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Direct FeX_3-Based Stereocontrolled Access to (*Z*)-3-Alkenyl-oxindoles from Allenols

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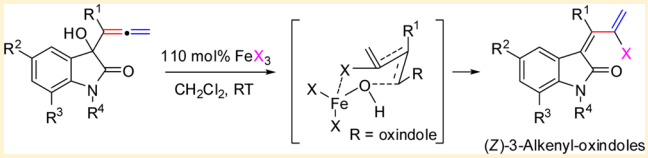
Supporting Information

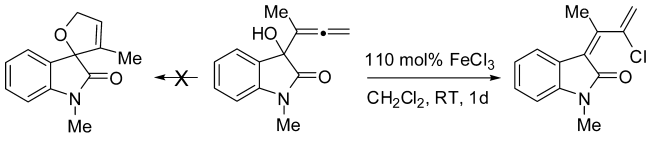
ABSTRACT: Iron trihalides ($FeCl_3$ and $FeBr_3$) smoothly promote the halogenation/rearrangement of 2-indolinone-tethered allenols to efficiently afford 3-halodienyl-oxindoles with good yield and total selectivity. Also, 2-halo-1,3-dienes are synthetically interesting building blocks for the preparation of functionalized 3-alkenyl-oxindoles through a Suzuki−Miyaura reaction.



The carbon−carbon double bond of allenes, a class of compounds with two π-orbitals perpendicular to each other, is ~10 kcal mol^{-1} less stable than that of simple alkenes,[1] rendering them significantly more reactive. Thus, allenes have metamorphosed from a laboratory curiosity to a versatile and uniquely reactive functional group, allowing chemists to prepare a variety of compounds of chemical and biological interest.[2] On the other hand, the potent biological activities of natural and man-made 3-alkenyl-oxindoles are also increasingly appreciated, mainly due to their antiangiogenic, antibacterial, antifungal, antitumor, and antiviral properties.[3] The 1,3-diene moiety is ubiquitous in a variety of natural products of biological interest.[4] Besides, the 1,3-diene functionality has led to many synthetically useful transformations.[5] In particular, 2-halo-1,3-dienes are useful compounds in organic synthesis because the halide atom acts as a directing group prone to further transformations.[6] Main previous strategies for the preparation of 2-halo-1,3-dienes have been centered on coupling protocols, and their syntheses from allenol derivatives usually proceeded with poor diastereoselectivity.[7] Following up on our combined interest in the area of lactams and allenes,[8] and considering the inexpensiveness and environmentally friendliness of iron species, we chose to study the FeX_3-promoted reaction of 2-indolinone-tethered allenols as a route to access 3-alkenyl-oxindoles because of the potential biological activities.

Starting allenols **1a**−**i** were achieved via indium-mediated Barbier-type allenylation reactions of isatins in aqueous media following our previously described methodology.[9] Originally, we were attempting the iron-catalyzed cycloisomerization reaction of allenol **1a** under $FeCl_3$ catalysis (10 mol %), but surprisingly, a 9% yield of the (*Z*)-3-(3-chlorobut-3-en-2-ylidene)indolin-2-one **2a** was obtained. Considering the economic attractiveness and the environmentally friendliness of iron species, we became interested in developing an allenol-based methodology for the preparation of functionalized (*Z*)-3-alkenyl-oxindoles. Our initial studies focused on developing a more efficient transformation, and we used the reaction of allenol **1a** with $FeCl_3$ as a model system. The reaction product **2a** could only be obtained in reasonable yield using a higher reagent loading. An optimal yield of **2a** was obtained at 20 °C by using 110 mol % of $FeCl_3$ and dichloromethane as the solvent (Scheme 1). A brief optimization of the halide source

Scheme 1. Chlorination/Rearrangement Reaction of Indolinone-Tethered Allenol 1a to (*Z*)-3-(3-Chlorobut-3-en-2-ylidene)indolin-2-one 2a by $FeCl_3$ Treatment



revealed that employment of other metal halides did not improve the yield of compound **2a**. In addition to $FeCl_3$, $BiCl_3$ was also tested with allenol **1a**. Next, both $HfCl_4$ and $ZnCl_2$ were investigated. Substrate **1a** did not react in the presence of $HfCl_4$ or $ZnCl_2$ under otherwise identical conditions. The use of $BiCl_3$ as a halide source provided 2-halo-1,3-diene **2a**, but in a low 51% yield after 2 days of reaction.

With optimized conditions in hand, we then examined the generality of this iron-promoted halogenation/rearrangement protocol. As shown in Table 1, all the reactions proceeded smoothly and afforded the desired products in reasonable to good yields upon isolation. We observed that allenic *NH*-indolinones (Table 1, entries 4−7) exhibited excellent reactivity and yielded full conversion of benchmark substrates. Electron-withdrawing and -donating substituents on the aryl ring of the

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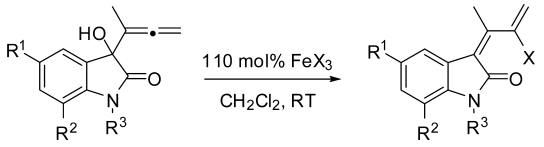
Table 1. Halogenation/Rearrangement Reaction of Indolinone-Tethered Allenols 1 to (Z)-3-(3-Halobut-3-en-2-ylidene)indolin-2-ones 2 by FeX_3 Treatment[a]



entry	allenol	X	time (h)	R^1	R^2	R^3	yield (%)
1	**1a**	Cl	22	H	H	Me	**2a** (71)
2	**1b**	Cl	22	Cl	H	Me	**2b** (63)
3	**1c**	Cl	22	H	Cl	Me	**2c** (88)
4	**1d**	Cl	3	H	H	H	**2d** (70)
5	**1e**	Cl	40	Cl	H	H	**2e** (82)
6	**1f**	Cl	22	H	Cl	H	**2f** (93)
7	**1g**	Cl	22	H	MeO	H	**2g** (65)
8	**1a**	Br	40	H	H	Me	**2h** (74)
9	**1b**	Br	136	Cl	H	Me	**2i** (50)
10	**1e**	Br	136	Cl	H	H	**2j** (72)
11	**1h**	Br	22	H	MeO	Me	**2k** (75)
12	**1i**	Cl	20	Br	H	H	**2l** (77)
13	**1i**	Br	40	Br	H	H	**2m** (70)

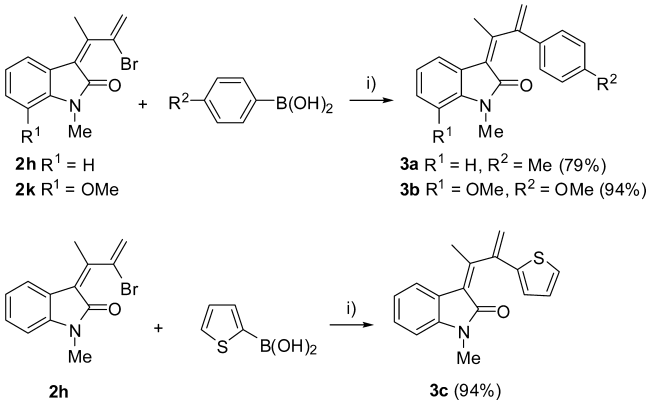
[a]The stereochemistry of products **2** was unambiguously determined by the NOE analysis of **2b** (see Supporting Information). NOE irradiation of the C-methyl group (δ = 2.58 ppm) resulted in enhancements of different intensity in the signals corresponding to the vinylic protons (δ = 5.42 ppm and δ = 5.58 ppm) and (C4)-aromatic proton (δ = 7.66 ppm). On the basis of these data, a (*Z*)-stereochemistry was assigned.

oxindoles were tolerated with only little influence on the reactivity (Table 1, entries 1−7). The placement of a bromine or chlorine atom at the C5 and C7 positions of the indole ring was tolerated in the presence of $FeCl_3$, providing a handle for subsequent orthogonal reactivity. It is often the case that reaction conditions optimized for one class of halides are less effective with others. However, the exact same conditions also promote the efficient reaction of $FeBr_3$ with a diverse range of 2-indolinone-tethered allenols **1**. Notably, the bromination/rearrangement reactions of allenols **1** with $FeBr_3$ gave the corresponding products in fair yields (Table 1, entries 8−11).

Owing to the efficacy and functional group tolerance of transition metal catalyzed cross-coupling reactions in forming C−C bonds, we envisioned that our 2-halo-1,3-dienes may be synthetically interesting building blocks for the preparation of functionalized 3-alkenyl-oxindoles through a Suzuki−Miyaura reaction. Indeed, the Pd-catalyzed coupling between bromodienes **2h** and **2k** with arylboronic acids afforded products **3a**−**c** (Scheme 2).[10]

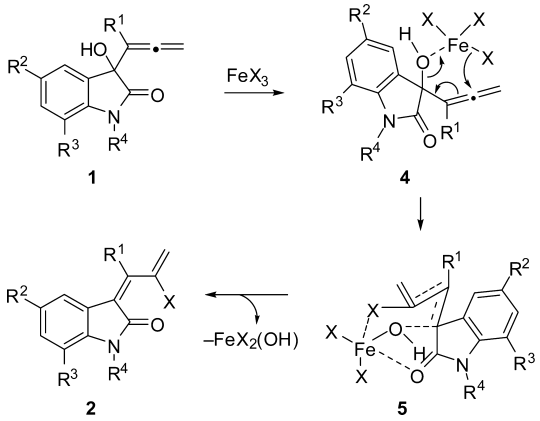
The proposed mechanism for the formation of our 2-halo-1,3-dienes is outlined in Scheme 3. In the diene formation, the iron trihalide salt FeX_3 acts as a Lewis acid interacting with the alcohol group in the allenol moiety to give complex **4**. The extremely high (*Z*)-selectivity observed in the formation of dienes **2** may indicate a concerted pseudopericyclic reaction[11] pathway rather than a stepwise path, namely, separation of the hydroxyl group of allenols **1** by FeX_3 leading to a carbonium species. The process probably proceeds via a chairlike six-membered cyclic transition structure **5**, through delivery of the halide ion (from the less hindered side) with concomitant detachment of the hydroxyl group, to afford the halobutenylidene indolinones with *Z* selectivity. Probably, the C═O

Scheme 2. Preparation of 2-Aryl-1,3-dienyl Oxindoles 3 through Suzuki−Miyaura Reaction[a]



[a]Conditions: 2.5 mol % $Pd(PPh_3)_4$, $NaHCO_3$, toluene−EtOH−H_2O (18:1:1), reflux, 4 h.

Scheme 3. Mechanistic Explanation for the Halogenation/Rearrangement of 2-Indolinone-Tethered Allenols through Reaction with Iron Trihalide



moiety takes a (pseudo)axial position. An axial position of the C═O group could be rationalized by its smaller size compared to the aryl ring system. Furthermore, an axial position of C═O might be stabilized by the iron center through a coordinating interaction. In other words, the (*Z*)-selectivity could be the consequence of chelating both the C═O unit and the OH group of the indolinone ring to the metal.[12]

In conclusion, iron trihalides ($FeCl_3$ and $FeBr_3$) smoothly promote the halogenation/rearrangement of 2-indolinone-tethered allenols to efficiently afford 3-halodienyl-oxindoles with good yield and total selectivity.

EXPERIMENTAL SECTION

General Methods. ^1H and ^{13}C NMR spectra were recorded on 300 MHz spectrometers. NMR spectra were recorded in $CDCl_3$ solutions, unless otherwise stated. Chemical shifts are given in ppm relative to TMS (^1H, 0.0 ppm) or $CDCl_3$ (^{13}C, 76.9 ppm). Low and high resolution mass spectra were taken on a QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. All commercially available compounds were used without further purification.

Indium-Promoted Reaction between 1-Bromo-2-butyne and Substituted Isatins; General Procedure for the Synthesis of α-Allenic Alcohols 1a−i. 1-Bromo-2-butyne (3.0 mmol) was added to a well stirred suspension of the corresponding isatin (1.0 mmol) and indium powder (6.0 mmol) in THF/NH_4Cl (aq. sat.) (1:5,

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5 mL) at 0 °C. After the disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for previously unreported α-allenic alcohols **1g**−**1i** follow.

α-Allenic Alcohol 1g. From 200 mg (1.13 mmol) of 7-methoxyisatin, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, compound **1g** (198 mg, 76%) was obtained as a pale brown solid; mp 121−123 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.76 (br s, 1H), 7.11−7.00 (m, 2H), 6.90 (dd, J = 8.2, 0.9 Hz, 1H), 5.08 (q, J = 3.1 Hz, 2H), 3.91 (s, 3H), 1.63 (t, J = 3.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 204.6, 177.7, 143.9, 130.1, 129.6, 123.7, 116.9, 112.2, 100.5, 80.4, 77.1, 55.7, 13.6; IR ($CHCl_3$, cm^{-1}): ν 3259, 2934, 1715, 1329. HRMS (ES): calcd for $C_{13}H_{13}NO_3$ $[M + H]^+$, 232.0974; found, 232.0974.

α-Allenic Alcohol 1h. From 90 mg (0.47 mmol) of *N*-methyl 7-methoxyisatin, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, compound **1h** (74 mg, 64%) was obtained as a colorless solid; mp 126−128 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.06−6.96 (m, 2H), 6.90 (d, J = 8.0 Hz, 1H), 5.02 (q, J = 3.1 Hz, 2H), 3.85 (s, 3H), 3.46 (s, 3H), 3.40 (br s, 1H), 1.53 (t, J = 3.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 204.7, 176.8, 145.3, 131.4, 130.6, 123.7, 116.9, 113.7, 100.8, 80.2, 76.1, 55.9, 29.6, 13.6; IR ($CHCl_3$, cm^{-1}): ν 3379, 2934, 1715, 1329. HRMS (ES): calcd for $C_{14}H_{15}NO_3$ $[M]^+$, 245.1052; found, 245.1044.

α-Allenic Alcohol 1i. From 600 mg (2.65 mmol) of 5-bromoisatin, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, compound **1i** (494 mg, 67%) was obtained as a pale yellow solid; mp 183−185 °C; ^{1}H NMR (300 MHz, acetone-δ_6, 25 °C) δ: 9.41 (br s, 1H), 7.42−7.39 (m, 2H), 6.88 (d, J = 8.9, Hz, 1H), 4.77 (q, J = 3.2 Hz, 2H), 1.75 (t, J = 3.2 Hz, 3H); ^{13}C NMR (75 MHz, acetone-δ_6, 25 °C) δ: 206.9, 177.6, 142.1, 134.7, 133.0, 128.7, 114.7, 112.5, 101.3, 78.4 (2C), 13.9; IR (KBr, cm^{-1}): ν 3323, 2986, 1725, 1618, 1476. HRMS (ES): calcd for $C_{12}H_{11}BrNO_2$ $[M + H]^+$, 279.9973; found, 279.9970.

FeX_3-Promoted Reaction of Allenols 1. *Synthesis of 3-Halodienyl-oxindoles* ***2***. To a solution of the appropriate allenol **1** (0.14 mmol) in dichloromethane (2.5 mL), anhydrous FeX_3 (0.154 mmol) was added under argon. The reaction mixture was stirred at rt until the starting material disappeared as indicated by TLC. After filtration through a pad of Celite, the mixture was concentrated under vacuum and purified by flash column chromatography eluting with an ethyl acetate/hexanes mixture. Spectroscopic and analytical data for pure forms of compounds **2** follow.

3-Chlorodienyl-oxindole ***2a***. From 30 mg (0.14 mmol) of indolin-2-one-tethered allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound **2a** (24 mg, 71%) was obtained as a yellow solid; mp 96−98 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.71 (d, J = 7.6 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 6.90 (t, J = 7.8 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 5.53 and 5.41 (d, J = 1.8 Hz, each 1H), 3.16 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.8, 147.7, 142.7, 139.1, 129.2, 123.8, 123.7, 121.8, 121.2, 115.3, 107.7, 25.7, 19.2; IR ($CHCl_3$, cm^{-1}): ν 3056, 2927, 1699, 1607, 1474, 1329. HRMS (ES): calcd for $C_{13}H_{13}ClNO$ $[M + H]^+$, 234.0686; found, 234.0686.

3-Chlorodienyl-oxindole ***2b***. From 30 mg (0.12 mmol) of indolin-2-one-tethered allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, compound **2b** (20 mg, 63%) was obtained as a yellow solid; mp 97−99 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.66 (d, J = 2.0 Hz, 1H), 7.17 (dd, J = 8.3, 2.0 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 5.58 and 5.42 (d, J = 1.9 Hz, each 1H), 3.15 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.4, 149.6, 141.2, 138.5, 128.8, 127.2, 123.9, 123.0, 122.4, 115.7, 108.6, 25.8, 19.4; IR ($CHCl_3$, cm^{-1}): ν 2930, 1700, 1462. HRMS (ES): calcd for $C_{13}H_{11}Cl_2NO$ $[M]^+$, 267.0218; found, 267.0213.

3-Chlorodienyl-oxindole ***2c***. From 30 mg (0.12 mmol) of indolin-2-one-tethered allenol **1c**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, compound **2c** (28 mg, 88%) was obtained as a yellow solid; mp 116−118 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.64 (d, J = 7.6 Hz, 1H), 7.11 (d, J = 7.9 Hz, 1H), 6.81 (t, J = 7.9 Hz, 1H), 5.52 and 5.38 (d, J = 1.9 Hz, each 1H), 3.55 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.9, 149.1, 138.9, 138.6, 131.2, 123.8, 122.8, 122.4, 122.3, 115.3, 29.1, 19.9; IR ($CHCl_3$, cm^{-1}): ν 2923, 1698, 1458, 1129. HRMS (ES): calcd for $C_{13}H_{11}Cl_2NO$ $[M]^+$, 267.0218; found, 267.0216.

3-Chlorodienyl-oxindole ***2d***. From 26 mg (0.13 mmol) of indolin-2-one-tethered allenol **1d**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, compound **2d** (20 mg, 70%) was obtained as a yellow solid; mp 122−124 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.42 (br s, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 6.89 (t, J = 7.6 Hz, 1H), 6.78 (d, J = 7.7 Hz, 1H), 5.54 and 5.43 (d, J = 1.7 Hz, each 1H), 2.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 169.7, 148.3, 140.0, 139.0, 129.2, 124.1 (2C), 121.9, 121.8, 115.3, 109.6, 19.2; IR ($CHCl_3$, cm^{-1}): ν 3199, 1698, 1466. HRMS (ES): calcd for $C_{12}H_{10}ClNO$ $[M]^+$, 219.0451; found, 219.0447.

3-Chlorodienyl-oxindole ***2e***. From 30 mg (0.13 mmol) of indolin-2-one-tethered allenol **1e**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, compound **2e** (23 mg, 82%) was obtained as a yellow solid; mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.99 (br s, 1H), 7.71 (d, J = 1.9 Hz, 1H), 7.18 (dd, J = 8.3, 1.9 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 5.66 and 5.52 (d, J = 1.9 Hz, each 1H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 169.6, 150.3, 138.5, 138.3, 128.9, 127.2, 124.1, 123.4, 123.2, 115.8, 110.5, 19.4; IR ($CHCl_3$, cm^{-1}): ν 3194, 1700, 1462. HRMS (ES): calcd for $C_{12}H_9Cl_2NO$ $[M]^+$, 253.0061; found, 253.0057.

3-Chlorodienyl-oxindole ***2f***. From 25 mg (0.10 mmol) of indolin-2-one-tethered allenol **1f**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, compound **2f** (24 mg, 93%) was obtained as a yellow solid; mp 138−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.19 (br s, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.21 (dd, J = 8.0, 0.6 Hz, 1H), 6.92 (t, J = 8.0 Hz, 1H), 5.63 and 5.50 (d, J = 1.9 Hz, each 1H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 168.4, 150.3, 138.5, 137.5, 128.7, 123.9, 123.2, 122.5, 122.3, 115.6, 114.8, 19.4; IR ($CHCl_3$, cm^{-1}): ν 3144, 2923, 1702, 1440. HRMS (ES): calcd for $C_{12}H_{10}Cl_2NO$ $[M + H]^+$, 254.0139; found, 254.0136.

3-Chlorodienyl-oxindole ***2g***. From 40 mg (0.17 mmol) of indolin-2-one-tethered allenol **1g**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, compound **2g** (27 mg, 65%) was obtained as a yellow solid; mp 138−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.96 (br s, 1H), 7.43 (d, J = 7.8 Hz, 1H), 6.95 (t, J = 8.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 5.64 and 5.53 (d, J = 1.8 Hz, each 1H), 3.91 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 168.7, 148.7, 143.5, 138.9, 129.2, 124.6, 122.5, 122.0, 116.6, 115.4, 111.3, 55.7, 19.1; IR ($CHCl_3$, cm^{-1}): ν 3193, 2933 1701, 1210. HRMS (ES): calcd for $C_{13}H_{13}ClNO_2$ $[M + H]^+$, 250.0635; found, 250.0637.

3-Bromodienyl-oxindole ***2h***. From 40 mg (0.14 mmol) of indolin-2-one-tethered allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound **2h** (29 mg, 74%) was obtained as a pale brown solid; mp 123−125 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.81 (d, J = 7.7 Hz, 1H), 7.28 (td, J = 7.7, 1.0 Hz, 1H), 7.00 (td, J = 7.7, 1.0 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 5.85 and 5.81 (d, J = 2.1 Hz, each 1H), 3.24 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.4, 149.4, 142.7, 129.6, 129.1, 124.1, 123.0, 121.8, 121.2, 119.0, 107.7, 25.7, 19.4; IR ($CHCl_3$, cm^{-1}): ν 3054, 2926, 1699, 1605, 1474. HRMS (ES): calcd for $C_{13}H_{13}BrNO$ $[M + H]^+$, 278.0181; found, 278.0180.

3-Bromodienyl-oxindole ***2i***. From 40 mg (0.16 mmol) of indolin-2-one-tethered allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound **2i** (25 mg, 50%) was obtained as a yellow solid; mp 95−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.76 (s, 1H), 7.27−7.24 (m, 1H), 6.72 (d, J = 8.3 Hz, 1H), 5.88−5.86 (m, 2H), 3.23 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.4, 151.3, 141.1, 128.8, 127.3, 124.2 (2C), 122.5, 122.2, 119.5, 108.6, 25.9, 19.7; IR ($CHCl_3$, cm^{-1}): ν 2930, 1700, 1462. HRMS (ES): calcd for $C_{13}H_{12}$ BrClNO $[M + H]^+$, 311.9791; found, 311.9795.

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3-Bromodienyl-oxindole ***2j***. From 30 mg (0.13 mmol) of indolin-2-one-tethered allenol **1e**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound **2j** (28 mg, 72%) was obtained as a pale brown solid; mp 136−138 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.88 (br s, 1H), 7.74 (d, J = 1.9 Hz, 1H), 7.20 (dd, J = 8.3, 2.0 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 5.90 and 5.87 (d, J = 2.3 Hz, each 1H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 169.5, 151.9, 138.4, 128.9, 128.6, 127.3, 124.5, 123.3, 122.6, 119.5, 110.5, 19.6; IR ($CHCl_3$, cm^{-1}): ν 3198, 2921, 1700, 1464. HRMS (ES): calcd for $C_{12}H_9BrClNO$ $[M]^+$, 296.9556; found, 296.9557.

3-Bromodienyl-oxindole ***2k***. From 27 mg (0.11 mmol) of indolin-2-one-tethered allenol **1h**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound **2k** (25 mg, 75%) was obtained as a pale brown solid; mp 98−100 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.47 (dd, J = 7.4, 1.0 Hz, 1H), 6.94−6.84 (m, 2H), 5.82 and 5.78 (d, J = 2.1 Hz, each 1H), 3.85 (s, 3H), 3.51 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 167.9, 149.6, 145.0, 130.9, 129.7, 123.2, 122.6, 122.0, 118.9, 117.1, 113.0, 56.0, 29.1, 19.6; IR ($CHCl_3$, cm^{-1}): ν 2928, 1693, 1459, 1250. HRMS (ES): calcd for $C_{14}H_{14}BrNO_2$ $[M]^+$, 307.0208; found, 307.0199.

3-Chlorodienyl-oxindole ***2l***. From 37 mg (0.13 mmol) of indolin-2-one-tethered allenol **1i**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, compound **2l** (30 mg, 77%) was obtained as a yellow solid; mp 149−151 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.85 (br s, 1H), 7.85 (d, J = 1.9 Hz, 1H), 7.33 (dd, J = 8.2, 1.9 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 5.67 and 5.52 (d, J = 1.9 Hz, each 1H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 169.4, 150.3, 138.9, 138.3, 131.8, 126.9, 123.6, 123.2, 115.8, 114.5, 111.0, 19.5; IR ($CHCl_3$, cm^{-1}): ν 3194, 1701, 1466. HRMS (ES): calcd for $C_{12}H_{10}BrClNO$ $[M + H]^+$, 297.9634; found, 297.9626.

3-Bromodienyl-oxindole ***2m***. From 28 mg (0.10 mmol) of indolin-2-one-tethered allenol **1i**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, compound **2m** (24 mg, 70%) was obtained as a pale brown solid; mp 129−131 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 8.71 (br s, 1H), 7.87 (d, J = 1.9 Hz, 1H), 7.34 (dd, J = 8.2, 1.9 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 5.89 and 5.86 (d, J = 2.2 Hz, each 1H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 169.3, 151.9, 138.8, 131.7, 128.6, 127.2, 123.7, 122.4, 119.6, 114.6, 110.9, 19.6; IR ($CHCl_3$, cm^{-1}): ν 3214, 2923, 1700, 1466. HRMS (ES): calcd for $C_{12}H_{10}Br_2NO$ $[M + H]^+$, 341.9129; found, 341.9126.

General Procedure for the Suzuki−Miyaura Cross-Coupling Reaction of Bromodienes 2 with Boronic Acids. Preparation Aryl-butylidenes 3. The corresponding bromodiene **2** (0.08 mmol) was added under argon to a stirred suspension of the appropriate arylboronic acid (0.12 mmol) and sodium bicarbonate (0.25 mmol) in toluene/ethanol/water (18:1:1) (1.68 mL), and the resulting mixture was stirred for 15 min. Then, $Pd(PPh_3)_4$ (2.5 mol %) was added and the reaction mixture was heated at reflux temperature for 3 h. The reaction mixture was allowed to cool to ambient temperature, before being partitioned between ethyl acetate and water. The organic extract was washed with water (2 × 1 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue eluting with a hexanes/ethyl acetate mixture gave analytically pure compounds **3**.

Aryl-butylidene ***3a***. From 25 mg (0.09 mmol) of bromodiene **2h**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, compound **3a** (21 mg, 79%) was obtained as a pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.55 (d, J = 7.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.22−7.19 (m, 1H), 7.16 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 7.7 Hz, 2H), 5.75 and 5.22 (s, each 1H), 3.30 (s, 3H), 2.64 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 168.1, 155.0, 149.5, 142.3, 138.5, 133.2, 129.6 (2C), 128.1, 126.1 (2C), 123.5 (2C), 122.4, 121.6, 111.4, 107.4, 25.7, 21.5, 21.2; IR ($CHCl_3$, cm^{-1}): ν 1695. HRMS (ES): calcd for $C_{20}H_{19}NO$ $[M]^+$, 289.1467; found, 289.1458.

Aryl-butylidene ***3b***. From 18 mg (0.057 mmol) of bromodiene **2k**, and after chromatography of the residue using hexanes/ethyl acetate (7:1) as eluent, compound **3b** (22 mg, 94%) was obtained as a pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.38 (d, J = 8.9 Hz, 2H), 7.20 (dd, J = 7.3, 1.5 Hz, 1H), 6.86 (d, J = 8.9 Hz, 2H), 6.79−6.69 (m, 2H), 5.64 and 5.12 (s, each 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.57 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 168.3, 159.8, 155.5, 149.1, 144.9, 130.5, 128.4, 127.4 (2C), 123.8, 123.7, 121.8, 116.7, 114.2 (2C), 112.1, 110.1, 56.0, 55.2, 29.1, 21.8; IR ($CHCl_3$, cm^{-1}): ν 1700. HRMS (ES): calcd for $C_{21}H_{22}NO_3$ $[M + H]^+$, 336.1600; found, 336.1587.

Aryl-butylidene ***3c***. From 30 mg (0.11 mmol) of bromodiene **2h**, and after chromatography of the residue using hexanes/ethyl acetate (8:1) as eluent, compound **3c** (29 mg, 94%) was obtained as a pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.50 (d, J = 7.6 Hz, 1H), 7.25−7.17 (m, 2H), 6.94−6.77 (m, 4H), 5.70 and 5.10 (s, each 1H), 3.28 (s, 3H), 2.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ: 168.0, 152.8, 143.9, 142.3, 140.6, 128.3, 127.8, 125.7, 125.6, 123.8, 123.6, 121.9, 121.7, 110.7, 107.5, 25.7, 21.6; IR ($CHCl_3$, cm^{-1}): ν 1696. HRMS (ES): calcd for $C_{17}H_{15}NOS$ $[M]^+$, 281.0874; found, 281.0875.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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