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Gallium-Catalyzed Domino Arylation/Oxycyclization of Allenes with Phenols

Benito Alcaide,*[,†] Pedro Almendros,*[,‡] Fernando Herrera,[†] Amparo Luna,[†] M. Elena de Orbe,[†] and M. Rosario Torres[§]

[†]Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica I, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid, Spain

[‡]Instituto de Química Orgánica General, IQOG-CSIC, Juan de la Cierva 3, 28006-Madrid, Spain

[§]CAI Difracción de Rayos X, Facultad de Química, Universidad Complutense de Madrid, 28040 Madrid, Spain

E-mail: alcaideb@quim.ucm.es; Palmendros@iqog.csic.es

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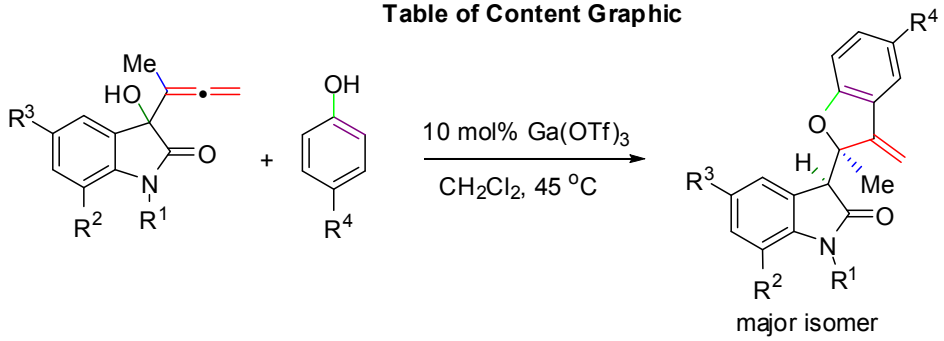


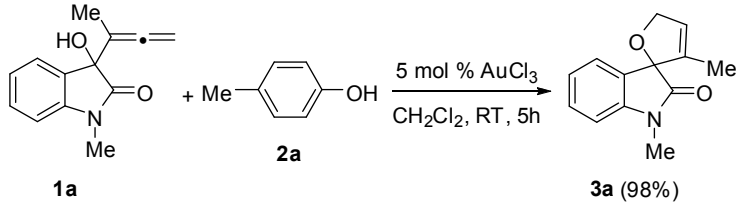
ABSTRACT: The synthesis of dihydrobenzofuran-appended oxindoles has been accomplished taking advantage of an unprecedented reaction between allenols and phenols under metal catalysis.

The dihydrobenzofuran motif is present in a wide variety of natural products and biologically relevant compounds,[1] and the synthesis of this heterocycle is of current interest.[2] Numerous reports are available on metal-catalyzed cyclization or cross-coupling reactions of functionalized allenes.[3]

In contrast, such reactions that involve the coupling of the allene moiety and a phenol are scarcely accessible in literature.[4] Despite that phenols are readily available chemicals, their use is problematic due to selectivity issues. Recently, we have successfully reported selective transformations of both indolinone-tethered allenols[5] and phenols.[6] We envisioned that different behaviour of the allenol moiety might be achieved utilizing a phenol as coupling partner. Herein, we present a gallium-catalyzed coupling–cyclization between phenols and indolinone-tethered allenols towards the preparation of dihydrobenzofuran-linked oxindoles.

To explore the possibility of an allene–phenol coupling, allenol **1a** and phenol **2a** were initially chosen. The $AuCl_3$-catalyzed reaction of allenol **1a** and 4-methylphenol **2a** afforded the spirocyclic 2,5-dihydrofuran **3a** (Scheme 1). Hence, the hydroxy group in allenol **1a** exclusively suffers 5-*endo* oxycyclization reaction,[7] without the participation of the phenol moiety.

Scheme 1. Non-Productive Gold-Catalyzed Reaction of Indolinone-Tethered Allenol 1a and Phenol 2a

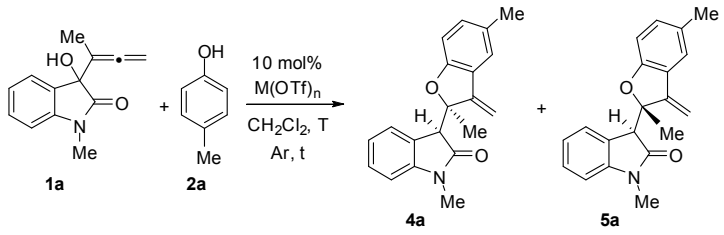


1a **2a** **3a** (98%)

When a π acid such as $AuCl_3$ is used, it might coordinate with one of the allene double bonds via a monodentade mode. When a Lewis acid is employed, it might coordinate with the OH of the allenol moiety via monodentade or bidentade modes. This activation might generate a carbocation intermediate. Consequently, we decided to use a main-group salt instead of a transition-metal derivative. Happily, after assessing various metal catalysts, we found that a catalytic amount of metal triflate specifically promoted the domino allenol–phenol coupling reaction (Table 1). The domino reaction took place at 40ºC under $M(OTf)_n$ catalysis, which specifically promoted the generation of the desired dihydrobenzofuran-appended oxindole scaffold, and the domino addition–cyclization reaction took place readily.[8] Diastereoselectivities were modest, in all cases giving rise to mixtures of adducts **4a** and **5a**. Based on conversion and isolated yields, gallium(III) triflate

proved to be the most efficient Lewis acid catalyst (Table 1, entry 12).[9,10] An experiment using molecular sieves as additive led to comparable results, thus indicating that this transformation could be efficiently catalyzed by metal triflates. A screening of solvents (acetonitrile, tetrahydrofuran, toluene) revealed that the reaction is best performed in dichloromethane. A Brønsted acid such as trifluoromethanesulfonic acid (TfOH) was also tested. The corresponding rearranged α,β-unsaturated ketone was the major reaction product under stoichiometric TfOH conditions. However, the use of 10 mol% TfOH afforded adducts **4a** and **5a** along with minor rearranged ketone, but did not get the reaction to completion, remaining some unreacted starting material. Comparatively, the use of TfOH led to limited reactivity.

Table 1. Reaction between Indolinone-Tethered Allenol 1a and Phenol 2a under Modified Metal-Catalyzed Conditions

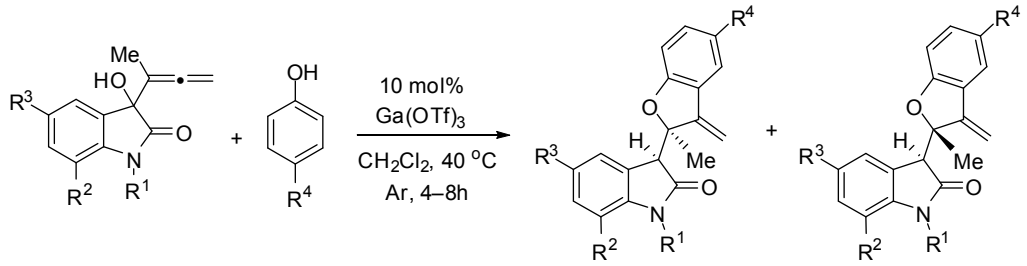


entry	catalyst	temperature (°C)	time (h)	**4a:5a** yield (%)[a]
1	$In(OTf)_3$	40	11	25/8
2	$Zn(OTf)_2$	40	12	22/7
3	$Fe(OTf)_3$	40	10	29/9
4	$Yb(OTf)_3$	40	12	20/6
5	$Bi(OTf)_3$	40	1	26/19
6	$Bi(OTf)_3$	30	3	23/17
7	$Bi(OTf)_3$	130/sealed tube	0.5	6/4[b]
8	$Bi(OTf)_3$	80/microwave	0.5	19/14
9	$Bi(OTf)_3$/PTSA	40	1	11/15
10	$Ga(OTf)_3$[c]	40	30	23/13
11	$Ga(OTf)_3$[d]	40	12	30/17
12	$Ga(OTf)_3$	40	4	35/20

[a]Yield of pure, isolated product with correct analytical and spectral data. [b]Decomposition of the starting allenol **1a** was observed in appreciable extension. [c]Catalyst loading of 2 mol%. [d]Catalyst loading of 5 mol%.

With the optimized reaction conditions in hand we then examined the scope and generality of the Ga-catalyzed method. Thus, various methyl-substituted allenols and phenols were reacted to give a range of dihydrobenzofuran-appended oxindoles **4** and **5** (Scheme 2).[11] The two products obtained from the coupling reaction are not identical but rather stand in an epimeric relationship at the allylic position. Although the diastereoselectivity of the reaction between **1a** and **2a** is poor under the conditions (Table 1), efforts for further improvements were not in vain. Interestingly, both the use of NH-free allenols **1b–d** and phenols bearing bulkier substituents (such as Br o *t*-Bu) resulted in improved diastereoselectivities (Scheme 2). The influence of the electronic nature of the substituents at the phenol reactant was first examined by submitting 4-methoxyphenol **1d** to various allenols **1**. In the event, phenol **1e** reacted well and the corresponding adducts **4d**, **4l**, **5d**, and **5l** were obtained. Unfortunately, a negative result was observed using either 4-hydroxybenzonitrile or methyl 4-hydroxybenzoate, which indicated that electron-withdrawing groups on the aromatic ring were not compatible with this catalytic arylation/oxycyclization reaction sequence. The R_f values of the two dihydrobenzofuran isomers **4a–l** and **5a–l** were very close to each other. Fortunately, the diastereomeric adducts **4** and **5** could be separated by flash chromatography, thus providing readily two structurally complex and valuable heterocyclic products. However, characterization of minor adducts **5c**, **5d**, **5f–i**, **5k**, and **5l** was performed on a mixture containing small amounts of their major counterparts **4**. Because most of the reactions were conducted in a 50 mg scale, it was desirable to scale-up the procedure. Worthy of note, when we performed a 4 mmol-scale reaction starting from allenol **1a** and phenol **2a**, adducts **4a** and **5a** were isolated in a combined yield of 59%, which is slightly higher than that achieved at a smaller scale during the scope study. The structure of dihydrobenzofuran **5a** was unambiguously confirmed with the help of a X-ray diffraction analysis on suitable crystals of this compound (Figure 1, see the Supporting Information).[12]

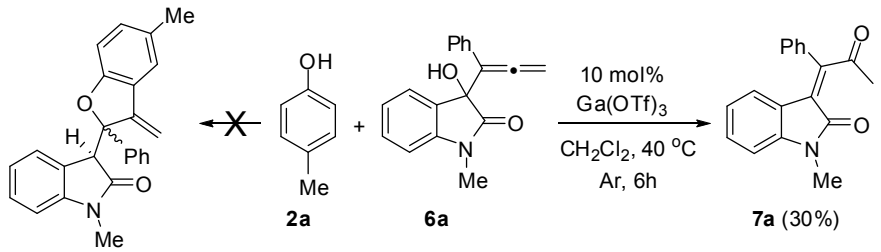
Scheme 2. Synthesis of Dihydrobenzofuran-Appended Oxindoles 4 and 5 through Domino Addition–Cyclization Reaction under Gallium Catalysis



1a R^1 = Me, R^2 = H, R^3 = H	**2b** R^4 = *t*-Bu	**4b** (67%)	**5b** (17%)
1a R^1 = Me, R^2 = H, R^3 = H	**2c** R^4 = Br	**4c** (50%)	**5c** (10%)
1a R^1 = Me, R^2 = H, R^3 = H	**2d** R^4 = MeO	**4d** (42%)	**5d** (20%)
1b R^1 = H, R^2 = H, R^3 = H	**2a** R^4 = Me	**4e** (60%)	**5e** (24%)
1b R^1 = H, R^2 = H, R^3 = H	**2b** R^4 = *t*-Bu	**4f** (52%)	**5f** (6%)
1b R^1 = H, R^2 = H, R^3 = H	**2c** R^4 = Br	**4g** (38%)	**5g** (6%)
1b R^1 = H, R^2 = H, R^3 = H	**2e** R^4 = H	**4h** (55%)	**5h** (10%)
1c R^1 = H, R^2 = H, R^3 = Br	**2a** R^4 = Me	**4i** (49%)	**5i** (9%)
1d R^1 = H, R^2 = OMe, R^3 = H	**2a** R^4 = Me	**4j** (69%)	**5j** (7%)
1d R^1 = H, R^2 = OMe, R^3 = H	**2b** R^4 = *t*-Bu	**4k** (48%)	**5k** (9%)
1b R^1 = H, R^2 = H, R^3 = H	**2d** R^4 = MeO	**4l** (50%)	**5l** (17%)

Next, the reaction of aryl-substituted allenol derivatives and phenols was examined. To test the reactivity of aryl allenes **6**, we started the initial investigation on the gallium-catalyzed reaction of phenyl-substituted allene **6a** under otherwise identical reaction conditions used for its methyl-counterpart **1a**. In the event, it was found that substrate **6a** was exclusively transformed into the rearranged product **7a** (Scheme 3).[13] Noticeably, despite the above ability (Schemes 1 and 2) of metal triflate-based catalysis for the coupling reaction of allenols **1** and phenols into dihydrobenzofurans **4**/**5**, no traces of oxacycles were detected using gallium(III) triflate as promoter. Possibly, attempts to use aryl-substituted substrates **6** proved to be unsuccessful for the construction of the corresponding dihydrobenzofurans, because of both unfavourable steric factors as well as a direct interaction of the π-aromatic system with the metal center from the catalyst.

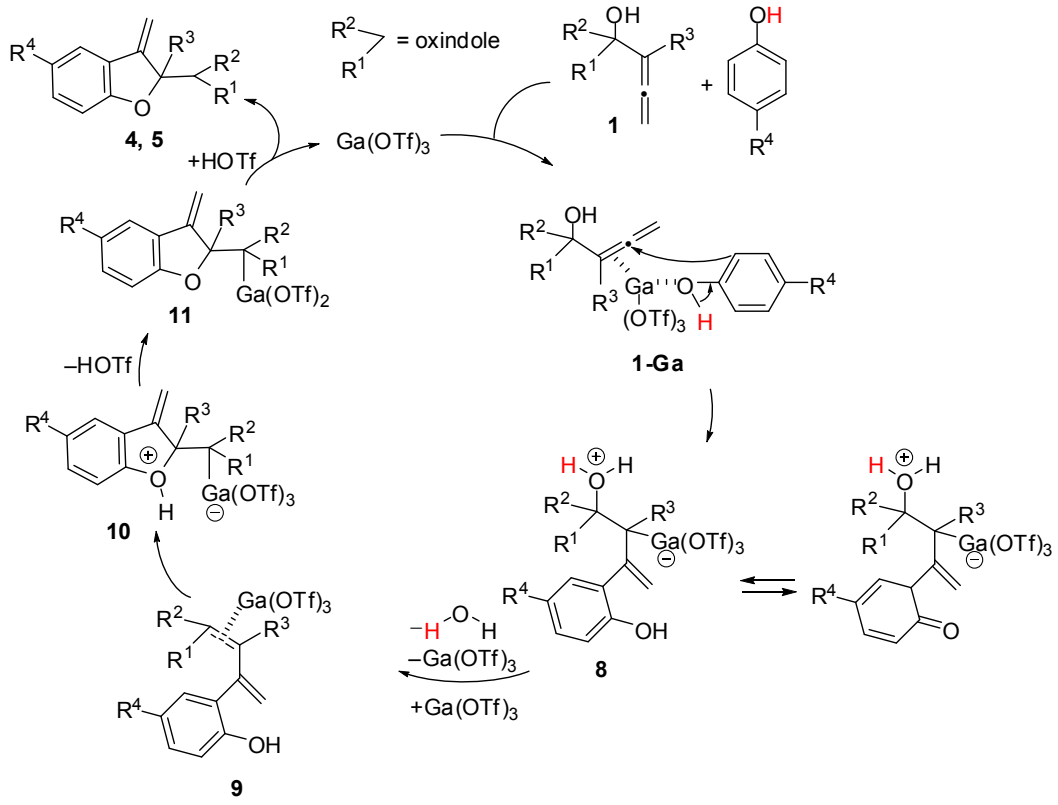
Scheme 3. Reaction of Phenyl-Substituted Allenol 6a under Metal Triflate Catalysis



2a **6a** **7a** (30%)

A possible pathway for the gallium-catalyzed generation of dihydrobenzofuran-linked oxindoles **4** and **5** is outlined in Scheme 4. Initially, $Ga(OTf)_3$ acts as a Lewis acid interacting with the allene and phenol moieties simultaneously via a bidentade mode. The formation of a complex **1**-Ga through both π-coordination of the metal to the allene group of allenols **1** as well as σ-coordination to the hydroxy group of phenols **2** may be involved. Subsequent nucleophilic addition of the phenol moiety at the sterically less hindered carbon center in complex **1**-Ga would lead to a ketone intermediate, which after tautomerization afforded the more stable enol-form **8**. Then, an elimination of water and $Ga(OTf)_3$ from zwitterionic intermediate **8** occurs to generate gallium species **9** through η-coordination of the gallium salt to the more substituted double bond. Species **9** suffers an intramolecular chemo- and regioselective 5-*exo*-trig oxycyclization reaction to produce zwitterionic dihydrobenzofurans **10**. This nucleophilic attack from the *O*-phenol site occurs as a result of the stability of the intermediate oxonium type cation **10**. Loss of HOTf in zwitterionic dihydrobenzofurans **10** generates neutral metal species **11**. Finally, protonolysis of the carbon–gallium bond of **11** liberates dihydrobenzofurans **4** and **5** with concomitant regeneration of the Ga(III) catalytic species (Scheme 4).

Scheme 4. Mechanistic Explanation for the Ga(III)-Catalyzed Synthesis of Dihydrobenzofurans 4 and 5 from Allenols 1 and Phenols



In conclusion, the synthesis of dihydrobenzofuran-linked oxindoles has been accomplished taking advantage of an unprecedented reaction between allenols and phenols under Lewis acid catalysis. Probably, $Ga(OTf)_3$ merges allene and phenol moieties simultaneously via a bidentade mode.

Experimental Section

General methods: NMR spectra were recorded at 25 °C on 700 or 300 MHz spectrometers: ^{1}H NMR (300 or 700 MHz) and ^{13}C NMR (75 or 175 MHz). NMR spectra were recorded in $CDCl_3$ or C_6D_6 solutions, except otherwise stated. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm), or $CDCl_3$ (^{13}C, 76.9 ppm), or C_6D_6 (^{13}C, 128.4 ppm). Low and high resolution mass spectra were taken on a QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray modes (ES).

Typical Procedure for the $Ga(OTf)_3$-Catalyzed Coupling Reaction of α-Allenols 1 and Phenols 2. General Procedure for the Preparation of Dihydrobenzofuran-Appended Oxindoles 4 and 5. To a solution of the appropriate allenol **1** (0.46 mmol) in dichloromethane (5 mL) at room temperature, $Ga(OTf)_3$ (0.046 mmol) was added under argon atmosphere and stirring was continued for 5 minutes. Then, the corresponding phenol **2** (1.28 mmol) was added and stirring was continued for other 5 minutes. Then, the reaction mixture was stirred at reflux temperature 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 ethyl acetate/hexanes or dicloromethane/ethyl acetate mixtures. Spectroscopic and analytical data for pure forms of compounds **4** and **5** follow.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4a and 5a. From 32 mg (0.14 mmol) of α-allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, 15 mg (35%) of the less polar compound **4a** and 8 mg (20%) of the more polar compound **5a** were obtained.

Dihydrobenzofuran-Appended Oxindole 4a. Yellow oil (15 mg, 35%); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.19 (d, J = 7.5 Hz, 1H), 7.12 (t, J = 7.7 Hz, 1H), 6.99 (m, 1H), 6.91 (s, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.72 (m, 2H), 5.09 and 4.76 (s, each 1H), 3.88 (s, 1H), 3.20 (s, 3H), 2.20 (s, 3H), 1.94 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 173.1, 158.4, 148.0, 144.2, 131.4, 129.7, 128.1, 126.3, 126.1, 125.1, 122.2, 121.0, 109.5, 107.5, 100.0, 91.0, 54.0, 26.1, 25.9, 20.7; IR (CH_2Cl_2, cm^{-1}): ν 1710, 1611, 1471; HRMS (ES): calcd for $C_{20}H_{19}NO_2$ $[M]^+$: 305.1416; found: 305.1412.

Dihydrobenzofuran-Appended Oxindole 5a. Colorless solid (8 mg, 20%); mp 134–136 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.29 (d, J = 7.6 Hz, 1H), 7.17 (m, 2H), 6.91 (dd, J = 6.9, 1.5 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 7.7 Hz, 1H), 6.53 (d, J = 8.3 Hz, 1H), 5.53 and 4.99 (s, each 1H), 3.63 (s, 1H), 3.20 (s, 3H), 2.27 (s, 3H), 1.80 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 174.0, 159.0, 150.8, 145.0, 131.5, 129.8, 128.2, 125.6, 125.2, 124.6, 121.7, 121.0, 109.8, 107.5, 101.0, 90.2, 52.8, 26.1, 24.8, 20.8; IR (CH_2Cl_2, cm^{-1}): ν 1709, 1612, 1487; HRMS (ES): calcd for $C_{20}H_{19}NO_2$ $[M]^+$: 305.1416; found: 305.1419.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4b and 5b. From 43 mg (0.20 mmol) of α-allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (8:1) as eluent, 47 mg (67%) of the less polar compound **4b** and 12 mg (17%) of the more polar compound **5b** were obtained.

Dihydrobenzofuran-Appended Oxindole 4b. Pale yellow solid (47 mg, 67%); mp 90–92 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.19 (m, 4H), 6.82 (d, *J* = 8.5 Hz, 1H), 6.77 (m, 1H), 6.73 (t, *J* = 7.6 Hz, 1H), 5.12 and 4.76 (s, each 1H), 3.89 (s, 1H), 3.21 (s, 3H), 1.94 (s, 3H), 1.22 (s, 9H); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 173.0, 159.7, 149.7, 145.0, 143.8, 129.0, 128.9, 126.9, 126.7, 126.0, 122.5, 118.1, 110.1, 108.0, 100.3, 92.0, 54.5, 34.6, 31.9 (3C), 27.2, 25.9; IR (CH_2Cl_2, cm^{-1}): ν 1700, 1610, 1489; HRMS (ES): calcd for $C_{23}H_{25}NO_2$ $[M]^+$: 347.1885; found: 347.1888.

Dihydrobenzofuran-Appended Oxindole 5b. Yellow oil (12 mg, 17%); ^{1}H-NMR (700 MHz, $CDCl_3$, 25 ºC) δ: 7.39 (d, *J* = 1.8 Hz,1H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.16 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.7 Hz, 1H), 6.59 (d, *J* = 8.5 Hz, 1H), 5.58 and 5.05 (s, each 1H), 3.64 (s, 1H), 3.20 (s, 3H), 1.77 (s, 3H), 1.29 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 174.0, 158.7, 150.9, 144.9, 143.6, 128.2, 128.1, 125.8, 124.8, 124.7, 121.7, 117.3, 109.5, 107.5, 101.1, 90.3, 52.7, 34.3, 31.6 (3C), 26.2, 24.5; IR (CH_2Cl_2, cm^{-1}): ν 1708, 1612, 1487; HRMS (ES): calcd for $C_{23}H_{25}NO_2$ $[M]^+$: 347.1885; found: 347.1889.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4c and 5c. From 50 mg (0.23 mmol) of α-allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, 43 mg (50%) of the less polar compound **4c** and 9 mg (10%) of the more polar compound **5c** (containing ca. 40% of its epimer **4c**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4c. Yellow solid (43 mg, 50%); mp 164–166 ºC; ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 7.03 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.92 (d, *J* = 2.2 Hz, 1H), 6.88 (s, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.56 (t, *J* = 7.6 Hz, 1H), 6.45 (d, *J* = 8.5 Hz, 1H), 6.13 (d, *J* = 7.7 Hz, 1H), 4.87 and 4.75 (s, each 1H), 3.58 (s, 1H), 2.68 (s, 3H), 2.0 (s, 3H); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 172.6, 160.3, 147.5, 145.0, 141.9, 133.9, 129.4, 126.8, 124.7, 123.1, 122.6, 113.4, 112.0, 108.1, 102.8, 92.7, 54.4, 26.7, 25.9; IR (CH_2Cl_2, cm^{-1}): ν 3334, 1682, 1489; HRMS (ES): calcd for $C_{19}H_{16}BrNO_2$ $[M]^+$: 369.0364; found: 369.0370.

Dihydrobenzofuran-Appended Oxindole 5c. Yellow solid (9 mg, 10%; containing ca. 40% of its epimer **4c**); mp 124–126 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.48 (d, *J* = 2.0 Hz, 0.4H, m), 7.20 (m, 3.6H, M+m), 6.77 (m, 2.6H, M+m), 6.52 (d, *J* = 8.5 Hz, 0.4H, m), 5.56 (s, 0.4H, m), 5.13 (s, 0.6H, M), 5.03 (s, 0.4H, m), 4.85 (s, 0.6H, M), 3.87 (s, 0.6H, M), 3.63 (s, 0.4H, m), 3.20 (s, 3H, M+m), 1.95 (s, 1.8H, M), 1.82 (s, 1.2H, m); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 173.6 (m), 172.7 (M), 159.3 (M+m), 149.3 (m), 146.6 (M), 144.9 (m), 144.1 (M), 133.3 (m), 133.2 (M), 128.4 (M), 128.3 (M+m), 126.2 (M+m), 125.5 (m), 124.6 (M), 124.1 (m), 123.7 (M+m), 122.3 (M), 121.9 (m), 112.7 (M), 112.6 (m), 111.9 (m), 111.5 (M), 107.8 (M), 107.7 (m), 102.9 (m), 102.1 (M), 91.9 (M), 91.1 (m), 53.9 (M), 52.7 (m), 26.2 (m), 26.0 (M) 26.0 (M), 24.9 (m); IR (CH_2Cl_2, cm^{-1}): ν 3299, 1706, 1466; HRMS (ES): calcd for $C_{19}H_{16}BrNO_2$ $[M]^+$: 369.0364; found: 369.0357.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4d and 5d. From 52 mg (0.24 mmol) of α-allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (8:1) as eluent, 33 mg (42%) of the less polar compound **4d** and 15 mg (20%) of the more polar compound **5d** (containing ca. 20% of its epimer **4d**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4d. Yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.18 (d, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.75 (m, 4H), 6.61 (d, *J* = 1.6 Hz, 1H), 5.09 and 4.79 (s, each 1H), 3.88 (s, 1H), 3.70 (s, 3H), 3.20 (s, 3H), 1.94 (s, 3H), 1.94 (s, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 173.1, 154.8, 148.3, 144.1, 138.3, 128.1, 126.3, 125.0, 122.2, 117.6, 114.1, 110.2, 107.5, 104.9, 100.5, 91.2, 54.8, 54.9, 26.1, 26.0; IR (CH_2Cl_2, cm^{-1}): ν 1706, 1612, 1482; HRMS (ES): calcd for $C_{20}H_{19}NO_3$ $[M]^+$: 321.1365; found: 321.1373.

Dihydrobenzofuran-Appended Oxindole 5d. Yellow oil; ^{1}H-NMR (700 MHz, C_6D_6, 25 ºC) δ: 7.30 (d, *J* = 7.5 Hz, 0.8H, m), 7.26 (d, *J* = 8.1 Hz, 0.2H, M), 7.04 (s, 0.2H, M), 6.93 (t, *J* = 7.7 Hz, 0.2H, M), 6.89 (m, 1.6H, m), 6.74 (d, *J* = 8.7 Hz, 0.2H, M), 6.70 (t, *J* = 7.2 Hz, 0.2H, M), 6.61 (t, *J* = 7.3 Hz, 0.8H, m), 6.48 (d, *J* = 2.6 Hz, 0.2H, M), 6.43 (d, *J* = 1.4 Hz, 1.6H, m), 6.20 (d, *J* = 7.7 Hz, 0.8H, m), 6.17 (d, *J* = 7.8 Hz, 0.2H, M), 5.31 (s, 0.8H, m), 4.99 and 4.97 (s, each 0.2H, M), 4.79 (s, 0.8H, m), 3.33 (s, 0.8H, m), 3.23 (s, 3H, M+m), 3.11 (s, 0.2H, M), 2.71 (s, 2.4H, m), 2.65 (s, 0.6H, M), 1.97 (s, 2.4H, m), 1.84 (s, 0.6H, M); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 173.9 (M+m), 156.7 (m), 155.1 (M), 152.8 (m), 150.4 (M), 146.0 (m), 143.6 (M), 129.7 (m), 128.0 (m),

127.5 (M), 127.0 (M), 126.6 (M), 126.1 (m), 125.6 (M), 123.1 (m), 122.5 (M), 122.4 (m), 121.9 (m), 121.3 (M), 118.7 (M), 118.2 (m), 111.5 (m), 111.0 (M), 108.3 (M), 108.0 (m), 105.9 (m), 105.6 (M), 101.4 (m), 100.8 (M), 91.5 (M+m), 55.6 (m), 55.4 (M), 53.2 (M+m), 26.1 (M), 26.0 (m) 25.6 (m), 25.5 (M); IR (CH_2Cl_2, cm^{-1}): ν 1708, 1611, 1482; HRMS (ES): calcd for $C_{20}H_{19}NO_3$ $[M]^+$: 321.1365; found: 321.1372.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4e and 5e. From 40 mg (0.20 mmol) of α-allenol **1b**, and after chromatography of the residue using dicloromethane/ethyl acetate (40:1) as eluent, 35 mg (60%) of the less polar compound **4e** and 14 mg (24%) of the more polar compound **5e** were obtained.

Dihydrobenzofuran-Appended Oxindole 4e. Colorless solid (35 mg, 60%); mp 166–168 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.88 (br s, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.07 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.95 (s, 1H), 6.75 (m, 3H), 5.18 and 4.92 (s, each 1H), 3.90 (s, 1H), 2.21 (s, 3H), 1.92 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 174.9, 158.4, 147.9, 141.0, 131.4, 129.8, 128.1, 126.7, 126.0, 125.7, 122.2, 121.1, 109.5, 109.0, 100.4, 90.8, 54.4, 26.1, 20.7; IR (CH_2Cl_2, cm^{-1}): ν 3252, 1705, 1482; HRMS (ES): calcd for $C_{19}H_{17}NO_2$ $[M]^+$: 291.1259; found: 291.1246.

Dihydrobenzofuran-Appended Oxindole 5e. Colorless solid (14 mg, 24%); mp 164–166 ºC;^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.53 (br s, 1H), 7.28 (m, 1H), 7.19 (s, 1H), 7.11 (t, J = 7.7 Hz, 1H), 6.92 (dd, J = 7.7, 1.4 Hz, 1H), 6.78 (m, 2H), 6.57 (d, J = 8.2 Hz, 1H), 5.53 and 4.97 (s, each 1H), 3.65 (s, 1H), 2.27 (s, 3H), 1.80 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 175.6, 159.0, 150.5, 141.8, 131.6, 129.9, 128.3, 126.1, 125.8, 125.2, 121.8, 121.1, 109.8, 109.0, 101.2, 90.1, 53.1, 24.7, 20.8; IR (CH_2Cl_2, cm^{-1}): ν 3253, 1708, 1480; HRMS (ES): calcd for $C_{19}H_{17}NO_2$ $[M]^+$: 291.1259; found: 291.1250.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4f and 5f. From 40 mg (0.20 mmol) of α-allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, 35 mg (52%) of the less polar compound **4f** and 4 mg (6%) of the more polar compound **5f** (containing ca. 50% of its epimer **4f**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4f. Pale yellow solid (35 mg, 52%); mp 203–205 ºC; ^{1}H-NMR (700 MHz, C_6D_6, 25 ºC) δ: 7.30 (d, *J* = 7.5 Hz, 1H), 7.27 (s, 1H), 7.09 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.05 (s, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 6.70 (t, *J* = 7.7 Hz, 1H) 6.49 (t, *J* = 7.2 Hz, 1H), 6.04 (m, 1H), 5.17 and 5.13 (s, each 1H), 3.66 (s, 1H), 2.06 (s, 3H), 1.07 (s, 9H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 174.2, 159.6, 149.5, 143.8 (2C), 142.0, 129.0, 128.0, 127.3, 126.7, 126.6, 122.4, 118.2, 110.1, 109.3, 100.6, 91.9, 54.7, 34.6, 31.9 (3C), 27.0; IR (CH_2Cl_2, cm^{-1}): ν 3214, 1706, 1487; HRMS (ES): calcd for $C_{22}H_{23}NO_2$ $[M]^+$: 333.1729; found: 333.1721.

Dihydrobenzofuran-Appended Oxindole 5f. Yellow solid (4 mg, 6%; containing ca. 50% of its epimer **4f**); mp 182–184 ºC; ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 8.20 (br s, 0.5H, m), 8.14 (br s, 0.5H, M), 7.45 (d, *J* = 1.9 Hz, 0.5H, m), 7.30 (m, 1.5H, 2M+m), 7.16 (m, 0.5H, M), 7.10 (m, 1H, 2M), 6.81 (m, 2H, 2M+2m), 6.54 (m, 1H, M+m), 6.35 (d, *J* = 7.7 Hz, 0.5H, m), 6.27 (d, *J* = 7.7 Hz, 0.5H, m), 5.41 (s, 0.5H, m), 5.18 and 5.15 (s, each 0.5H, M), 4.79 (s, 0.5H, m), 3.70 (s, 0.5H, M), 3.35 (s, 0.5H, m), 2.06 (s, 1.5H, M), 1.90 (s, 1.5H, m), 1.15 (s, 4.5H, m), 1.08 (s, 4.5H, M); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 176.6 (m), 175.7 (M), 160.2 (m), 159.6 (M), 152.3 (m), 149.5 (M), 144.0 (m), 143.9 (M), 143.3(m), 142.3 (M), 129.1 (m), 129.0 (M), 128.7 (m), 128.0 (M),127.2 (M), 126.8 (m), 126.7 (M), 126.6 (M), 126.3 (m), 125.7 (m), 122.5 (M), 121.9 (m), 118.2 (M), 117.8 (m), 110.7 (m), 110.1 (M), 109.8 (m), 109.7 (M), 100.9 (m), 100.7 (M), 91.9 (M), 91.3 (m), 55.0 (M), 53.6 (m), 34.7 (m), 34.6 (M), 32.0 (3C, m), 31.9 (3C, M), 27.1 (M), 25.6 (m); IR (CH_2Cl_2, cm^{-1}): ν 3212, 1704, 1486; HRMS (ES): calcd for $C_{22}H_{23}NO_2$ $[M]^+$: 333.1729; found: 333.1710.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4g and 5g. From 40 mg (0.20 mmol) of α-allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, 27 mg (38%) of the less polar compound **4g** and 4 mg (6%) of the more polar compound **5g** (containing ca. 20% of its epimer **4g**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4g. Pale yellow solid (27 mg, 38%); mp 204-206 ºC; ^{1}H-NMR (700 MHz, C_6D_6, 25 ºC) δ: 7.10 (dd, *J* = 8.2, 6.2 Hz, 1H), 7.02 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 6.72 (t, *J* = 7.7 Hz, 1H), 6.50 (t, *J* = 7.7 Hz, 1H), 6.44 (d, *J* = 8.5 Hz, 1H), 6.32 (d, *J* = 8.7 Hz, 1H), 6.12 (d, *J* = 7.7 Hz, 1H), 4.99 and 4.83 (s, each 1H), 3.54 (s, 1H),

1.93 (s, 3H); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 174.0, 160.3, 147.4, 142.1, 133.9, 133.0, 129.4, 127.1, 126.2, 124.8, 122.4, 113.5, 112.0, 109.5, 103.1, 92.5, 54.7, 26.6; IR (CH_2Cl_2, cm^{-1}): ν 3256, 1699, 1464; HRMS (ES): calcd for $C_{18}H_{14}BrNO_2$ $[M]^+$: 355.0208; found: 355.0192.

Dihydrobenzofuran-Appended Oxindole 5g. Yellow solid (4 mg, 6%; containing ca. 20% of its epimer **4g**); mp 194–196 ºC; ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 7.46 (m, 0.2H, m), 7.31 (d, *J* = 2.0 Hz, 0.8H, M), 7.11 (m, 1H, M+m), 7.02 (dd, *J* = 8.5, 2.0 Hz, 1H, M+m), 6.96 (d, *J* = 2.0 Hz, 1H, M+m), 6.77 (m, 1H, M+m), 6.52 (td, *J* = 7.7, 1.0 Hz, 1H, M+m), 6.44 (d, *J* = 8.5 Hz, 1H, M+m), 6.20 (m, 1H, M+m), 5.09 (s, 0.2H, m), 5.00 and 4.84 (s, each 0.8H, M), 4.62 (s, 0.2H, m), 3.55 (s, 0.8H, M), 3.18 (s, 0.2H, m), 1.93 (s, 2.4H, M), 1.79 (s, 0.6H, m); ^{13}C-NMR (75 MHz, C_6D_6, 25 ºC) δ: 174.6 (M+m), 160.3 (M+m), 147.4 (M+m), 142.2 (M+m), 134.1 (m), 133.9 (3C, 2M + 1m), 129.4 (M), 128.9 (m), 127.1 (M), 126.4 (m), 126.2 (M), 125.7 (m), 124.8 (M+m), 124.5 (m), 122.5 (M), 122.0 (m), 113.5 (M), 112.7 (m), 112.0 (M), 109.7 (M+m), 103.1 (M+m), 92.5 (M), 91.9 (m), 54.8 (M), 53.4 (m), 26.6 (M), 25.4 (m); IR (CH_2Cl_2, cm^{-1}): ν 3187, 1708, 1464; HRMS (ES): calcd for $C_{18}H_{14}BrNO_2$ $[M]^+$: 355.0208; found: 355.0218.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4h and 5h. From 43 mg (0.21 mmol) of α-allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (7:1) as eluent, 32 mg (55%) of the less polar compound **4h** and 6 mg (10%) of the more polar compound **5h** (containing ca. 40% of its epimer **4h**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4h. Colorless solid (32 mg, 55%); mp 164–166 ºC; ^{1}H-NMR (700 MHz, $CDCl_3$, 25 ºC) δ: 7.65 (s, 1H), 7.20 (td, *J* = 8.4, 1.3 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.14 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.78 (td, *J* = 7.5, 0.8 Hz, 1H), 6.73 (d, *J* = 7.7 Hz, 1H), 6.70 (td, *J* = 7.7, 0.8 Hz, 1H), 5.22 and 4.96 (s, each 1H), 3.92 (s, 1H), 1.94 (s, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 174.6, 160.3, 147.6, 140.9, 130.6, 128.2, 126.7, 126.2, 125.6, 122.2, 120.8, 120.6, 109.9, 108.9, 100.9, 90.7, 50.4, 26.0; IR (CH_2Cl_2, cm^{-1}): ν 3244, 1702, 1468; HRMS (ES): calcd for $C_{18}H_{15}NO_2$ $[M]^+$: 277.1103; found: 277.1105.

Dihydrobenzofuran-Appended Oxindole 5h. Yellow solid (6 mg, 10%; containing ca. 40% of its epimer **4h**); mp 124–126 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.91 (m, 1H, M+m), 7.38

(dd, *J* = 7.6, 0.9 Hz, 0.4H, m), 7.29-7.04 (m, 3.6H, M+m), 6.90 (d, *J* = 8.0 Hz, 0.6H, M), 6.86 (dd, *J* = 7.5, 0.8 Hz, 0.4H, m), 6.82-6.65 (m, 3H, M+m), 5.58 (s, 0.4H, m), 5.22 (s, 0.6H, M), 5.02 (s, 0.4H, m), 4.95 (s, 0.6H, M), 3.92 (s, 0.6H, M), 3.66 (s, 0.4H, m), 1.94 (s, 1.8H, M), 1.83 (s, 1.2H, m); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 174.5 (M+m), 160.3 (M+m), 147.5 (M+m) 140.9 (M+m), 130.6 (M+m), 128.4 (m), 128.2 (M), 126.8 (m), 126.7 (M), 126.2 (M+m), 125.5 (M+m), 122.3 (m), 122.1 (M), 120.8 (M+m), 120.6 (M+m), 109.9 (M+m), 108.9 (M+m), 100.9 (M+m), 90.7 (M+m), 54.3 (M+m), 26.0 (M+m); IR (CH_2Cl_2, cm^{-1}): ν 3231, 1707, 1468; HRMS (ES): calcd for $C_{18}H_{15}NO_2$ $[M]^+$: 277.1103; found: 277.1111.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4i and 5i. From 50 mg (0.18 mmol) of α-allenol **1c**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, 33 mg (49%) of the less polar compound **4i** and 6 mg (9%) of the more polar compound **5i** (containing ca. 50% of its epimer **4i**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4i. Yellow oil (33 mg, 49%); ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 7.42 (s, 1H), 6.89–6.66 (m, 4H), 5.72 (d, *J* = 8.2 Hz, 1H), 5.08 and 5.03 (s, each 1H), 3.47 (s, 1H), 1.97 (s, 3H), 1.88 (s, 3H); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 173.6, 159.7, 149.1, 141.1, 132.6 (2C), 131.5, 131.0, 130.6, 126.9, 122.3, 115.1, 110.7, 110.3, 101.0, 91.4, 55.1, 26.7, 21.0; IR (CH_2Cl_2, cm^{-1}): ν 3249, 1707, 1485; HRMS (ES): calcd for $C_{19}H_{16}BrNO_2$ $[M]^+$: 369.0364; found: 369.0347.

Dihydrobenzofuran-Appended Oxindole 5i. Yellow oil (6 mg, 9%; containing ca. 50% of its epimer **4i**); ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 7.42 (s, 1H, M+m), 7.22-6.66 (m, 4H, M+m), 6.58 (d, *J* = 7.4 Hz, 0.5H, m), 6.46 (d, *J* = 8.2 Hz, 0.5H, m), 5.73 (d, *J* = 8.3 Hz, 0.5H, M), 5.69 (d, *J* = 8.3 Hz, 0.5H, m), 5.26 (s, 0.5H, m), 5.07 and 5.03 (s, each 0.5H, M), 4.69 (s, 0.5H, m), 3.47 (s, 0.5H, M), 3.08 (s, 0.5H, m), 2.00 (s, 1.5H, m), 1.97 (s, 1.5H, M), 1.88 (s, 1.5H, M), 1.80 (s, 1.5H, m); ^{13}C-NMR (75 MHz, C_6D_6, 25 ºC) δ: 174.4 (M+m), 159.5 (M+m), 149.0 (M+m), 141.1 (M+m), 132.5, (4C, 2M + 2m), 131.4 (M+m), 130.8 (M+m), 130.5 (M), 129.2 (m), 127.5 (m), 126.7 (M), 122.1 (M+m), 115.5 (m), 115.1 (M), 110.8 (M+m), 110.1 (M+m), 100.9 (M+m), 91.2 (M+m), 60.4 (m), 55.2 (M), 26.6 (M+m), 21.0 (M+m); IR (CH_2Cl_2, cm^{-1}): ν 3245, 1703, 1475; HRMS (ES): calcd for $C_{19}H_{16}BrNO_2$ $[M]^+$: 369.0364; found: 369.0383.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4j and 5j. From 40 mg (0.17 mmol) of α-allenol **1d**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, 38 mg (69%) of the less polar compound **4j** and 4 mg (7%) of the more polar compound **5j** were obtained.

Dihydrobenzofuran-Appended Oxindole 4j. Colorless solid (38 mg, 69%); mp 103–105 ºC; ^{1}H-NMR (700 MHz, $CDCl_3$, 25 ºC) δ: 7.76 (br s, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.94 (s, 1H), 6.68 (m, 2H), 6.67 (m, 2H), 5.17 and 4.93 (s, each 1H), 3.93 (s, 1H), 3.80 (s, 3H), 2.21 (s, 3H), 1.92 (s, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 174.2, 158.4, 147.8, 143.0, 131.3, 129.9, 129.7, 126.5, 126.0, 122.5, 121.0, 119.0, 110.3, 109.5, 100.5, 90.8, 55.4, 55.1, 29.6, 26.0; IR (CH_2Cl_2, cm^{-1}): ν 3228, 1709, 1493, 1462; HRMS (ES): calcd for $C_{20}H_{19}NO_3$ $[M]^+$: 321.1365; found: 321.1358.

Dihydrobenzofuran-Appended Oxindole 5j. Colorless oil (4 mg, 7%); ^{1}H-NMR (700 MHz, $CDCl_3$, 25 ºC) δ: 7.43 (s, 1H), 7.19 (s, 1H), 6.93 (m, 1H), 6.76 (m, 1H), 6.71 (d, J = 8.2 Hz, 1H), 6.59 (d, J = 8.2 Hz, 1H), 5.52 and 4.96 (s, each 1H), 3.82 (s, 3H), 3.67 (s, 1H), 2.27 (s, 3H), 1.79 (s, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 174.8, 158.9, 150.4, 143.0, 131.5, 130.8, 129.9, 125.9, 125.3, 122.1, 121.1, 118.5, 110.5, 109.9, 101.2, 90.1, 55.5, 53.7, 29.7, 24.7; IR (CH_2Cl_2, cm^{-1}): ν 3221, 1704, 1494, 1461; HRMS (ES): calcd for $C_{20}H_{19}NO_3$ $[M]^+$: 321.1365; found: 321.1357.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4k and 5k. From 40 mg (0.17 mmol) of α-allenol **1d**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, 29 mg (48%) of the less polar compound **4k** and 6 mg (9%) of the more polar compound **5k** (containing ca. 50% of its epimer **4k**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4k. Pale yellow solid (29 mg, 48%); mp 193–195 ºC; ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 8.44 (m, 1H), 7.13 (m, 2H), 7.03 (d, J = 7.5 Hz, 1H), 6.89 (dd, J = 8.3, 0.7 Hz, 1H), 6.47 (t, J = 8.0 Hz, 1H), 6.10 (d, J = 8.3 Hz, 1H), 5.23 and 5.16 (s, each 1H), 3.80 (s, 1H), 3.05 (s, 3H), 2.12 (s, 3H), 1.09 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 174.9, 159.7, 149.4, 143.9, 143.8, 131.4, 129.0, 127.5, 126.7, 122.9, 119.7, 118.2, 111.1, 110.1,

100.9, 92.0, 55.7, 55.1, 34.6, 31.9 (3C), 27.0; IR (CH_2Cl_2, cm^{-1}): ν 3225, 1708, 1490; HRMS (ES): calcd for $C_{23}H_{25}NO_3$ $[M]^+$: 363.1834; found: 363.1841.

Dihydrobenzofuran-Appended Oxindole 5k. Yellow solid (6 mg, 9%; containing ca. 50% of its epimer **4k**); mp 181–183 ºC; ^{1}H-NMR (300 MHz, C_6D_6, 25 ºC) δ: 8.22 (br s, 0.5H, m), 8.12 (br s, 0.5H, M), 7.47 (d, *J* = 2.0 Hz, 0.5H, m), 7.13 (m, 1.5H, M+m+M), 7.01 (m, 1H, M+m), 6.91 (m, 1H, M+m), 6.55 (m, 1H, m), 6.48 (t, *J* = 8.0 Hz, 0.5H, M), 6.22 (d, *J* = 8.3 Hz, 0.5H, m), 6.10 (d, *J* = 8.3 Hz, 0.5H, M), 5.45 (s, 0.5H, m), 5.21 and 5.15 (s, each 0.5H, M), 4.868 (s, 0.5H, m), 3.79 (s, 0.5H, M), 3.42 (s, 0.5H, m), 3.12 (s, 1.5H, m), 3.04 (s, 1.5H, M), 2.12 (s, 1.5H, M), 1.94 (s, 1.5H, m), 1.16 (s, 4.5H, m), 1.09 (s, 4.5H, M); ^{13}C-NMR (75 MHz, C_6D_6, 25 ºC) δ: 175.6 (m), 174.8 (M), 160.2 (m), 159.7 (M), 152.5 (m), 149.4 (M), 143.9 (m), 143.9 (m), 143.7 (2C, M), 132.3 (m), 131.3 (M), 129.1 (m), 129.0 (M), 127.5 (M), 127.0 (m), 126.7 (M), 125.8 (m), 122.9 (M), 122.2 (m), 119.7 (M), 119.3 (m), 118.2 (M), 117.8 (m), 111.1 (M), 111.0 (m), 110.8 (m), 110.1 (M), 101.0 (m), 100.8 (M), 92.0 (M), 91.4 (m), 55.7 (M), 55.1 (m), 55.1 (M), 54.1 (m), 34.7 (M), 32.0 (3C, m), 31.9 (3C, M), 30.6 (m), 27.1 (M), 25.5 (m); IR (CH_2Cl_2, cm^{-1}): ν 3220, 1710, 1391; HRMS (ES): calcd for $C_{23}H_{25}NO_3$ $[M]^+$: 363.1834; found: 363.1845.

Preparation of Dihydrobenzofuran-Appended Oxindoles 4l and 5l. From 35 mg (0.17mmol) of α-allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, 26 mg (50%) of the less polar compound **4l** and 9 mg (17%) of the more polar compound **5l** (containing ca. 40% of its epimer **4l**) were obtained.

Dihydrobenzofuran-Appended Oxindole 4l. Colorless oil; ^{1}H-NMR (700 MHz, C_6D_6, 25 ºC) δ: 7.31 (d, *J* = 7.5 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.7 Hz, 1H), 6.70 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 6.51 (m, 1H), 6.29 (m, 1H), 5.13 and 5.06 (s, each 1H), 3.69 (m, 1H), 3.12 (s, 3H), 2.1 (s, 3H); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 175.8, 155.9, 155.0, 149.5, 142.3, 128.7, 127.5, 127.4, 126.7, 122.5, 118.7, 111.0, 109.7, 105.6, 101.2, 91.8, 55.4, 55.1, 26.9; IR (CH_2Cl_2, cm^{-1}): ν 3263, 1706, 1482; HRMS (ES): calcd for $C_{19}H_{17}NO_3$ $[M]^+$: 307.1208; found: 307.1218.

Dihydrobenzofuran-Appended Oxindole 5l. Yellow oil; ^{1}H-NMR (700 MHz, C_6D_6, 25 ºC) δ: 7.31 (d, *J* = 7.5 Hz, 0.4H, M), 7.24 (d, *J* = 7.5 Hz, 0.6H, m), 7.23 (d, *J* = 7.7 Hz, 0.6H, m), 6.87

(m, 0.6H, m), 6.77 (t, J = 7.7 Hz, 0.4H, M), 6.73 (d, J = 8.7 Hz, 0.4H, M), 6.70 (dd, J = 8.7, 2.6 Hz, 0.4H, M), 6.66 (t, J = 7.7 Hz, 0.6H, m), 6.58 (m, 1H, M+m), 6.51 (m, 0.4H, M), 6.45 (m, 0.6H, m), 6.35 (m, 2H, M+m), 5.30 (s, 0.6H, m), 5.12 and 5.05 (s, each 0.4H, M), 4.75 (s, 0.6H, m), 3.69 (s, 0.4H, M), 3.32 (s, 0.6H, m), 3.23 (s, 1.8H, m), 3.13 (s, 1.2H, M), 2.37 (s, 1.8H, m), 2.07 (s, 1.2H, m); ^{13}C-NMR (175 MHz, C_6D_6, 25 ºC) δ: 176.8 (m), 175.8 (M), 156.6 (m), 155.9 (M), 155.2 (M), 152.4 (m), 151.1 (m), 149.5 (M), 143.4 (m), 142.5 (M), 141.2 (m), 129.8 (m), 128.7 (M), 127.5 (M), 127.3 (M), 126.5 (M), 126.3 (m), 123.5 (m), 122.5 (M), 122.0 (m), 118.7 (M), 118.2 (m), 111.5 (m), 111.0 (M), 110.4 (m), 109.8 (M), 105.9 (m), 105.6 (M), 101.5 (m), 101.3 (M), 91.8 (M), 91.3 (m), 55.6 (m), 55.4 (M), 55.2 (M), 53.7 (m), 28.0 (m), 27.0 (M); IR (CH_2Cl_2, cm^{-1}): ν 3263, 1707, 1480; HRMS (ES): calcd for $C_{19}H_{17}NO_3$ $[M]^+$: 307.1208; found: 307.1210.

Ketone 7a. From 44 mg (0.16 mmol) of the allenol **6a** and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, gave compound **7a** (14 mg, 30%) as yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.27 (m, 1H), 7.00 (m, 2H), 6.79 (d, J = 8.1 Hz, 1H), 6.53 (m, 3H), 3.00 (s, 3H), 2.24 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 204.0, 166.7, 151.4, 144.5, 132.8, 130.0, 129.9, 129.8, 129.2, 127.8, 123.8, 123.1, 121.9, 120.6, 115.0, 108.2, 29.0, 25.9; IR (CH_2Cl_2, cm^{-1}): ν 2926, 1697, 1606, 1487; HRMS (ES): calcd for $C_{18}H_{15}NO_2$ $[M]^+$: 277.1103; found: 277.1104.

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Supporting Information Available: ORTEP drawing of compound **5a** as well as copies of the ^{1}H NMR and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For selected reviews, see: (a) Donnelly, D. M. X.; Meegan, M. J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A.R., Rees, C. W., Eds.; Pergamon: Oxford, UK, 1984; Vol. 4. (b) Ayers, A. C.; Loike, J. K. *Lignans: Chemical, Biological and Clinical Properties*, Cambridge, 1990. (c) Watzke, A.; O'Malley, S. J.; Bergman, R. G.; Ellman, J. A. *J. Nat. Prod.* **2006**, *69*, 1231. (d) Veitch, N. C. *Nat. Prod. Rep.* **2007**, *24*, 417. (e) Shen, T.; Wang, X.-N.; Lou, H.-X. *Nat. Prod. Rep.* **2009**, *26*, 916.

(2) For a review, see: Sheppard, T. D. *J. Chem. Res.* **2011**, *35*, 337.

(3) For recent selected reviews, see: (a) Fensterbank, L.; Malacria, M. *Acc. Chem. Res.* **2014**, *47*, 953. (b) Alcaide, B.; Almendros, P. *Acc. Chem. Res.* **2014**, *47*, 939. (c) Lechel, T.; Pfrengle, F.; Reissig, H.-U.; Zimmer, R. *ChemCatChem* **2013**, *5*, 2100. (d) Yu, S.; Ma, S. *Angew. Chem. Int. Ed.* **2012**, *51*, 3074. (e) Yang, W.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2014**, *43*, 2941.

(4) For the coupling of an allene intermediate with halogenated phenols, see: (a) Bi, H.-P.; Liu, X.-Y.; Gou, F.-R.; Guo, L.-N.; Duan, X.-H.; Shu, X.-Z.; Liang, Y.-M. *Angew. Chem. Int. Ed.* **2007**, *46*, 7068. For the condensation of allenoates and phenols, see: (b) Kim, S.; Kang, D.; Lee, C.-H.; Lee, P. H. *J. Org.Chem.* **2012**, *77*, 6530. For the gold-catalyzed chromane formation from allenamides and phenols, see: (c) Slater, N. H.; Brown, N. J.; Elsegood, M. R. J.; Kimber, M. C. *Org. Lett.* **2014**, *16*, 4606.

(5) (a) Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Quirós, M. T. *Chem. Eur. J.* **2009**, *15*, 3344. (b) Alcaide, B.; Almendros, P.; Luna, A.; Cembellín, S.; Arnó, M.; Domingo, L. R. *Chem. Eur. J.* **2011**, *17*, 11559. (c) Alcaide, B.; Almendros, P.; Luna, A.; Prieto, N. *J. Org. Chem.* **2012**, *77*, 11388.

(6) Alcaide, B.; Almendros, P.; Quirós, M. T.; López, R.; Menéndez, M. I.; Sochacka-Ćwikła, A. *J. Am. Chem. Soc.* **2013**, *135,* 898.

(7) (a) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537. (b) Hashmi, A. S. K.; Blanco, M. C.; Fischer, D.; Bats, J. W. *Eur. J. Org. Chem.* **2006**, 1387. (c) Asikainen, M.; Krause, N. *Adv. Synth. Catal.* **2009**, *351*, 2305. (d) Brasholz, M.; Dugovič, B.; Reissig, H.-U. *Synthesis* **2010**, 3855. (e) Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Fernández, I. *Chem. Commun.* **2011**, *47*, 9054.

(8) For a different reactivity of 3-hydroxy-2-oxindoles and phenols under Lewis acid catalysis, see: (a) Kinthada, L. K.; Ghosh, S.; Babu, K. N.; Sharique, M.; Biswas, S.; Bisai, A. *Org. Biomol. Chem.* **2014**, *12*, 8152. (b) Ghosh, S.; Kinthada, L. K.; Bhunia, S.; Bisai, A. *Chem. Comm.* **2012**, *48*, 10132. (c) Zhou, F.; Cao, Z.- Y.; Zhang, J. ; Yang, H.-B.; Zhou, J. *Chem. Asian J.* **2012**, *7*, 233. For a different reactivity of 3-hydroxy-2-oxindoles and phenols under organocatalysis, see: (d) Liu, Y.; Zhang, H.-H.; Zhang, Y.-C.; Jiang, Y.; Shi, F.; Tu, S.-J. *Chem. Comm.* **2014**, *50*, 12054. For a different reactivity of allenes and phenols, see: (e) Nemoto, T.; Nozaki, T.; Yoshida, M.; Hamada, Y. *Adv. Synth. Catal.* **2013**, *355,* 2693.

(9) Slighly improved yields were obtained by the use of $Ga(OTf)_3$ in comparison with $Bi(OTf)_3$, $In(OTf)_3$, $Zn(OTf)_2$, $Fe(OTf)_3$, and $Yb(OTf)_3$.

(10) For a review on the use of $Ga(OTf)_3$ in organic reactions, see: (a) Prakash, G. K. S.; Mathew, T.; Olah, G. A. *Acc. Chem. Res.* **2012** , *45*, 565. For a recent use, see: (b) Zhang, S.; Xu, Z.; Jia, J.; Tung, C.-H.; Xu, Z. *Chem. Comm.* **2014**, *50*, 12084.

(11) Compounds **4a–i** and **5a–i** can be considered as hybrid scaffolds as combination of the biologically relevant oxindole and dihydrobenzofuran frameworks. For reviews on hybrid chemical entities, see: (a) Decker, M. *Curr. Med. Chem.* **2011**, *18*, 1464. (b) Tsogoeva, S. B. *Mini-Rev. Med. Chem.* **2010**, *10*, 773. (c) Meunier, B. *Acc. Chem. Res.* **2008**, *41*, 69. (d) Tietze, L. F.; Bell, H. P.; Chandrasekhar, S. *Angew. Chem. Int. Ed.* **2003**, *42*, 3996.

(12) CCDC-907155 contains the supplementary crystallographic data for this paper (www.ccdc.cam.ac.uk/data_request/cif).

(13) The transformation of isoindolinone-tethered alkoyallenols into oxopropylidene isoindolinones has been reported by treatment with aqueous sulphuric acid: (a) Kaden, S.; Reissig, H.-U.; Brüdgam, I.; Hartl, H. *Synthesis,* **2006**, 1351. For the acid-catalyzed synthesis of α,β-disubstituted conjugated enones by a Meyer–Schuster-type rearrangement in allenols, see: (b) Alcaide, B.; Almendros, P.; Cembellín, S.; Martínez del Campo, T. *Adv. Synth. Catal.* **2015**, *357*, 1070.