% yield for the subsequent investigations (Scheme 2, eq 2).

Metal triflates and other Lewis acids are known to release traces of protons that might act as the active catalyst.[20,21] We carried out some control experiments to exclude this type of "hidden Brønsted acid" catalysis in the $Sc(OTf)_3$-catalyzed process (see Table S2). In the presence of 2,6-di-*tert*-butylpyridine (DTBP), which is known to be a noncoordinating and selective proton scavenger,[20,22] no difference in reaction time or yield was obtained in comparison to the results without the base. Moreover, we performed the same reaction with 10 mol % TfOH, which gave rise to **3a** in 87% yield within 1 day. Addition of DTBP to the TfOH-catalyzed reaction significantly decreased the conversion of starting material and furnished the product with less than 10% yield after 3 days. These experiments strongly indicated that $Sc(OTf)_3$ itself was the active catalyst, but traces of TfOH generated in situ can also assist in this transformation.

We next studied the influence of different substituted indoles on the nucleophilic attack to oxazolines (*Z*)- and (*E*)-**2**. It turned out that electron-donating as well as electron-withdrawing groups were well-tolerated, leading to the corresponding products with good to excellent yields and high (*Z*)-selectivities (Table 1). Reactions that started from the (*E*)-isomer of oxazoline **2** afforded the products **3** within generally

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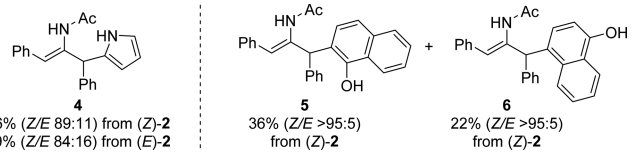
longer reactions times but with similar yields as indicated by comparing entries 1 and 2. The lower reactivity of (*E*)-**2** likely resulted from the enhanced 1,3-allylic strain between the two phenyl groups. This led to double bond isomerization into the more reactive (*Z*)-configured oxazoline **2**, which was observed by TLC monitoring of the reaction mixtures. Indoles with electron-donating substituents typically furnished the products with very high yields and in most cases exclusively as (*Z*)-isomers (entries 3−10). *N*-Methylated as well as 2-methylindole were suitable nucleophiles but required longer reaction times (entries 3 and 4). However, placing a phenyl group at the 2-position of indole provided the corresponding product in quantitative yield within 1 day (entry 10). C-4-substituted indoles showed slower conversion of starting material and a slight decrease of product yield because of steric hindrance to the nucleophilic center (entries 9 and 11). The 4-bromoindole-substituted product **3j** was the only case in which a significantly lower *Z*/*E* ratio was observed (entry 11). Other functional groups like halides (entries 12 and 13) or esters (entries 14 and 15) also delivered the corresponding products **3k**−**3n** with excellent yields. Indoles carrying strongly electron-withdrawing cyano or nitro groups showed a significant decrease in reactivity with oxazoline (*Z*)-**2**. After column chromatography, **3o** and **3p** were isolated in 62 and 60% yields, respectively, and with high (*Z*)-selectivities (entries 16 and 17).

We also investigated other π- as well as σ-nucleophiles to extend the substrate scope of our established protocol. When oxazolines (*Z*)- and (*E*)-**2** were treated with pyrrole and 10 mol % $Sc(OTf)_3$ in $CHCl_3$ at 60 °C, *E*/*Z*-mixtures of pyrrolylenamide **4** were obtained with good overall yields and high *Z*/*E* ratios after 17 and 64 h, respectively. Both isomers could be separated by column chromatography. Under identical conditions, the nucleophilic addition of 1-naphthol to (*Z*)-**2** resulted in a separable mixture of *ortho*-product **5** and *para*-product **6** in a ratio of 62:38 after 17 h. Both isomers were isolated in moderate yields and excellent (*Z*)-selectivities (Scheme 3). Other potential π-nucleophiles such as β-diketones, enol ethers, and enamines did not furnish any product but exclusively gave rise to decomposition of starting material.

Scheme 3. Addition Products of 2 with Pyrrole and 1-Naphthol



Mechanistically, we propose that the Lewis acid will first coordinate to the basic nitrogen atom of oxazolines (*Z*)- and (*E*)-**2** resulting in ring-opening of the heterocycle and formation of 2-amidoallyl cation **7**. This symmetrical and highly reactive intermediate can exist in three different conformations. W-form **7a** is generally preferred over sickle form **7b** and U-form **7c** due to minimized 1,3-allylic strain between the two Ph-groups. However, in analogy to reported Lewis acid-catalyzed formations of 2-aminoallyl cations, W-form **7a** might be less favored compared to sickle form **7b** because of additional 1,3-allylic strain between one Ph group and the bulky, coordinating Lewis acid.[12,13] Intramolecular attack of the acetyl group to **7** regenerates oxazoline **2**. The addition of indole finally forms product **3a** in an irreversible step (Scheme 4). It is unclear whether the (*Z*)-configuration of **3a** is directly related to the 2-amidoallyl cation intermediate **7** or whether double bond isomerization of a potential (*E*)-**3a**-isomer had taken place in the reaction medium. Although a possible S_N2 or S_N2' mechanism cannot be fully ruled out in this reaction, we rather assume a S_N1-type mechanism because of the high resonance stabilization of intermediate **7**. Moreover, our successful experiments with DPP in TFE suggest a unimolecular mechanism based on stabilization of **7** by the protic solvent (see Scheme 2, eq 1).

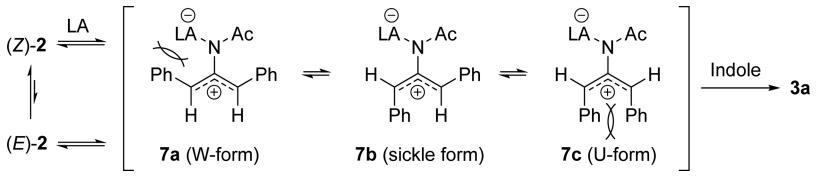
CONCLUSIONS

In summary, we have reported a novel strategy to form 2-amidoallyl cations by $Sc(OTf)_3$-catalyzed ring-opening of 4-alkylidene-substituted 2-oxazolines. A broad range of indoles as well as pyrrole and 1-naphthol have proven to be suitable π-nucleophiles to give rise to highly α-substituted enamides with good-to-excellent yields and (*Z*)-selectivities. We could prove that $Sc(OTf)_3$ itself acts as an active catalytic species. Furthermore, we were able to run the same reaction under mild Brønsted acidic conditions using catalytic amounts of diphenylphosphate in trifluoroethanol providing addition product **3a** with high yield and (*Z*)-selectivity.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all reactions were carried out in oven-dried glassware and in dry solvents under an argon atmosphere. ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 or $CDCl_3$ at 26 °C using a Mercury plus 300 MHz and a Bruker Avance DRX 400 MHz spectrometer. The spectra were referenced to residual DMSO (2.50 ppm, ^1H; 39.52 ppm, ^{13}C) or $CHCl_3$ (7.26 ppm, ^1H; 77.16 ppm, ^{13}C). Chemical shifts are reported in ppm; multiplicities are indicated by s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and related permutations. Coupling constants, *J*, are reported in hertz. All high-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics Apex II FT-ICR. Melting points were determined uncorrected on a Boetius measurement device. The used solvents dichloromethane and tetrahydrofuran (THF) were dried using a MBraun Solvent Purification System (SPS) 800. Dry chloroform and methanol were purchased from Acros Organics and stored over molecular sieve. Acetonitrile was technical grade. Solvents for column chromatography were of technical grade and distilled from the indicated drying reagents: dichloromethane (CaH_2), diethyl ether (KOH), methyl-*tert*-butyl ether (KOH), ethyl acetate ($CaCl_2$), and *n*-hexane (KOH).

Scheme 4. Proposed Mechanism for the Formation of Indolylenamide 3a



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Methanol was technical grade. Triethylamine was distilled freshly prior to use. Flash column chromatography was performed using silica gel (Fluka, 60 Å, 230−400 mesh size). Analytical thin-layer chromatography (TLC) was performed on Macherey−Nagel precoated TLC sheets AlugramXtra SIL G/UV_{254}. Visualization of the spots was achieved by UV-light and treatment with a vanillin staining solution.

Synthesis of Oxazoline 2. Methyl α-acetamidocinnamate was synthesized from α-acetamidocinnamic acid **1** according to known literature.[23]

A solution of methyl α-acetamidocinnamate (17.5 g, 80.0 mmol, 1.00 equiv) in 150 mL of dry THF was added dropwise to a suspension of $LiAlH_4$ (10.6 g, 280 mmol, 3.50 equiv) in 400 mL of dry THF over 30 min at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then transferred into 300 mL of ice-cold EtOAc. It was filtered over Celite, and the residue was washed with EtOAc and MeOH. The filtrate was treated with sat. NH_4Cl solution. The organic phase was separated, and the aqueous phase was extracted twice with EtOAc. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (30% EtOAc/*n*-hexane → EtOAc), *N*-(3-hydroxy-1-phenylprop-1-en-2-yl)acetamide was isolated as a white solid (9.65 g, 63%). R_f (EtOAc) 0.42; mp 80 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (bs, 1H), 7.40 (m, 2H), 7.32 (m, 2H), 7.21 (m, 1H), 6.27 (s, 1H), 5.12 (t, 1H, *J* = 6.0 Hz), 4.13 (d, 2H, *J* = 6.0 Hz), 1.95 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 169.0, 137.6, 135.6, 128.3, 126.7, 118.3, 62.3, 22.9; IR (KBr) ṽ 3239, 3172, 3062, 3049, 3021, 2940, 2919, 1646, 1556, 1489, 1437, 1373, 1348, 1310, 1183, 1037, 850, 755, 692, 526 cm^{-1}; HRMS (ESI+) *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{13}NO_2Na$ 214.0838, found 214.0835.

To a solution of *N*-(3-hydroxy-1-phenylprop-1-en-2-yl)acetamide (9.65 g, 50.5 mmol, 1.00 equiv) in 200 mL of CH_3CN was added activated MnO_2 (88% w/w, 40.0 g, 404 mmol, 8.00 equiv), and the mixture was stirred at rt for 15 h. It was filtered over Celite, and the residue was washed with EtOAc. The filtrate was concentrated in vacuo, and the crude product was purified by flash column chromatography (30% EtOAc/*n*-hexane → EtOAc). *N*-(3-Oxo-1-phenylprop-1-en-2-yl)acetamide was isolated as a white solid (8.36 g, 88%). R_f (80% EtOAc/*n*-hexane) 0.50; mp 104−105 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.55 (bs, 1H), 9.45 (s, 1H), 7.69 (m, 2H), 7.48−7.43 (m, 3H), 7.32 (s, 1H), 2.05 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 190.8, 168.9, 139.7, 134.7, 133.4, 130.2, 128.7, 22.6; IR (KBr) ṽ 3464, 3250, 3016, 2847, 1698, 1687, 1659, 1634, 1490, 1419, 1382, 1372, 1321, 1277, 1189, 980, 764, 746, 684, 536, 438 cm^{-1}; HRMS (ESI+) *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{11}NO_2Na$ 212.0682, found 212.0681.

Bromobenzene (13.4 mL, 128 mmol, 3.50 equiv) was added dropwise to a mixture of activated magnesium turnings (3.20 g, 132 mmol, 3.60 equiv) in 80 mL of dry THF over 20 min. After complete addition, the resulting black suspension was heated under reflux in an oil bath for 90 min and then cooled to 0 °C. *N*-(3-Oxo-1-phenylprop-1-en-2-yl)acetamide (6.79 g, 36.6 mmol, 1.0 equiv) was dissolved in 80 mL of dry THF and added dropwise to the Grignard reagent at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then quenched with 200 mL of sat. NH_4Cl solution. The organic phase was separated, and the aqueous phase was extracted twice with EtOAc. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (10% EtOAc/*n*-hexane → EtOAc), *N*-(3-hydroxy-1,3-diphenylprop-1-en-2-yl)acetamide was isolated as a yellowish solid (9.31 g, 95%). R_f (70% Et_2O/*n*-hexane) 0.22; mp 115−117 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.01 (bs, 1H), 7.43−7.40 (m, 2H), 7.35−7.28 (m, 6H), 7.27−7.17 (m, 2H), 6.58 (s, 1H), 5.92 (d, 1H, *J* = 5.0 Hz), 5.48 (d, 1H, *J* = 5.0 Hz), 1.85 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 169.0, 143.3, 139.2, 135.6, 128.4, 128.2, 127.9, 127.0, 126.8, 126.7, 119.3, 72.8, 22.8; IR (KBr) ṽ 3396, 3246, 3166, 3054, 3021, 1660, 1645, 1540, 1489, 1447, 1410, 1375, 1319, 1305, 1276, 1179, 1041, 1014, 756, 712, 696 cm^{-1}; HRMS (ESI+) *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}NO_2Na$ 290.1151, found 290.1148.

To a solution of *N*-(3-hydroxy-1,3-diphenylprop-1-en-2-yl)-acetamide (3.00 g, 11.2 mmol, 1.00 equiv) in 50 mL of dry CH_2Cl_2, triethylamine (6.20 mL, 44.8 mmol, 4.00 equiv) and methanesulfonyl chloride (1.30 mL, 16.8 mmol, 1.50 equiv) were added dropwise at 0 °C. After 10 min of stirring, the reaction mixture was quenched with sat. $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (10% → 50% Et_2O/*n*-hexane), oxazoline (*Z*)-**2** was isolated as a white solid (1.23 g, 44%). In another fraction, oxazoline (*E*)-**2** was obtained as a white solid (1.23 g, 44%). (*Z*)-Isomer: R_f (70% Et_2O/*n*-hexane) 0.85; mp 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.45−7.37 (m, 5H), 7.33 (m, 2H), 7.18 (m, 1H), 6.01 (d, 1H, *J* = 2.5 Hz), 5.58 (d, 1H, *J* = 2.5 Hz), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.2, 152.9, 138.8, 136.4, 129.2, 129.0, 128.6, 128.4, 127.7, 126.4, 112.1, 85.8, 15.2; IR (KBr) ṽ 3083, 3063, 3039, 3029, 3019, 1613, 1593, 1492, 1387, 1307, 1295, 1273, 1248, 1205, 977, 926, 755, 695 cm^{-1}; HRMS (ESI+) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}NO$ 250.1226, found 250.1223. (*E*)-Isomer: R_f (70% Et_2O/*n*-hexane) 0.41; mp 80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.37 (m, 2H), 7.34−7.31 (m, 3H), 7.15−7.11 (m, 2H), 7.07−7.01 (m, 3H), 6.74 (d, 1H, *J* = 2.5 Hz), 6.34 (d, 1H, *J* = 2.5 Hz), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.4, 152.3, 136.1, 135.6, 129.3, 129.1, 128.4, 128.3, 127.7, 126.4, 116.3, 84.5, 14.7; IR (KBr) ṽ 3433, 3086, 3063, 3046, 3026, 1665, 1607, 1589, 1572, 1492, 1446, 1422, 1387, 1318, 1308, 1387, 1230, 1187, 1141, 960, 917, 909, 870, 765, 759, 712, 692, 621, 605, 513 cm^{-1}; HRMS (ESI+) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}NO$ 250.1226, found 250.1228.

General Procedure for the Synthesis of Indolylenamides 3. Oxazoline (*Z*)-**2** or (*E*)-**2** (50 mg, 0.20 mmol, 1.00 equiv), $Sc(OTf)_3$ (4.9 mg, 10 μmol, 0.05 equiv), and indole (1.20 equiv) were dissolved in dry $CHCl_3$ (0.5 mL) and stirred at 60 °C in an oil bath for the indicated time. The reaction mixture was quenched with sat. $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The crude products were purified by flash column chromatography (CH_2Cl_2 → 1% MeOH/CH_2Cl_2) and dried under high vacuum (0.1 mbar) at 60 °C overnight.

Indolylenamide ***3a***. This compound was obtained from oxazoline (*Z*)-**2** and indole (28 mg, 0.24 mmol) after 16 h as a white solid (69 mg, 95%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.28; mp 175−177 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (bs, 1H), 9.22 (bs, 1H), 7.62 (d, 1H, *J* = 8.0 Hz), 7.34−7.24 (m, 10H), 7.19−7.14 (m, 1H), 7.05 (t, 1H, *J* = 7.5 Hz), 6.92 (t, 1H, *J* = 7.5 Hz) 6.73 (s, 1H), 5.84 (s, 1H), 5.62 (s, 1H), 1.86 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.9, 142.1, 139.4, 136.6, 135.8, 128.8, 128.2, 128.1, 126.8, 126.6, 126.4, 124.2, 122.5, 121.1, 119.7, 118.3, 116.1, 111.4, 47.3, 23.0; IR (KBr) ṽ 3413, 3056, 3024, 2924, 2853, 1655, 1491, 1455, 1267, 745, 698 cm^{-1}; HRMS (ESI+) *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{22}N_2ONa$ 389.1624, found 389.1626.

Indolylenamide ***3b***. This compound was obtained from oxazoline (*E*)-**2** and 1-methylindole (31 μL, 0.24 mmol) after 96 h as a white solid (62 mg, 82%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.44; mp 154−157 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (bs, 1H), 7.69 (d, 1H, *J* = 8.0 Hz), 7.39−7.35 (m, 5H), 7.30−7.24 (m, 5H), 7.19−7.14 (m, 1H), 7.13 (t, 1H, *J* = 7.5 Hz), 6.97 (t, 1H, *J* = 7.5 Hz), 6.71 (s, 1H), 5.88 (s, 1H), 5.64 (s, 1H), 3.71 (s, 3H), 1.86 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 169.0, 142.0, 139.4, 137.1, 135.7, 128.7, 128.5, 128.3, 128.3, 128.1, 127.1, 126.7, 126.4, 122.6, 121.2, 120.0, 118.5, 115.5, 109.5, 47.2, 32.3, 23.0; IR (KBr) ṽ 3406, 3055, 3023, 2930, 1655, 1614, 1490, 1449, 1371, 1330, 1273, 743, 700 cm^{-1}; HRMS (ESI+) *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{24}N_2ONa$ 403.1781, found 403.1782.

Indolylenamide ***3c***. This compound was obtained from oxazoline (*E*)-**2**, 2-methylindole (53 mg, 0.40 mmol, 2.00 equiv), and $Sc(OTf)_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 96 h as a brown solid (55 mg, 72%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.21; mp 103−108 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (bs, 1H), 9.18 (bs, 1H), 7.33−7.23 (m,

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10H) 7.20−7.15 (m, 2H), 6.94 (t, 1H, J = 7.5 Hz) 6.82 (t, 1H, J = 7.5 Hz), 5.91 (s, 1H), 5.81 (s, 1H), 2.26 (s, 3H), 1.81 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.7, 142.3, 139.3, 135.8, 135.3, 133.2, 128.9, 128.2, 128.1, 128.0, 126.6, 125.9, 122.5, 119.7, 118.7, 118.2, 110.5, 110.0, 46.0, 23.0, 11.8; IR (KBr) $\tilde{\nu}$ 3399, 3056, 3023, 1660, 1621, 1490, 1458, 746, 698 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2ONa$ 403.1781, found 403.1780.

Indolylenamide ***3d***. This compound was obtained from oxazoline (*Z*)-**2** and 5-methylindole (32 mg, 0.24 mmol) after 21 h as a white solid (70 mg, 92%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.45; mp 88−95 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.79 (bs, 1H), 9.23 (bs, 1H), 7.40 (s, 1H), 7.34−7.33 (m, 4H), 7.31−7.24 (m, 6H), 7.18−7.14 (m, 1H), 6.89 (dd, 1H, J = 8.5, 1.5 Hz, 1H), 6.72 (d, 1H, J = 2.0 Hz) 5.84 (s, 1H), 5.64 (s, 1H), 2.31 (s, 3H), 1.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.8, 142.3, 139.6, 135.9, 135.0, 128.8, 128.2, 128.1, 127.1, 126.7, 126.6, 126.3, 124.3, 122.7, 122.4, 119.1, 115.5, 111.1, 47.1, 23.0, 21.4; IR (KBr) $\tilde{\nu}$ 3407, 3296, 3055, 3023, 1661, 1599, 1491, 1448, 1424, 1369, 796, 753, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2ONa$ 403.1781, found 403.1777.

Indolylenamide ***3e***. This compound was obtained from oxazoline (*Z*)-**2** and 7-methylindole (32 mg, 0.24 mmol) after 20 h as a white solid (74 mg, 97%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.36; mp 95−98 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.87 (bs, 1H), 9.24 (bs, 1H), 7.46 (dd, 1H, J = 7.0, 2.0 Hz), 7.35−7.23 (m, 9H), 7.17−7.14 (m, 1H), 6.87−6.82 (m, 2H), 6.75 (d, 1H, J = 2.0 Hz), 5.86 (s, 1H), 5.65 (s, 1H), 2.46 (s, 3H), 1.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.9, 142.2, 139.5, 136.2, 135.9, 128.8, 128.2, 128.1, 126.6, 126.5, 126.4, 123.9, 122.6, 121.6, 120.4, 118.6, 117.3, 116.6, 47.4, 23.0, 16.8; IR (KBr) $\tilde{\nu}$ 3420, 3054, 3024, 1655, 1492, 1448, 749, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2ONa$ 403.1781, found 403.1777.

Indolylenamide ***3f***. This compound was obtained from oxazoline (*E*)-**2** and 5-methoxyindole (35 mg, 0.24 mmol) after 15 h as a white solid (70 mg, 89%, 94:6 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.22; mp 86−90 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.70 (bs, 1H), 9.20 (bs, 1H), 7.36−7.35 (m, 4H), 7.28−7.22 (m, 7H), 7.18−7.14 (m, 1H), 6.71 (dd, 1H, J = 8.5, 2.5 Hz), 6.63 (d, 1H, J = 2.0 Hz), 5.69 (s, 1H), 5.51 (s, 1H), 3.66 (s, 3H), 1.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.1, 152.8, 142.0, 139.3, 135.9, 131.8, 128.8, 128.2, 128.0, 127.2, 126.7, 126.4, 124.8, 122.9, 116.1, 111.9, 111.0, 102.0, 55.2, 47.6, 22.9; IR (KBr) $\tilde{\nu}$ 3411, 3056, 3024, 2936, 2829, 1656, 1626, 1485, 1451, 1209, 1171, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_2Na$ 419.1730, found 419.1729.

Indolylenamide ***3g***. This compound was obtained from oxazoline (*E*)-**2**, 7-methoxyindole (35 mg, 0.24 mmol), and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 69 h as a white solid (63 mg, 80%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.29; mp 94−98 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.97 (bs, 1H), 9.21 (bs, 1H), 7.34−7.33 (m, 4H), 7.27−7.20 (m, 6H), 7.17−7.14 (m, 1H), 6.85 (t, 1H, J = 8.0 Hz), 6.63−6.61 (m, 2H), 5.83 (s, 1H), 5.60 (s, 1H), 3.89 (s, 3H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.9, 146.0, 142.2, 139.4, 135.8, 128.8, 128.3, 128.2, 128.1, 126.7, 126.6, 126.4, 123.8, 122.5, 118.9, 116.7, 112.6, 101.6, 55.0, 47.3, 23.0; IR (KBr) $\tilde{\nu}$ 3422, 3055, 3024, 2934, 1655, 1578, 1494, 1465, 1448, 1370, 1261, 1232, 1091, 1046, 782, 752, 731, 716, 700 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_2Na$ 419.1730, found 419.1729.

Indolylenamide ***3h***. This compound was obtained from oxazoline (*Z*)-**2** and 4,5-ethylenedioxyindole (42 mg, 0.24 mmol) after 44 h as a white solid (61 mg, 72%, 94:6 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.18; mp 104−109 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.77 (bs, 1H), 9.13 (bs, 1H), 7.31−6.57 (m, 10H), 6.81−6.77 (m, 2H), 6.58 (d, 1H, J = 8.5 Hz), 5.77 (s, 1H), 5.64 (s, 1H), 4.12−4.08 (m, 3H) 4.02−3.98 (m, 1H), 1.80 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 167.8, 143.6, 140.0, 136.5, 136.3, 134.9, 134.9, 128.9, 128.0, 127.8, 127.7, 126.3, 125.8, 123.7, 122.2, 117.1, 114.8, 112.3, 104.0, 64.0, 63.7, 48.4, 23.1; IR (KBr) $\tilde{\nu}$ 3417,3055, 3023, 2926, 2870, 1668, 1503, 1446, 1368, 1338, 1274, 1257, 1222, 1085, 962, 714, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{27}H_{24}N_2O_3Na$ 447.1679, found 447.1680.

Indolylenamide ***3i***. This compound was obtained from oxazoline (*Z*)-**2** and 2-phenylindole (46 mg, 0.24 mmol) after 15 h as a white solid (87 mg, 99%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.24; mp 107−112 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.34 (bs, 1H), 9.14 (bs, 1H), 7.59 (m, 2H), 7.50−7.46 (m, 3H), 7.42−7.37 (m, 2H), 7.28−7.22 (m, 8H), 7.19−7.13 (m, 2H), 7.06 (t, 1H, J = 7.5 Hz), 6.90 (t, 1H, J = 7.5 Hz), 6.10 (s, 1H), 5.84 (s, 1H), 1.70 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.5, 142.4, 139.0, 136.5, 135.8, 132.6, 128.9, 128.6, 128.5, 128.2, 128.1, 128.0, 127.7, 126.7, 125.9, 123.4, 121.1, 120.5, 118.8, 111.5, 110.6, 46.8, 22.8; IR (KBr) $\tilde{\nu}$ 3397, 3281, 3056, 3023, 1668, 1600, 1490, 1449, 1426, 764, 746, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{31}H_{26}N_2ONa$ 465.1937, found 465.1941.

Indolylenamide ***3j***. This compound was obtained from oxazoline (*Z*)-**2**, 4-bromoindole (50 μL, 0.40 mmol, 2.00 equiv) and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 96 h as a white solid (73 mg, 82%, 85:15 *Z*/*E*). (*Z*)-isomer: R_f (1% MeOH/CH_2Cl_2) 0.26; mp 93−95 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.41 (bs, 1H), 9.22 (bs, 1H), 7.40 (d, 1H, J = 8.0 Hz), 7.08−7.31 (m, 11H) 7.01 (d, 1H, J = 2.0 Hz), 6.95 (t, 1H, J = 8.0 Hz), 6.16 (s, 1H), 5.52 (s, 1H), 1.79 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 167.8, 143.1, 139.9, 138.2, 136.4, 129.2, 128.0, 127.9, 126.4, 126.0, 124.5, 122.9, 122.7, 122.2, 115.5, 113.1, 111.3, 47.3, 23.2; IR (KBr) $\tilde{\nu}$ 3419, 3056, 3024, 1669, 1652, 1491, 1335, 1184, 746, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{25}H_{21}{}^{79}BrN_2ONa$ 467.0730, found 467.0726.

Indolylenamide ***3k***. This compound was obtained from oxazoline (*E*)-**2** and 6-chloroindole (36 mg, 0.24 mmol) after 64 h as a white solid (74 mg, 93%, 94:6 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.33; mp 205−206 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.05 (bs, 1H), 9.24 (bs, 1H), 7.66 (d, 1H, J = 8.5 Hz), 7.40 (d, 1H, J = 1.5 Hz), 7.36−7.33 (m, 4H), 7.29−7.24 (m, 5H), 7.18−7.15 (m, 1H), 6.95 (dd, 1H, J = 8.5, 1.5 Hz), 6.74 (d, 1H, J = 1.5 Hz), 5.83 (s, 1H), 5.59 (s, 1H), 1.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.1, 141.7, 139.3, 137.0, 135.7, 128.8, 128.3, 128.2, 128.1, 126.7, 126.5, 125.9, 125.6, 125.4, 122.8, 121.1, 118.7, 116.6, 111.0, 47.2, 22.9; IR (KBr) $\tilde{\nu}$ 3420, 3223, 3057, 3022, 1649, 1518, 1491, 1450, 907, 812, 749, 716, 700 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{25}H_{21}{}^{35}ClN_2ONa$ 423.1235, found 423.1231.

Indolylenamide ***3l***. This compound was obtained from oxazoline (*Z*)-**2** and 5-fluoroindole (32 mg, 0.24 mmol) after 18 h as a white solid (69 mg, 90%, 92:8 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.29; mp 84−89 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.97 (bs, 1H), 9.25 (bs, 1H), 7.46 (dd, 1H, J = 10.0, 2.5 Hz), 7.38−7.24 (m, 10H), 7.20−7.16 (m, 1H), 6.90 (td, 1H, J = 9.0, 2.5 Hz), 6.76 (d, 1H, J = 2.5 Hz), 5.88 (s, 1H), 5.54 (s, 1H), 1.89 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.2, 156.5 (d, J = 231.0 Hz), 141.7, 139.2, 135.7, 133.3, 128.8, 128.3, 128.2, 128.1, 127.0 (d, J = 10.0 Hz), 126.8, 126.6, 126.3, 122.8, 116.7 (d, J = 4.5 Hz), 112.4 (d, J = 10.0 Hz), 109.3 (d, J = 26.0 Hz), 104.5 (d, J = 23.5 Hz), 47.4, 22.9; IR (KBr) $\tilde{\nu}$ 3417, 3383, 3283, 3056, 3024, 2922, 1661, 1582, 1486, 1451, 1369, 1263, 1166, 940, 798, 751, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{25}H_{21}FN_2ONa$ 407.1530, found 407.1533.

Indolylenamide ***3m***. This compound was obtained from oxazoline (*Z*)-**2**, methylindole-5-carboxylate (42 mg, 0.24 mmol) and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 48 h as a white solid (81 mg, 95%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.11; mp 199−201 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.37 (bs, 1H), 9.26 (bs, 1H), 8.32 (s, 1H), 7.71 (d, 1H, J = 8.5 Hz), 7.44 (d, 1H, J = 8.5 Hz), 7.35−7.24 (m, 9H), 7.18−7.14 (m, 1H), 6.94 (d, 1H, J = 2.5 Hz), 5.81 (s, 1H), 5.74 (s, 1H), 3.79 (s, 3H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.8, 167.2, 141.9, 139.3, 139.2, 135.7, 128.7, 128.3, 128.2, 128.1, 126.7, 126.5, 126.4, 126.2, 122.5, 122.2, 122.1, 120.1, 117.4, 111.5, 51.6, 46.8, 23.0; IR (KBr) $\tilde{\nu}$ 3420, 3023, 2949, 1691, 1654, 1617, 1491, 1436, 1279, 1244, 1109, 754, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{27}H_{24}N_2O_3Na$ 447.1679, found 447.1680.

Indolylenamide ***3n***. This compound was obtained from oxazoline (*Z*)-**2**, methylindole-6-carboxylate (42 mg, 0.24 mmol), and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 69 h as a white solid (78 mg, 92%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.19; mp 99−104 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.32 (bs, 1H), 9.25 (bs, 1H), 8.05 (s, 1H),

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7.73 (d, 1H, J = 8.5 Hz), 7.44 (d, 1H, J = 8.5 Hz), 7.36−7.35 (m, 4H), 7.29−7.25 (m, 5H), 7.18−7.14 (m, 1H), 7.01 (d, 1H, J = 2.0 Hz), 5.84 (s, 1H), 5.67 (s, 1H), 3.83 (s, 3H), 1.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.0, 167.2, 141.1, 139.2, 135.9, 135.7, 130.3, 128.8, 128.3, 128.2, 128.1, 126.8, 126.6, 122.8, 122.2, 119.5, 119.1, 116.8, 113.5, 51.7, 47.1, 23.0; IR (KBr) $\tilde{\nu}$ 3411, 3323, 3057, 3024, 2949, 1694, 1665, 1623, 1492, 1455, 1435, 1320, 1276, 1218, 1086, 776, 749, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{27}H_{24}N_2O_3Na$ 447.1679, found 447.1677.

Indolylenamide ***3o***. This compound was obtained from oxazoline (*Z*)-**2**, 5-cyanoindole (34 mg, 0.24 mmol) and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 96 h as a pink solid (48 mg, 62%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.18; mp 107−110 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.47 (bs, 1H), 9.30 (bs, 1H), 8.26 (s, 1H), 7.53 (d, 1H, J = 8.5 Hz), 7.42 (d, 1H, J = 8.5 Hz), 7.39−7.35 (m, 4H), 7.32−7.25 (m, 5H), 7.20−7.16 (m, 1H), 6.87 (d, 1H, J = 2.5 Hz), 5.87 (s, 1H), 5.60 (s, 1H), 1.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.4, 141.2, 139.2, 138.4, 135.5, 128.8, 128.4, 128.3, 128.1, 126.9, 126.8, 126.6, 125.5, 123.9, 123.2, 120.9, 117.8, 112.8, 100.5, 47.2, 22.9; IR (KBr) $\tilde{\nu}$ 3387, 3296, 3057, 3025, 2220, 1656, 1617, 1492, 1473, 1448, 1368, 807, 753, 699 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{26}H_{21}N_3ONa$ 414.1577, found 414.1578.

Indolylenamide ***3p***. This compound was obtained from oxazoline (*Z*)-**2**, 5-nitroindole (39 mg, 0.24 mmol), and Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv) after 96 h as a yellow solid (49 mg, 60%, >95:5 *Z*/*E*). R_f (1% MeOH/CH_2Cl_2) 0.20; mp 109−114 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.32 (bs, 1H), 9.30 (bs, 1H), 8.76 (d, 1H, J = 2.0 Hz), 7.98 (dd, 1H, J = 9.0, 2.0 Hz), 7.53 (d, 1H, J = 9.0 Hz), 7.38−7.36 (m, 4H), 7.31−7.25 (m, 5H), 7.19−7.15 (m, 1H), 6.97 (s, 1H), 5.87 (s, 1H), 5.71 (s, 1H), 1.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.3, 141.3, 140.4, 139.8, 139.1, 135.5, 128.8, 128.5, 128.2, 128.1, 126.9, 126.8, 126.1, 123.0, 119.2, 117.0, 116.7, 112.0, 47.0, 22.9; IR (KBr) $\tilde{\nu}$ 3408, 3058, 3025, 1654, 1624, 1518, 1492, 1472, 1332, 1100, 700 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{25}H_{21}N_3O_3Na$ 434.1475, found 434.1472.

Pyrrolylenamides ***4***. Oxazoline (*Z*)-**2** (50 mg, 0.20 mmol, 1.00 equiv), Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv), and pyrrole (28 μL, 0.40 mmol, 2.00 equiv) were dissolved in dry $CHCl_3$ (0.5 mL) and stirred at 60 °C in an oil bath for 17 h. The reaction mixture was quenched with sat. $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The crude products were purified by flash column chromatography (20% → 50% MTBE/*n*-hexane) and dried under high vacuum (0.1 mbar) at 60 °C overnight. Compound (*Z*)-**4** was obtained as an orange solid (38 mg, 59%). R_f (50% MTBE/*n*-hexane) 0.25; mp 49−52 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.61 (bs, 1H), 9.21 (bs, 1H), 7.33−7.16 (m, 10H), 6.67−6.64 (m, 1H), 5.97−5.94 (m, 1H), 5.78−5.75 (m, 2H), 5.46 (s, 1H), 1.83 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6) δ 168.8, 142.2, 139.5, 135.7, 131.2, 128.7, 128.21, 128.15, 128.07, 126.7, 126.3, 122.6, 117.3, 107.1, 106.9, 48.8, 23.0; IR (KBr) $\tilde{\nu}$ 3419, 3372, 3269, 3057, 3024, 2924, 2853, 1656, 1516, 1492, 1369, 1276, 1075, 1028, 751, 711, 698 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{21}H_{20}N_2ONa$ 339.1468, found 339.1466; Compound (*E*)-**4** was obtained as an orange solid (5 mg, 7%). R_f (50% MTBE/*n*-hexane) 0.40; mp 102−105 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (bs, 1H), 7.81 (bs, 1H), 7.50 (s, 1H), 7.35−7.18 (m, 8H), 7.10 (m, 2H), 6.75−6.73 (m, 1H), 6.03−6.01 (m, 1H), 5.91−5.89 (m, 1H), 5.45 (s, 1H), 1.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.1, 140.6, 136.7, 135.4, 129.4, 128.5, 128.4, 127.8, 126.7, 126.3, 118.0, 117.3, 107.6, 107.4, 44.0, 24.2; IR (KBr) $\tilde{\nu}$ 3410, 3344, 3024, 2924, 1675, 1647, 1517, 1494, 1267, 734, 700 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{21}H_{20}N_2ONa$ 339.1468, found 339.1466.

1-Hydroxynaphthalenylenamides ***5*** *and* ***6***. Oxazoline (*Z*)-**2** (50 mg, 0.20 mmol, 1.00 equiv), Sc(OTf)$_3$ (9.8 mg, 20 μmol, 0.10 equiv), and 1-naphthol (35 mg, 0.24 mmol, 1.20 equiv) were dissolved in dry $CHCl_3$ (0.5 mL) and stirred at 60 °C in an oil bath for 17 h. The reaction mixture was quenched with sat. $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The crude products were purified by flash column chromatography (10% → 70% MTBE/*n*-hexane) and dried under high vacuum (0.1 mbar) at 60 °C overnight. Compound **5** was obtained as a white solid (28 mg, 36%, >95:5 *Z*/*E*). R_f (30% MTBE/*n*-hexane) 0.26; mp 210−212 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.30 (bs, 1H), 10.00 (bs, 1H), 8.23−8.21 (m, 1H), 7.78−7.76 (m, 1H), 7.46−7.40 (m, 4H), 7.37−7.26 (m, 8H), 7.23−7.20 (m, 1H), 6.80 (d, 1H, J = 8.5 Hz), 5.94 (s, 1H), 5.65 (s, 1H), 2.03 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 171.9, 150.1, 139.9, 138.2, 134.7, 133.2, 129.4, 128.6, 128.4, 128.2, 127.4, 127.2, 127.0, 126.8, 125.8, 125.6, 124.83, 124.77, 122.2, 121.3, 118.2, 49.9, 22.3; IR (KBr) $\tilde{\nu}$ 3407, 3250, 3056, 3025, 2925, 1654, 1569, 1508, 1492, 1383, 1279, 752, 698 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{27}H_{23}NO_2Na$ 416.1621, found 416.1611; Compound **6** was obtained as a white solid (17 mg, 22%, >95:5 *Z*/*E*). R_f (70% MTBE/*n*-hexane) 0.56; mp 127−133 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (bs, 1H), 9.30 (bs, 1H), 8.36 (d, 1H J = 8.5 Hz), 8.16 (dd, 1H, J = 8.0, 1.5 Hz), 7.48−7.39 (m, 2H), 7.36−7.32 (m, 2H), 7.25−7.23 (m, 7H), 7.18−7.13 (m, 1H), 6.89 (d, 1H, J = 8.0 Hz), 6.80 (d, 1H, J = 8.0 Hz), 6.26 (s, 1H), 5.53 (s, 1H), 1.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.0, 152.2, 141.9, 139.6, 135.6, 132.9, 129.4, 128.4, 128.2, 128.1, 127.9, 127.1, 126.8, 126.5, 126.2, 125.1, 124.6, 124.2, 123.5, 122.3, 107.3, 50.6, 23.0; IR (KBr) $\tilde{\nu}$ 3384, 3058, 3025, 2925, 1656, 1625, 1598, 1586, 1516, 1491, 1378, 1271, 765, 754, 700 cm^{-1}; HRMS (ESI+) m/z [M + Na]$^+$ calcd for $C_{27}H_{23}NO_2Na$ 416.1621, found 416.1626.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00791.

^{1}H and ^{13}C NMR spectra for all new compounds and crystallographic data for compound **3a** (CCDC 1541861) (PDF)

Crystal data and structure refinement for indolylenamide **3a** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: schneider@chemie.uni-leipzig.de.

ORCID

Christoph Schneider: 0000-0001-7392-9556

Notes

The authors declare no competing financial interest.

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