Heck reaction on protected 3-alkyl-1,2-dien-1-ols: an approach to substituted 3-alkenylindoles, 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes and -indolidines†

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A phosphine-free annulation reaction has been exploited for the preparation of substituted 3-alkenylindoles, 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes and -indolidines in good to excellent yields. This has been done by reaction of protected 3-alkyl-1,2-dienols with *o*-iodophenols or protected *o*-iodoanilines. Two different heterocyclic skeletons were obtained, depending on the electron-donating properties of the heteroatom involved in the annulation process.

Introduction

The palladium-catalysed annulation process is one of the most useful methods to synthesise highly functionalised heterocycles. In recent years, this reaction has been exploited as a route to a wide variety of heterocycles and carbocycles using 1,2-, 1,3- and 1,4-dienes, as well as internal alkynes, which were placed to react with aryl or vinyl halides and triflates.[1,2] Allenes represent a very attractive class of compounds due to their increased reactivity with respect to other classes of dienic substrates.[3–5] They undergo carbopalladation very readily, and moreover, many examples of catalysed annulations involving 1,2-dienes have so far been reported.[6–12]

Recently, we have described the synthetic use of the Heck[13–15] coupling applied to 1-alkoxy-functionalised 1,3-dienes,[16,17] and more recently, we have addressed our attention to protected 3-alkyl-1,2-dienols as synthetic precursors of α-arylated α,β-unsaturated aldehydes.[18] In particular, alkoxy-substituted allenes are characterised by unique reactivity, and they have been exploited in different reactions with organometallic, nucleophilic, and electrophilic reagents.[19] The synthesis of carbocycles and heterocycles, exploiting lithiated alkoxyallenes, have been recently reviewed.[20] The reactivity of 1-alkoxy-π-allylpalladium complexes, obtained from the corresponding alkoxyallenes, has been explored, and the dramatic effect of the alkoxy group on the regioselectivity of the Pd(0)-catalysed coupling reactions has been demonstrated. Actually, the most reactive position is that adjacent to the alkoxy group.[21]

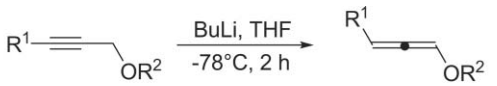
The indolic scaffold represents a privileged motif that is found in various natural and synthetic products,[22] many efforts have been consequently directed towards the synthesis of substituted indoles.[23–25] In particular, vinylindoles represent a valuable class of precursors of biologically important derivatives, such as alkaloids, carbazoles and carbolines.[26,27]

As far as we know, few syntheses of alkenyl indoles have so far been reported in the literature. Some procedures utilise the suitable phosphorane and indole-3-carbaldehydes,[28] or the gramine framework coupled with aldehydes.[29] The Heck coupling has also been exploited.[30–34] Since the proposed procedures resort to the indole scaffold as a starting reagent, their applicability to the synthesis of variously substituted targets is limited, as few functionalised indoles are commercially available.

As far as 3-alkylidene-2,3-dihydrobenzofuranes are concerned, they can be the starting point to synthesise several biologically relevant molecules, such as, for example, the rocaglates[35,36] that show potent antitumor activity.

Discussion

In this paper, we report the synthesis of highly functionalised benzoheterocycles by Heck reaction using various phenols or protected *o*-iodoanilines, and protected alkyl-1,2-dien-1-ols. 1,2-Dienols were synthesised as previously described by the reaction of the protected alkynes **1a–e** with 2 equiv. of BuLi, as shown in Scheme 1.[18] According to the literature, internal allenols afford a mixture of 1,2-dienol and the starting alkyne.[37]



1a R^1= Me, R^2 = CH_2OEt — **2a** R^1= Me, R^2 = CH_2OEt (66%)
1b R^1= Me, R^2 = THP — **2b** R^1= Me, R^2 = THP (60%)
1c R^1= *n*-Pr, R^2 = CH_2OEt — **2c** R^1= *n*-Pr, R^2 = CH_2OEt (62%)
1d R^1= *n*-Pr, R^2 = MEM — **2d** R^1= *n*-Pr, R^2 = MEM (68%)
1e R^1= Ph, R^2 = MEM — **2e** R^1= Ph, R^2 = MEM (51%)

Scheme 1 Synthesis of protected 1,2-dienols starting from protected alkynols.

The reaction of 1-(ethoxymethoxy)hex-1,2-diene (**2c**) with 2-iodophenol was selected in order to optimise the process. This was done by evaluating the effect of the catalyst, solvent, and base, as well as the influence of added phosphines and ionic liquids on the coupling yield and the diastereoselectivity.

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† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra of products **4a–f** and **5a–g**. NOESY spectra of products **4a** (*E* and *Z*) and **4b**. See DOI: 10.1039/b925550h

The *E* and *Z* configuration of the double bond of 3-butylidene-2-(ethoxymethoxy)-2,3-dihydrobenzofuran (**4a**) was determined by a NOESY experiment in which the correlation point between $\mathbf{H_a}$ (5.81 ppm) and $\mathbf{H_b}$ (6.12 ppm) for the *E* isomer, or $\mathbf{H_a}$ (6.12 ppm) and $\mathbf{H_c}$ (7.19 ppm) for the *Z* isomer, was observed. The *E*/*Z* ratio was determined by ^{1}H NMR analysis on the crude reaction mixture. In particular, the *E*/*Z* ratio was deduced by comparing the integration area of the signal centred at 5.81 ppm, pertinent to the $\mathbf{H_a}$ proton of the *E* isomer, with the signal centred at 6.35 ppm, due to the $\mathbf{H_b}$ proton of the *Z* isomer. The results are listed in the Table 1.

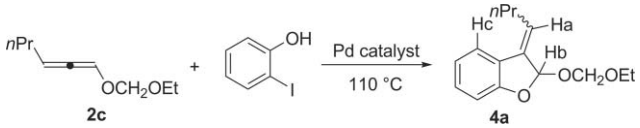
Examining the results reported in Table 1, it can be observed that the highest stereoselectivity is achieved when the reaction is carried out in pure TBAB (entry 6), while a mixture of DMSO/TBAB (entry 8) is the best compromise in order to attain good yields with reasonable stereoselectivities. The improvement of the reaction stereoselectivity which was observed when changing from pure DMSO to pure TBAB might be attributed to the effect of the ionic liquid and to a higher polarity of the reaction medium.

Several ionic liquids were tested, in each case either the cation or the anion were changed, the TBA cation seems to be necessary to obtain good reaction outcomes; actually, the use of DMSO/bmimBr (entry 17) decreases the yield. On the one hand, reaction yield does not seem to be strongly influenced by the nature of the anion in the ionic liquid, and good yields are always observed, even if bromide appears to be the preferred selection. On the other hand, data in Table 1 suggest that the reaction stereoselectivity is favored by a small anion, in fact the use of TBAC (*E*/*Z* ratio = 82/18, entry 18), favours a higher stereoselectivity in comparison with TBAB (*E*/*Z* ratio = 72/28, entry 8), and even more with respect to TBAI (*E*/*Z* ratio = 52/48, entry 19). Moreover, the use of phosphines, PBu_3 (entry 12), PPh_3 (entry 13), and DPPP (entry 14), does not improve reaction results, on the contrary PBu_3 and DPPP lower the reaction yields. $Pd(OAc)_2$ (3% mol) was selected as the catalyst, mainly for economical and stability reasons, even if $Pd(PPh_3)_4$ and $Pd_2(dba)_3$ lead to comparable yield and stereoselectivity. Finally, anhydrous NaOAc was selected as the base, though anhydrous K_2CO_3 (entry 10) produced comparable results.

The coupling reaction was then attempted with *o*-bromophenols, and no coupling product was recovered, despite the use of phosphines,[38,39] and the presence of a greater quantity of $Pd(OAc)_2$ or Herrmann's catalyst. The reactivity of *o*-bromophenols is probably lowered by the steric hindrance of the hydroxyl group in the *ortho* position. Furthermore, any attempt to carry out the reaction with 1-(ethoxymethoxy)-hex-1,2-diene (**2c**) and unprotected 2-iodoaniline was unsuccessful. The Heck coupling was, therefore, carried out using functionalised 1,2-dienes and protected 2-iodoaniline, or 2-iodophenols, which contain both electron-donating and electon-withdrawing substituents. Surprisingly, as shown in Scheme 2, the reaction led to two different scaffolds, depending on the nature of the nucleophile (oxygen or nitrogen) and of the *N*-protecting function. Substituted 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or -indolines **4a–f** in one case, and substituted 3-alkenylindoles **5a–g** in the other, were isolated.

The hypothesised reactivity pattern is illustrated in Scheme 2. The addition of arylpalladium compounds to protected alkoxy-allenes **2a–e** produced the π-allylpalladium intermediate **A**. Then, the following intramolecular nucleophilic substitution afforded the products **4a–f**. The elimination of the OR^2 group, assisted by the nitrogen lone pair, which gave the intermediate **B**, could occur,

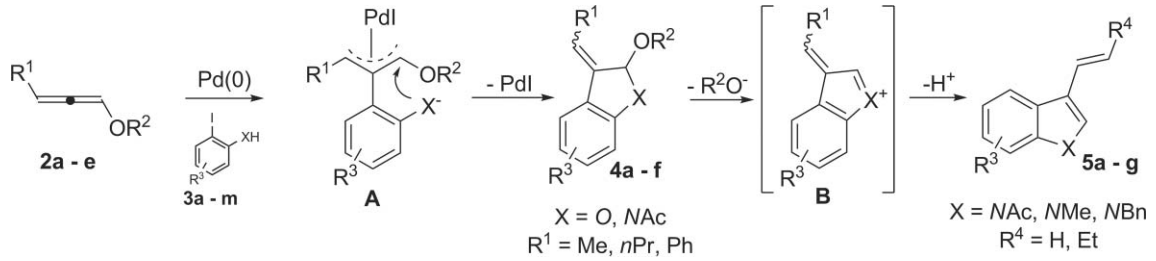
Table 1 Coupling reaction between 1-(ethoxymethoxy)hex-1,2-diene (**2c**) and 2-iodophenol[a]



2c 4a

Entry	Base	Catalyst (mol%)	Solvent	Time/h	Yield (%)[b]	*E*/*Z*[c]
1	An. NaOAc	$Pd(OAc)_2$ (5)/**PPh_3**	DMSO	1.5	36	47/53
2	An. NaOAc	$Pd(OAc)_2$ (**5**)	DMSO	3	92	66/34
3	An. NaOAc	$Pd(OAc)_2$ (**2**)	DMSO	3	46	64/36
4	An. NaOAc	$Pd(OAc)_2$ (**3**)	DMSO	1.5	91	64/36
5	An. NaOAc	$Pd(OAc)_2$ (3)	**DMF**	3	35	75/25
6	An. NaOAc	$Pd(OAc)_2$ (3)	**TBAB**	1.5	57	99/1
7	**An. K_2CO_3**	$Pd(OAc)_2$ (3)	DMSO	1.5	46	67/33[c]
8	An. NaOAc	$Pd(OAc)_2$ (3)	**DMSO/TBAB**	1	96	72/28
9	**Et_3N**	$Pd(OAc)_2$ (3)	DMSO/TBAB	1.5	75	84/16
10	**An. K_2CO_3**	$Pd(OAc)_2$ (3)	**DMSO/TBAB**	1.5	95	72/28[d]
11	**TBAA**	$Pd(OAc)_2$ (3)	DMSO/TBAB	2	40	63/37[d]
12	An. NaOAc	$Pd(OAc)_2$ (3)/**PBu_3**	DMSO/TBAB	1.5	68	75/25
13	An. NaOAc	$Pd(OAc)_2$ (3)/**PPh_3**	DMSO/TBAB	1	98	71/29
14	An. NaOAc	$Pd(OAc)_2$ (3)/**DPPP**	DMSO/TBAB	1.5	61	73/27
15	An. NaOAc	**$Pd(PPh_3)_4$** (3)	DMSO/TBAB	1	87	72/28
16	An. NaOAc	**$Pd_2(dba)_3$** (3)	DMSO/TBAB	1	98	74/26
17	An. NaOAc	$Pd(OAc)_2$ (3)	**DMSO/bmimBr**	24	44	78/22
18	An. NaOAc	$Pd(OAc)_2$ (3)	**DMSO/TBAC**	1	90	82/18
19	An. NaOAc	$Pd(OAc)_2$ (3)	**DMSO/TBAI**	1	87	52/48

[a] Reaction conditions: PhIOH, 0.5 mmol; **2c** 0.75 mmol; solvent 3 mL; ionic liquid 300 mg, base 0.5 mmol, $T = 110\,^{\circ}C$. In bold are indicated the modified conditions. [b] Isolated products, purified by column chromatography. [c] Determined by NMR analysis. [d] Determined by GC analysis.



Scheme 2 Proposal of reactivity pattern.

depending on the electron-donating properties of the heteroatom X. The final deprotonation at the C^3 of the alkyl chain allowed the formation of the 3-alkenylindoles **5a–g**. It should be pointed out that the last step is not possible in the case of terminal 1,2-allen-2-ols. Moreover, when the coupling was carried out with 2-iodo-*N*-acetylaniline (entry 6 in Table 2), the corresponding substituted alkylideneindoline **4f** was isolated first. Besides, when this reaction was not quenched just after the disappearance of the starting materials, the indolidinic derivative **4f** was converted into the corresponding *N*-acetylalkenylindole **5f** (entry 12), that was isolated as the sole pure product after 3 h.

The results of the reaction shown are reported in Table 2. The effects on the reaction outcome of the substituents on the aromatic ring, the protecting groups of allenols and the nitrogen, R^3 and R^2, have been evaluated. As far as the *o*-iodophenols are concerned, good yields were obtained (entries 1–5), regardless of the nature of the R^3 substituents that, moreover, slightly affect the stereoselectivity of the reaction, whereas when the 1-(ethoxymethoxy)but-1,2-diene (**2a**, entries 2 and 5) was used, better stereoselectivities were obtained. In fact an *E*/*Z* ratio of 90/10 was observed in the case of the products **4b** and **4e**. Unprotected 2-iodoaniline did not react, and *N*-tosyl and *N*-acetyliodoanilines were tested first. In the first case, the coupling proceeded smoothly (1.5 h), and the ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the signals of the corresponding alkylideneindoline derivatives. Unfortunately, any chromatographic purification was unsuccessful. As reported above, with *N*-acetyliodoaniline, both the corresponding alkenylindolidine **4f** (entry 6) and the 3-alkenyl-*N*-acetylindole **5f** (entry 12) were obtained at different reaction times. *N*-methyl-protected anilines were used next, and afforded the corresponding 3-alkenyl-*N*-methyl indoles **5b–e** (entries 8–11). The reactions were totally stereoselective and fast, regardless of the R^2 protecting group (THP in entry 7, $MeOCH_2$ in entries 8 and 12, and MEM in entries 9–11 and 13). Finally, with the aim of confirming the electronic effects of the *N*-protecting group, *N*-benzyliodoaniline was used (entry 13), and the corresponding 3-alkenylindole **5g** was isolated. This shows that the yield and stereoselectivity were comparable to those obtained with *N*-methyliodoaniline.

Conclusions

In summary, a phosphine-free Pd(0)-catalysed heteroannulation process involving 2-alkyl-1,2-dienols and *o*-iodophenols, or *o*-iodoanilines, has been proposed. Two different frameworks have been achieved, which depend on the electronic features of the nucleophile attacking the Pd π-allyl complex. When *o*-iodophenols, or *o*-iodoanilines protected with an electron-withdrawing group, are used, 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or -indolines, respectively, were obtained in good yield. On the other hand, when *N*-methyl and *N*-benzyliodoanilines were used, the nucleophile stereoselectively promoted the elimination of the alkoxy leaving group, affording the corresponding substituted alkenylindoles.

Experimental

General

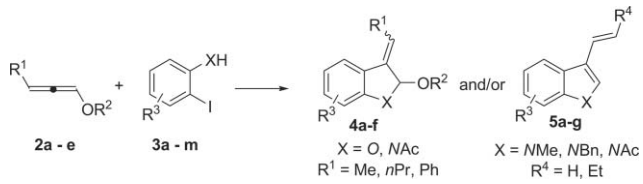
Flasks and all equipment used for the generation and reaction of moisture-sensitive compounds were dried by electric heat gun under Ar. THF and CH_2Cl_2 were distilled from sodium benzophenone ketyl and CaH_2, respectively. BuLi (1.6 M in hexanes) was obtained from Aldrich. All commercially obtained reagents and solvents were used as received. Products were purified by preparative column chromatography on Macherey Nagel silica gel for flash chromatography, 0.04–0.063 mm/230–400 mesh. *N*-Acetyl, *N*-benzyl and *N*-methylanilines were synthesised according to the literature procedures.[40]

Reactions were monitored by TLC using silica gel on TLC-PET foils Fluka, 2–25 μm, layer thickness 0.2 mm, medium pore diameter 60 Å. ^1H NMR spectra were recorded at 200 MHz, ^{13}C NMR spectra at 50.2 MHz, in $CDCl_3$. Data were reported as follows: chemical shifts in ppm from Me_4Si as an internal standard, integration, multiplicity (qm = quartet of multiplets, qd = quartet of doublets), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent peak as an internal standard. GC-MS spectra were obtained on a mass selective detector HP 5970 B instrument operating at an ionizing voltage of 70 eV connected to a HP 5890 GC with a cross linked methyl silicone capillary column (25 m × 0.2 mm × 0.33 μm film thickness). IR spectra were recorded on a Perkin Elmer BX FT-IR.

Procedure for the protection of alkynols[40]

In a 250 mL three-necked round bottom flask the alkynol (10.0 mmol) was dissolved in anhydrous CH_2Cl_2 (100 mL) and the solution was cooled to 0° C. Then, *N*-ethyldiisopropylamine (2.0 eq., 20.0 mmol, 3.82 mL) followed by the alkyl chloride (1.9 eq., 19.0 mmol) were added dropwise. The reaction mixture was stirred overnight at r.t. under Ar, then a 10% aqueous solution of $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2, then washed with a 5% aqueous solution of HCl (1 × 20 mL) and brine (1 × 20 mL), dried over K_2CO_3, filtered and evaporated

Table 2 Annulation of protected 3-alkyl-1,2-dien-1-ols and 2-iodophenols, and protected 2-iodoanilines[a]



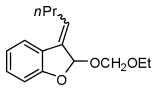
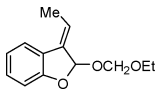
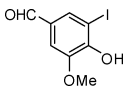
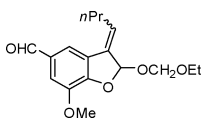
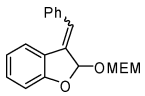
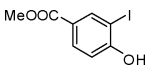
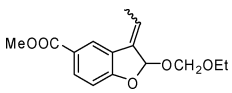
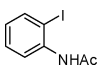
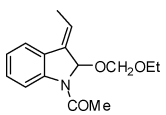
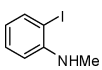
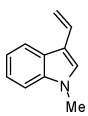
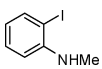
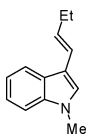
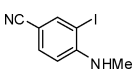
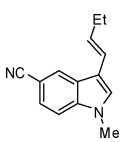
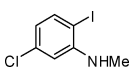
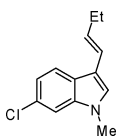
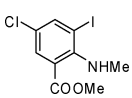
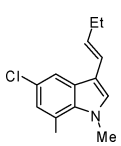
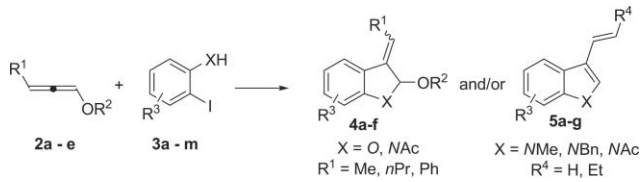
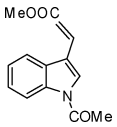
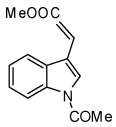
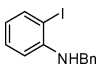
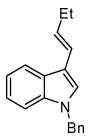
Entry	Allenol	Iodophenol or iodoaniline		Product		Time/h	Yield (%)[b]	E/Z[c]
1	**2c**	**3a**		**4a**		1	95	72/28
2	**2a**	**3a**		**4b**		1	93	90/10
3	**2c**	**3b**		**4c**		1	99	60/40
4	**2e**	**3a**		**4d**		1.5	94	76/24
5	**2a**	**3d**		**4e**		1.5	96	90/10
6	**2a**	**3e**		**4f**		1	54	>99/<1
7	**2b**	**3f**		**5a**		1.5	90	—
8	**2c**	**3f**		**5b**		1.5	80	>99/<1
9	**2d**	**3h**		**5c**		1.5	87	>99/<1
10	**2d**	**3i**		**5d**		1.5	77	>99/<1
11	**2d**	**3l**		**5e**		1.5	76	>99/<1

Table 2 *(Contd.)*



Entry	Allenol	Iodophenol or iodoaniline	Product	Time/h	Yield (%)[b]	*E*/*Z*[c]
12	**2a**	**3e** 	**5f** 	3	85	—
13	**2d**	**3m** 	**5g** 	2.5	84	>99/<1

[a] Reactions conditions: ArI, 0.5 mmol; protected allenol 0.75 mmol; DMSO 3 mL; TBAB 300 mg, NaOAc 0.5 mmol, $T = 110$ °C. [b] Isolated products, purified by column chromatography. [c] Determined by NMR analysis. [d] Determined by GC analysis.

under reduced pressure, to give the crude reaction product, that was used in the subsequent step without further purification.

1-(Ethoxymethoxy)but-2-yne (1a). Following the general procedure previously described, 0.70 g of 2-butyn-1-ol and 1.97 g of chloromethoxyethane were dissolved in CH_2Cl_2. 1.96 g of a pale yellow oil were obtained (76%). Found C, 65.01; H, 9.50%. Calc. for $C_7H_{12}O_2$: C, 65.60; H, 9.44%. ν_{max}(neat)/cm^{-1} 2950, 1730, 1450, 1360, 1047. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.21 (3 H, t, $J = 7.1$ Hz, CH_3), 1.82 (3 H, bs, CH_3), 3.60 (2 H, q, $J = 7.1$ Hz, CH_2 CH_3), 4.20 (2 H, s, CH_2O), 4.72 (2 H, s, OCH_2O); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 2.79 (1 × q), 14.551 (1 × q), 53.97 (1 × t), 62.87 (1 × t), 74.35 (1 × s), 83.00 (1 × s), 92.68 (1 × t). MS (EI, 70 eV): m/z (%) = 128 (1) [M$^+$], 82 (19), 59 (18), 53 (100), 52 (17).

1-(Ethoxymethoxy)hex-2-yne (1c). Following the general procedure previously described, 1.08 g of 2-hexyn-1-ol and 1.97 g of chloromethoxyethane were dissolved in CH_2Cl_2. 1.48 g of a pale yellow oil were obtained (95%). Found C, 69.75; H, 11.00%. Calc. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.93 (3 H, t, $J = 6.8$ Hz, CH_3), 1.09 (3 H, t, $J = 7.1$ Hz, CH_3), 1.55 (2 H, sext., $J = 7.0$ Hz, CH_2), 2.20 (2 H, t, $J = 6.7$ Hz, CH_2), 3.57 (2 H, q, $J = 6.0$ Hz, CH_2O), 4.16 (2 H, s, CH_2), 4.69 (2 H, s,OCH_2O); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.16 (1 × q), 14.81 (1 × q), 20.44 (1 × t), 21.74 (1 × t), 54.37 (1 × t), 63.18 (1 × t), 75.31 (1 × s), 86.38 (1 × s), 92.92 (1 × t). MS (EI, 70 eV): m/z (%) = 127 (2) [M$^+$ – Et], 97 (35), 81 (54), 67 (100), 59 (52).

1-((2-Methoxyethoxy)methoxy)hex-2-yne (1d). Following the general procedure previously described, 1.08 g of 2-hexyn-1-ol and 2.36 g of 2-methoxyethoxymethyl chloride were dissolved in CH_2Cl_2. 1.75 g of a pale yellow oil were obtained (94%). Found C, 63.80; H, 9.61%. Calc. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.94 (3 H, t, $J = 6.9$ Hz, CH_3), 1.48 (2 H, sext., $J = 7.1$ Hz, CH_2), 2.12 (2 H, t, $J = 6.7$ Hz, CH_2), 3.48 (3 H, s, CH_3O), 3.52 (2 H, t, $J = 4.8$ Hz, CH_2O), 3.66 (2 H, t, $J = 4.8$ Hz, CH_2O), 4.20 (2 H, t, $J = 2.1$ Hz, CH_2), 5.28 (2 H, s,OCH_2O); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.00 (1 × q), 20.20 (1 × t), 21.67 (1 × t), 54.25 (1 × q), 58.42 (1 × t), 66.64 (1 × t), 71.35 (1 × t), 75.17 (1 × s), 86.24 (1 × s), 93.10 (1 × t). MS (EI, 70 eV): m/z (%) = 127 (1) [M$^+$ – $CH_3OCH_2CH_2$], 81 (68), 73 (28), 59 (100), 53 (40).

(3-((2-Methoxyethoxy)methoxy)prop-1-ynyl)benzene (1e). Following the general procedure previously described, 1.32 g of 3-phenylprop-2-yn-1-ol and 2.36 g of of 2-methoxyethoxymethyl chloride were dissolved in CH_2Cl_2. 1.61 g of a pale yellow oil were obtained (98%). Found C, 70.72; H, 7.27%. Calc. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%. δ_H (200 MHz; $CDCl_3$, Me_4Si) 3.30–4.10 (7 H, m, OCH_2CH_2O, CH_3O), 4.50 (2 H, s, CH_2O), 4.90 (2 H, s, OCH_2O), 7.49 (5 H, m, Ar).

Procedure for the synthesis of 2-(but-2-ynyloxy)tetrahydro-2*H*-pyran (1b)

In a 100 mL three-necked round bottom flask, 0.70 g of 2-butyn-1-ol (10.0 mmol) was dissolved in 25 mL of anhydrous CH_2Cl_2 at r.t., then DHP (1.5 eq., 15.0 mmol, 1.26 g) followed by PPTS (0.1 eq., 1.0 mmol, 0.25 g) were added. The reaction mixture was stirred overnight at r.t. under Ar, then the solvent was partly evaporated. The mixture was diluted with Et_2O then washed with brine (2 × 20 mL), dried over K_2CO_3, filtered, and evaporated under reduced pressure, to give 1.43 g of a pale yellow oil (93%). The crude reaction product, was used in the subsequent step without further purification. Spectral data corresponded to those reported in the literature.[41]

General procedure for the isomerization of alkynes to allenes

In a Schlenk vessel, alkynol (10.0 mmol) was dissolved in anhydrous THF (20 mL) and cooled to –95 °C, then *n*-BuLi (2.0 eq., 20.0 mmol, 12.5 mL) was added. The reaction mixture

was stirred for 2 h at –95 °C, then a solution of THF–H_2O was added (20 mL). The mixture was extracted with Et_2O (2 × 20 mL), then washed with brine (2 × 20 mL), dried (K_2CO_3), filtered and evaporated under reduced pressure. The product was purified by column chromatography.

1-(Ethoxymethoxy)but-1,2-diene (2a). (EP/EE 95/5, 1% Et_3N (EP = petroleum ether, EE = diethyl ether)) pale yellow oil (0.84 g, 66%). Spectral data corresponded to those reported in the literature.[18]

2-(Buta-1,2-dienyloxy)tetrahydro-2*H*-pyran (2b). (EP/EE 98/2, 1% Et_3N; diastereomeric mixture 60/40) pale yellow oil (0.92 g, 60%). Spectral data corresponded to those reported in the literature.[41]

1-(Ethoxymethoxy)hex-1,2-diene (2c). (EP/EE 95/5, 1% Et_3N) pale yellow oil (0.96 g, 62%). Found C, 69.60; H, 10.25%. Calc. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.94 (3 H, t, J = 6.6 Hz, CH_3), 1.23 (3 H, t, J = 7.1 Hz, CH_3CH$_2$O), 1.48 (2 H, sext, J = 7.5 Hz, CH$_3$CH_2CH$_2$), 2.08 (2 H, qd, J = 5.4 Hz, 1.0 Hz, CH_2CH=C), 3.66 (2 H, q, J = 7.1 Hz, CH_2O), 4.84 (2 H, s, OCH_2O), 5.81 (1 H, q, J = 5.3 Hz, CH$_2$CH=C), 6.56 (1 H, m, =CHO); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.5 (1 × q), 15.6 (1 × q), 21.5 (1 × t), 32.8 (1 × t), 64.0 (1 × t), 93.4 (1 × t), 105.9 (1 × d), 117.7 (1 × d), 193.3 (1 × s).

1-((2-Methoxyethoxy)methoxy)hexa-1,2-diene (2d). (EP/EE 95/5, 1% Et_3N) pale yellow oil (1.26 g, 68%). Found C, 69.60; H, 10.25%. Calc. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.94 (3 H, t, J = 7.5 Hz, CH_3), 1.48 (2 H, sext, J = 7.5 Hz, CH_2CH$_2$), 2.08 (2 H, qm, J = 5.4 Hz, CH_2CH=C), 3.40 (3 H, s, CH_3O), 3.55 (2 H, m, OCH$_2$CH_2O), 3.71 (2 H, m, OCH_2CH$_2$O), 4.84 (2 H, s, OCH_2O), 5.81 (1 H, q, J = 5.3 Hz, CH$_2$CH=C), 6.56 (1 H, bs, =CHO); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 14.3 (1 × q), 25.6 (1 × t), 38.0 (1 × t), 59.3 (1 × q), 69.5 (1 × t), 71.9 (1 × t), 95.2 (1 × t), 110.2 (1 × d), 134.2 (1 × d), 189.9 (1 × s).

(3-((2-Methoxyethoxy)methoxy)propa-1,2-dienyl)benzene (2e). (EP/EE 95/5, 1% Et_3N) pale yellow oil (1.12 g, 51%). Found C, 70.95; H, 7.34%. Calc. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%. ν_{max}(neat)/cm^{-1} 3446, 2928, 2359, 2339, 758. δ_H (200 MHz; $CDCl_3$, Me_4Si) 3.36 (3 H, s, CH_3O), 3.57 (2 H, t, J = 5.1 Hz, CH_2CH$_2$), 3.71 (2 H, t, J = 5.0 Hz, CH$_2$CH_2), 4.93 (2 H, s, OCH_2O), 6.71 (1 H, d, J = 5.5 Hz, CH$_2$CH=C), 6.96 (1 H, d, J = 5.5 Hz, PhCH=C), 7.31 (5 H, m, *Ar*). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 58.7 (1 × q), 67.7 (1 × t), 71.4 (1 × t), 93.8 (1 × t), 107.6 (1 × d), 120.6 (1 × d), 127.3 (2 × d), 127.7 (1 × d), 128.4 (2 × d), 134.4 (1 × s), 195.3 (1 × s). MS (EI, 70 eV): m/z (%) = 220 (5) [M$^+$], 146 (21), 115 (100), 77 (53), 63 (27).

Typical procedure for the Heck couplings between protected allenols and iodoarenes

$Pd(OAc)_2$ (3% mol, 0.015 mmol, 3.4 mg) was dissolved in anhydrous DMSO (3 mL) and 300 mg of TBAB, the solution so obtained was degassed with Ar for 10 min at r.t. Then, NaAcO (0.5 mmol, 41 mg), iodoarene (0.5 mmol), and protected allenol (0.75 mmol) were subsequently added. The reaction was stirred in a sealed tube at 110 °C until the disappearance of the allenol was observed by TLC and GC on a sample taken and partitioned between Et_2O and H_2O. Then, H_2O was added and the mixture was extracted with Et_2O (2 × 20 mL), then washed with brine (2 × 20 mL), dried (K_2CO_3), filtered, and evaporated under reduced pressure.

(*E*)-3-butylidene-2-(ethoxymethoxy)-2,3-dihydrobenzofuran (4a). (EP/EE 93/7, 1% Et_3N) pale yellow oil (85 mg, 68%). Found C, 72.80; H, 8.13%. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.15%. ν_{max}(neat)/cm^{-1} 2978, 2357, 1721, 1587, 1463, 922. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.02 (3 H, t, J = 7.1 Hz, CH_3), 1.19 (3 H, t, J = 6.9 Hz, CH_3), 1.59 (2 H, sext, J = 7.3 Hz, CH$_3$CH_2), 2. 48 (2 H, q, J = 6.9 Hz, CH$_3$CH$_2$CH_2), 3.75 (2 H, m, CH$_3$CH_2O), 4.84 (1 H, d, J = 6.9 Hz, OCH_{2a}O), 5.12 (1 H, d, J = 6.9 Hz, OCH_{2b}O), 6.12 (1 H, bt, J = 7.5 Hz, CH$_2$CH=C), 6.35 (1 H, s, OCHO), 6.89 (2 H, m, Ar), 7.19 (1 H, m, Ar), 7.50 (1 H, d, J = 7.4, Ar); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (1 × q), 14.9 (1 × q), 22.5 (1 × t), 31.0 (1 × t), 64.2 (1 × t), 92.4 (1 × t), 101.1 (1 × d), 110.1 (1 × d), 119.9 (1 × d), 121.0 (1 × d), 124.6 (1 × d), 125.3 (1 × d), 129.1 (1 × s), 135.0 (1 × s), 159.9 (1 × s). MS (EI, 70 eV): m/z (%) = 248 (34) [M$^+$], 173 (36), 131 (44), 91 (25), 59 (100).

(*Z*)-3-butylidene-2-(ethoxymethoxy)-2,3-dihydrobenzofuran (4a). (EP/EE 93/7, 1% Et_3N) pale yellow oil (34 mg, 27%). Found C, 73.01; H, 8.12%. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.15%. ν_{max}(neat)/cm^{-1} 2978, 2357, 1748, 1532, 1419, 922. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.02 (3 H, t, J = 7.1 Hz, CH_3), 1.19 (3 H, t, J = 6.9 Hz, CH_3), 1.59 (2 H, sext., J = 7.4 Hz, CH$_3$CH_2), 2. 48 (2 H, q, J = 6.9 Hz, CH$_3$CH$_2$CH_2), 3.75 (2 H, m, CH$_3$CH_2O), 4.84 (1 H, d, J = 6.9 Hz, OCH_{2a}O), 5.12 (1 H, d, J = 6.9 Hz, OCH_{2b}O), 5.81 (1 H, bt, J = 7.6 Hz, CH$_2$CH=C), 6.12 (1 H, s, OCHO), 6.89 (2 H, m, Ar), 7.19 (1 H, m, Ar), 7.50 (1 H, d, J = 7.4 Hz, Ar); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.8 (1 × q), 14.9 (1 × q), 22.3 (1 × t), 30.4 (1 × t), 63.9 (1 × t), 92.8 (1 × t), 103.5 (1 × d), 110.2 (1 × d), 120.9 (1 × d), 124.0 (1 × d), 124.1 (1 × d), 128.3 (1 × d), 129.3 (1 × s), 134.8 (1 × s), 161.0 (1 × s). MS (EI, 70 eV): m/z (%) = 248 (34) [M$^+$], 173 (36), 131 (44), 91 (25), 59 (100).

(*E*)- and (*Z*)-2-(ethoxymethoxy)-3-ethylidene-2,3-dihydrobenzofuran (4b). (EP/EE 93/7, 1% Et_3N) pale yellow oil (102.4 mg, 93%). Found C, 71.35; H, 7.29%. Calc. for $C_{15}H_{20}O_3$: C, 70.89; H, 7.32%. ν_{max}(neat)/cm^{-1} 2982, 1730, 1588, 1465, 925. δ_H major isomer (200 MHz; $CDCl_3$, Me_4Si) 0.90 (3 H, t, J = 7.1 Hz, CH_3), 1.95 (3 H, dd, J = 7.3, 1.5 Hz, CH_3CH=C), 3.63 (2 H, quint., J = 7.1 Hz, CH$_3$CH_{2a}O), 3.82 (2 H, quint., J = 7.1 Hz, CH$_3$CH_{2b}O), 4.83 (1 H, d, J = 6.8 Hz, OCH_{2a}O), 5.11 (1 H, d, J = 6.8 Hz, OCH_{2b}O), 5.90 (1 H, qd, J = 7.4, 1.5 Hz, CH$_3$CH=C), 6.12 (1 H, quint., J = 1.4 Hz, OCHO), 6.89 (2 H, m, Ar), 7.20 (1 H, td, J = 7.3, 1.5 Hz, Ar), 7.52 (1 H, d, J = 7.3 Hz, Ar); δ_C major isomer (50.2 MHz; $CDCl_3$, Me_4Si) 14.2 (1 × q), 14.9 (1 × q), 63.9 (1 × t), 92.7 (1 × t), 103.3 (1 × d), 110.2 (1 × d), 120.9 (1 × d), 122.2 (1 × s), 124.2 (2 × d), 129.3 (1 × d), 135.7 (1 × s), 161.1 (1 × s). MS (*Z*) (EI, 70 eV): m/z (%) = 220 (18) [M$^+$], 147 (25), 145 (43), 115 (30), 59 (100). MS (*E*) (EI, 70 eV): m/z (%) = 220 (15) [M$^+$], 147 (20), 145 (38), 115 (33), 59 (100).

(*E*)- and (*Z*)-3-butylidene-2-(ethoxymethoxy)-7-methoxy-2,3-dihydrobenzofuran-5-carbaldehyde (4c). (EP/EE 93/7, 1% Et_3N) (*E*/*Z* = 60/40) pale yellow oil (147 mg, 99%). Found C, 66.48; H, 7.29%. Calc. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24%. ν_{max}(neat)/cm^{-1} 3010, 2902, 1725, 1583, 1455, 1030, 935, 747. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.98 (3 H, m, CH_3CH$_2$), 1.25 (3 H, m, CH_3CH$_2$O), 1.60 (2 H, sext, J = 6.3 Hz, CH$_3$CH_2CH$_2$), 2.28 (2 H, t, J = 7.1 Hz,

$CH_3CH_2CH_2$, isomer *Z*), 2.52 (2 H, q, $J = 7.1$ Hz, $CH_3CH_2CH_2$, isomer *E*), 3.63 (1 H, m, $CH_3CH_{2a}O$), 3.80 (1 H, m, $CH_3CH_{2b}O$), 3.93 (3 H, s, CH_3O), 4.81 (1 H, d, $J = 5.5$ Hz, $OCH_{2a}O$, isomer *E*), 4.83 (1 H, d, $J = 5.5$ Hz, $OCH_{2a}O$, isomer *Z*), 5.17 (1 H, d, $J = 5.5$ Hz, $OCH_{2b}O$, isomer *Z*), 5.19 (1 H, d, $J = 5.5$ Hz, $OCH_{2b}O$, isomer *E*), 5.08 (1 H, d, $J = 7.0$ Hz, $OCH_{2b}O$), 5.85 (1 H, t, $J = 7.8$ Hz, C*H*=C, isomer *Z*), 6.25 (1 H, t, $J = 7.8$ Hz, C*H*=C, isomer *E*), 6.29 (1 H, s, OC*H*O, isomer *Z*), 6.51 (1 H, s, OC*H*O, isomer *E*), 7.36 (1 H, s, Ar, isomer *Z* and *E*), 7.48 (1 H, s, Ar), 7.62 (1 H, s, Ar), 9.84 (1 H, s, C*H*O, isomer *Z*), 9.84 (1 H, s, C*H*O, isomer *E*); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (1 × q), 14.8 (1 × q), 22.2 (1 × t), 22.4 (1 × t), 30.4 (1 × t), 30.9 (1 × t), 56.0 (1 × q), 64.1 (1 × t), 64.4 (1 × t), 92.9 (1 × t), 93.1 (1 × t), 103.1 (1 × d), 105.2 (1 × d), 111.5 (1 × d), 111.8 (1 × d), 116.6 (1 × d), 120.4 (1 × d),. 125.5 (1 × d),. 127.6 (1 × d), 128.3 (1 × s), 129.0 (1 × s), 130.4 (1 × d), 131.2 (1 × d), 131.4 (1 × d), 133.3 (1 × s), 133.4 (1 × s), 145.1 (1 × s), 157.5 (1 × s), 158.8 (1 × s), 190.5 (1 × s), 190.6 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 306 (25) [M^+], 231 (10), 189 (19), 77 (9), 59 (100). MS (*E*) (EI, 70 eV): *m*/*z* (%) = 306 (10) [M^+], 216 (12), 205 (13), 189 (24), 59 (100).

(*E*)- and (*Z*)-3-benzylidene-2-((2-methoxyethoxy)methoxy)-2,3-dihydrobenzofuran (4d). (EP/EE 93/7, 1% Et_3N) (*E*/*Z* = 76/24) pale yellow oil (147 mg, 94%). Found C, 73.33; H, 6.44%. Calc. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45%. ν_{max}(neat)/cm^{-1} 3014, 2893, 1588, 1460, 1028, 938, 747, 697. δ_H (200 MHz; $CDCl_3$, Me_4Si) 3.44 (3 H, s, OCH_3), 3.64 (2 H, t, $J = 5.9$ Hz, OCH_2CH_2O), 3. 85 (2 H, m, OCH_2CH_2O), 4.96 (1 H, d, $J = 6.7$ Hz, $OCH_{2a}O$), 5.26 (1 H, d, $J = 6.7$ Hz, $OCH_{2b}O$), 6.31 (1 H, s, OC*H*O), 6.74 (2 H, m, Ar), 7.45 (6 H, m, Ar, C*H*=C); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 58.9 (1 × q), 67.6 (1 × t), 71.5 (1 × t), 93.4 (1 × t), 104.0 (1 × d), 110.4 (2 × d), 120.6 (2 × d), 122.6 (1 × s), 123.4 (1 × d), 125.7 (1 × d), 127.7 (1 × d), 128.2 (2 × d),. 128.3 (1 × d),. 130.5 (1 × d),. 136.0 (1 × s),. 136.2 (1 × s), 161.9 (1 × s). MS (EI, 70 eV): *m*/*z* (%) = 312 (3) [M^+], 207 (9), 178 (12), 89 (50), 59 (100).

(*E*)- and (*Z*)-methyl-3-ethylidene-2-(ethoxymethoxy)-2,3-dihydrobenzofuran-5-carboxylate (4e). (EP/EE 90/10, 1% Et_3N) (*E*/*Z* = 60/40) pale yellow oil (133 mg, 96%). Found C, 65.01; H, 6.51%. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52%. ν_{max}(neat)/cm^{-1} 3020, 2901, 1601, 1455, 1025, 941, 750, 700. δ_H major isomer (200 MHz; $CDCl_3$, Me_4Si) 1.27 (3 H, t, $J = 7.1$ Hz, CH_3CH_2), 2.14 (3 H, dd, $J = 7.4$, 1.4 Hz, CH_3CH=C), 3.70 (2 H, m, CH_3CH_2O), 3.89 (3 H, s, CH_3O), 4.84 (1 H, d, $J = 6.8$ Hz, $OCH_{2a}O$), 5.12 (1 H, d, $J = 6.8$ Hz, $OCH_{2b}O$), 5.96 (1 H, qd, $J = 7.4$, 1.4 Hz, C*H*=C), 6.21 (1 H, bs, OC*H*O), 6.88 (1 H, d, $J = 8.5$ Hz, Ar), 7.94 (1 H, dd, $J = 8.5$, 1.5 Hz, Ar), 8.21 (1 H, d, $J = 1.5$ Hz, Ar); δ_C major isomer (50.2 MHz; $CDCl_3$, Me_4Si) 14.3 (1 × q), 14.9 (1 × q), 51.8 (1 × q), 64.0 (1 × t), 92.9 (1 × t), 104.3 (1 × d), 109.8 (1 × d), 123.1 (1 × s), 124.0 (1 × d), 124.5 (1 × q), 125.8 (1 × d), 131.8 (1 × d), 134.3 (1 × s), 164.5 (1 × s), 166.6 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 278 (37) [M^+], 203 (62), 159 (23), 59 (100), 31 (25). MS (*E*) (EI, 70 eV): *m*/*z* (%) = 278 (37) [M^+], 205 (26), 203 (67), 115 (23), 59 (100).

(*E*)-1-(2-(ethoxymethoxy)-3-ethylideneindolin-1-yl)ethanone (4f). (EP/EE 93/7, 1% Et_3N) pale yellow oil (70 mg, 54%). Found C, 68.48; H, 7.31%. Calc. for $C_{15}H_{18}NO_3$: C, 68.94; H, 7.33%. ν_{max}(neat)/cm^{-1} 3015, 2891, 1590, 1460, 1031, 940, 748, 700. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.16 (3 H, t, $J = 7.1$ Hz, CH_3CH_2), 2.10 (3 H, d, $J = 7.3$ Hz, CH_3CH=C), 2.41 (3 H, s, CH_3CON), 3.59 (2 H, q, $J = 7.1$ Hz, CH_3CH_2O), 4.65 (1 H, m, $OCH_{2a}O$), 4.81 (1 H, d, $J = 6.9$ Hz, $OCH_{2b}O$), 5.99 (1 H, m, OC*H*N), 6.09 (1 H, q, $J = 7.3$ Hz, C*H*=C), 7.09 (1 H, t, $J = 7.6$ Hz, Ar), 7.27 (1 H, t, $J = 7.8$ Hz, Ar), 7.55 (1 H, d, $J = 7.6$ Hz, Ar), 8.27 (1 H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 14.2 (1 × q), 14.7 (1 × q), 23.2 (1 × q), 64.1 (1 × t), 88.8 (1 × d), 89.5 (1 × t), 116.9 (1 × d), 123.6 (1 × d), 123.9 (1 × d), 124.9 (1 × d), 126.0 (1 × s), 128.8 (1 × d), 133.3 (1 × s), 143.0 (1 × s), 169.1 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 261 (20) [M^+], 187 (31), 144 (100), 130 (35), 59 (21).

1-Methyl-3-vinyl-1*H*-indole (5a). (EP/EE 93/7, 1% Et_3N) pale yellow oil (71 mg, 90%). Found C, 83.351; H, 8.96%. Calc. for $C_{11}H_{11}N$: C, 84.04; H, 7.05, N, 8.91%. ν_{max}(neat)/cm^{-1} 2961, 1711, 1468, 1070, 1013, 738. δ_H (200 MHz; $CDCl_3$, Me_4Si) 3.78 (3 H, s, CH_3N), 5.14 (1 H, dd, $J = 11.2$, 1.6 Hz, $CH_{2(cis)}$=CH), 5.69 (1 H, dd, $J = 17.8$, 1.6 Hz, $CH_{2(trans)}$=CH), 6.89 (1 H, dd, $J = 17.8$, 11.2 Hz, CH_2=C*H*), 7.23 (4 H, m, Ar), 7.90 (1 H, d, $J = 6.5$ Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 32.6 (1 × q), 109.2 (1 × d), 109.8 (1 × d), 114.0 (1 × s), 119.7 (1 × d), 120.0 (1 × d), 121.9 (1 × t), 125.9 (1 × s), 128.0 (1 × s), 128.0 (1 × s), 129.1 (1 × d). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 157 (100) [M^+], 156 (33), 154 (8), 128 (8), 115 (28).[28]

(*E*)-3-(but-1-enyl)-1-methyl-1*H*-indole (5b). (EP/EE 93/7, 1% Et_3N) pale yellow oil (74 mg, 80%). Found C, 84.31; H, 8.08, N, 7.61%. Calc. for $C_{13}H_{15}N$: C, 84.28; H, 8.16, N, 7.56%. ν_{max}(neat)/cm^{-1} 2961, 1711, 1468, 1070, 1013, 738. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.13 (3 H, t, $J = 7.1$ Hz, CH_3CH_2), 2.27 (2 H, quint., $J = 7.1$ Hz, CH_3CH_2), 3.71 (3 H, s, CH_3N), 6.19 (1 H, dt, $J = 16.4$, 6.8 Hz, CH_2CH=CH), 6.53 (1 H, d, $J = 16.2$ Hz, CH_2CH=C*H*), 7.08 (1 H, s, C*H*N), 7.29 (3 H, m, Ar), 7.87 (1 H, d, $J = 6.7$ Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 14.1 (1 × q), 26.5 (1 × t), 32.5 (1 × q), 109.2 (1 × d), 113.9 (1 × s), 119.3 (1 × d), 119.9 (1 × d), 120.9 (1 × d), 121.7 (1 × d), 126.0 (1 × s), 126.6 (1 × d), 129.0 (1 × d), 137.3 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 185 (78) [M^+], 170 (100), 154 (21), 144 (23), 115 (13).

(*E*)-3-(but-1-enyl)-1-methyl-1*H*-indole-5-carbonitrile (5c). (EP/EE 95/5, 1% Et_3N) pale yellow oil (91 mg, 87%). Found C, 80.22; H, 6.75, N, 13.40%. Calc. for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71, N, 13.32%. ν_{max}(neat)/cm^{-1} 2940, 2260, 1720, 1477, 1068, 1013, 803. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.13 (3 H, t, $J = 6.9$ Hz, CH_3CH_2), 2.28 (2 H, quint., $J = 7.1$ Hz, CH_3CH_2), 3.79 (3 H, s, CH_3N), 6.20 (1 H, dt, $J = 17.1$, 6.9 Hz, CH_2CH=CH), 6.49 (1 H, bd, $J = 17.0$ Hz, CH_2CH=C*H*), 7.13 (1 H, s, C*H*N), 7.31 (1 H, m, Ar), 7.44 (1 H, d, $J = 7.3$ Hz, Ar), 8.16 (1 H, s, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (1 × q), 26.3 (1 × t), 32.7 (1 × q), 102.2 (1 × s), 109.9 (1 × d), 115.0 (1 × s), 119.4 (1 × d), 120.7 (1 × s), 124.5 (1 × d), 125.5 (1 × d), 125.8 (1 × s), 128.3 (1 × d), 131.2 (1 × d), 170.9 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 210 (59) [M^+], 195 (100), 179 (14), 169 (21), 154 (14).

(*E*)-3-(but-1-enyl)-4-chloro-1-methyl-1*H*-indole (5d). (EP/EE 95/5, 1% Et_3N) pale yellow oil (85 mg, 77%). Found C, 71.69; H, 6.47, N, 6.41%. Calc. for $C_{13}H_{14}ClN$: C, 71.07; H, 6.42, N, 6.38%. ν_{max}(neat)/cm^{-1} 2930, 1719, 1610, 1068, 960, 854. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.13 (3 H, t, $J = 7.4$ Hz, CH_3CH_2), 2.27 (2 H, quint., $J = 6.4$ Hz, CH_3CH_2), 3.71 (3 H, s, CH_3N), 6.19 (1 H, dt, $J = 16.4$, 6.9 Hz, CH_2CH=CH), 6.51 (1 H, bd, $J = 16.7$ Hz, CH_2CH=C*H*), 7.02 (1 H, s, C*H*N), 7.12 (1 H, d, $J = 6.7$ Hz, Ar),

7.28 (1 H, s, Ar), 7.73 (1 H, d, $J = 9.0$ Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.9 (1 × q), 26.4 (1 × t), 32.5 (1 × q), 109.2 (1 × d), 114.1 (1 × s), 119.9 (1 × d), 120.3 (1 × d), 120.7 (1 × d), 124.6 (1 × s), 127.1 (1 × s), 127.7 (1 × d), 129.7 (1 × d), 137.6 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 221 (25) [M^+], 204 (83), 178 (27), 169 (100), 168 (57).

(*E*)-methyl 3-(but-1-enyl)-5-chloro-1-methyl-1*H*-indole-7-carboxylate (5e). (EP/EE 95/5, 1% Et_3N) pale yellow oil (105.3 mg, 76%). Found C, 80.22; H, 6.75, N, 4.99%. Calc. for $C_{15}H_{16}ClNO_2$: C, 64.87; H, 5.81, N, 5.04%. ν_{max}(neat)/cm^{-1} 2961, 1718, 1540, 1457, 1075. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.13 (3 H, t, $J = 6.9$ Hz, CH_3CH$_2$), 2.26 (2 H, quint., $J = 6.8$ Hz, CH$_3$CH_2), 3.79 (3 H, s, CH_3N), 3.97 (3 H, s, CH_3O), 6.15 (1 H, dt, $J = 16.0$, 6.8 Hz, CH$_2$CH=CH), 6.49 (1 H, bd, $J = 16.0$ Hz, CH$_2$CH=CH), 7.08 (1 H, s, CHN), 7.61 (1 H, s, Ar), 7.27 (1 H, s, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (1 × q), 26.3 (1 × t), 37.1 (1 × q), 52.2 (1 × q), 114.0 (1 × d), 116.7 (1 × s), 119.1 (1 × d), 123.1 (1 × s), 124.0 (1 × d), 124.6 (1 × s), 130.0 (1 × s), 130.4 (1 × s), 130.8 (2 × d), 166.6 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 279 (36) [$M^+ + 2$], 277 (100) [M^+], 262 (91), 227 (25), 203 (22).

1-(3-Vinyl-1*H*-indol-1-yl)ethanone (5f). EP/EE 93/7, 1% Et_3N) pale yellow oil (110 mg, 85%). Found C, 77.65; H, 6.01, N, 7.61%. Calc. for $C_{15}H_{18}NO_3$: C, 77.81; H, 5.99, H, 7.56%. ν_{max}(neat)/cm^{-1} 3134, 2927, 1702, 1452, 1129, 989, 746, 645. δ_H (200 MHz; $CDCl_3$, Me_4Si) 2.62 (3 H, s, CH_3), 5.38 (1 H, dd, $J =$ 11.3, 1.2 Hz, CH_{2a}=C), 5.85 (1 H, dd, $J = 17.8$, 1.2 Hz, CH_{2b}=C), 6.79 (1 H, dd, $J = 17.8$, 11.3 Hz, CH$_2$=CH), 7.36 (3 H, m, Ar, CHN), 7.81 (1 H, $J = 6.7$ Hz, Ar), 8.51 (1 H, d, $J = 6.7$ Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 23.8 (1 × q), 115.2 (1 × d), 116.5 (1 × s), 119.7 (1 × d), 120.7 (1 × t), 122.9 (1 × d), 123.7 (1 × d), 125.3 (1 × d), 127.6 (1 × d), 128.5 (1 × s), 136.1 (1 × s), 168.3 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 185 (25) [M^+], 143 (100), 115 (50), 89 (21), 63 (23).

(*E*)-1-benzyl-3-(but-1-enyl)-1*H*-indole (5g). (EP/EE 95/5, 1% Et_3N) pale yellow oil (110 mg, 84%). Found C, 86.97; H, 7.29, N, 5.38%. Calc. for $C_{19}H_{19}N$: C, 87.31; H, 7.33, N, 5.36%. ν_{max}(neat)/cm^{-1} 3032, 2974, 1717, 161540, 1456, 1352, 1117. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.13 (3 H, t, $J = 7.0$ Hz, CH_3CH$_2$), 2.28 (2 H, quint., $J = 7.0$ Hz, CH$_3$CH_2), 5.28 (2 H, s, ArCH_2N), 6.25 (1 H, dt, $J = 16.0$, 6.4 Hz, CH$_2$CH=CH), 6.49 (1 H, dt, $J =$ 16.0, 0.6 Hz, CH$_2$CH=CH), 7.08–7.41 (9 H, m, CHN, Ar), 7.90 (1 H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.9 (1 × q), 26.4 (1 × t), 49.7 (1 × t), 109.6 (1 × d), 114.5 (1 × s), 119.5 (1 × d), 120.0 (1 × d), 120.7 (1 × d), 121.9 (1 × d), 126.0 (1 × s), 126.3 (1 × d), 126.6 (2 × d), 127.4 (1 × d), 128.6 (2 × d), 129.4 (1 × d), 136.9 (1 × s), 137.1 (1 × s). MS (*Z*) (EI, 70 eV): *m*/*z* (%) = 261 (17) [M^+], 246 (17), 92 (9), 91 (100), 65 (30).

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Notes and references

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