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Synthesis of Highly Functionalised Dihydrobenzofurans and Indolines by Palladium Catalysed Mizoroki-Heck - Heteroannulation Cascade Reaction of Alkoxy-1,3-dienes

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Abstract

A Mizoroki – Heck – Heteroannulation cascade reaction has been used for the preparation of substituted dihydrobenzofurans and indolines in good yields. This has been done via a reaction between functionalised alkoxy-1,3-dienes and several *o*-iodophenols and protected *o*-iodoanilines depending on the starting material structure, the substitution on the aromatic ring and the amino protecting group.

Keywords: Mizoroki-Heck couplings, heteroannulation, cascade reactions, dihydrobenzofurans, indolines, alcoxydienes.

Introduction

The palladium catalysed annulation process is one of the most useful methods for the synthesis of 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-, 1,4-dienes, as well as internal alkynes, which were reacted with aryl or vinyl halides and triflates.[1-3] We have previously described the synthetic use of the Heck coupling on 1-alkoxy-functionalised 1,3-dienes,[4, 5] and more recently we have turned our attention to protected 3-alkyl-1,2-dienols as synthetic precursors of α-arylated α,β-unsaturated aldehydes[6] and

substituted 3-alkenylindoles, 2-alkoxy 3-alkylidene-2,3-dihydrobenzofuranes and indolines.[7] The general reactivity of conjugated dienes and the direct formation of their palladium π-allyl complexes had already been described by Heck.[8] Grigg's research group studied the palladium catalysed tandem cyclisation anion capture processes and the cases of carbon-, nitrogen- and oxygen- centered nucleophiles were described.[9] Larock and coworkers greatly contributed to the description of the chemistry of the Heck coupling of 1,2- and 1,3-dienes.[3, 10-12] They initially described the carbo- and heteroannulation of dienes and later the enantioselective version was also investigated.[13] More recently these authors reported the palladium-catalysed annulation of 1,3-dienes by *o*-iodoaryl acetates as an efficient approach to biologically interesting dihydrobenzofurans.[14] 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 Pd(0) catalysed coupling reactions has been demonstrated. Actually, the most reactive position is adjacent to the alkoxy group.[15] The palladium catalysed methodologies which afford five- and six-membered fused heterocycles have been recently reviewed,[16] and of the described strategies, the multi-step syntheses of natural products, and the development and the use of multiple palladium catalysed transformations, performed in a domino fashion, occupy a special position.[17-22]

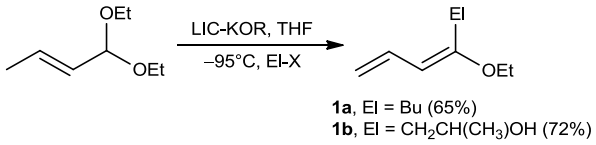
The 2,3-dihydrobenzofuran skeleton, is present in a vast array of natural products and numerous synthetic compounds with useful biological activity.[23] Dihydrobenzofuran containing natural products have been reported with activity against cancer,[24-26] tuberculosis,[27] malaria[28] and cataracts,[29] others show antioxidant and/or cytoprotective properties[30] and insecticidal activity.[31]

The importance of the indolinic moiety is also well established, especially in the alkaloid systems.[32, 33] For instance, correlated structures such as Toussaintines have shown antimicrobial properties.[34] The Pauson-Khand reaction has been exploited for the synthesis of tri-[35] and tetracyclic[36] indolines correlated to the alkaloid asperparaline.

Results and Discussion

In this paper we wish to report the results obtained when studying the Pd(0) catalysed heteroannulation of functionalised 1-alkoxybuta-1,3-dienes with *o*-iodophenols and *N*-protected *o*-iodoanilines in order to obtain highly functionalised dihydro-2,3-benzofurans and indolines in a domino fashion. The possibility of

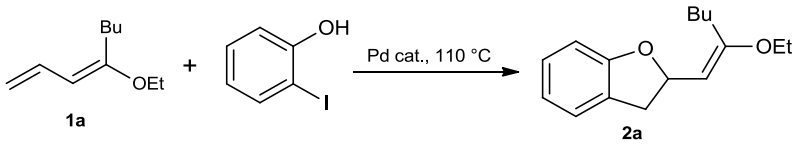
introducing several electrophiles to the dienic skeleton broaden the synthetic applications of the methodology. Moreover, the alkoxydic function is readily hydrolysed to the corresponding carbonylic group. Two alkoxybutadienes were prepared via the reaction between the (*E*)-crotonaldehyde diethylacetal and 2 equiv of Schlosser's superbase LIC-KOR (LIC, butyllithium, KOR, potassium *tert*-butoxide) respectively quenched with 1-iodobutane and propylene oxide (Scheme 1).[37-39]



Scheme 1 Synthesis of (*E*)-4-ethoxyocta-1,3-diene (1a) and (*E*)-4-ethoxyocta-1,3-dien-ol (1b)

The reaction of (*E*)-4-ethoxyocta-1,3-diene (**1a**) 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. The results are reported in Table 1.

Table 1 Coupling reaction between (*E*)-4-ethoxyocta-1,3-diene (**1a**) and 2-iodophenol[a]

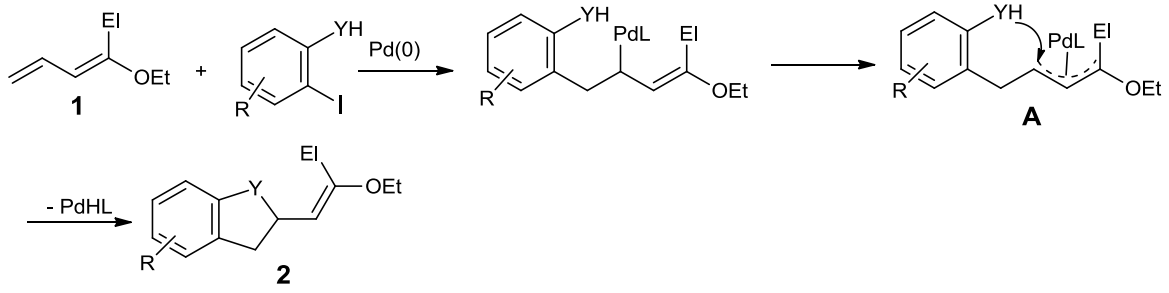


Entry	1a : iodophenol	Base	Catalyst (%)	Solvent	Time (h)	Yield (%)[b]	*E/Z*[c]
1	1 : 1	an. NaOAc	$Pd(OAc)_2$ (3)	DMSO/TBAB	2	23	99/1
2	**2 : 1**	an. NaOAc	$Pd(OAc)_2$ (3)	DMSO/TBAB	2	28	99/1
3	**1.2 : 1**	an. NaOAc	$Pd(OAc)_2$ (3)	DMSO/TBAB	2	54	99/1
4	1.2 : 1	an. NaOAc	$Pd(OAc)_2$ (3)	**DMSO**	4	18	99/1
5	1.2 : 1	an. NaOAc	$Pd(OAc)_2$ (3)	**DMSO/bmim$^+$Cl$^-$**	16	0	-
6	1.2 : 1	an. NaOAc	**$Pd(OAc)_2$ (1)**	DMSO/TBAB	16	0	-
7	1.2 : 1	an. NaOAc	**$Pd(OAc)_2$ (2)**	DMSO/TBAB	16	0	-
8	1.2 : 1	an. NaOAc	**$Pd(PPh_3)_4$ (3)**	DMSO/TBAB	16	0	-
9	1.2 : 1	an. NaOAc	**$Pd(dba)_2$ (3)**	DMSO/TBAB	16	0	-
10	1.2 : 1	**Et_3N**	$Pd(OAc)_2$ (3)	DMSO/TBAB	16	0	-

11	1.2 : 1	**an. K_2CO_3**	$Pd(OAc)_2$ (3)	DMSO/TBAB	3	20	99/1

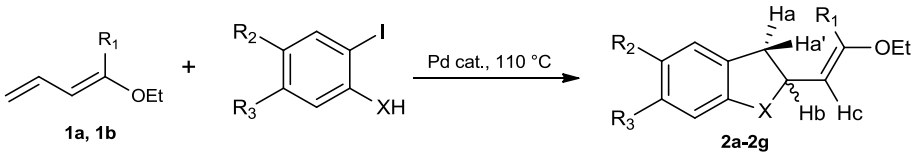
[a] Reactions conditions: DMSO 3 mL; ionic liquid 300 mg, base 0.5 mmol, T = 110 °C. [b] Isolated products, purified by column chromatography. [c] Determined by NMR analysis.

Firstly, the reagents ratio was studied (entry 1–3), best results were obtained when a slight excess of alkoxydiene **1a** was used. The presence of TBAB was crucial to increase the yields, in fact when it was absent (entry 4), or substituted with a different ionic liquid such as $bmim^+Cl$ (entry 5), little or no product was obtained. The substitution of $Pd(OAc)_2$ with $Pd(PPh_3)_4$ (entry 8) or $Pd(dba)_2$ (entry 9) afforded no products, while, a minimum amount of 3% allowed the coupling to be successful (see entry 6 and 7). Finally, only the use of NaOAc as the base afforded the desired product **2a**, in acceptable yields. In all the cases a good regio- and diasterereoselectivity was afforded with the predominance of the *E* isomer. The diastereomeric ratio was determined by the ^{1}H NMR spectrum, where the α position proton signals (with respect to the oxygen) were observed at 5.43 and 5.70 ppm respectively. The *E* configuration of the double bond was assigned via a NOESY experiment, where a correlation spot between the vinylic signal (H_c in scheme 3, 4.65 ppm) and the CH_2 of the ethoxy group (H_b in scheme 3, 3.72 ppm) was observed. The hypothesised reactivity pattern is illustrated in Scheme 2. The addition of an arylpalladium compound to alkoxy-1,3-diene **1** produced the π-allylpalladium intermediate **A**, and the subsequent intramolecular nucleophilic substitution afforded product **2**. The regioselective outcome can be easily explained if we consider that the nucleophile attacks the diene γ-C, which is sterically hindered compared to the α-C, then in this case steric factors overcome electronic factors which would favour the nucleophilic attack on the α-carbon over the γ-carbon, because the first is more electrophilic due to the presence of the alkoxide function.

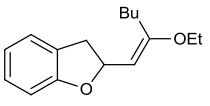


Scheme 2 Proposed mechanism for the Pd(0) catalysed heteroannulation of functionalised 1-alkoxy-1,3-butadienes with *o*-iodophenols and *o*-iodoprotected anilines

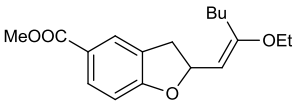
The optimised cross coupling reaction was then extended to different alkoxy-1,3-dienes, *o*-iodophenols and *N*-protected *o*-iodoanilines in order to evaluate the influence of the substituents present both on the aromatic ring and on the alkoxydiene, the nature of the heteroatom on the yields and the amino protecting group in the starting *o*-iodoanilines. The reaction was then successfully carried out on (*E*)-4-ethoxyocta-1,3-diene (**1a**) and (*E*)-4-ethoxyocta-1,3-dien-ol (**1b**) with *o*-iodophenol, 4-hydroxy-3-iodomethylbenzoate, 4-hydroxymethyl-*o*-iodophenol, *N*-methyl-*o*-iodoaniline and *N*-tosyl-*o*-iodoaniline. The annulation process led to the corresponding 2-(2ethoxyvinyl)-dihydrobenzofuran and indoline **2a-g** (Scheme 3). The formation of the bicyclic structures was proven by the presence of the doublets, attributable to the olefinic proton H_c, and the doublet of doublets pertinent to the H_b proton (see Scheme 3) in their ^{1}H NMR spectra. Moreover, the signals relevant to H_a and $H_{a'}$ showed the typical pattern of diastereotopic protons, which demonstrate the formation of a cycle which contained an asymmetric C. When *o*-iodophenols were employed, good yields were observed in all the cases, both when electronwithdrawing (**2b**) and electrondonor substituent (**2c**) on the aromatic ring were present. In the latter case a slightly better yield was observed. Highest yields were obtained when *N*-tosyl-*o*-iodoaniline (**2f** and **2g**) was employed, both with diene **1a** and **1b**, probably because of the bulky protecting group present on the amino group which helps the annulation process.



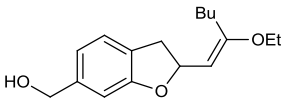
1a, 1b **2a-2g**



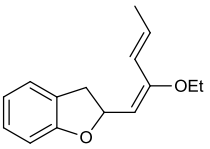
2a, 52%, *E/Z* 99/1



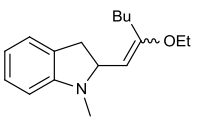
2b, 56%, *E/Z* 99/1



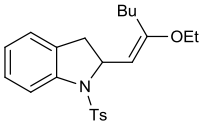
2c, 60%, *E/Z* 99/1



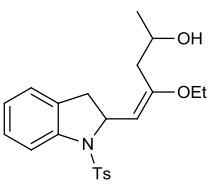
2d, 32%, *E/Z* 99/1



2e, 45%, *E/Z* 60/40



2f, 72%, *E/Z* 99/1



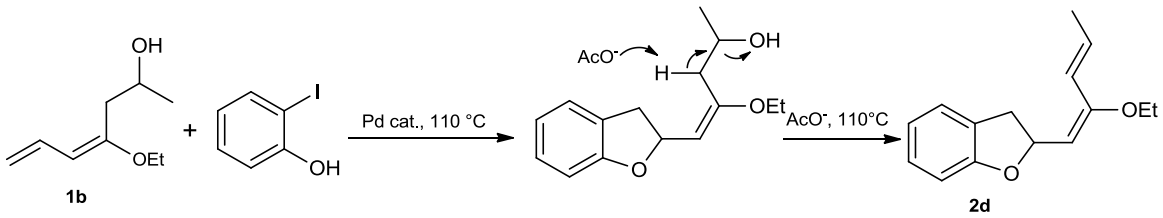
2g, 68%, *E/Z* 50/50

Scheme 3 Cross coupling between (*E*)-4-ethoxyocta-1,3-diene (**1a**) and (*E*)-4-ethoxyocta-1,3-dien-ol (**1b**) and substituted *o*-iodophenol, *N*-methyl-*o*-iodoaniline and *N*-tosyl-*o*-iodoaniline

The diastereomeric ratio of products **2a-g** was deduced both by NMR analysis, comparing the areas of the signals pertinent to H_c and H_b and by gas chromatography. In cases **2a-d** and **2f** only (*E*) isomer was obtained whereas the data clearly indicate a lower diastereoselectivity when *N*-methyl-*o*-iodoaniline was used as a reagent (**2e**). This decrease could be explained by a possible post-reaction isomerisation process which would lead to the thermodynamic mixture. It would be promoted by a readdition of PdHL to the double bond.[40] The probability of this isomerisation, which would need a rotation of the substituents, is higher in the case of poor sterically demanding methyl group than in the tosyl group. Moreover it should be noticed that the ^{1}H NMR spectrum of derivative **2e** shows a H_b typical chemical shift of 4.0 and 4.5 ppm for the two isomers respectively. In all other cases this signal is observed between approximately 5.5 ppm for the dihydrobenzofuran derivatives and 5.0 ppm for *N*-tosylindolines. This upfield shift could depend on a higher electron density on H_b proton in 2-(2-ethoxyhexa-1-enyl)-1-methylindoline (**2e**) which could facilitate the PdH elimination – addition process.

A 50/50 diastereomeric mixture (**2g**) was also obtained when *N*-tosyl-*o*-iodoaniline was coupled with (*E*)-4-ethoxyocta-1,3-dien-ol (**1b**). In this case it was not obvious if the lack of stereoselectivity was due to the formation of a (*E*) or (*Z*) isomer mixture pertinent to the C1 double bond or to the presence of three stereocenters in the annulation product which would lead to different diastereoisomers. The first hypothesis might be confirmed by the fact that the mild acidic hydrolysis of 2-(-2-ethoxyexa-4-hydroxypent-1-yl)-1-tosylindoline (**2g**), as shown in Scheme 5, afforded only one product (**3g**). Since in the case of 2-((1*E*)-2-ethoxyexa-1-enyl)-1-tosylindoline (**2f**), which differs from **2g** by the presence of a linear butyl instead of a 2-hydroxypropyl group, only a diastereoisomer was recovered, it might be hypothesised a steric influence of this latter group together with the hindered tosyl group.

Diene **1b** was reacted with both *o*-iodophenol and *N*-tosyl-*o*-iodoaniline and two different reactivity pattern were observed. In fact in the first case, the annulation process was followed by an E_2 elimination reaction affording the 2-((1*E*,3*E*)-2-ethoxypenta-1,3-dienyl)-2,3-dihydrobenzofuran **2d**. The process was probably favored by the formation of the more stable conjugated system and the basic medium (Scheme 4) and afforded only the 1*E*,3*E* isomer.



Scheme 4 Formation of 2-((1*E*,3*E*)-2-ethoxypenta-1,3-dienyl)-2,3-dihydrobenzofuran **2d** by E_2 elimination

When *N*-tosyl-*o*-iodoaniline was used, the elimination process did not occur probably because of the steric hindrance of the tosyl group in the anti-periplanar conformation which did not favour the proton extraction, as evidenced in Figure 1. 2-((1*E*)-2-Ethoxyexa-4-hydroxypent-1-yl)-1-tosylindoline **2g** was obtained, as as matter of fact both the ^{1}H and the ^{13}C spectra showed the typical signals of a CH bonded to an hydroxyl group at 4.1 and 66 ppm respectively.

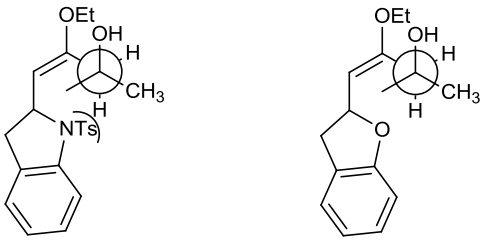
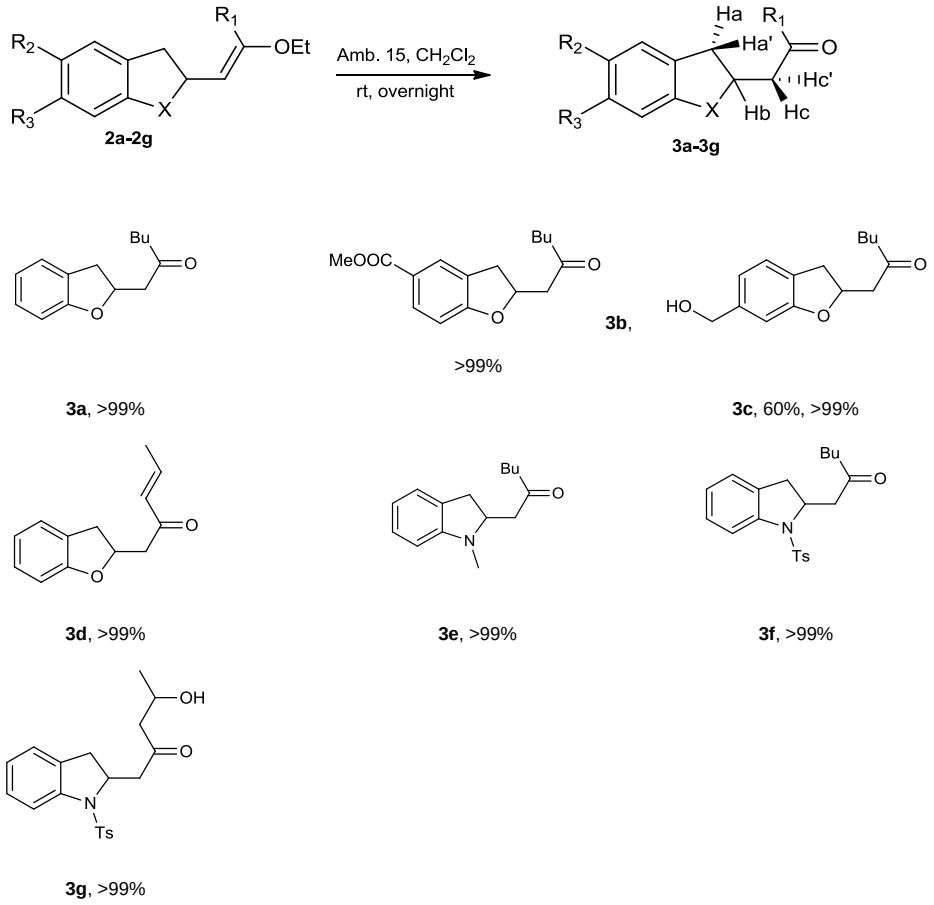


Figure 1 Anti-periplanar conformation of the diene **1b** Heck coupling products with *N*-tosyl-*o*-iodoaniline and *o*-iodophenol respectively.

Moreover, derivatives **2a-g** can be converted into ketones by mild acidic treatment because of the presence of the vinyl ether function in accord to an *umpolung* approach. They were then treated overnight with catalytic amounts of Amberlyst-15, in CH_2Cl_2 at r.t. affording the corresponding carbonyl derivatives **3a-g** in quantitative yield (Scheme 5). NMR data indicated the formation of a dyhydrobenzofuran or indoline structure bearing an oxomethylenic group in position 2. In fact, in the ^{1}H NMR spectrum the signals corresponding to the olefinic proton disappeared, the ^{13}C spectra showed a typical

carbonyl signal centered at approximately 210 ppm, according to the product structure. Finally all the product spectra (**3a-g**) showed four doublets of doublet typical of Ha, Ha', Hc, Hc' diastereomeric protons (see Scheme 5).



Scheme 5 Hydrolysis of derivatives **2a-g** in mild acidic conditions

Conclusions

In summary, a Pd(0)-catalysed heteroannulation cascade process on differently functionalised alkoxy-1,3-dienes and substituted *o*-iodophenols and protected *o*-iodoanilines has been reported. Several substituted dihydrobenzofurans and indolines were obtained in function of the starting alkoxy-1,3-diene, *o*-iodophenol and *o*-iodoaniline, the substitution of the iodophenol aromatic ring and the protection of the amino group. The reaction was regio- and mainly stereoselective according to the heteroatom involved in the annulation process and its steric hindrance. Steric factors were predominant over electronic factors in determining the process regioselectivity. Finally, the presence of the enolether group extended the synthetic applications of

the cross-coupling because ketones can be obtained via simple hydrolysis in mild acidic conditions in quantitative yields.

General

Flasks and all equipments used for the generation and reaction of moisture-sensitive compounds were dried by electric heat gun under Ar. THF was distilled from sodium benzophenone ketyl, 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. Alcoxy-1,3-dienes and *N*-protected *o*-iodoanilines were synthesised as previously reported.

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. ^{1}H 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, coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured with complete proton decoupling. Chemical shifts were reported in ppm from the residual pick solvent 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 tickness). IR spectra were recorded on a Perkin Elmer BX FT-IR. Enantiomeric purity of derivatives **1b** and **2g** was determines using a PerKin Elmer Autosystem GC equipped with a chiral column Cyclosil 6® (JW Scientific, 30 m × 0.25 mm × 0.25 μm film tickness).

Procedure for the Palladium catalysed coupling of alcoxydienes and *o*-iodophenols or protected *o*-iodoanilines. $Pd(OAc)_2$ (3% mol, 0.015 mmol, 3.36 mg) and TBAB (300 mg) were dissolved in anhydrous DMSO (3 mL) and the solution was degassed with Ar for 10 min. at r**.t..** Then NaOAc (0.5 mmol, 41 mg), the suitable *o*-iodophenol or protected *o*-iodoaniline (0.5 mmol), and the alcoxy-1,3-diene (0.55 mmol) were subsequently added. The reaction was stirred in a sealed

tube at 110 °C until the disappearance of the alcoxy-1,3-diene 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.

2-((1*E*)-2-Ethoxyhexa-1-enyl)-2,3-dihydrobenzofuran (**2a**) As previously reported 110 mg (0.5 mmol) of *o*-iodophenol and 84.7 mg (0.55 mmol) of 4-ethoxyocta-1,3-diene **1a** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 95/5) a pale yellow oil was obtained (65 mg, 54%). Found C, 77.98; H, 9.02%. Calc. for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00%. ν_{max}(neat)/cm^{-1} 2958, 1656, 1599, 1479, 1225. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.95 (3H, t, *J* = 7.0 Hz, C*H*$_3$CH$_2$CH$_2$), 1.31 (3H, t, *J* =7.0 Hz, C*H*$_3$CH$_2$O), 1.42-1.64 (4H, m, CH$_3$C*H*$_2$C*H*$_2$), 2.27 (2H, m, C*H*$_2$C=CH), 2.96 (1H, dd, *J* = 15.6, 8.6 Hz, C*H*$_2$ ring), 3.34 (1H, dd, *J* =15.6, 8.6 Hz, C*H*$_2$ ring), 3.73 (2H, q, *J* =6.8 Hz, CH$_3$C*H*$_2$O), 4.66 (1H, d, *J* =9.4 Hz, C*H*=C), 5.45 (1H, q, *J* =8.8 Hz, C*H*CH=C), 6.81 (2H, m, Ar), 7.12 (2H, m, Ar); δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.8 (CH_3), 14.4 (CH_3), 22.3 (CH_2), 30.2 (CH_2), 30.6 (CH_2), 37.5 (CH_2), 62.2 (CH_2), 80.9 (CH), 97.4 (CH), 109.2 (CH), 119.9 (CH), 124.5 (CH), 127.2 (Cq), 127.8 (CH), 159.2 (Cq), 161.7 (Cq). MS (EI, 70 eV): *m/z* (%) = 246 (M^+, 100), 217 (35), 133 (38), 131 (32), 85 (34).

Methyl-2-((1*E*)-2-ethoxyhexa-1-enyl)-2,3-dihydrobenzofuran-5-carboxylate (**2b**) As previously reported 153 mg (0.5 mmol) of 4-hydroxy-3-iodomethylbenzoate and 79.2 mg (0.55 mmol) of 4-ethoxyocta-1,3-diene **1a** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 95/5) a pale yellow oil was obtained (65 mg, 54%). Found C, 71.00; H, 7.93%. Calc. for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95%. ν_{max}(neat)/ cm^{-1} 2958, 1656, 1599, 1479, 1225. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.96 (3H, t, *J* = 7.0 Hz, C*H*$_3$CH$_2$CH$_2$), 1.10-1.60 (7H, m, C*H*$_3$CH$_2$O, CH$_3$C*H*$_2$C*H*$_2$), 2.26 (2H, t, *J* = 7.0, C*H*$_2$C=CH), 3.05 (1H, dd, *J* = 18.0, 9.0 Hz, C*H*$_2$ ring), 3.40 (1H, dd, *J* = 16.0, 6.8 Hz, C*H*$_2$ ring), 3.71 (2H, q, *J* = 7.0 Hz, CH$_3$C*H*$_2$O), 3.87 (3H, s, COOC*H*$_3$), 4.62 (1H, d, *J* = 9.6 Hz, C*H*=C), 5.45 (1H, q, *J* = 9.0 Hz, C*H*CH=C), 6.74 (1H, d, *J* = 7.0 Hz, Ar), 7.85 (2H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (CH_3), 14.2 (CH_3), 22.2 (CH_2), 30.1 (CH_2), 30.6 (CH_2), 36.7 (CH_2),

51.6 (CH_3), 62.3 (CH_2), 82.3 (CH), 96.8 (CH), 108.8 (CH), 122.0 (Cq), 126.3 (CH), 127.6 (Cq), 130.9 (CH), 162.3 (Cq), 163.4 (Cq), 166.9 (Cq). MS (EI, 70 eV): *m/z* (%) = 304 (M^+, 100), 275 (23), 243 (22), 159 (16), 85 (14).

2-((1*E*)-2-Ethoxyhex-1-enyl)-6-hydroxymethyl-2,3-dihydrobenzofuran (**2c**) As previously reported 153 mg (0.5 mmol) of 4-hydroxymethyl-*o*-iodophenol and 79.2 mg (0.55 mmol) of 4-ethoxyocta-1,3-diene **1a** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 80/20) a pale yellow oil was obtained (83 mg, 60%). Found C, 73.90; H, 8.73%. Calc. for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75%. ν_{max}(neat)/ cm^{-1} 3401, 2930, 1657, 1497, 1382, 1233. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.96 (3H, t, *J* = 7.0 Hz, C*H*$_3$CH$_2$CH$_2$), 1.10-1.60 (7H, m, C*H*$_3$CH$_2$O, CH$_3$C*H*$_2$C*H*$_2$), 1.76 (1H, bs, O*H*), 2.26 (2H, m, C*H*$_2$C=CH), 2.93 (1H, dd, *J* = 15.4, 9.0 Hz, C*H*$_2$ ring), 3.40 (1H, dd, *J* = 15.4, 9.0 Hz, C*H*$_2$ ring), 3.71 (2H, q, *J* = 7.0 Hz, CH$_3$C*H*$_2$O), 4.63 (3H, m, C*H*$_2$OH, C*H*=C), 5.48 (1H, q, *J* = 8.6 Hz, C*H*CH=C), 6.82 (2H, m, Ar), 7.13 (1H, m, Ar) . δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (CH_3), 14.2 (CH_3), 22.2 (CH_2), 30.1 (CH_2), 30.6 (CH_2), 37.2 (CH_2), 62.2 (CH_2), 65.2 (CH_2), 81.2 (CH), 97.2 (CH), 107.9 (CH), 118.6 (CH), 124.4 (CH), 126.8 (Cq), 141.1 (Cq), 159.6 (Cq), 161.7 (Cq). MS (EI, 70 eV): *m/z* (%) = 276 (M^+, 12), 148 (100), 131 (32), 119 (49), 86 (47).

2-((1*E*,3*E*)-2-Ethoxypenta-1,3-dienyl)-2,3-dihydrobenzofuran (**2d**) As previously reported 110 mg *o*-iodophenol (0.5 mmol) and 85.2 mg (0.55 mmol) of 4-ethoxyepta-4,6-dien-2-ol **1b** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 95/5) a pale yellow oil was obtained (37 mg, 32%). Found C, 78.25; H, 7.87%. Calc. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88%. ν_{max}(neat)/ cm^{-1} 2921, 1604, 1230, 963. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.32 (3H, t, *J* = 6.9 Hz, C*H*$_3$CH$_2$O), 1.82 (3H, m, C*H*$_3$CH=CH), 2.95 (1H, dd, *J* = 13.8, 8.0 C*H*$_2$ ring), 3.40 (1H, dd, *J* = 13.8, 8.0 Hz, C*H*$_2$ ring), 3.82 (2H, q, *J* = 6.9 Hz, CH$_3$C*H*$_2$O), 4.72 (1H, d, *J* = 8.0 Hz, C*H*=C), 5.65 (1H, q, *J* = 8.0 Hz, C*H*CH=C), 6.30 (2H, m, CH$_3$C*H*=C*H*), 6.82 (2H, m, Ar), 7.15 (2H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 14.3 (CH_3), 18.1 (CH_3), 37.4 (CH_2), 62.4 (CH_2), 79.6 (CH), 99.5 (CH), 109.2 (CH), 119.9 (CH), 122.1 (CH), 124.5 (CH), 127.0 (Cq), 127.8 (CH), 129.5 (CH), 155.5 (Cq), 159.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 230 (M^+, 100), 215 (24), 201 (24), 187 (49), 131 (29), 69 (53).

2-(2-Ethoxyhex-1-enyl)-1-methylindoline (**2e**) As previously reported 116 mg (0.5 mmol) of *N*-methyl-*o*-iodoaniline and 84.7 mg (0.55 mmol) of 4-ethoxyocta-1,3-diene **1a** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 90/10) a pale yellow oil was obtained (58 mg, 45%). Diastereomeric mixture 60:40: δ_H (200 MHz; $CDCl_3$, Me_4Si): 0.94 (3H, m, C*H*$_3$CH$_2$CH$_2$), 1.19-1.65 (7H, m, C*H*$_3$CH$_2$O, CH$_3$C*H*$_2$C*H*$_2$), 2.30 (2H, t, *J* = 7.0 Hz, C*H*$_2$C=CH), 2.68 (3H, s, NC*H*$_3$), 3.05 (1H, m, C*H*$_2$ ring), 3.12 (1H, m, C*H*$_2$ ring), 3.77 (2H, q, *J* = 7.0 Hz, CH$_3$C*H*$_2$O), 4.00 (1H, q, *J* = 9.7 Hz, NC*H*, minor isomer), 4.38 (1H, q, *J* = 9.7 Hz, NC*H*, major isomer), 4.50 (1H, d, *J* = 9.7 Hz, C=C*H*, minor isomer), 4.72 (1H, d, *J* = 9.7 Hz, C=C*H*, major isomer), 6.50 (1H, d, *J* = 6.5 Hz, Ar), 6.70 (1H, m, Ar), 7.05-7.27 (2H, m, Ar). Diastereomeric mixture δ_C (50 MHz, $CDCl_3$, Me_4Si) 13.7 (CH_3), 14.4 (CH_3), 15.2 (CH_3), 22.1 (CH_2), 22.3 (CH_2), 29.1 (CH_2), 30.2 (CH_2), 30.4 (CH_2), 31.1 (CH_2), 33.3 (CH), 33.6 (CH), 36.2 (CH_2), 37.4 (CH_2), 62.0 (CH_2), 62.6 (CH_3), 63.6 (CH_2), 65.8 (CH_3), 98.2 (CH), 107.1 (CH), 107.2 (CH), 110.7 (CH), 117.5 (CH), 117.7 (CH), 123.7 (CH), 127.1 (CH), 127.2 (CH), 129.1 (Cq), 129.3 (Cq), 152.9 (Cq), 153.1 (Cq), 157.5 (Cq), 159.4 (Cq). MS (EI, 70 eV): *m/z* (%) major isomer = 259 (M^+, 50), 230 (22), 146 (44), 144 (29), 132 (100). MS (EI, 70 eV): *m/z* (%) minor isomer = 259 (M^+, 100), 230 (47), 144 (72), 132 (68), 131 (40).

2-((1*E*)-2-Ethoxyexa-1-enyl)-1-tosylindoline (**2f**) As previously reported 191 mg (0.5 mmol) of *N*-tosyl-*o*-iodoaniline and 84.7 mg (0.55 mmol) of 4-ethoxyocta-1,3-diene **1a** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 95/5) a pale yellow oil was obtained (143 mg, 72%). Found C, 69.17; H, 7.30, N, 3.50, S, 8.04%. Calc. for $C_{23}H_{29}NO_3S$: C, 69.14; H, 7.32, N, 3.51, S, 8.03%. ν_{max}(neat)/ cm^{-1} 2959, 1660, 1600, 1479, 1167. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.96 (3H, t, *J* = 7.0 Hz, C*H*$_3$CH$_2$CH$_2$), 1.20 (3H, t, *J* = 7.0 Hz, C*H*$_3$CH$_2$O), 1.26-1.66 (4H, m, CH$_3$C*H*$_2$C*H*$_2$), 2.20 (2H, m, C*H*$_2$C=CH), 2.32-2.68 (1H, m, C*H*$_2$ ring), 2.3 (3H, s, C*H*$_3$Ar), 3.12 (1H, dd, *J* = 16.0, 6.8 Hz, C*H*$_2$ ring), 3.40 (2H, m, CH$_3$C*H*$_2$O), 4.38 (1H, d, *J* = 9.4 Hz, C=C*H*), 5.45 (1H, td, *J* = 9.4, 3.0 Hz, C*H*CH=C), 6.96-7.27 (5H, m, Ar), 7.45-7.75 (3H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 13.9 (CH_3), 14.3 (CH_3), 21.3 (CH_3), 22.4 (CH_2), 29.9 (CH_2), 30.4 (CH_2), 32.1 (CH_2), 61.0 (CH), 61.9 (CH_2), 98.4 (CH), 115.8 (CH), 123.6 (CH), 125.0 (CH), 126.9 (CH), 127.5

(CH), 129.2 (CH), 131.5 (Cq), 136.5 (Cq), 141.2 (Cq), 143.4 (Cq), 158.4 (Cq). MS (EI, 70 eV): *m/z* (%) = 399 (M^+, 2), 272 (100), 271 (20), 155 (46), 91 (37).

2-(-2-Ethoxyexa-4-hydroxypent-1-yl)-1-tosylindoline (**2g**) As previously reported 191 mg (0.5 mmol) of *N*-tosyl-*o*-iodoaniline and 85.2 mg (0.55 mmol) of 4-ethoxyepta-4,6-dien-2-ol **1b** were suspended in the DMSO-TBAB mixture. After chromatographic purification (EP/EE 50/50) a pale yellow oil was obtained (143 mg, 72%). Diastereomeric mixture 50:50: δ_H (200 MHz; $CDCl_3$, Me_4Si): 1.25 (7H, m, C*H*$_3$CHOH, C*H*$_3$CH$_2$O, O*H*), 2.36 (3H, s, C*H*$_3$ArSO$_2$), 2.50–2.61 (3H, m, C*H*$_2$C=CH, C*H*$_2$ ring), 3.06 (1H, dd, *J* = 16.0, 9.6 Hz, C*H*$_2$ ring), 3.51 (2H, m, CH$_3$C*H*$_2$O), 4.11 (1H, m, C*H*OH), 4.58 (1H, d, *J* = 9.8 Hz, C=C*H*, isomer a), 4.63 (1H, d, *J* = 9.6 Hz, C=C*H*, isomer b), 6.50 (1H, m, C*H*CH=C), 7.03 (5H, m, Ar), 7.60 (3H, m, Ar). Diastereomeric mixture δ_C (50 MHz, $CDCl_3$, Me_4Si) 14.2 (CH_3), 21.2 (CH_3), 22.9 (CH_3), 23.2 (CH), 37.0 (CH_2), 37.1 (CH_2), 39.6 (CH_2), 40.0 (CH_2), 60.7 (CH), 62.1 (CH_2), 66.0 (CH), 100.9 (CH), 101.3 (CH), 115.8 (CH_2), 115.9 (CH), 123.8 (CH), 123.9 (CH), 125.0 (CH), 126.8 (CH), 126.9 (CH), 127.5 (CH), 129.3 (CH), 129.4 (CH), 131.0 (Cq), 131.1 (Cq), 135.6 (Cq), 136.1 (Cq), 140.9 (Cq), 141.0 (Cq), 143.5 (Cq), 143.6 (Cq), 155.2 (Cq), 155.4 (Cq). MS (EI, 70 eV): *m/z* (%) isomer a= 357 (M^+ - EtOH, 36), 202 (100), 174 (26), 130 (52), 91 (30). MS (EI, 70 eV): *m/z* (%) minor isomer b= 357 (M^+ - EtOH, 7), 272 (100), 271 (22), 155 (54), 91 (42).

General procedure for the acid catalysed hydrolysis of ethoxysubstituted dihydrobenzofurans and indolines. In a 50 mL round bottom flask**,** the suitable substrate (0.5 mmoles) was dissolved in 3 mL of CH_2Cl_2, then 0,1 g of Amberlyst 15 were added. The solution was stirred overnight at r. t. filtered and the solvent evaporated under reduced pressure.

1-(2,3-dihydrobenzofuran-2-yl)-hexan-2-one (**3a**) As previously reported 123 mg (0.5 mmol) of 2-((1*E*)-2-ethoxyhex-1-enyl)-2,3-dihydrobenzofuran **2a** were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (109 mg). Found C, 77.06; H, 8.30%. Calc. for

$C_{14}H_{18}O_2$: C, 77.03; H, 8.31%. ν_{max}(neat)/cm^{-1} 2958, 1714, 1598, 1480, 1230. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.90 (3H, t, *J* =7.7 Hz, C*H*$_3$CH$_2$CH$_2$), 1.31 (2H, sest, *J* = 7.7, CH$_3$C*H*$_2$CH$_2$), 1.61 (2H, quint, *J* = 6.4, CH$_3$CH$_2$C*H*$_2$), 2.48 (2H, t, *J* = 7.2 Hz, COC*H*$_2$), 2.73 (1H, dd, *J* = 16.6, 6.4, C*H*$_2$ ring), 2.84 (1H, dd, *J* = 15.6, 8.0, C*H*$_2$CO), 3.05 (1H, dd, *J* = 16.6, 6.8, C*H*$_2$ ring), 3.44 (1H, dd, *J* = 15.8, 9.0, C*H'*$_2$CO), 5.19 (1H, m, C*H*CH$_2$CO), 6.85 (2H, m, Ar), 7.15 (2H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) 13.7 (CH$_3$), 22.1 (CH$_2$), 25.5 (CH$_2$), 35.4 (CH$_2$), 43.2 (CH$_2$), 48.4 (CH$_2$), 78.5 (CH), 109.3 (CH), 120.3 (CH), 124.8 (CH), 126.1 (Cq), 127.8 (CH), 158.9 (Cq), 208.8 (Cq). MS (EI, 70 eV): *m/z* (%) = 218 (M^+, 13), 119 (15), 118 (100), 91 (11), 57 (9).

Methyl-2-(2-oxyhexyl)-2,3-dihydrobenzofuran-5-carboxylate (**3b**) As previously reported 152 mg of methyl-2-((1*E*)-2-ethoxyhexa-1-enyl)-2,3-benzodihydrofuran-5-carboxylate **2b** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (138 mg). Found C, 69.57; H, 7.32%. Calc. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30%. ν_{max}(neat)/cm^{-1} 2958, 1715, 1613, 1489, 1270. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.92 (3H, t, *J* = 7.2 Hz, C*H*$_3$CH$_2$CH$_2$), 1.17-1.49 (2H, m, CH$_3$C*H*$_2$CH$_2$), 1.47-1.76 (2H, m, CH$_3$CH$_2$C*H*$_2$), 2.48 (2H, t, *J* = 7.3 Hz, COC*H*$_2$), 2.75 (1H, dd, *J* = 16.0, 6.0 Hz, C*H*$_2$ ring), 2.85 (1H, dd, *J* = 16.0, 8.0 Hz, C*H*$_2$CO), 3.06 (1H, dd, *J* = 18.0, 8.0 Hz, C*H*$_2$ ring), 3.46 (1H, dd, *J* = 15.9, 10.1 Hz, C*H'*$_2$CO), 3.87 (3H, s, OC*H*$_3$), 5.28 (1H, m, C*H*CH$_2$CO), 6.76 (1H, d, *J* = 9.0 Hz, Ar), 7.85 (2H, bs, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 13.6 (CH$_3$), 22.0 (CH$_2$), 25.4 (CH$_2$), 34.8 (CH$_2$), 43.2 (CH$_2$), 48.2 (CH$_2$), 51.7 (CH$_3$), 79.7 (CH), 109.0 (CH), 122.6 (Cq), 126.6 (CH), 131.0 (CH), 163.0 (Cq), 166.7 (Cq), 208.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 276 (M^+, 13), 177 (100), 176 (67), 145 (53), 105 (14).

6-Hydroxymethy-2-(2-oxyhexyl)-2,3-dihydrobenzofurane (**3c**) As previously reported 138 mg of 2-((1*E*)-2-ethoxyexa-1-enyl)-6-hydroxymethyl-2,3-dihydrobenzofuran **2c** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (100 mg). Found C, 72.53; H, 8.13%. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%. ν_{max}(neat)/cm^{-1} 3352, 2961,

1705, 1408, 1260, 1017. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.92 (3H, t, *J* = 7.2 Hz, C*H*$_3$CH$_2$CH$_2$), 1.31-1.66 (5H, m, CH$_3$C*H*$_2$C*H*$_2$, O*H*), 2.48 (2H, t, *J* = 7.2 Hz, COC*H*$_2$), 2.75 (1H, dd, *J* = 16.6, 6.6 Hz, C*H*$_2$ ring), 2.83 (1H, dd, *J* = 16.6, 8.8 Hz, C*H*$_2$CO), 3.06 (1H, dd, *J* = 16.9, 6.7 Hz, C*H*$_2$ ring), 3.48 (1H, dd, *J* = 16.6, 9.2 Hz, C*H'*$_2$CO), 4.62 (2H, s, C*H*$_2$OH), 5.20 (1H, m, C*H*CH$_2$CO), 6.82 (2H, m, Ar), 7.13 (1H, d, *J* = 7.4 Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 15.0 (CH_3), 22.0 (CH_2), 25.4 (CH_2), 35.1 (CH_2), 43.2 (CH_2), 48.4 (CH_2), 65.6 (CH_2), 78.8 (CH), 108.0 (CH), 119.0 (CH), 124.7 (Cq), 125.6 (CH), 141.3 (Cq), 159.3 (Cq), 209.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 248 (M^+, 8), 148 (100), 147 (19), 131 (22), 119 (24).

(*E*)-1-(2,3-dihydrobenzofuran-2-yl)-penta-3-en-2-one (**3d**) As previously reported 115 mg of 2-((1*E*,3*E*)-2-ethoxypenta-1,3-dienyl)-2,3-dihydrobenzofuran **2d** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (124 mg). Found C, 77.18; H, 6.99%. Calc. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. ν_{max}(neat)/cm^{-1} 2925, 1674, 1481, 1232, 971, 750. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.92 (3H, dd, *J* = 6.8, 1.4 Hz, C*H*$_3$CH=CH), 2.92-2.80 (2H, bdd, C*H*$_2$ ring, C*H'*$_2$CO), 3.20 (1H, dd, *J* = 16.6, 6.4 Hz, C*H*$_2$ ring), 3.43 (1H, dd, *J* = 16.6, 9.2 Hz, C*H*$_2$CO), 5.23 (1H, m, C*H*CH$_2$CO),), 6.18 (1H, dm, *J* = 15.8, 1.6 Hz, COC*H*=CH), 6.75-6.99 (3H, m, Ar, COCH=C*H*), 7.13 (2H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 18.2 (CH_3), 35.5 (CH_2), 45.6 (CH_2), 78.7 (CH), 109.3 (CH), 120.3 (CH), 124.9 (CH), 125.2 (Cq), 127.9 (CH), 132.1 (CH), 143.7 (CH), 159.0 (Cq), 197.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 202 (M^+, 18), 118 (100), 84 (30), 69 (41), 41 (13).

1-(*N*-Methylindolin-2-yl)-hexan-2-one (**3e**) As previously reported 130 mg of 2-((1*E*)-2-ethoxyhexa-1-enyl)-1-methylindoline **2e** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (116 mg). Found C, 77.85; H, 9.14, N, 6.03%. Calc. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15, N, 6.05%. ν_{max}(neat)/cm^{-1} 2958, 1713, 1609, 1486, 1376, 1270, 748. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.92 (3H, t, *J* = 6.8, C*H*$_3$CH$_2$CH$_2$), 1.26-1.67 (4H, m, CH$_3$C*H*$_2$C*H*$_2$), 2.48 (2H, t, *J* = 7.0, COC*H*$_2$CH$_2$), 2.63 (2H, m, C*H*$_2$ ring, C*H*$_2$CO), 2.71 (3H, s, N-C*H*$_3$), 2.96 (1H, dd, *J* = 16.8, 6.6 Hz, C*H*$_2$ ring), 3.29 (1H, dd, *J* = 15.6, 8.4 Hz, C*H'*$_2$CO), 3.73 (1H, m, C*H*CH$_2$CO),),

6.47 (1H, d, *J* = 7.8 Hz, Ar), 6.69 (1H, td, *J* = 7.2, 0.8 Hz, Ar), 7.05 (2H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 13.7 (CH_3), 22.1 (CH_2), 25.6 (CH_2), 34.2 (CH_3), 35.6 (CH_2), 43.4 (CH_2), 46.6 (CH_2), 62.6 (CH), 107.1 (CH), 117.9 (CH), 124.0 (CH), 127.2 (CH), 128.5 (Cq), 152.6 (Cq), 209.6 (Cq). MS (EI, 70 eV): *m/z* (%) = 231 (M^+, 16), 132 (100), 131 (27), 130 (19), 117 (14).

1-(*N*-Tosylindolin-2-yl)-hexan-2-one (**3f**) As previously reported 200 mg of 2-((1*E*)-2-ethoxyhexa-1-enyl)-1-tosylindoline **2f** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (185 mg). Found C, 67.93; H, 6.79, N, 3.75, S 8.64%. Calc. for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78, N, 3.77, S 8.63%. ν_{max}(neat)/cm^{-1} 3010, 2958, 1711, 1479, 1355, 1168. δ_H (200 MHz; $CDCl_3$, Me_4Si) 0.91 (3H, t, *J* = 7.2, C*H*$_3$CH$_2$CH$_2$), 1.26-1.37 (2H, m, CH$_3$C*H*$_2$CH$_2$), 1.49-1.60 (2H, m, CH$_3$CH$_2$C*H*$_2$), 2.36-2.51 (6H, m, COC*H*$_2$CH$_2$, C*H*$_2$ ring, C*H*$_3$Ar), 2.83-3.03 (2H, m, C*H*$_2$ ring, C*H*$_2$CO), 3.25 (1H, dd, *J* = 17.8, 3.2 Hz, C*H'*$_2$CO), 4.58 (1H, m, C*H*CH$_2$CO), 7.02 (2H, bd, *J* = 4.2 Hz, Ar), 7.17 (3H, m, Ar), 7.55 (2H, m, *J* = 7.8 Hz, Ar), 7.70 (1H, m, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 13.6 (CH_3), 21.3 (CH_3), 22.1 (CH_2), 25.6 (CH_2), 35.0 (CH_2), 42.9 (CH_2), 49.6 (CH_2), 58.0 (CH), 116.8 (CH), 124.4 (CH), 125.1 (CH), 126.9 (CH), 127.6 (CH), 129.4 (CH), 131.2 (Cq), 134.3 (Cq), 140.9 (Cq), 143.8 (Cq), 209.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 371 (M^+, 2), 271 (96), 216 (100), 132 (43), 91 (41).

4-Hydroxy-1-(*N*-tosylindolin-2-yl)-pentan-2-one (**3g**) As previously reported 202 mg of 2-(2-ethoxyexa-4-hydroxy-1-pentyl)-1-tosylindoline **2g** (0.5 mmol) were dissolved in CH_2Cl_2 and stirred overnight in the presence of Amberlyst 15. After filtration and the solvent evaporation a pale yellow oil was obtained in quantitative yield (187 mg). Found C, 64.35; H, 6.19, N, 3.76, S 8.60%. Calc. for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21, N, 3.75, S 8.59%. ν_{max}(neat)/cm^{-1} 3543, 3056, 2973, 1705, 1599, 1351, 814. δ_H (200 MHz; $CDCl_3$, Me_4Si) 1.19 (3H, d, *J* = 6.2, C*H*$_3$CHOH), 2.35 (3H, s, C*H*$_3$Ar), 2.43-3.10 (7H, m, C*H*$_2$ ring, C*H*$_2$CO, C*H*$_2$COCHOH, O*H*), 4.28 (1H, m, CH$_3$C*H*OH), 4.58 (1H, m, C*H*CH$_2$CO), 7.02 (2H, bd, *J* = 4.3 Hz, Ar), 7.19 (3H, m, Ar), 7.55 (2H, d, *J* = 8.1 Hz, Ar), 7.70 (1H, d, *J* = 8.1 Hz, Ar). δ_C (50.2 MHz; $CDCl_3$, Me_4Si) δ (ppm): 21.3 (CH_3), 22.5 (CH_3), 35.0 (CH_2), 51.2 (CH_2),

53.0 (CH_2), 57.8 (CH), 63.6 (CH), 116.8 (CH), 124.6 (CH), 125.1 (CH), 126.9 (CH), 127.6 (CH), 129.5 (CH), 131.2 (Cq), 134.1 (Cq), 140.8 (Cq), 144.0 (Cq), 209.0 (Cq). MS (EI, 70 eV): *m/z* (%) = 329 (M^+ - C_2H_4O, 8), 271 (95), 174 (100), 132 (80), 91 (49).

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Supporting informations ^1H, ^{13}C and DEPT spectra of products **2a-g** and **3a-g.** NOESY spectra of product **2**

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