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Diels–Alder Reactions of 2-Vinylindoles with Open-Chain C=C Dienophiles

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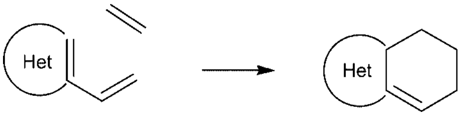
The synthesis of diastereoisomeric 3,4-disubstituted 1,2,3,4-tetrahydrocarbazoles by Diels–Alder cycloaddition reactions between [(*E*)-2-vinyl]indole-1-carboxylic acid ethyl esters and open-chain C=C dienophiles is reported and discussed. The reactions proceed with high regioselectivity whereas the diastereoselectivity ranges from moderate to excellent depending on the substitution pattern on both the dienes and dienophiles and on the catalyst employed.

Introduction

The Diels–Alder reaction is one of the most innovative and helpful reactions in synthetic organic chemistry.[1] The substituent array in diene and dienophile moieties allows the construction of a wide range of carbo- and hetero(poly)cyclic compounds often in a stereospecific manner. In particular, the Diels–Alder reactions of internal-external-ring dienes derived from heterocyclic compounds with activated C=C dienophiles represent an attractive approach to polyheterocyclic compounds (Scheme 1).[2]

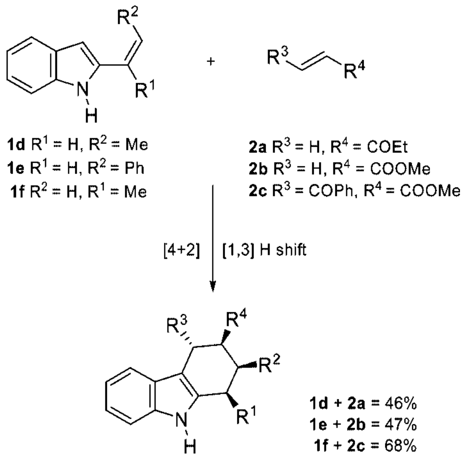


Scheme 1.

Recently, in connection with our ongoing interest in the transition-metal-catalyzed synthesis of indoles and polycyclic indole derivatives,[3] we realized a novel and valuable palladium-catalyzed approach to 3-unsubstituted 2-substituted indoles starting from a new indol-2-yl triflate.[3k] Among these the [(*E*)-2-vinyl]indole-1-carboxylic acid ethyl esters **1a**–**c** (Scheme 3) could represent useful 4π components in Diels–Alder reactions with open-chain C=C dienophiles in the synthesis of tetrahydrocarbazole derivatives.

The tetrahydrocarbazole nucleus is found in numerous naturally occurring alkaloids and synthetic analogues of medicinal importance[4] and the preparation of new and variously substituted derivatives is still a highly pursued objective.[5]

The [4+2] cycloaddition reactions of [(*E*)-2-vinyl]indoles with open-chain C=C dienophiles have not yet been extensively explored, excepting the investigations of Pindur and co-workers,[2f,2g,2l] although a few examples of this reaction have appeared in the literature over the past 25 years.[2a,2c,2e,2i] In particular, about 15 years ago, Pindur and co-workers realized the synthesis of several *N*,3-unsubstituted 2-vinylindoles and investigated, both from a theoretical and synthetic point of view, their participation in Diels–Alder reactions with different substituted dienophiles.[2l] Their results with open-chain C=C dienophiles are reported in Scheme 2.



Scheme 2.

The cycloaddition reactions were performed in toluene at reflux and in the presence of 4 Å molecular sieves or in the liquid dienophile at room temperature and in the presence of silica gel and proceeded with high regio- and *endo* diastereoselectivity, giving rise to the corresponding tetrahydrocarbazoles in moderate-to-good yields. The regio- and stereochemical outcomes were in agreement with the predictions of FMO theory and with a concerted HOMO$_{\text{diene}}$–LUMO$_{\text{dienophile}}$-controlled Diels–Alder process.

Thus, we decided to investigate both from a synthetic and mechanistic point of view the reactivity of [(*E*)-2-vinyl]-

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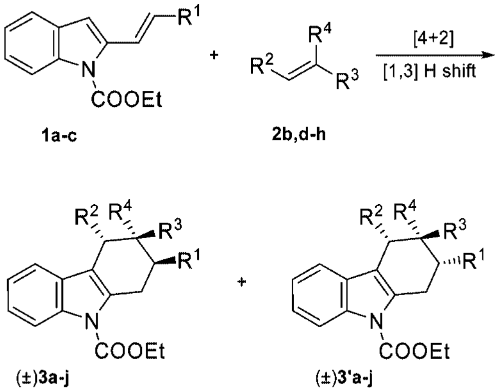
indole-1-carboxylic acid ethyl esters **1a**–**c** with open-chain C=C dienophiles. Herein we report the full details of our research.



1	R^1
a	*p*-tolyl
b	CH_3
c	C_4H_9

2	R^2	R^3	R^4
b	H	COOMe	H
d	H	COMe	H
e	H	COOEt	Me
f	COOMe	COOMe	H
g	Me	CHO	H
h	Ph	CHO	H

Scheme 3.

Results and Discussion

The [4+2] cycloaddition reactions between indoles **1a**–**c** and electron-poor alkenes **2b,d**–**h** were performed in toluene at reflux using an excess of the dienophile and in the presence of 15% magnesium perchlorate as Lewis acid. Under the conditions reported by Eitel and Pindur[21] the reactions are extremely slow (**1a** + **2b**: molecular sieves, toluene, 20% conversion after 10 days under reflux, *endo*/*exo* ratio = 1:1) or do not proceed at all (**1a** + **2b**: silica gel, room temp.). The reactions were monitored by TLC and the crude mixtures purified by flash chromatography over silica gel giving rise regioselectively to the corresponding diastereoisomeric 1,2,3,4-tetrahydrocarbazoles (±)-**3a**–**j** and (±)-**3′a**–**j** (Scheme 3, Table 1). The structures of **3a**–**j and 3′a**–**j** were assigned on the basis of analytical and spectroscopic data.

In particular, combined one- (^{1}H NMR, APT) and two-dimensional (COSY, HETCOR) experiments performed at 500 MHz using C_6D_6 as solvent allowed the complete assignment of chemical shifts and coupling constants, whereas the stereochemistry was assigned on the basis of spatial coupling interactions detected by two-dimensional NOE experiments, as exemplified in Figure 1 for compounds **3b** and **3′b**.

With a view to supporting this experimental evidence and to elucidating the conformational preferences of the isomers **3b** (3,4-*cis*) and **3′b** (3,4-*trans*) we performed a computational investigation on both conceivable conformers ascribable to each isomer.

The four hypothetical structures, **3b** (3,4-*cis* ax,eq), **3b** (3,4-*cis* eq,ax), **3′b** (3,4-*trans* eq,eq) and **3′b** (3,4-*trans* ax,ax), were subjected to a preliminary conformational analysis at a molecular mechanics level using the MM+ force field (an implemented version of the Allinger MM2[6] force field included in the Hyperchem® molecular modelling program[7]) specifically developed for small- and middle-sized organic molecules. The minima were reoptimized at the ab initio level using DFT (B3LYP/6-31G*). Ab initio calculations were performed with the Gaussian 03® molecular modelling program[8] using the default options. The characteristics of the minima of the optimized geometries were confirmed by the absence of imaginary frequencies. The results are reported in Table 2.

The experimental results and structural assignments are in agreement with computational analyses. In particular, it is interesting to note that the energetic difference between

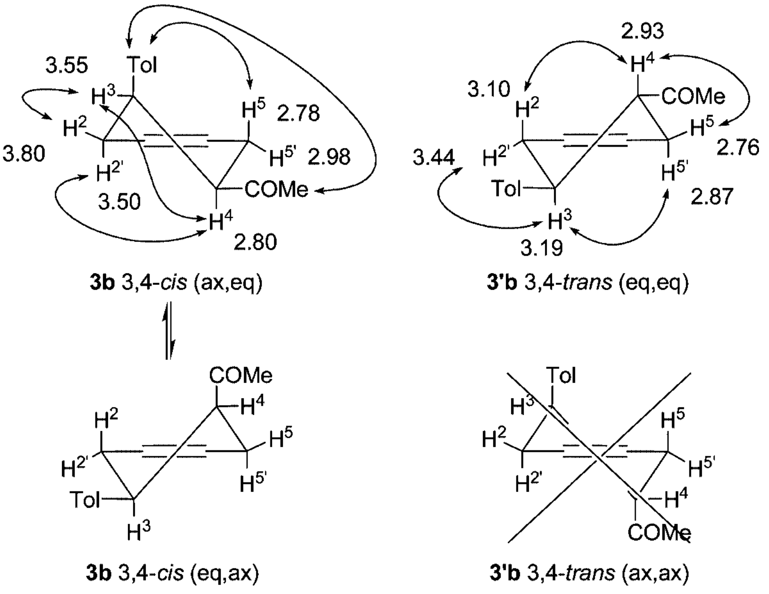
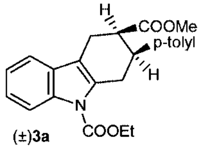
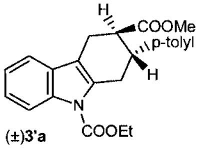
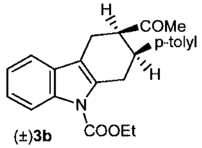
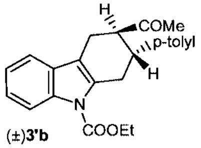
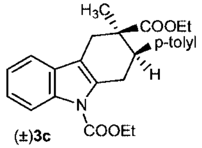
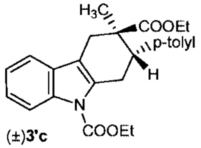
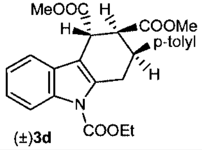
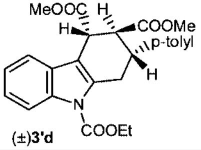
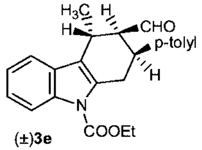
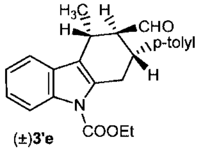
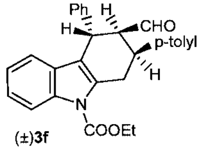
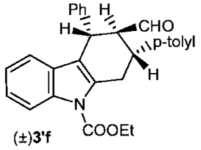
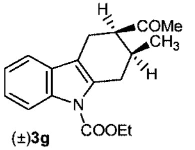
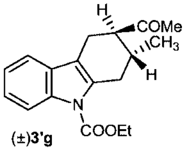
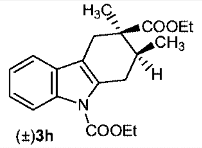
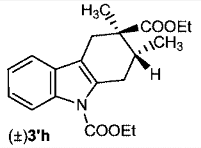
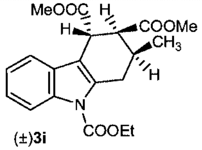
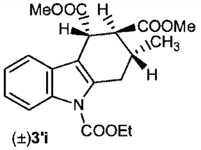
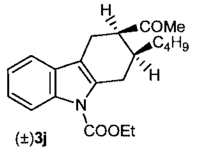
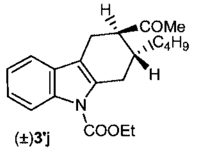


Figure 1. Chemical shifts [ppm] and NOE interactions for compounds **3b** and **3′b**.

Table 1. Reactions of indoles with electron-poor alkenes.

1 + 2	1:2	3	3'	Time	Yield (%)	3:3'	*de* (%)
1a + 2b	1:2.5	 (±)**3a**	 (±)**3'a**	24 h	60	3.3:1	53
1a + 2d	1:2.5	 (±)**3b**	 (±)**3'b**	24 h	77	2.5:1	43
1a + 2e	1:2.5	 (±)**3c**	 (±)**3'c**	24 h	66	54:1	96
1a + 2f	1:1.2	 (±)**3d**	 (±)**3'd**	6 d	54	1.7:1	26
1a + 2g	1:2.5	 (±)**3e**	 (±)**3'e**	24 h	80	2.7:1	46
1a + 2h	1:1	 (±)**3f**	 (±)**3'f**	24 h	76	1.4:1	17
1b + 2d	1:2.5	 (±)**3g**	 (±)**3'g**	2 d	67	1.4:1	17
1b + 2e	1:2.5	 (±)**3h**	 (±)**3'h**	6 d	45	2:1	33
1b + 2f	1:1.2	 (±)**3i**	 (±)**3'i**	2 d	46	1:2.2	38
1c + 2d	1:2.5	 (±)**3j**	 (±)**3'j**	4 h	66	1.1:1	5

the two conformers of **3b** is quite small (0.3 kcal/mol), suggesting a rapid equilibrium between the two *cis* isomers. This hypothesis is confirmed by the observation that the measured coupling constants of **3b** show average values with respect to the range of coupling constants computed for conformers **3b** (3,4-*cis* ax,eq) and **3b** (3,4-*cis* eq,ax). Moreover, the measured NOE interactions and calculated interatomic distances are also in agreement with this suggestion. In fact, although isomer **3b** (3,4-*cis* ax,eq) shows the best fit between measured and calculated data,

Table 2. Measured ^{1}H–^{1}H coupling constants and NOE interactions versus the calculated ^{1}H–^{1}H coupling constant range (derived from dihedral angles given) and interatomic distances.

	3b Exp. data	**3b** 3,4-*cis* (ax,eq) Calcd. data	**3b** 3,4-*cis* (eq,ax) Calcd. data	**3′b** Exp. data	**3′b** 3,4-*trans* (eq,eq) Calcd. data	**3′b** 3,4-*trans* (ax,ax) Calcd. data
E_{rel}[a] [kcal/mol]	–	3.0	2.7	–	0.0	3.4
$^3J_{\text{H2–H3}}$	4.0 Hz	82° (0.0–1.0 Hz)	167° (8.9–13.9 Hz)	10.5 Hz	164° (8.6–13.4 Hz)	80° (0.0–1.0 Hz)
$^3J_{\text{H2′–H3}}$	6.6 Hz	32° (5.5–9.5 Hz)	51° (3.0–5.5 Hz)	5.0 Hz	49° (3.2–6.1 Hz)	35° (5.4–9.4 Hz)
$^3J_{\text{H3–H4}}$	4.0 Hz	58° (2.0–4.0 Hz)	61° (1.8–3.8 Hz)	10.5 Hz	175° (9.4–14.4 Hz)	65° (1.5–2.8 Hz)
$^3J_{\text{H4–H5}}$	5.5 Hz	170° (9.1–14.2 Hz)	76° (0.2–1.3 Hz)	4.0 Hz	49° (3.2–6.0 Hz)	42° (4.2–7.8 Hz)
$^3J_{\text{H4–H5′}}$	7.3 Hz	55° (2.5–5.0 Hz)	39° (4.5–8.5 Hz)	10.5 Hz	165° (8.7–13.6 Hz)	74° (0.2–1.3 Hz)
NOE H2′–H4	Yes	2.7 Å	4.3 Å	No	3.8 Å	3.9 Å
NOE H2′–H3	Indet.[b]	2.3 Å	2.4 Å	Yes	2.4 Å	2.3 Å
NOE H2–H3	Yes	2.6 Å	3.1 Å	No	3.1 Å	2.6 Å
NOE H2–H4	No	3.8 Å	4.0 Å	Yes	2.8 Å	4.3 Å
NOE H3–H4	Yes	2.4 Å	2.4 Å	No	3.0 Å	2.4 Å
NOE H4–H5	Indet.[b]	3.1 Å	2.6 Å	Yes	2.4 Å	2.4 Å
NOE[c] Tol–H5	Yes	2.7 Å	5.2 Å (I)	No	5.0 Å (I)	3.0 Å (P)
NOE[c] Tol–Me	Yes	2.8 Å	3.8 Å (P)	No	3.1 Å (P)	3.4 Å (I)

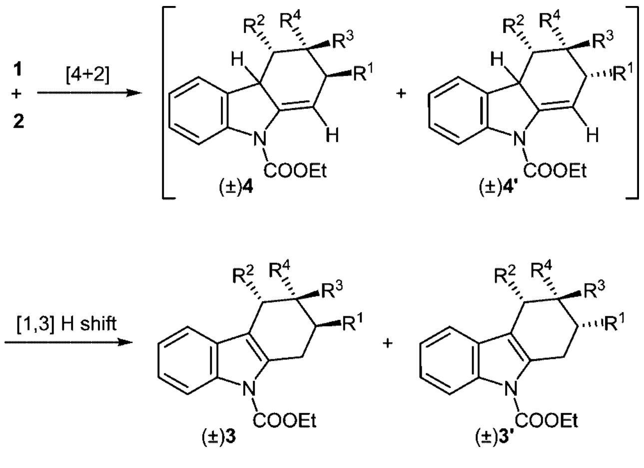
[a] Calculated by DFT (B3LYP/6-31G*); ZPE corrected. [b] This NOE was experimentally indeterminable because the proton signals have the same chemical shift. [c] Tolyl and methyl groups have some degree of freedom; the reported interatomic distances refer to the most vicinal proton of each group in the minima conformation. P (possible) and I (impossible) indicate that they can exist (or otherwise) in at least one alternative conformation resulting from the simple rotation of tolyl and/or methyl groups around the C–C single bond in which the drop off in the interatomic distance is less than 3 Å.

the potential critical data (NOE H2′–H3, H2–H4, and H4–H5 versus calculated interatomic distances) do not rule out the conformer **3b** (3,4-*cis* eq,ax).

In contrast, the conformer **3′b** (3,4-*trans* eq,eq) is 3.4 kcal/mol more stable than **3′b** (3,4-*trans* ax,ax) and on the basis of Boltzmann factors, this energetic difference is consistent with a shift in the ratio between **3′b** (3,4-*trans* eq,eq) and **3′b** (3,4-*trans* ax,ax) towards the former at room temperature. This statement is supported by the fact that the experimental data is in agreement with only the data calculated for the conformer **3′b** (3,4-*trans* eq,eq).

The reaction mechanism involves a Diels–Alder cycloaddition step giving rise to the primary cycloadducts **4** and **4′** that rearrange through a [1,3] hydrogen shift towards the more stable 1,2,3,4-tetrahydrocarbazoles **3** and **3′** (Scheme 4). An alternative stepwise process giving rise to Michael-type adducts able to undergo a subsequent 6π electrocyclization to carbazoles can be ruled out because in none of the performed reactions was it possible to detect intermediates arising from the nucleophilic attack of indole C3 on the electrophilic terminus of activated alkenes.[21] Moreover, structurally correlated 2-(*p*-tolyl)indole-1-carboxylic acid ethyl ester was recovered unreacted when treated under the usual reaction conditions with **2b** or **2d**.

The regiochemical outcome of all these cycloaddition reactions can be easily understood by applying the FMO concept to the interactions between a 1,2,4-trisubstituted diene containing an electron-releasing group in the 2-position and an electron-withdrawing substituted dienophile.[9]



Scheme 4.

On the other hand, in contrast with the results obtained by Pindur and co-workers for the cycloaddition reactions performed between the *N*-unsubstituted 2-vinylindoles **1d**–**f** and open-chain carbodienophiles (Scheme 2), which afford, under silica gel catalysis, exclusively the *endo* carbazole adducts, the [(*E*)-2-vinyl]indole-1-carboxylic acid ethyl esters **1a**–**c** provide *endo*/*exo* ratios ranging from 1:2.2 to 54:1 in the presence of magnesium perchlorate as catalyst (Scheme 3, Table 1). In particular, the 2-[(*E*)-2-(*p*-tolyl)vinyl]indole-1-carboxylic acid ethyl ester (**1a**) reacts with moderate *endo* selectivity with alkenes **2b**, **2d** and **2g** monosubstituted with an electron-withdrawing π group (**2b** and **2d**) or α,β-disubstituted with an electron-withdrawing and a methyl group (**2g**), respectively. Lower *endo* selectivities were observed with dienophiles **2f** and **2h** α,β-disubstituted with π groups, whereas the *endo* adduct was almost the only product isolated when the reaction was carried out with the alkene **2e** α,α-disubstituted with a π and methyl group. Finally, when the reactions were performed with (*E*)-2-prop-1-enylindole-1-carboxylic acid ethyl ester (**1b**) or (*E*)-2-hex-1-enylindole-1-carboxylic acid ethyl ester (**1c**) and alkenes **2d**,**e** a loss of *endo* selectivity was observed and with **2f** the *exo* adduct was the main cycloaddition product.

The *endo*/*exo* ratio in a cycloaddition reaction is affected by several factors including primary orbital interactions, steric and electrostatic effects, closed-shell repulsions and secondary orbital interactions. The discussion on the significance of all these effective control mechanisms on the reaction course is beyond the scope of this work, however, it seems that the presence of a terminal *p*-tolyl group on the diene moiety that is able to interact with the π system of the carbonyl group in the dienophile (**1a** + **2b**, **2d** and **2g**) favours the formation of an *endo* transition state and this effect is deeply enhanced by the presence of a bulky substituent α to the alkene carbonyl group (**1a** + **2e**) and lowered by the presence of a competitive π interaction between the β-alkene carbonyl group and the π system of the indole nucleus (**1a** + **2f**). This hypothesis is supported by the results obtained with the alkyl-substituted vinylindoles **1b**,**c** which are unable to establish a carbonyl/π-interaction and react with dienophile **2d** to yield almost equimolecular amounts of *endo* and *exo* adducts. Moreover, the *endo* diastereoselectivity can be enhanced by using a hindered dienophile (**1b** + **2e**), whereas the *exo* adduct is the main product when a carbonyl/π-indole interaction occurs (**1b** + **2f**).

It is well known that Diels–Alder reactions catalysed by simple Lewis acid (LA) salts proceed faster than their thermal counterparts and often with improved regio- and stereoselectivity. In agreement with this statement when more active[10] LA salts such as copper or scandium triflate were employed in the reaction between **1a** and **2d** the cycloaddition reactions occur in 3 h at room temperature and in dichloromethane yielding **3b** and **3′b** with a *de* of 83%, as determined by HPLC analysis of the crude reaction mixtures. These results demonstrate once again that selectivity does not generally decrease with increasing reactivity and additional information is always necessary to predict the effects of structural variation on selectivity.[11] In this case FMO theory has been successfully applied to explain the role of the Lewis acid catalysts which, by means of donor–acceptor interactions, lower the energy of both the HOMO and the LUMO of the dienophile thus increasing the stabilization of the transition state.[12]

Conclusions

Our recent successful synthesis of several [(*E*)-2-vinyl]indole-1-carboxylic acid ethyl esters in excellent yield and in multigram quantities has stimulated our research group to investigate the behaviour of these derivatives in the synthesis of the 1,2,3,4-tetrahydrocarbazole nucleus by [4+2] cycloaddition reactions. The reactions with classical open-chain C=C dienophiles afford the desired products in good yields, with excellent regioselectivity and moderate diastereoselectivity in accordance with FMO theory for a normal Diels–Alder reaction. From a preparative point of view, the more interesting results have been achieved with α,α-disubstituted alkenes and 2-vinylindole **1a**, which give rise to the desired product with almost complete *endo* selectivity.

Thus, this synthetic approach to the 1,2,3,4-tetrahydrocarbazole nucleus could represent a valuable tool for the synthesis of more complex and interesting structures. Consequently, our efforts are currently focussed on the modulation of the substitution pattern of both the diene and dienophile moieties in order to access new and biologically active structures and on the selection of more appropriate catalysts with the aim being to perform these reactions in a stereocontrolled fashion.

Experimental Section

General Details: All chemicals and solvents are commercially available and were used after distillation or treatment with drying agents. Silica gel F_{254} thin-layer plates were employed for thin-layer chromatography (TLC). Silica gel 40–63 micron/60 Å was employed for flash column chromatography. Melting points were measured with a Perkin-Elmer DSC 6 calorimeter at a heating rate of 5 °C/min and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer FT-IR 16 PC spectrometer using KBr tablets for both solids and oils. ^{1}H and ^{13}C NMR spectra were determined with a Varian-Gemini 200, a Bruker 300 or a 500 Avance spectrometer at room temperature in $CDCl_3$ or C_6D_6 with residual solvent peaks as the internal reference. The APT or DEPT sequences were used to distinguish the methine and methyl carbon signals from those arising from methylene and quaternary carbon atoms. Two-dimensional NMR experiments were performed, where appropriate, to aid the assignment of structures. Low-resolution MS spectra were recorded with a Thermo-Finnigan LCQ advantage AP electrospray/ion trap equipped instrument using a syringe pump device to directly inject sample solutions. 2-Vinylindoles **1a**–**c** were prepared according to literature procedures.[3k]

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with Methyl Acrylate (2b): A mixture of **1a** (100 mg, 0.328 mmol), **2b** (0.074 mL, 0.82 mmol) and $Mg(ClO_4)_2$ (11 mg, 0.049 mmol) in toluene (4 mL) was refluxed for 24 h, then cooled to room temperature and freed from solvent in vacuo. The residue was purified by flash column chromatography over silica gel (hexane/ethyl acetate, 98:2), yielding progressively **3′a** (59 mg, 46%) and **3a** (18 mg, 14%).

Data for 3′a: Yellow solid; m.p. 154.6 °C. IR (KBr): $\tilde{\nu}$ = 2915, 2849, 1735 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.42 (t, *J* = 7.3 Hz, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 3.11 (m, 3 H, 1-H, 3-H, 4-H), 3.41 (m, 3 H, 1-H, 2-H, 4-H), 3.46 (s, 3 H, OCH_3), 4.44 (q, *J* = 7.3 Hz, 2 H, OCH_2), 7.15 (AA′BB′ system, *J* = 8.4 Hz, 4 H, arom., tolyl), 7.31 (m, 3 H, arom.), 8.15 (m, 1 H, arom.) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.4 (CH_3), 24.0 (CH_2), 20.3 (CH_3), 42.8 (CH_3), 32.4 (CH_2), 40.5 (CH), 51.5 (CH), 62.2 (OCH_2), 114.3, 129.3, 133.6, 135.3, 135.7, 139.2 (quat. C_{sp2}), 114.8, 117.0, 122.3, 123.1, 126.7 (2 C), 128.5 (2 C) ($C_{sp2}H$), 151.2 (COOEt), 173.9 (COOMe) ppm. ESI(+)-MS: *m*/*z* (%) = 392 (100) [M + 1]$^{+}$294 (10). $C_{24}H_{25}NO_4$ (391.46): calcd. C 73.64, H 6.44, N 3.58; found C 73.61, H 6.39, N 3.52.

Data for 3a: Colourless oil. IR (KBr): $\tilde{\nu}$ = 3050, 2980, 2946, 1732 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.47 (t, *J* = 7.3 Hz, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 2.8 (ddt, *J* = 2.1, 9.6, 16.6 Hz, 1 H, 4-H), 3.0 (dd, *J* = 5.1, 16.6 Hz, 1 H, 4a-H), 3.18 (ddd, *J* = 3.7, 5.1, 9.6 Hz, 1 H, 3-H), 3.57 (m, 2 H, 1-H), 3.7 (s, 3 H, OCH_3), 3.84 (m, 1 H, 2-H), 4.51 (m, 2 H, OCH_2), 7.04 (AA′BB′ system, *J* = 3.7, 8.3 Hz, 4 H, arom., tolyl), 7.32 (m, 2 H, arom.), 7.48 (dd, *J* = 0.8, 6.9 Hz, 1 H, 5-H), 8.23 (d, *J* = 8.1 Hz 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.4 (CH_3), 20.4 (CH_2), 21.0 (CH_3), 43.9 (CH_3), 30.9 (CH_2), 40.4 (CH), 51.6 (CH), 62.9 (OCH_2), 115.8, 129.3, 134.4, 136.2, 136.5, 138.5 (quat. C_{sp2}), 115.6, 117.8, 122.9, 123.9, 127.6 (2 C), 129.1 (2 C) (C_{sp2}H), 152.2 (COOEt), 173.9 (COOMe) ppm. ESI(+)-MS: *m*/*z* (%) = 392 (100) [M + 1]$^+$, 360 (70), 332 (40).

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with But-3-en-2-one (2d)

Method A: Mg(ClO$_4$)$_2$: A mixture of **1a** (100 mg, 0.328 mmol), **2d** (0.068 mL, 0.82 mmol) and $Mg(ClO_4)_2$ (11 mg, 0.049 mmol) in toluene (4 mL) was refluxed for 24 h, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (hexane/ethyl acetate, 95:5), yielding progressively **3′b** (27 mg, 22%) and **3b** (68 mg, 55%).

Data for 3′b: White solid; m.p. 166.2 °C. IR (KBr): ṽ = 2916, 2849, 1723 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 0.99 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.72 (s, 3 H, OCH_3), 2.21 (s, 3 H, CH_3), 2.76 (dd, *J* = 4.0, 15.6 Hz, 1 H, 4a′-H), 2.87 (dd, *J* = 10.5, 15.6 Hz, 1 H, 4′-H), 2.93 (ddd, *J* = 4.0, 10.5, 10.5 Hz, 1 H, 3′-H), 3.1 (dd, *J* = 10.5, 17.5 Hz, 1 H, 1a′-H), 3.19 (ddd, *J* = 5.0, 10.5, 10.5 Hz, 1 H, 2′-H), 3.44 (dd, *J* = 5.0, 17.5 Hz, 1 H, 1′-H), 4.23 (m, 2 H, OCH_2), 7.08 and 7.17 (AA′BB′ system, *J* = 7.9 Hz, 4 H, arom., tolyl), 7.38 (m, 1 H, arom.), 7.47 (m, 2 H, arom.), 8.63 (d, *J* = 8.2 Hz, 8′-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.9 (CH_3), 20.8 (CH_3), 24.5 (CH_2), 29.7 (CH_3), 33.9 (CH_2), 43.6 (CH), 52.4 (CH), 62.4 (OCH_2), 115.2, 129.6, 134.4, 136.2, 136.5, 140.7 (quat. C_{sp2}), 115.2, 117.8, 123.0, 124.1, 128.0 (2 C), 129.4 (2 C) (C_{sp2}H), 151.6 (COOEt), 209.0 (COMe) ppm. ESI(+)-MS: *m*/*z* (%) = 376 (40) [M + 1]$^+$, 304 (100). $C_{24}H_{25}NO_3$ (375.46): calcd. C 76.77, H 6.71, N 3.73; found C 76.68, H 6.58, N 3.67.

Data for 3b: White solid; m.p. 142.7 °C. IR (KBr): ṽ = 3054, 2921, 1722, 1701 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.02 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.83 (s, 3 H, OCH_3), 2.14 (s, 3 H, CH_3), 2.78 (dd, *J* = 5.5, 18.1 Hz, 1 H, 4-H), 2.80 (m, 1 H, 3-H), 2.98 (dd, *J* = 7.3, 18.1 Hz, 1 H, 4a-H), 3.50 (dd, *J* = 6.6, 17.6 Hz, 1 H, 1a-H), 3.55 (ddd, *J* = 4.0, 4.0, 6.6 Hz, 1 H, 2-H), 3.80 (dd, *J* = 4.0, 17.6 Hz, 1 H, 1-H), 4.1 (q, *J* = 7.1 Hz, 2 H, OCH_2), 6.96 and 7.16 (AA′BB′ system, *J* = 7.9 Hz, 4 H, arom., tolyl), 7.32–7.50 (m, 3 H, arom.), 8.61 (d, *J* = 8.3 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 21.1 (CH_2), 29.3 (CH_3), 30.4 (CH_3), 31.7 (CH_2), 41.2 (CH), 51.5 (CH), 62.8 (OCH_2), 116.1, 130.1, 135.1, 136.6, 137.1, 139.6 (quat. C_{sp2}), 116.5, 118.3, 123.4, 124.5, 129.6 (4 C) (C_{sp2}H), 152.4 (COOEt), 209.0 (COMe) ppm. ESI(+)-MS: *m*/*z* (%) = 376 (25) [M + 1]$^+$, 304 (100), 100 (70). $C_{24}H_{25}NO_3$ (375.46): calcd. C 76.77, H 6.71, N 3.73; found C 76.71, H 6.65, N 3.68.

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with Ethyl Methacrylate (2e): A mixture of **1a** (300 mg, 0.984 mmol), **2e** (0.309 mL, 2.46 mmol) and $Mg(ClO_4)_2$ (33 mg, 0.148 mmol) in toluene (12 mL) was refluxed for 24 h, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (hexane/ethyl acetate, 98:2), yielding progressively **3c** (266 mg, 65%) and **3′c** (5 mg, 1.2%).

Data for 3c: White solid; m.p. 111.3 °C. IR (KBr): ṽ = 3052, 2986, 2916, 1731, 1716 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.14 (m, 6 H, OCH_2CH_3), 1.43 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3, tolyl), 2.87 (d, *J* = 15.8 Hz, 1 H, 4a-H), 3.46 (dd, *J* = 3.5, 5.3 Hz, 1 H, 2-H), 3.52 (d, *J* = 15.8 Hz, 1 H, 4-H), 3.60 (dd, *J* = 5.3, 17.6 Hz, 1 H, 1a-H), 3.81 (dd, *J* = 3.5, 17.6 Hz, 1 H, 1-H), 4.0 (m, 4 H, OCH_2), 6.98 (d, *J* = 7.8 Hz, 2 H, arom.), 7.4 (m, 5 H, arom.), 8.23 (d, *J* = 8.3 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 14.3 (CH_3), 21.1 (CH_3), 24.7 (CH_3), 28.9 (CH_2), 30.5 (CH_2), 47.6 (CH), 60.4 (OCH_2), 62.8 (OCH_2), 116.1, 130.4, 134.2, 136.7, 137.2, 139.3, 140.5 (quat. C_{sp2}), 116.4, 118.4, 123.4, 124.5, 128.9 (2 C), 129.4 (2 C) (C_{sp2}H), 152.1 (NCOOEt), 175.6 (COOEt) ppm. ESI(+)-MS: *m*/*z* (%) = 420 (47.5) [M + 1]$^+$, 348 (100). $C_{26}H_{29}NO_4$ (419.51): calcd. C 74.44, H 6.97, N 3.34; found C 74.34, H 6.82, N 3.29.

Data for 3′c: Yellow oil. IR (KBr): ṽ = 3049, 2963, 2853, 1733 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.46 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 2.3 (s, 3 H, CH_3, tolyl), 3.45 (m, 3 H, 2 × 4-H + 2-H), 4.1 (m, 2 H, OCH_2), 4.50 (m, 3 H, OCH_2, 1-H), 4.85 (m, 1 H, 1-H), 6.59 (d, *J* = 7.0 Hz, 2 H, arom.), 6.89 (d, *J* = 7.1 Hz, 2 H, arom.), 7.18 (m, 3 H, arom.), 7.91 (d, *J* = 7.3 Hz, 1 H, arom.) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 14.3 (CH_3), 21.1 (CH_3), 24.7 (CH_3), 28.9 (CH_2), 30.5 (CH_2), 44.4 (CH), 60.4 (OCH_2), 62.8 (OCH_2), 59.7, 115.9, 128.5, 135.1, 135.3, 139.0, 139.9 (quat. C_{sp2}), 114.7, 118.6, 121.9, 123.1, 127.2 (2 C), 128.2 (2 C) (C_{sp2}H), 151.1 (NCOOEt), 176.3 (COOEt) ppm. ESI(+)-MS: *m*/*z* (%) = 420 (10) [M + 1]$^+$.

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with Dimethyl Fumarate (2f): A mixture of **1a** (200 mg, 0.656 mmol), **2f** (113 mg, 0.787 mmol) and $Mg(ClO_4)_2$ (22 mg, 0.098 mmol) in toluene (8 mL) was refluxed for 6 d, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (toluene), yielding progressively **3d** (101 mg, 34%) and **3′d** (59 mg, 20%).

Data for 3d: Yellow solid; m.p. 174.9 °C. IR (KBr): ṽ = 3050, 2978, 2956, 1729 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 0.99 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.18 (s, 3 H, CH_3, tolyl), 3.26 (s, 3 H, OCH_3), 3.5 (s, 3 H, OCH_3), 3.51 (m, 1 H, 1-H), 3.96 (m, 1 H, 1a-H), 4.03 (m, 1 H, 3-H), 4.05 (m, 2 H, OCH_2), 4.06 (m, 1 H, 2-H), 4.54 (d, *J* = 5.0 Hz, 1 H, 4-H), 7.04 and 7.42 (AA′BB′ system, *J* = 8.0 Hz, 4 H, arom., tolyl), 7.37 (m, 1 H, CH, arom.), 7.4 (m, 1 H, CH, arom.), 7.93 (d, *J* = 7.2 Hz, 1 H, 5-H), 8.59 (d, *J* = 8.0 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.0 (CH_3), 20.0 (CH_3), 28.6 (CH_2), 38.5 (CH), 40.2 (CH), 46.7 (CH), 50.2 (OCH_3), 50.9 (OCH_3), 61.8 (OCH_2), 111.8, 128.3, 135.6, 136.0, 136.1, 138.4 (quat. C_{sp2}), 115.3, 118.3, 122.5, 123.5, 127.0 (2 C), 128.6 (2 C) (C_{sp2}H), 150.7 (COOEt), 171.2, 172.2 (COOMe) ppm. APCI(+)-MS: *m*/*z* (%) = 450 (100) [M + 1]$^+$, 390 (50). $C_{26}H_{27}NO_6$ (449,50): calcd. C 69.47, H 6.05, N 3.12; found C 69.46, H 5.92, N 3.05.

Data for 3′d: Yellow oil. IR (KBr): ṽ = 2953, 1731 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 0.94 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.2 (s, 3 H, CH_3, tolyl), 3.13 (ddd, ^5J = 2.9, ^3J = 11.4, 17.5 Hz, 1 H, 1a′-H), 3.26 (ddd, *J* = 4.8, 11.4, 11.4 Hz, 1 H, 2′-H), 3.28 (s, 3 H, OCH_3), 3.36 (ddd, ^5J = 3.6, ^3J = 4.8, 17.5 Hz, 1 H, 1′-H), 3.53 (s, 3 H, OCH_3), 3.74 (dd, *J* = 10.7, 11.4 Hz, 1 H, 3′-H), 4.01 (m, 2 H, OCH_2), 4.60 (m, 1 H, 4′-H), 7.08 and 7.22 (AA′BB′ system, *J* = 8.0 Hz, 4 H, arom., tolyl), 7.45 (m, 1 H, CH, arom.), 7.4 (m, 1 H, CH, arom.), 7.72 (d, *J* = 7.7 Hz, 1 H, 5′-H), 8.60 (d, *J* = 8.2 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.1 (CH_3), 20.1 (CH_3), 32.7 (CH_2), 42.7 (CH), 44.4 (CH), 49.8 (CH), 50.5 (OCH_3), 51.0 (OCH_3), 61.8 (OCH_2), 112.4, 127.8, 135.0, 135.8, 135.9, 138.6 (quat. C_{sp2}), 115.3, 117.6, 122.6, 123.6, 127.0 (2 C), 128.6 (2 C) (C_{sp2}H), 150.6 (COOEt), 172.2, 172.3 (COOMe) ppm. APCI(+)-

MS: *m*/*z* (%) = 450 (100) [M + 1]$^{+}$, 391 (20). $C_{26}H_{27}NO_6$ (449.50): calcd. C 69.47, H 6.05, N 3.12; found C 69.56, H 6.11, N 3.04.

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with *trans*-Crotonaldehyde (2g): A mixture of **1a** (250 mg, 0.819 mmol), **2g** (0.169 mL, 2.048 mmol) and $Mg(ClO_4)_2$ (27 mg, 0.123 mmol) in toluene (10 mL) was refluxed for 24 h, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (toluene/hexane, 6:4), yielding progressively **3e** (67 mg, 22%) and **3′e** (180 mg, 58%).

Data for 3e: Yellow solid; m.p. 155.4 °C. IR (KBr): $\tilde{\nu}$ = 2916, 2698, 1729 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 0.96 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.44 (d, *J* = 6.7 Hz, 3 H, CH_3), 2.21(s, 3 H, CH_3, tolyl), 2.64 (ddd, *J* = 3.8, 6.7, 11.2 Hz, 1 H, 3-H), 2.88 (ddd, *J* = 4.6, 11.2, 11.2 Hz, 1 H, 2-H), 3.06 (ddd, ^{5}J = 2.1, ^{3}J = 11.2, 17.6 Hz, 1 H, 1-H), 3.26 (m, 1 H, 4-H), 3.34 (dd, *J* = 4.6, 17.6 Hz, 1 H, 1a-H), 4.05 (m, 2 H, OCH_2), 7.08 (s, 4 H, arom., tolyl), 7.33 (m, 1 H, CH, arom.), 7.42 (m, 1 H, CH, arom.), 7.6 (d, *J* = 7.6 Hz, 1 H, 5-H), 8.63 (d, *J* = 8.3 Hz, 1 H, 8-H), 9.42 (d, *J* = 3.8 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 19.7 (CH_3), 21.2 (CH_3), 28.9 (CH), 34.6 (CH_2), 42.6 (CH), 60.4 (CH), 62.8 (OCH_2), 119.7, 129.5, 134.5, 136.9, 137.2, 139.5 (quat. C_{sp2}), 116.4, 119.9, 123.2, 124.3, 128.1 (2 C), 130.1 (2 C) ($C_{sp2}H$), 151.9 (COOEt), 202.5 (CHO) ppm. ESI (+)-MS: *m*/*z* (%) = 376 (100) [M + 1]$^{+}$. $C_{24}H_{25}NO_3$ (375.46): calcd. C 76.77, H 6.71, N 3.73; found C 76.63, H 6.57, N 3.68.

Data for 3′e: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2959, 2917, 2849, 1736 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.03 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.37 (d, *J* = 7.0 Hz, 3 H, CH_3), 2.24 (s, 3 H, CH_3, tolyl), 2.58 (m, 1 H, 3′-H), 3.45–3.65 (m, 4 H, 4′-H, 2′-H, 2 × 1′-H), 4.09 (m, 2 H, OCH_2), 7.10 and 7.25 (AA′BB′ system, *J* = 8.1 Hz, 4 H, arom., tolyl), 7.33 (m, 1 H, CH, arom.), 7.41 (m, 1 H, CH, arom.), 7.53 (d, *J* = 7.5 Hz, 1 H, 5′-H), 8.57 (d, *J* = 8.2 Hz, 1 H, 8′-H), 9.65 (d, *J* = 0.7 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 20.4 (CH_3), 21.1 (CH_3), 27.3 (CH), 29.1 (CH_2), 37.6 (CH), 58.1 (CH), 62.8 (OCH_2), 119.6, 129.1, 134.1, 136.2, 136.9, 139.1 (quat. C_{sp2}), 116.2, 118.5, 123.0, 124.1, 128.2 (2 C), 129.5 (2 C) ($C_{sp2}H$), 151.6 (COOEt), 201.9 (CHO) ppm. ESI(+)-MS: *m*/*z* (%) = 376 (100) [M + 1]$^{+}$, 358 (30). $C_{24}H_{25}NO_3$ (375.46): calcd. C 76.77, H 6.71, N 3.73; found C 76.65, H 6.64, N 3.71.

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with *trans*-Cinnamaldehyde (2h): A mixture of **1a** (50 mg, 0.164 mmol), **2h** (0.021 mL, 0.164 mmol) and $Mg(ClO_4)_2$ (6 mg, 0.025 mmol) in toluene (2 mL) was refluxed for 24 h, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (hexane/ethyl acetate, 99:1), yielding progressively **3′f** (23 mg, 32%) and **3f** (32 mg, 44%).

Data for 3′f: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2906, 2895, 2786, 1732 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.01 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.20 (s, 3 H, CH_3, tolyl), 3.11 (m, 1 H, 2′-H), 3.23 (dd, *J* = 2.9, 9.8 Hz, 1 H, 3′-H), 3.35 (m, 1 H, 1-H), 3.52 (m, 1 H, 1a-H), 4.64 (m, 1 H, 4′-H), 4.23 (m, 2 H, OCH_2), 6.94–7.33 (m, 12 H, 4 H, arom., tolyl, 5 H Ph, 5′-H, 6′-H, 7′-H), 8.56 (m, 1 H, 8′-H), 9.42 (d, *J* = 2.9 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 21.2 (CH_3), 35.2 (CH_2), 42.3 (CH), 44.1 (CH), 61.1 (CH), 63.0 (OCH_2), 118.4, 135.7, 136.6, 136.9, 137.1, 139.0, 142.8 (quat. C_{sp2}), 116.1, 120.5, 123.3, 124.4, 127.4, 129.1, 129.3, 130.0, 130.3 ($C_{sp2}H$), 152.0 (COOEt), 202.7 (CHO) ppm. ESI(+)-MS: *m*/*z* (%) = 460 (100) [M + 23]$^{+}$. $C_{29}H_{27}NO_3$ (437.53): calcd. C 79.61, H 6.22, N 3.20; found C 79.74, H 7.04, N 3.66.

Data for 3f: Yellow oil. IR (KBr): $\tilde{\nu}$ = 3027, 2924, 2853, 1734 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.06 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.17 (s, 3 H, CH_3, tolyl), 3.07 (m, 1 H, 3-H), 3.58 (m, 1 H, 2-H), 3.67 (m, 2 H, 1-H), 4.23 (m, 2 H, OCH_2), 4.87 (d, *J* = 2.9 Hz, 1 H, 4-H), 7.02–7.53 (m, 12 H, 4 H, arom., tolyl, 5 H Ph, 5-H, 6-H, 7-H), 8.56 (d, *J* = 8.3 Hz, 1 H, 8-H), 9.74 (d, *J* = 0.7 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 21.1 (CH_3), 29.3 (CH_2), 37.4 (CH), 38.6 (CH), 60.3 (CH), 63.0 (OCH_2), 117.1, 129.5, 136.5, 136.6, 137.3, 139.0, 143.2 (quat. C_{sp2}), 116.3, 119.7, 123.5, 124.6, 127.2, 129.0, 129.1, 129.7, 130.0 ($C_{sp2}H$), 152.0 (COOEt), 201.5 (CHO) ppm. ESI(+)-MS: *m*/*z* (%) = 460 (100) [M + 23]$^{+}$. $C_{29}H_{27}NO_3$ (437.53): calcd. C 79.61, H 6.22, N 3.20; found C 79.75, H 6.37, N 3.31.

Reaction of Ethyl (*E*)-2-Propenylindole-1-carboxylate (1b) with But-3-en-2-one (2d): A mixture of **1b** (300 mg, 1.309 mmol), **2d** (0.272 mL, 3.273 mmol) and $Mg(ClO_4)_2$ (44 mg, 0.196 mmol) in toluene (15 mL) was refluxed for 2 d, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (hexane/ethyl acetate, 92:8), yielding progressively **3g** (111 mg, 28.5%) and **3′g** (151 mg, 38.8%).

Data for 3g: Yellow oil. IR (KBr): $\tilde{\nu}$ = 3076, 2953, 2917, 2884, 1735, 1703 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 0.95 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.06 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.27 (t, *J* = 12.2 Hz, 1 H, 4-H), 1.57 (m, 1 H, 2-H), 1.80 (m, 1 H, 4a-H), 1.88 (s, 3 H, OCH_3), 2.50 (ddd, *J* = 3.0, 10.8, 17.9 Hz, 1 H, 1-H), 3.17 (m, 1 H, 1a-H), 3.83 (m, 1 H, 3-H), 4.14 (q, *J* = 7.1 Hz, 2 H, OCH_2), 7.32 (m, 2 H, CH, arom.), 7.49 (d, *J* = 7.6 Hz, 1 H, 5-H), 8.50 (d, *J* = 8.3 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.3 (CH_3), 21.9 (CH_3), 25.6 (CH_3), 29.7 (CH), 34.2 (CH_2), 34.8 (CH_2), 50.4 (CH), 62.8 (OCH_2), 115.1, 129.3, 136.8, 137.4 (quat. C_{sp2}), 116.3, 118.8, 123.6, 124.4 ($C_{sp2}H$), 151.90 (COOEt), 208.7 (COMe) ppm. ESI(+)-MS: *m*/*z* (%) = 300 (100) [M + 1]$^{+}$. $C_{18}H_{21}NO_3$ (299.36): calcd. C 72.22, H 7.07, N 4.68; found C 72.37, H 7.15, N 4.53.

Data for 3′g: Pink solid; m.p. 88.2 °C. IR (KBr): $\tilde{\nu}$ = 3034, 2914, 2873, 1727, 1706 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.51 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.29 (s, 3 H, OCH_3), 2.78 (m, 1 H, 2′-H), 2.79 (m, 1 H, 4a′-H), 2.89 (m, 1 H, 4′-H), 2.89 (m, 1 H, 3′-H), 3.1 (m, 1 H, 1a′-H), 3.3 (m, 1 H, 1′-H), 4.51 (q, *J* = 7.1 Hz, 2 H, OCH_2), 7.32 (m, 2 H, CH, arom.), 7.47 (d, *J* = 6.9 Hz, 1 H, 5′-H), 8.14 (d, *J* = 7.6 Hz, 1 H, CH, 8′-H) ppm. ^{13}C NMR (125 MHz) $CDCl_3$): δ = 14.4 (CH_3), 14.6 (CH_3), 18.3 (CH_2), 28.5 (CH), 29.3 (CH_3), 33.3 (CH_2), 50.7 (CH), 62.8 (OCH_2), 114.7, 129.5, 133.6, 136.1 (quat. C_{sp2}), 115.5, 117.7, 122.8, 123.7 ($C_{sp2}H$), 152.0 (COOEt), 210.0 (COMe) ppm. APCI(+)-MS: *m*/*z* (%) = 300 (100) [M + 1]$^{+}$. $C_{18}H_{21}NO_3$ (299.36): calcd. C 72.22, H 7.07, N 4.68; found C 72.17, H 7.05, N 4.64.

Reaction of Ethyl (*E*)-2-Propenylindole-1-carboxylate (1b) with Ethyl Methacrylate (2e): A mixture of **1b** (200 mg, 0.873 mmol), **2e** (0.274 mL, 2.183 mmol) and $Mg(ClO_4)_2$ (30 mg, 0.131 mmol) in toluene (8 mL) was refluxed for 6 d, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (toluene/hexane, 7:3), yielding progressively **3h** (90 mg, 30%) and **3′h** (45 mg, 15%).

Data for 3h: Yellow oil. IR (KBr): $\tilde{\nu}$ = 3050, 2934, 1737 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 0.95 (t, *J* = 7.1 Hz, 3 H, $NCOOCH_2CH_3$), 1.03 (m, 3 H, OCH_2CH_3), 1.10 (d, *J* = 6.6 Hz, 3 H, $CHCH_3$), 1.81 (m, 1 H, 1-H), 1.85 (s, 3 H, $CH_3CCOOEt$), 1.92 (m, 1 H, 2-H), 2.12 (t, *J* = 12.6 Hz, 1 H, 1a-H), 2.55 (d, *J* = 17.8 Hz, 1 H, 4-H), 3.21 (dd, *J* = 4.1, 17.8 Hz, 1 H, 4a-H), 4.02 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.10 (m, 2 H, $NCOOCH_2CH_3$), 7.33 (m, 2 H, CH, arom.), 7.73 (d, *J* = 7.6 Hz, 1 H, 5-H), 8.54 (d, *J* =

8.2 Hz, 1 H, 8-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.1 (CH_3), 13.3 (CH_3), 21.0 (CH_3), 22.6 (CH), 22.8 (CH_3), 33.3 (CH_2), 42.4 (CH_2), 59.9 (OCH_2), 61.5 (OCH_2), 59.3 (C), 118.9, 127.6, 134.9, 135.9 (quat. C_{sp2}), 115.4, 118.0, 122.1, 123.0 (C_{sp2}H), 150.8 (NCOOEt), 175.6 (COOEt) ppm. ESI(+)-MS: *m/z* (%) = 366 (100) $[M + 23]^+$, 344 (25) $[M + 1]^+$. $C_{20}H_{25}NO_4$ (343,42): calcd. C 69.95, H 7.34, N 4.08; found C 70.08, H 7.46, N 4.17.

Data for 3′h: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2980, 2872, 1738 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 0.98 (t, *J* = 7.1 Hz, 3 H, $NCOOCH_2CH_3$), 1.04 (m, 3 H, OCH_2CH_3), 1.13 (d, *J* = 6.9 Hz, 3 H, $CHCH_3$), 1.30 (m, 1 H, 1a′-H), 1.84 (s, 3 H, CH_3CCOOEt), 2.35 (m, 1 H, 2′-H), 2.45 (d, *J* = 19.1 Hz, 1 H, 4a′-H), 2.49 (t, *J* = 11.0 Hz, 1 H, 1′-H), 3.25 (dd, *J* = 4.9, 19.1 Hz, 1 H, 4′-H), 4.03 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.1 (m, 2 H, $NCOOCH_2CH_3$), 7.35 (m, 2 H, CH, arom.), 7.95 (d, *J* = 7.5 Hz, 1 H, 5′-H), 8.58 (d, *J* = 8.2 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.1 (CH_3), 13.2 (CH_3), 20.9 (CH_3), 25.6 (CH_3), 33.7 (CH_2), 34.8 (CH), 44.2 (CH_2), 59.8 (OCH_2), 61.6 (OCH_2), 59.5 (C), 118.5, 128.3, 135.0, 136.0 (quat. C_{sp2}), 115.2, 117.1, 121.9, 122.7 (C_{sp2}H), 150.9 (NCOOEt), 174.8 (COOEt) ppm. ESI(+)-MS: *m/z* (%) = 366 (100) $[M + 23]^+$, 344 (25) $[M + 1]^+$. $C_{20}H_{25}NO_4$ (343.42): calcd. C 69.95, H 7.34, N 4.08; found C 70.12, H 7.42, N 4.02.

Reaction of Ethyl (*E*)-2-Propenylindole-1-carboxylate (1b) with Dimethyl Fumarate (2f): A mixture of **1b** (200 mg, 0.873 mmol), **2f** (151 mg, 1.047 mmol) and $Mg(ClO_4)_2$ (13 mg, 0.131 mmol) in toluene (8 mL) was refluxed for 2 d, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (toluene), yielding progressively **3i** (47 mg, 14%) and **3′i** (103 mg, 32%).

Data for 3i: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2957, 2931, 1732 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.01 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.11 (d, *J* = 7.0 Hz, 3 H, CH_3), 2.55 (m, 1 H, 2-H), 3.17 (m, 2 H, 1-H), 3.49 (s, 3 H, OCH_3), 3.52 (s, 3 H, OCH_3), 3.62 (m, 1 H, 3-H), 4.1 (m, 2 H, OCH_2), 4.53 (m, 1 H, 4-H), 7.35 (m, 2 H, CH, arom.), 7.92 (m, 1 H, 5-H), 8.51 (d, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 14.2 (CH_3), 19.7 (CH_3), 29.4 (CH), 33.4 (CH_2), 41.0 (CH), 47.0 (CH), 51.6 (OCH_3), 52.0 (OCH_3), 62.8 (OCH_2), 113.4, 129.4, 136.3, 137.0, (quat. C_{sp2}), 116.4, 119.2, 123.5, 124.4 (C_{sp2}H), 151.7 (COOEt), 173.5, 174.2 (COOMe) ppm. ESI(+)-MS: *m/z* (%) = 396 (100) $[M + 23]^+$. $C_{20}H_{23}NO_6$ (373.40): calcd. C 64.33, H 6.21, N 3.75; found C 64.28, H 6.09, N 3.71.

Data for 3′i: Yellow solid; m.p. 100.6 °C. IR (KBr): $\tilde{\nu}$ = 3448, 3079, 2963, 2917, 2849, 1741 cm^{-1}. ^{1}H NMR (500 MHz, C_6D_6): δ = 1.04 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.07 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.17 (m, 1 H, 2′-H), 2.55 (ddd, ^5J = 2.8, ^3J = 10.6, 17.9 Hz, 1 H, 1a′-H), 3.11 (m, 1 H, 3′-H), 3.12 (m, 1 H, 1′-H), 3.50 (s, 3 H, OCH_3), 3.53 (s, 3 H, OCH_3), 4.1 (m, 2 H, OCH_2), 4.49 (ddd, ^5J = 1.6, 2.8, ^3J = 9.9 Hz, 1 H, 4′-H), 7.3 (m, 1 H, CH, arom.), 7.37 (m, 1 H, CH, arom.), 7.67 (d, *J* = 7.5 Hz, 1 H, 5′-H), 8.59 (d, *J* = 8.2 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 13.1 (CH_3), 16.0 (CH_3), 31.0 (CH), 32.2 (CH_2), 43.7 (CH), 50.3 (CH), 50.5 (OCH_3), 50.9 (OCH_3), 61.7 (OCH_2), 112.3, 127.9, 134.9, 135.7, (quat. C_{sp2}), 115.3, 117.6, 122.4, 123.4 (C_{sp2}H), 150.7 (COOEt), 172.3, 173.1 (COOMe) ppm. ESI(+)-MS: *m/z* (%) = 396 (100) $[M + 23]^+$. $C_{20}H_{23}NO_6$ (373.40): calcd. C 64.33, H 6.21, N 3.75; found C 64.42, H 6.2621, N 3.77.

Reaction of Ethyl (*E*)-2-Hex-1-enylindole-1-carboxylate (1c) with But-3-en-2-one (2d): A mixture of **1c** (140 mg, 0.459 mmol), **2d** (0.095 mL, 1.147 mmol) and $Mg(ClO_4)_2$ (16 mg, 0.069 mmol) in toluene (6 mL) was refluxed for 4 h, cooled to room temperature and freed from the solvent in vacuo. The residue was purified by flash column chromatography over silica gel (cyclohexane/ethyl acetate, 99.9:0.1), yielding progressively **3j** (46 mg, 34.8%) and **3′j** (41 mg, 31.5%).

Data for 3j: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2957, 2928, 2859,1736 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.36 (m, 6 H, 3 CH_2), 1.47 (m, 1 H, 4a-H), 1.52 (t, *J* = 7.1 Hz, 3 H, OCH_2), 1.81 (m, 1 H, 2-H), 2.09 (s, 3 H, OCH_3), 2.21 (m, 1 H, 4-H), 2.61 (m, 1 H, 1-H), 3.32 (m, 1 H, 1a-H), 3.84 (m, 1 H, 3-H), 4.51 (m, 2 H, OCH_2), 7.25 (m, 3 H, CH, arom.), 8.14 (d, *J* = 7.9 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (CH_3), 14.8 (CH_3), 23.3 (CH_2), 26.5 (CH_3), 29.5 (CH_2), 32.6 (CH_2), 33.5 (CH_2), 34.9 (CH), 36.6 (CH_2), 50.2 (CH), 63.4 (OCH_2), 128.8, 136.4, 137.8, 137.9 (quat. C_{sp2}), 116.2, 118.1, 123.7, 124.5 (C_{sp2}H), 152.3 (COOEt), 211.5 (COMe) ppm. ESI(+)-MS: *m/z* (%) = 364 (100) $[M + 23]^+$, 296 (40). $C_{21}H_{27}NO_3$ (341.44): calcd. C 73.87, H 7.97, N 4.10; found C 73.92, H 7.90, N 4.06.

Data for 3′j: Yellow oil. IR (KBr): $\tilde{\nu}$ = 2955, 2926, 2870, 1735, 1707 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.6 Hz, 3 H, CH_3), 1.38 (m, 2 H, CH_2), 1.44 (m, 2 H, CH_2), 1.25 (m, 1 H, 4′-H), 1.51 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.21 (m, 1 H, 4a′-H), 2.28 (s, 3 H, OCH_3), 2.51 (m, 1 H, 2′-H), 2.8 (m, 2 H, CH_2), 2.9 (m, 1 H, 3-H), 3.2 (m, 2 H, 1-H), 4.52 (q, *J* = 7.1 Hz, 2 H, OCH_2), 7.38 (m, 3 H, CH, arom.), 8.12 (d, *J* = 7.1 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (CH_3), 14.8 (CH_3), 19.6 (CH_2), 23.2 (CH_2), 28.8 (CH_2), 29.1 (CH_3), 30.2 (CH_2), 30.7 (CH_2), 35.6 (CH), 51.4 (CH), 63.2 (OCH_2), 115.5, 129.4, 134.4, 136.4 (quat. C_{sp2}), 115.9, 118.1, 123.2, 124.1 (C_{sp2}H), 152.4 (COOEt), 210.5 (COMe) ppm. ESI(+)-MS: *m/z* (%) = 364 (100) $[M + 23]^+$. $C_{21}H_{27}NO_3$ (341.44): calcd. C 73.87, H 7.97, N 4.10; found C 74.01, H 8.12, N 4.01.

Reaction of Ethyl 2-[(*E*)-2-(*p*-Tolyl)vinyl]indole-1-carboxylate (1a) with But-3-en-2-one (2d)

Method B: $Cu(OTf)_2$ or $Sc(OTf)_3$: A mixture of **1a** (100 mg, 0.328 mmol), **2d** (0.068 mL, 0.82 mmol) and $Cu(OTf)_2$ (16 mg, 0.042 mmol) or $Sc(OTf)_3$ (20 mg, 0.042 mmol) in dichloromethane (4 mL) was stirred under nitrogen for 3 h and then freed from the solvent in vacuo. The diastereoisomeric excess was determined by HPLC analysis of the crude reaction mixtures performed on a Chiralcel OD column (250 × 4.6 mm) with mobile phase hexane/2-propanol (80:10), flow rate 0.8 mL/min, temperature 30 °C and detection wavelength 230 nm. For the results see the text.

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