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Ring closing metathesis strategies towards functionalised 1,7-annulated 4,6-dimethoxyindoles

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ABSTRACT

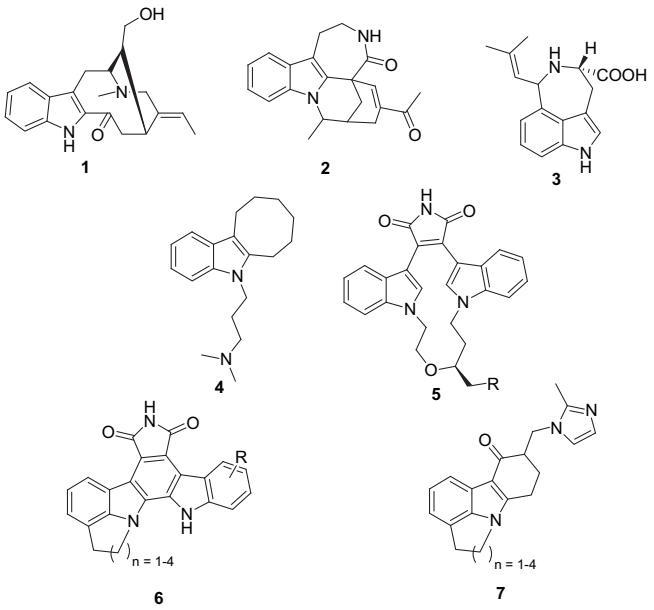
A ring closing metathesis approach has been used to prepare a novel range of indoles 1,7-annulated with nitromethyl and lactone functionalised medium-sized rings. Initial studies into the preparation of lactam functionalised rings are also discussed.

1. Introduction

The indole moiety is found extensively throughout terrestrial and aquatic natural products. Indole alkaloids have been subjected to intensive scrutiny over the years due to the frequency and variety of physiological activities displayed by these compounds. Meanwhile, many natural bioactive products possess functionalised medium-sized rings. Naturally occurring medium-sized lactones, for example, have shown anticancer[1] and antibiotic[2] activities while medium-sized lactams have potential applications in pharmaceuticals,[3–5] materials[6,7] and catalysis.[8]

Indoles annulated with medium-sized rings are an interesting class of compounds that have been found both in nature and throughout chemical synthesis. Natural examples include affinine **1** and tronocarpine **2**, which have been isolated from *Tabernaemontana hystrix*[9] and *Tabernaemontana corymbosa*,[10] respectively, as well as clavicipitic acid **3**, which is a derailment product of normal ergot metabolism.[11] Synthetic examples include iprindole **4**, which has been clinically used as an antidepressant[12] and the macrocyclic bisindolylmaleimides **5**, which are currently being developed to treat diabetic complications.[13]

However, there are only limited reports in the literature of indoles, which are 1,7-annulated with medium-sized rings, despite their potential for interesting bioactivities. The indolocarbazoles **6** are cyclin-dependent kinase inhibitors,[14] while the 1,7-annulated ondanstron derivatives **7** display a high affinity for the serotonin 5-HT_3 receptor.[15]



Synthetic approaches towards these structures are currently limited. One approach entails Stille coupling of 7-bromoindole **8** with tributylvinyltin followed by N-alkylation with 5-bromopentene and subsequent ring closing metathesis of precursor **10** (Scheme 1).[14]

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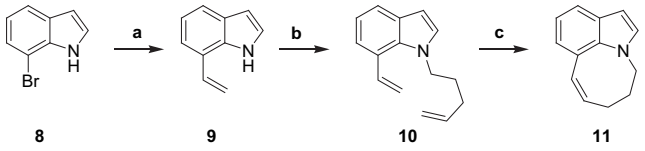
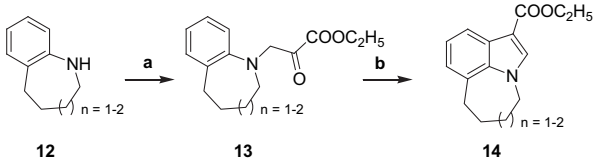


Scheme 1. (a) Tributylvinyltin, $PdPh_2Cl_2$, LiCl, PPh_3, DMF, 90 °C (b) NaH, 5-bromopentene, DMF, 0 °C (c) Grubbs' catalyst, DCM, rt.

Alternatively, the synthesis can begin from benzazepine **12** and ethylbromopyruvate followed by ring closure in the presence of magnesium chloride to form derivative **14** as reported by van Wijngaarden et al. (Scheme 2).[15]



Scheme 2. (a) $BrCH_2COCOOC_2H_5$, THF (b) $MgCl_2$, methylcellosolve.

However, neither of these approaches offers a ready capacity to introduce functionality into the medium-sized ring, which is an important goal given the high chemical functionality displayed in the natural examples. Our interest therefore lay in the development of versatile approaches to indoles 1,7-annulated with functionalised medium-sized rings. In particular, an alternative approach to cycloalkane rings and strategies towards lactone and amide functionalised rings were targeted.

In addition to the well known difficulties inherent in building eight to eleven-membered rings,[16,17] strategies towards indoles 1,7-annulated with medium-sized rings appear to be hampered by the lack of indole reactivity at C7. It has been previously shown, however, that indole C7 reactivity can be enhanced by the strategic placement of methoxy substituents on the benzenoid ring[18] and we have previously reported the C7 formylation, acylation, halogenation and nitration of a range of 4,6-dimethoxyindoles.[19–21] These 4,6-dimethoxyindoles subsequently facilitated the development of simple and versatile routes to various indoles 1,7-annulated with five- and six-membered rings[19,22–25] and were therefore selected as the starting point for this work.

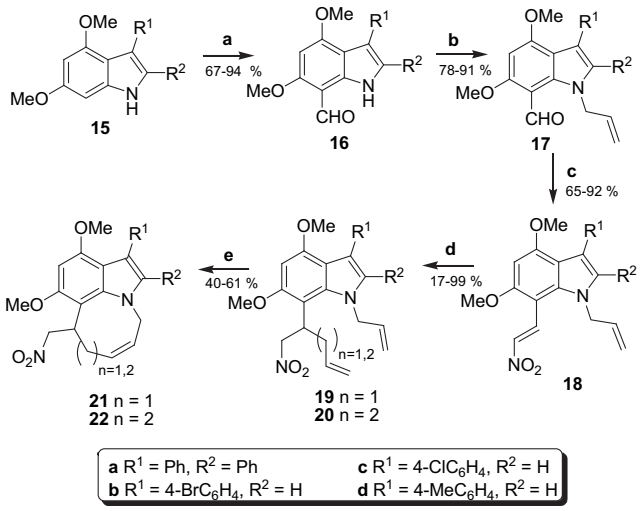
2. Results and discussion

2.1. Synthesis of cycloalkane fused indoles

Indoles 1,7-annulated with cycloalkanes bearing a nitroalkyl moiety were synthesised as shown in Scheme 3.[26] Formylation of indoles **15a**–**d** was performed at room temperature using 1 equiv of the Vilsmeier reagent. With the C2 position blocked, the reaction of indole **15a** occurred exclusively at C7. Indoles **15b**,**c** contain electron withdrawing groups at the 4′-position, which deactivates the C2 position, thus only the C7-isomers **16b**,**c** were obtained. Methylphenylindole **15d** displayed a stronger C2 electrophilic reactivity than the halogenated indoles. In the presence of 1 equiv of the Vilsmeier reagent the reaction was regioselective for C7 at room temperature, forming compound **16d**. In the presence of an excess of Vilsmeier regent, the 2,7-di-formyl product was formed at room temperature instead.

Treatment of indole-7-carbaldehydes **16a**–**d** at room temperature with potassium hydroxide and allyl bromide in dimethylsulfoxide for 1 h afforded *N*-allyl derivatives **17a**–**d** in high yields. The corresponding β-nitrostyrenes **18a**–**d** were then produced in 65–92% yields upon refluxing with nitromethane and ammonium acetate for 3 h.

Michael addition of allylmagnesium bromide to nitroalkenes **18a**–**d** was conducted under inert conditions in dry



Scheme 3. (a) $POCl_3$, DMF, rt, 2 h (b) allyl bromide, KOH, DMSO, rt, 1 h (c) CH_3NO_2, ammonium acetate, *i*-PrOH, reflux, 3 h (d) allylmagnesium bromide, THF, rt, 3 h (e) Grubbs' catalyst, toluene, reflux, 4 h.

tetrahydrofuran. The reaction mixture was quenched with aqueous ammonium chloride after 2–3 h and the resulting solution extracted with dichloromethane to give the eight-membered ring closing metathesis precursors **19a**–**d** as low melting solids. The corresponding nine-membered ring precursors **22b**–**d** were produced upon treatment of indoles **18b**–**d** with butenylmagnesium bromide in dry tetrahydrofuran. These reactions were noticeably slower, with the Michael addition typically requiring a large excess of the Grignard reagent and 3 days to reach completion. Precursors **20b**–**d** were obtained as oils in 17–54% yields.

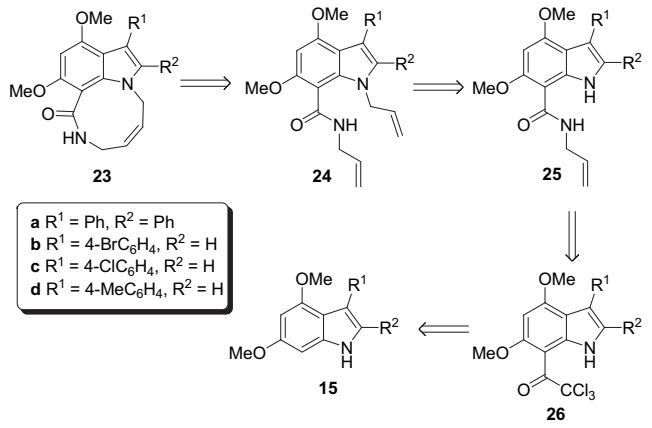
Ring closing metathesis of Michael adducts **19a**–**d** and **20b**–**d** afforded the indole fused eight-membered rings **21a**–**d** and indole fused nine-membered rings **22b**–**d**, respectively. Ring closing metathesis was achieved by refluxing in dry, degassed toluene in the presence of second generation Grubbs' catalyst for 4 h.

The corresponding synthesis of 10- and 11-membered ring systems was attempted via extension of the alkyl chain in the N-alkylation step. The 1-pentene and 1-hexene derivatives of **17** readily underwent the Henry reaction and subsequent Michael addition, however, the ring closing metathesis proved problematic and only starting materials were recovered after heating at reflux for 3 days. Direct ring closure of the 1-pentene derivative of **18** was also examined but again no reaction was apparent, likely due to the nitro group inhibiting the catalyst turnover.

2.2. Synthesis of lactone fused indoles

It was envisaged that indole fused lactones of type **23** could be prepared via the ring closing metathesis of precursor **24**, which in turn would be assessable through alkylation of the corresponding indole-7-carboxylic acids **25**. Previous work by Black et al.[19,27] indicated indole-7-carboxylic acids **25** could be obtained through trihaloacetylation of indoles **15** with trifluoroacetic anhydride followed by treatment with hydroxide ions (Scheme 4).

Trifluoroacetylation of indoles **15b** and **15d** was performed by stirring at room temperature for 2 h with trifluoroacetic anhydride in tetrahydrofuran. In contrast to the literature precedent, the *N*-trifluoroacetylindole isomer was produced in addition, or even in preference, to the desired 7-trifluoroacetylindoles **26b**,**d**. The efficiency of the reaction was therefore enhanced by the prior introduction of an N1 blocking group, with the *N*-allyl derivatives of **15b** and **15d** undergoing regioselective C7 trifluoroacetylation in good yields. However, subsequent conversion of the *N*-allyl derivatives of **26b**,**d** to the corresponding acids proved problematic.



Scheme 4.

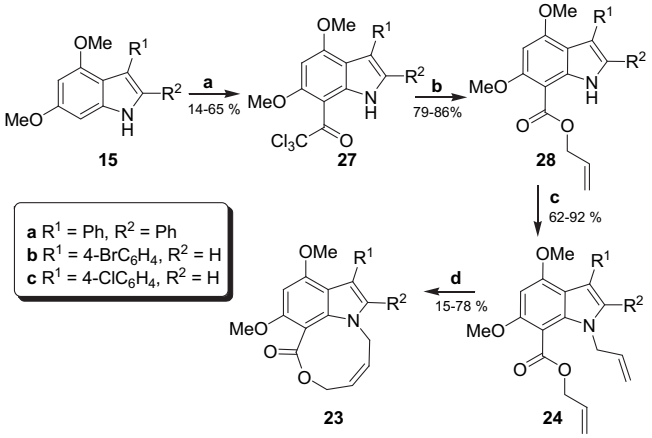
The reactions were very low yielding and the isolated solids were impure even after optimisation.

An alternate strategy was therefore to bypass the formation of the carboxylic acid intermediate and to form the ester directly from the trihaloacetylindole. Literature reports have shown that trifluoromethyl ketones cannot be directly converted into esters but that this can be achieved in a single step from the related trichloromethyl ketones.[27,28]

In contrast to trifluoroacetic anhydride, trichloroacetic anhydride does not react with indoles **15** even under vigorous conditions.[27] Trichloroacetylindole derivatives **27** were therefore formed via treatment with trichloroacetyl chloride. Heating 2,3-disubstituted indole **15a** at reflux with a five-times excess of trichloroacetyl chloride successfully afforded trichloroacetylindole **27a** as a single product. Similar treatment of the 3-substituted indoles **15b**,**c** afforded four compounds according to thin layer chromatography analysis. In accordance with the literature, the major reaction products were the 7-trichloroacetylindoles **27b**,**c** and the isomeric 2-trichloroacetylindoles. The minor products, present only in trace amounts, were identified as the *N*- and 2,7-disubstituted isomers.

Alcoholysis of 7-trichloroacetylindoles **27a**–**c** was achieved by heating at reflux in tetrahydrofuran for 2 h with allyl alcohol and potassium hydroxide. The indole-7-carboxylic esters **28a**–**c** were obtained in 79–86% yield. Ring closing metathesis precursors **24a**–**c** were subsequently synthesised by N-alkylation of indoles **28a**–**c** with allyl bromide in a basic solution of dimethylsulfoxide (Scheme 5).

Ring closing metathesis of precursor **24a** was performed by heating under reflux for 5 h in a dry, degassed solution of toluene with 5–10 mol % of second generation Grubbs' catalyst. The ^{1}H NMR spectrum of the resulting solid was not indicative of the target structure



Scheme 5. (a) Trichloroacetyl chloride, DCE, reflux, 3 h (b) allyl alcohol, THF, reflux, 2 h (c) allyl bromide, KOH, DMSO, rt, 4 h (d) Grubbs' catalyst, toluene, reflux, 5 h.

23a. Two methoxy groups were present as singlets at δ 3.74 and δ 3.96, the H5 proton appeared as a singlet at δ 6.29 and two phenyl rings appeared as multiplets at δ 7.14 and δ 7.29. In addition, two signals, integrating for 1H each, appeared at δ 5.63 and 6.03, which was consistent with a –CH=CH– group. These signals had a doublet of a triplet splitting pattern, which suggested that they each possessed a CH_2 neighbour, however, the only other signal present in the spectrum was a multiplet at δ 4.65, which integrated for 1H. Similarly, the DEPT135 experiment did not reveal the presence of any CH_2 groups.

High-resolution mass spectrometry showed the product had an *m*/*z* of 426.1705, which was consistent with $C_{27}H_{24}NO_4$ for the expected structure **23a**. It was therefore conjectured that the flexibility of the nine-membered ring was influencing the relaxation time of the CH_2 groups, resulting in an unusual NMR spectrum. A variable temperature ^{1}H NMR experiment was subsequently conducted. Heating the sample to 330 K resulted in a very broad peak appearing at δ 4.25. As the sample was cooled to 230 K this peak sharpened and merged with the original signal at δ 4.65. Despite the appearance of a missing signal in the variable temperature experiment, the integration of the peaks still lacked two hydrogens of the proposed structure **23a**. Final confirmation of structure **23a** was therefore obtained through X-ray crystallography (Fig. 1).

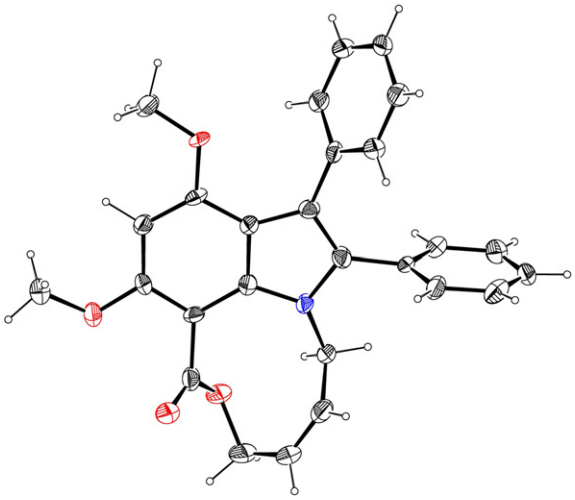
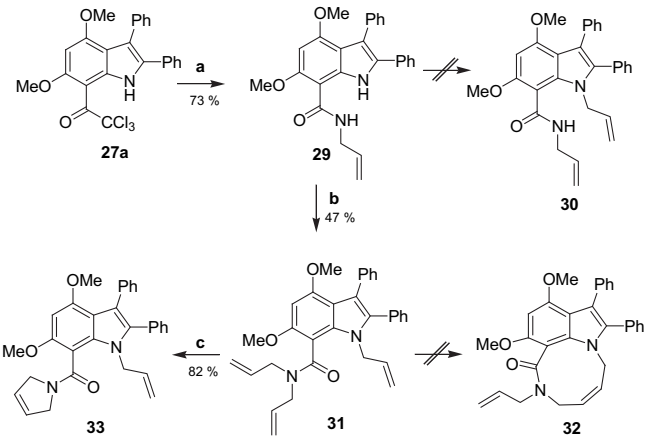


Fig. 1. OTREP diagram of compound **23a**.[29]

Ring closing metathesis of indoles **24b**,**c** led to the formation of the corresponding esters **23b**,**c**. In contrast to the ^{1}H NMR spectrum of compound **23a**, the spectra of analogues **23b**,**c** contained all the expected signals. The ^{1}H NMR spectrum of indole **23c** was characteristic for these compounds, displaying singlets at δ 3.79 and δ 3.84 (3H each) corresponding to the methoxy groups and doublets at δ 7.29 and 7.43 (each 2H, *J*=8.2 Hz) corresponding to the *p*-substituted aryl protons. H8 and H11 were present as singlets (1H each) at δ 6.83 and δ 6.28, respectively, while H3 and H6 appeared as doublets at δ 4.65 (2H, *J*=2.3 Hz) and δ 4.72 (2H, *J*=4.9 Hz). Finally, H4 and H5 appeared as doublet of triplets at δ 5.49 (1H, *J*=3.8 and 15.5 Hz) and δ 5.89 (1H, *J*=5.3 and 15.5 Hz).

2.3. Attempted synthesis of amide fused indoles

It was envisaged that amide analogues of structure **23** could be prepared through the treatment of trichloroacetylindole derivatives **27** with allyl amine followed by N-alkylation and ring closing metathesis. Indole-7-carboxamide **29** was successfully produced in 88% yield by heating the parent indole **27a** at reflux with allyl amine in tetrahydrofuran for 2 h (Scheme 6).



Scheme 6. (a) Allyl amine, THF, reflux, 2 h (b) allyl bromide, KOH, DMSO, rt, 3 h (c) Grubbs' catalyst, toluene, reflux, 5 h.

Subsequent N-alkylation proved to be problematic. When indole **29** was treated with potassium hydroxide and allyl bromide in dimethylsulfoxide for 3 h, alkylation occurred at both the amide and N1 positions to produce indole **31** in preference to the target precursor **30**. Conversely, heating indole **29** at reflux in acetone with allyl bromide and potassium carbonate resulted only in recovery of the starting material. Attention consequently turned to the use of a secondary amine for the preparation of carboxamides, with a benzyl group being initially selected as a blocking group because it could later be removed through hydrogenation. The reaction of indole **27a** with *N*-benzyl-*N*-allylamine was investigated but only a trace amount of a product was observed, even under vigorous conditions and in the presence of a large excess of the amine. The reaction of indole **27a** with the less bulky *N*-methyl-*N*-allylamine was also examined, but again only a trace amount of product was apparent by thin layer chromatography.

Ring closing metathesis of the over alkylated product **31** was performed by heating at reflux for 5 h in a dry, degassed solution of toluene with 5–10 mol% of second generation Grubbs' catalyst, affording a single product as an off white solid. It was anticipated that the five-membered ring structure **33** would be favoured over the desired nine-membered fused system **32**, however, Basu and Waldmann have reported a diene-ene ring closing metathesis reaction that gave a 2:3 ratio of five- and seven-membered cyclic ethers.[30] The ^{1}H NMR spectrum showed 11 alkyl protons, while four CH_2 groups appeared in the DEPT135 ^{13}C NMR experiment, indicating that ring closure had occurred. However, differentiating between structures **33** and **32** using 1D and 2D NMR was difficult due to the CH_2 groups having diastereotopic protons, which overlapped with the other alkyl signals. Structure confirmation was therefore obtained through X-ray crystallography, which showed that the five-membered ring compound **33** was produced (Fig. 2).

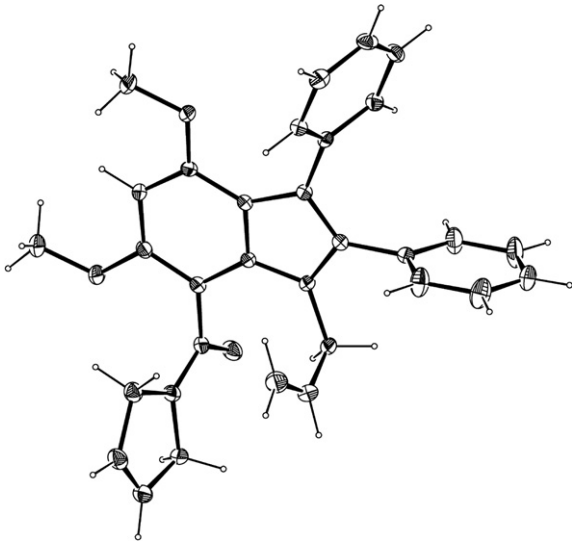


Fig. 2. ORTEP diagram of amide **33**.[29]

3. Conclusion

Ring closing metathesis strategies towards functionalised 1,7-annulated 4,6-dimethoxyindoles have been presented. The activation of the C7 indole position provided convenient access to cycloalkane and lactone fused indoles. Alternative pathways to lactam fused indoles needs to be investigated in order to overcome the similar reactivity of the indole and amide nitrogen atoms.

4. Experimental

4.1. General methods

Melting points were measured using a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Mattson Genesis Series FTIR spectrophotometer as KBr disks. Ultraviolet spectra were measured using a Varian Cary 100 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained in the designated solvents on a Bruker DPX 300 or a Bruker AVANCE DMX 600 spectrometer as designated. Low resolution ESI$^+$ mass spectra were recorded on a VG Quatro mass spectrometer at 70eV ionization voltage and 200 °C ion source temperature at the Bioanalytical Mass Spectrometry unit, UNSW. High-resolution mass spectrometry was performed by the Mass Spectrometry unit at the University of Otago, New Zealand or Mass Spectrometry Lab of Monash University. Microanalysis was performed on a Carlo Erba Elemental Analyzer EA 1108 at the Campbell Microanalytical Laboratory, University of Otago, New Zealand. Anhydrous solvents were obtained using a PureSolv MD Solvent Purification System. Ajax Finechem Silica 200–325 mesh was used for column chromatography and Merck silica gel 60H was used for flash chromatography.

*4.1.1. 4,6-Dimethoxy-2,3-diphenyl-1H-indole-7-carbaldehyde (**16a**).* Indole **15a** (1.99 g, 6.05 mmol) was added to a mixture of phosphorus oxychloride (0.7 mL, 7.65 mmol) in *N*,*N*-DMF (20 mL). The reaction was stirred at room temperature for 2.5 h before being quenched with water (100 mL) and made basic with sodium hydroxide solution (1 M). The resulting precipitate was collected to give the *title compound* **16a** as a yellow solid (1.98 g, 92%). Mp 180–182 °C. Lit.[31] mp 183–184 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 6.15 (s, 1H, H5), 7.23–7.36 (m, 10H, ArH), 10.41 (s, 1H, CHO), 10.59 (br s, 1H, NH).

*4.1.2. 3-(4-Bromophenyl)-4,6-dimethoxy-1H-indole-7-carbaldehyde (**16b**).* This compound was prepared by the same method as compound **16a**, from indole **15b** (1.01 g, 3.03 mmol), phosphorus oxychloride (0.5 mL, 5.5 mmol) and *N*,*N*-DMF (10 mL). The *title compound* **16b** desired indole was obtained as a yellow solid (1.03 g, 94%) mp 207–209 °C. Lit.[31] mp 203–206 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.19 (s, 1H, H5), 7.08 (s, 1H, H2), 7.43 (d, J=8.7 Hz, 2H, ArH), 7.48 (d, J=8.7 Hz, 2H, ArH), 10.38 (s, 1H, CHO), 10.54 (br s, 1H, NH).

*4.1.3. 3-(4-Chlorophenyl)-4,6-dimethoxy-1H-indole-7-carbaldehyde (**16c**).* This compound was prepared by the same method as compound **16a**, from indole **15c** (1.99 g, 6.95 mmol), phosphorus oxychloride (0.7 mL, 7.6 mmol) and *N*,*N*-DMF (10 mL). The *title compound* **16c** was obtained as a yellow solid (1.84 g, 84%). Mp

218–220 °C. Lit.[33] mp 223–224 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.92 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.19 (s, 1H, H5), 7.07 (d, J=2.3 Hz, 1H, H2), 7.33 (d, J=8.7 Hz, 2H, ArH), 7.49 (d, J=8.7 Hz, 2H, ArH), 10.38 (s, 1H, CHO), 10.53 (br s, 1H, NH).

*4.1.4. 4,6-Dimethoxy-3-(4-methylphenyl)-1H-indole-7-carbaldehyde (**16d**).* This compound was prepared by the same method as compound **16a**, from indole **15d** (1.95 g, 7.30 mmol), phosphorus oxychloride (0.7 mL, 7.6 mmol) and *N*,*N*-DMF (10 mL). The *title compound* **16d** was obtained as a light tan solid (1.51 g, 67%). Mp 217–219 °C. Found: C, 73.31; H, 5.91; N, 4.82%. $C_{18}H_{17}NO_3$ requires: C, 73.20; H, 5.80; N, 4.74%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.11 (s, 1H, H5), 7.00 (d, J=2.3 Hz, 1H, H2), 7.11 (d, J=7.9 Hz, 2H, ArH), 7.40 (d, J=7.9 Hz, 2H, ArH), 10.31 (s, 1H, CHO), 10.42 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 55.8, 56.7, 87.1, 104.8, 110.6, 119.2, 121.9, 128.9, 129.7, 132.8, 136.0, 138.1, 161.9, 163.4, 188.7. IR (KBr): ν_{max} 3392, 2995, 2933, 2838, 1627, 1585, 1547, 1511, 1451, 1332, 1258, 1214, 1143, 1085, 1044, 965, 822, 807 cm^{-1}. UV–vis (MeOH): λ_{max} 294 nm (ε 9793 cm^{-1} M^{-1}), 262 (14,518), 226 (29,480). MS (ESI$^+$): m/z 318.07, [M+Na]$^+$.

*4.1.5. 1-Allyl-4,6-dimethoxy-2,3-diphenyl-1H-indole-7-carbaldehyde (**17a**).* Indole **16a** (2.44 g, 6.83 mmol) and then allyl bromide (2.3 mL, 0.027 mol) were added to a solution of potassium hydroxide (1.49 g, 0.027 mol) in DMSO (80 mL). The reaction was stirred at room temperature for 1 h and then quenched with water (100 mL). The resulting precipitate was collected to give the *title compound* **17a** as a light yellow solid (2.11 g, 78%). Mp 152–154 °C. Lit.[32] mp 156–157 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.72 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.37 (dd, J=17.1, 1.5 Hz, 1H, H3′), 4.82 (dd, J=10.3, 1.5 Hz, 1H, H3′), 4.97–4.98 (m, 2H, H1′), 5.30–5.42 (m, 1H, H2′), 6.19 (s, 1H, H5), 7.06–7.20 (m, 10H, ArH), 10.42 (s, 1H, CHO).

*4.1.6. 1-Allyl-3-(4-bromophenyl)-4,6-dimethoxy-1H-indole-7-carbaldehyde (**17b**).* This compound was prepared by the same method as compound **17a**, from indole **16b** (1.03 g, 2.88 mmol), allyl bromide (0.48 mL, 5.55 mmol), potassium hydroxide (0.63 g, 1.10 mmol) and DMSO (15 mL). The *title compound* **17b** was obtained as a light tan solid (1.04 g, 91%). Mp 188–190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 4.83 (dd, J=17.3, 1.5 Hz, 1H, H3′), 5.05 (dd, J=10.2, 1.5 Hz, 1H, H3′), 5.12–5.14 (m, 2H, H1′), 5.79–5.91 (m, 1H, H2′), 6.25 (s, 1H, H5), 6.90 (s, 1H, H2), 7.36 (d, J=8.7 Hz, 2H, ArH), 7.46 (d, J=8.7 Hz, 2H, ArH), 10.44 (s, 1H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.8, 55.6, 57.4, 87.9, 107.4, 112.9, 116.7, 117.9, 120.4, 129.0, 130.9, 131.6, 134.6, 134.8, 136.3, 160.8, 164.9, 188.3. IR (KBr): ν_{max} 2938, 2847, 1656, 1577, 1558, 1543, 1459, 1360, 1260, 1215, 1187, 1130, 1070, 1035, 1010, 794, 592 cm^{-1}. UV–vis (MeOH): λ_{max} 338 nm (ε 13,247 cm^{-1} M^{-1}), 258 (29,019), 228 (25,593). HRMS (ESI$^+$): found m/z 422.0345, [M+Na]$^+$; $C_{20}H_{18}{}^{79}BrNNaO_3$ required 422.0368.

*4.1.7. 1-Allyl-3-(4-chlorophenyl)-4,6-dimethoxy-1H-indole-7-carbaldehyde (**17c**).* This compound was prepared by the same method as compound **17a**, from indole **16c** (1.95 g, 6.17 mmol), allyl bromide (0.8 mL, 9.24 mmol), potassium hydroxide (1.21 g, 2.20 mol) and DMSO (40 mL). The *title compound* **17c** was obtained as a white solid (1.24 g, 91%). Mp 188–190 °C. Lit.[32] mp 186–188 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.80 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.79–4.86 (m, 1H, H3′), 5.03–5.06 (m, 1H, H3′), 5.11–5.14 (m, 2H, H1′), 5.78–5.91 (m, 1H, H2′), 6.17 (s, 1H, H5), 6.83 (s, 1H, H2), 7.24 (d, J=8.5 Hz, 2H, ArH), 7.35 (d, J=8.5 Hz, 2H, ArH), 10.37 (s, 1H, CHO).

*4.1.8. 1-Allyl-4,6-dimethoxy-3-(4-methylphenyl)-1H-indole-7-carbaldehyde (**17d**).* This compound was prepared by the same method as compound **17a**, from indole **16d** (1.51 g, 4.89 mmol), allyl bromide (0.85 mL, 9.82 mmol), potassium hydroxide (1.13 g, 2.00 mol) and DMSO (15 mL). The *title compound* **17d** was obtained as a white solid (1.52 g, 89%). Mp 124–126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.77 (dd, J=1.5, 17.2 Hz, 1H, H3′), 4.97 (dd, J=1.5, 10.3 Hz, 1H, H3′), 5.04–5.07 (m, 2H, H1′), 5.72–5.83 (m, 1H, H2′), 6.17 (s, 1H, H5), 6.82 (s, 1H, H2), 7.09 (d, J=8.0 Hz, 2H, ArH), 7.33 (d, J=8.0 Hz, 2H, ArH), 10.37 (s, 1H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 53.7, 55.6, 57.4, 87.8, 107.3, 113.3, 116.6, 119.0, 128.7, 128.9, 129.9, 132.9, 134.8, 135.9, 136.3, 161.1, 164.8, 188.3. IR (KBr): ν_{max} 2938, 2847, 1654, 1578, 1563, 1548, 1461, 1435, 1395, 1362, 1330, 1264, 1215, 1182, 1127, 1036, 918, 797, 784, 545 cm^{-1}. UV–vis (MeOH): λ_{max} 339 nm (ε 8358 cm^{-1} M^{-1}), 258 (23,797), 225 (18,249). HRMS (ESI$^+$): found m/z 336.1593, [M+H]$^+$; $C_{21}H_{22}NO_3$ required 336.1600.

*4.1.9. 1-Allyl-4,6-dimethoxy-2,3-diphenyl-7-(2-nitrovinyl)-1H-indole (**18a**).* A mixture of indole **17a** (2.08 g, 5.24 mmol), nitromethane (2.2 mL, 0.041 mol) and ammonium acetate (1.75 g, 0.023 mol) were heated at reflux in isopropanol (70 mL) for 3 h. The precipitate produced upon cooling was collected to give the *title compound* **18a** as a red solid (1.884 g, 82%). Mp 202–204 °C. Found: C, 73.60; H, 5.50; N, 6.36%. $C_{27}H_{24}N_2O_4$ requires: C, 73.62; H, 5.49; N, 6.36%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.79 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.75–4.76 (m, 2H, H1′), 5.05 (dd, J=17.1, 0.9 Hz, 1H, H3′), 5.34 (dd, J=10.6, 0.9 Hz, 1H, H3′), 5.97–6.09 (m, 1H, H2′), 6.33 (s, 1H, H5), 7.16–7.29 (m, 10H, ArH), 8.02 (d, J=12.8 Hz, 1H, H2″), 8.77 (d, J=12.8 Hz, 1H, H1″). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.6, 55.3, 56.3, 88.3, 98.0, 113.0, 116.4, 117.5, 125.7, 126.8, 128.1, 128.3, 131.3, 131.3, 131.4, 132.7, 134.0, 135.2, 136.2, 137.4, 138.9, 158.7, 160.2. IR (KBr): ν_{max} 2938, 1637, 1611, 1582, 1487, 1463, 1358, 1303, 1251, 1207, 1182, 1155, 1126, 1041, 970, 744, 698 cm^{-1}. UV–vis (MeOH): λ_{max} 283 nm (ε 6992 cm^{-1} M^{-1}), 229 (15,637). MS (ESI$^+$): m/z 463.09, [M+Na]$^+$.

*4.1.10. 1-Allyl-3-(4-bromophenyl)-4,6-dimethoxy-7-(2-nitrovinyl)-1H-indole (**18b**).* This compound was prepared by the same method as compound **18a**, from indole **17b** (1.04 g, 2.59 mmol), nitromethane (1.1 mL, 0.021 mol), ammonium acetate (0.88 g, 0.011 mol) and isopropanol (80 mL). The *title compound* **18b** was obtained as a red solid (0.750 g, 65%). Mp 144–146 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.85 (t, J=2.1 Hz, 2H, H1′), 5.03 (d, J=17.2 Hz, 1H, H3′), 5.26 (d, J=10.5 Hz, 1H, H3′), 6.01–6.10 (m, 1H, H2′), 6.24 (s, 1H, H5), 6.81 (s, 1H, H2), 7.31 (d, J=8.5 Hz, 2H, H2‴, H6‴), 7.41 (d, J=8.5 Hz, 2H, H3‴, H5‴), 7.93 (d, J=12.9 Hz, 1H, H2″), 8.52 (d, J=12.9 Hz, 1H, H1″). ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.8, 55.7, 56.7, 88.5, 98.3, 112.3, 117.5, 118.4, 120.6, 128.8, 131.0, 131.6, 132.3, 133.2, 134.5, 136.6, 137.8, 158.9, 160.6. IR (KBr): ν_{max} 2934, 1612, 1577, 1485, 1462, 1359, 1303, 1256, 1239, 1207, 1177, 1138, 1071, 1049, 970 cm^{-1}. UV–vis (MeOH): λ_{max} 287 nm (ε 40,399 cm^{-1} M^{-1}), 225 (80,537). HRMS (ESI$^+$): found m/z 467.0384, [M+Na]$^+$; $C_{21}H_{19}{}^{81}BrN_2NaO_4$ required 467.0405.

*4.1.11. 1-Allyl-3-(4-chlorophenyl)-4,6-dimethoxy-7-(2-nitrovinyl)-1H-indole (**18c**).* This compound was prepared by the same method as compound **18a**, from indole **17c** (1.72 g, 4.84 mmol), nitromethane (2.0 mL, 0.037 mol), ammonium acetate (1.45 g, 0.019 mol) and isopropanol (50 mL). The *title compound* **18c** was obtained as a red solid (1.53 g, 79%). Mp 146–148 °C. Found: C, 63.08; H, 4.88; N, 6.72%. $C_{21}H_{19}ClN_2O_4$ requires: C, 63.24; H, 4.80; N, 7.02%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.93 (t, J=2.0 Hz, 2H, H1′), 5.11 (d, J=17.1 Hz, 1H, H3′), 5.34 (d, J=10.4 Hz, 1H, H3′), 6.09–6.19 (m, 1H, H2′), 6.32 (s, 1H, H5), 6.87 (s, 1H, H2), 7.32 (d, J=8.4 Hz, 2H, H3‴, H5‴), 7.44 (d, J=8.4 Hz, 2H, H2‴, H6‴), 7.80 (d, J=12.8 Hz, 1H, H2″), 8.60 (d, J=12.8 Hz, 1H, H1″). ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.8, 55.7, 56.7, 88.5, 98.3, 112.6, 117.6, 118.3, 128.0, 128.8, 131.2, 132.3, 132.4, 133.2, 134.0, 136.6, 137.8, 158.9, 160.6. IR (KBr): ν_{max} 2939, 2841, 1610, 1578, 1560, 1486, 1460,

1303, 1257, 1239, 1206, 1177, 1136, 1091, 1050, 971 cm^{-1}. UV–vis (MeOH): λ_{max} 281 nm (ε 15,382 cm^{-1} M^{-1}), 232 (30,580). MS (ESI^+): *m/z* 421.04, $[M+Na]^+$. 421.0931 (100.0%), 423.0902 (32.0%).

*4.1.12. 1-Allyl-3-(4-methylphenyl)-4,6-dimethoxy-7-(2-nitrovinyl)-1H-indole (**18d**).* This compound was prepared by the same method as compound **18a**, from indole **17d** (1.41 g, 4.04 mmol), nitromethane (1.9 mL, 0.035 mol), ammonium acetate (1.39 g, 0.018 mol) and isopropanol (50 mL). The *title compound* **18d** was obtained as a red solid (1.46 g, 92%). Mp 147–149 °C. Found: C, 70.09; H, 6.00; N, 7.52%. $C_{22}H_{22}N_2O_4$ requires: C, 69.83; H, 5.86; N, 7.40%. ^1H NMR (300 MHz, $CDCl_3$): δ 2.49 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.82–4.85 (m, 2H, H1′), 5.10 (dd, *J*=16.9, 0.6 Hz, 1H, H3′), 5.25 (dd, *J*=10.5, 0.6 Hz, 1H, H3′), 6.01–6.11 (m, 1H, H2′), 6.30 (s, 1H, H5), 6.86 (s, 1H, H2), 7.18 (d, *J*=7.9 Hz, 2H, H3‴, H5‴), 7.42 (d, *J*=7.9 Hz, 2H, H2‴, H6‴), 8.01 (d, *J*=12.9 Hz, 1H, H2″), 8.61 (d, *J*=12.9 Hz, 1H, H1″). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 52.8, 55.7, 56.7, 88.3, 98.3, 112.8, 118.2, 118.7, 128.7, 128.8, 129.9, 132.5, 133.3, 136.2, 136.4, 137.8, 159.3, 160.6. IR (KBr): ν_{max} 2936, 2839, 1608, 1578, 1460, 1357, 1298, 1257, 1239, 1208, 1177, 1044, 968, 800 cm^{-1}. UV–vis (MeOH): λ_{max} 278 nm (ε 13,244 cm^{-1} M^{-1}), 232 (28,273). MS (ESI^+): *m/z* 401.07, $[M+Na]^+$.

*4.1.13. 1-Allyl-4,6-dimethoxy-2,3-diphenyl-7-(1-nitropent-4-en-2-yl)-1H-indole (**19a**).* Allylmagnesium bromide (3 mL, 1 M) was added to indole **18a** (0.757 g, 1.72 mmol) in anhydrous THF (40 mL) and the reaction stirred at room temperature under an argon atmosphere for 18 h. The reaction was quenched with ammonium chloride solution (50 mL) and extracted with DCM (3×15 mL). The combined organic layers were dried over anhydrous sodium sulfate and reduced in vacuo to give the *title compound* **19a** as a light tan solid (0.697 g, 84%). Mp 172–174 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.67 (dd, *J*=7.1 Hz, 2H, H3″), 3.67 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.31–4.41 (m, 1H, H2″), 4.75–5.28 (m, 8H, H1′, H3′, H1″, H5″), 5.64–5.78 (m, 1H, H4″), 5.97–6.08 (m, 1H, H2′), 6.33 (s, 1H, H5), 7.10–7.25 (m, 10H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.0, 36.9, 48.6, 55.1, 56.2, 78.9, 89.6, 103.8, 113.4, 115.4, 116.1, 117.1, 125.1, 126.5, 127.8, 127.9, 131.3, 131.4, 132.0, 135.4, 135.9, 136.0, 136.2, 138.9, 153.7, 155.8. IR (KBr): ν_{max} 2936, 2838, 1598, 1586, 1548, 1502, 1442, 1408, 1379, 1360, 1320, 1256, 1208, 1176, 1122, 1069, 1039, 920, 733, 699 cm^{-1}. UV–vis (MeOH): λ_{max} 298 nm (ε 12,464 cm^{-1} M^{-1}), 238 (29,264), 223 (37,840). HRMS (ESI^+): found *m/z* 483.2271, $[M+H]^+$; $C_{30}H_{31}N_2O_4$ required 483.2284.

*4.1.14. 1-Allyl-3-(4-bromophenyl)-4,6-dimethoxy-7-(1-nitropent-4-en-2-yl)-1H-indole (**19b**).* This compound was prepared by the same method as compound **19a**, from indole **18b** (0.302 g, 0.68 mmol), allylmagnesium bromide (3 mL, 1 M) and anhydrous THF (15 mL) The *title compound* **19b** was obtained as a light brown solid (0.33 g, 99%). Mp 74–76 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.64 (dd, *J*=7.3 Hz, 2H, H3″), 3.78 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.17–4.26 (m, 1H, H2″), 4.84–5.25 (m, 8H, H1′, H3′, H1″, H5″), 5.59–5.72 (m, 1H, H4″), 6.07–6.19 (m, 1H, H2′), 6.33 (s, 1H, H5), 6.82 (s, 1H, H2), 7.38 (d, *J*=8.7 Hz, 2H, ArH), 7.45 (d, *J*=8.7 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.2, 36.6, 51.9, 54.9, 56.2, 78.6, 89.3, 103.6, 112.5, 115.9, 116.6, 117.3, 119.5, 128.9, 130.3, 131.2, 134.0, 134.8, 135.8, 136.3, 153.6, 155.7. IR (KBr): ν_{max} 3075, 2936, 2839, 1609, 1585, 1548, 1463, 1403, 1375, 1336, 1204, 1127, 1070, 1047, 1008, 918, 832, 797 cm^{-1}. UV–vis (MeOH): λ_{max} 295 nm (ε 13,104 cm^{-1} M^{-1}), 226 (28,097). HRMS (ESI^+): found *m/z* 507.0892, $[M]^+$; $C_{24}H_{25}{}^{79}BrN_2NaO_4$ required 507.0895.

*4.1.15. 1-Allyl-3-(4-chlorophenyl)-4,6-dimethoxy-7-(1-nitropent-4-en-2-yl)-1H-indole (**19c**).* This compound was prepared by the same method as compound **19a**, from indole **18c** (0.466 g, 1.17 mmol), allylmagnesium bromide (3.5 mL, 1 M) and anhydrous THF (15 mL). The *title compound* **19c** was obtained as a light brown solid (0.27 g, 52%). Mp 70–72 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.56 (dd, *J*=7.4 Hz, 2H, H3″), 3.71 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.15 (dt, *J*=7.2 Hz, 1H, H2″), 4.80–5.18 (m, 8H, H1′, H3′, H1″, H5″), 5.52–5.66 (m, 1H, H4″), 6.00–6.12 (m, 1H, H2′), 6.25 (s, 1H, H5), 6.74 (s, 1H, H2), 7.23 (d, *J*=8.6 Hz, 2H, H3‴, H5‴), 7.38 (d, *J*=8.6 Hz, 2H, H2‴, H6‴). ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.6, 37.1, 52.4, 55.4, 56.7, 79.1, 89.7, 104.2, 113.0, 116.4, 117.0, 117.8, 127.8, 129.4, 131.3, 131.9, 134.5, 134.8, 136.3, 136.8, 154.1, 156.2. IR (KBr): ν_{max} 3078, 2937, 2840, 1610, 1585, 1548, 1488, 1463, 1376, 1336, 1270, 1204, 1127, 1089, 1047, 919, 835, 798 cm^{-1}. UV–vis (MeOH): λ_{max} 295 nm (ε 12,579 cm^{-1} M^{-1}), 226 (26,779). HRMS (ESI^+): found *m/z* 441.1577, $[M+H]^+$; $C_{24}H_{26}{}^{35}ClN_2O_4$ required 441.1581.

*4.1.16. 1-Allyl-4,6-dimethoxy-3-(4-methylphenyl)-7-(1-nitropent-4-en-2-yl)-1H-indole (**19d**).* This compound was prepared by the same method as compound **19a**, from indole **18d** (0.752 g, 1.99 mmol), allylmagnesium bromide (5.5 mL, 1 M) and anhydrous THF (35 mL). The *title compound* **19d** was obtained as a brown sticky residue (0.30 g, 36%). ^1H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H, CH_3), 2.54–2.59 (m, 2H, H3″), 3.71 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.16 (dt, *J*=7.2 Hz, 1H, H2″), 4.75–5.17 (m, 8H, H1′, H3′, H1″, H5″), 5.52–5.66 (m, 1H, H4″), 6.00–6.13 (m, 1H, H2′), 6.24 (s, 1H, H5), 6.73 (s, 1H, H2), 7.08 (d, *J*=7.8 Hz, 2H, ArH), 7.35 (d, *J*=7.8 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.3, 36.7, 51.9, 55.1, 56.3, 78.8, 89.3, 103.6, 112.9, 116.5, 117.1, 117.3, 128.2, 128.9, 129.5, 132.9, 134.3, 135.1, 136.0, 136.3, 153.9, 155.6. IR (KBr): ν_{max} 2920, 1607, 1587, 1549, 1509, 1463, 1375, 1338, 1201, 1176, 1125, 1051, 823, 792 cm^{-1}. UV–vis (MeOH): λ_{max} 291 nm (ε 15,194 cm^{-1} M^{-1}), 233 (34,929). HRMS (ESI^+): found *m/z* 421.2124, $[M+H]^+$; $C_{25}H_{29}N_2O_4$ required 421.2127.

*4.1.17. 1-Allyl-3-(4-bromophenyl)-4,6-dimethoxy-7-(1-nitrohex-5-en-2-yl)-1H-indole (**20b**).* Butenylmagnesium bromide (8 mL, 0.5 M) was added to indole **18b** (0.767 g, 1.73 mmol) in anhydrous THF (20 mL) and the reaction stirred at room temperature under an argon atmosphere for 3 days. The reaction was quenched with ammonium chloride solution (50 mL) and extracted with DCM (3×15 mL). The combined organic layers were dried over anhydrous sodium sulfate and reduced in vacuo to give the *title compound* **20b** as a light orange sticky residue (0.465 g, 54%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.86–2.08 (m, 4H, H3″, H4″), 3.77 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.09–4.18 (m, 1H, H2″), 4.74 (dd, *J*=12.6, 5.6 Hz, 1H, H1″), 4.85–4.97 (m, 6H, H1′, H3′, H1″, H6′), 5.21 (dd, *J*=10.5, 1.0 Hz, 1H, H3′), 5.69–5.79 (m, 1H, H5″), 6.04–6.15 (m, 1H, H2′), 6.31 (s, 1H, H5), 6.82 (s, 1H, H2), 7.38 (d, *J*=8.6 Hz, 2H, H2‴, C6‴), 7.45 (d, *J*=8.6 Hz, 2H, H3‴, H5‴). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.3, 32.2, 35.8, 52.5, 55.4, 56.7, 79.7, 89.8, 104.1, 113.0, 115.3, 116.5, 117.0, 120.0, 129.4, 130.8, 131.6, 134.5, 135.3, 137.1, 138.5, 154.1, 156.3. IR (KBr): ν_{max} 3074, 2934, 2842, 1608, 1584, 1546, 1463, 1405, 1377, 1335, 1203, 1128, 1071, 1036, 1005, 920, 796 cm^{-1}. UV–vis (MeOH): λ_{max} 294 nm (ε 13,689 cm^{-1} M^{-1}), 226 (28,083). HRMS (ESI^+): found *m/z* 499.1226, $[M+H]^+$; $C_{25}H_{28}{}^{79}BrN_2O_4$ required 499.1232.

*4.1.18. 1-Allyl-3-(4-chlorophenyl)-4,6-dimethoxy-7-(1-nitrohex-5-en-2-yl)-1H-indole (**20c**).* This compound was prepared by the same method as compound **20b**, from indole **18c** (0.800 g, 2.00 mmol), butenylmagnesium bromide (6 mL, 0.5 M) and anhydrous THF (10 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **20c** as a light orange sticky residue (0.371 g, 45%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.86–2.12 (m, 4H, H3″, H4″), 3.77 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.09–4.18 (m, 1H, H2″), 4.70 (dd, *J*=12.5, 5.6 Hz, 1H, H1″), 4.85–4.98 (m, 6H, H1′, H3′, H1″, H6′), 5.21 (dd, *J*=10.5, 1.0 Hz, 1H, H3′), 5.66–5.79 (m, 1H, H5″), 6.04–6.16 (m, 1H, H2′), 6.31 (s, 1H, H5), 6.82 (s, 1H, H2), 7.29 (d, *J*=8.6 Hz, 2H, H3‴, H5‴), 7.43 (d, *J*=8.6 Hz, 2H, H2‴, C6‴). ^{13}C NMR (75 MHz, $CDCl_3$):

δ 31.3, 32.2, 35.8, 52.5, 55.4, 56.7, 79.8, 89.8, 104.1, 113.1, 115.3, 116.4, 117.0, 127.9, 129.5, 131.3, 131.9, 134.5, 134.8, 137.1, 138.5, 154.1, 156.3. IR (KBr): ν_{max} 3083, 2933, 2838, 1585, 1547, 1488, 1463, 1405, 1377, 1335, 1204, 1128, 1045, 916, 836, 796 cm^{-1}. UV–vis (MeOH): λ_{max} 294 nm (ε 13,528 cm^{-1} M^{-1}), 227 (27,715). HRMS (ESI^+): found *m/z* 455.1729, $[M+H]^+$; $C_{25}H_{28}{}^{35}ClN_2O_4$ required 455.1738.

*4.1.19. 1-Allyl-3-(4-methylphenyl)-4,6-dimethoxy-7-(1-nitrohex-5-en-2-yl)-1H-indole (**20d**).* This compound was prepared by the same method as compound **20b**, from indole **18d** (0.701 g, 1.85 mmol), butenylmagnesium bromide (11 mL, 0.5 M) and anhydrous THF (10 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **20d** as a light orange sticky residue (0.136 g, 17%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.85–2.16 (m, 4H, H3″, H4″), 3.77 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.15–4.19 (m, 1H, H2″), 4.71 (dd, *J*=12.5, 5.3 Hz, 1H, H1″), 4.86–4.98 (m, 6H, H1′, H3′, H1″, H6′), 5.18 (dd, *J*=10.5, 1.0 Hz, 1H, H3′), 5.72–5.79 (m, 1H, H5″), 6.04–6.15 (m, 1H, H2′), 6.30 (s, 1H, H5), 6.80 (s, 1H, H2), 7.14 (d, *J*=7.9 Hz, 2H, H3‴, H5‴), 7.41 (d, *J*=7.9 Hz, 2H, H2‴, C6‴). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 30.9, 31.7, 35.4, 51.9, 55.0, 56.2, 79.4, 89.2, 103.5, 112.9, 114.7, 116.4, 117.0, 128.1, 128.9, 129.4, 132.8, 134.2, 135.1, 136.5, 138.1, 153.7, 155.6. IR (KBr): ν_{max} 3078, 2932, 2838, 1603, 1585, 1548, 1463, 1377, 1334, 1203, 1125, 1068, 1041, 994, 913, 797, 733 cm^{-1}. UV–vis (MeOH): λ_{max} 289 nm (ε 19,816 cm^{-1} M^{-1}), 233 (46,678). HRMS (ESI^+): found *m/z* 435.2280, $[M+H]^+$; $C_{26}H_{31}N_2O_4$ required 435.2284.

*4.1.20. 4-(4-Bromophenyl)-10,11-dihydro-1,3-dimethoxy-11-(nitro methyl)-7H-azocino[3,2,1-hi]indole (**21b**).* Indole **19b** (0.220 g, 0.45 mmol) and Grubbs' catalyst (second gen, 5–10 mol %) were heated at reflux under an argon atmosphere in dry, degassed toluene (30 mL) for 4.5 h. The reaction mixture was then cooled and reduced in vacuo. Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **21b** as an off white solid (0.083 g, 40%). Mp 164–166 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.50–2.61 (m, 1H, H10), 2.75–2.82 (m, 1H, H10), 3.71 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.26 (dd, *J*=15.1, 8.3 Hz, 1H, H7), 4.78 (dd, *J*=12.8, 3.0 Hz, 1H, CH_2NO_2), 4.92–4.99 (m, 1H, H11), 5.01–5.09 (m, 1H, CH_2NO_2), 5.40 (dd, *J*=14.4, 7.7 Hz, 1H, H7), 5.63–5.71 (m, 2H, H8, H9), 6.20 (s, 1H, H2), 6.77 (s, 1H, H5), 7.32 (d, *J*=8.7 Hz, 2H, H2′, H6′), 7.38 (d, *J*=8.7 Hz, 2H, H3′, H5′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.2, 34.7, 46.1, 54.1, 55.4, 79.7, 88.5, 103.5, 111.6, 115.0, 118.6, 122.4, 127.8, 129.5, 130.0, 132.2, 133.7, 136.9, 152.9, 153.4. IR (KBr): ν_{max} 2929, 2834, 1613, 1587, 1547, 1510, 1463, 1375, 1337, 1201, 1178, 1125, 1070, 1051, 1007, 795 cm^{-1}. UV–vis (MeOH): λ_{max} 298 nm (ε 13,220 cm^{-1} M^{-1}), 227 (24,154). HRMS (ESI^+): found *m/z* 479.0581, $[M+Na]^+$; $C_{22}H_{21}{}^{79}BrN_2O_4Na$ required 479.0582.

*4.1.21. 4-(4-Chlorophenyl)-10,11-dihydro-1,3-dimethoxy-11-(nitro methyl)-7H-azocino[3,2,1-hi]indole (**21c**).* This compound was prepared by the same method as compound **21b**, from indole **19c** (0.220 g, 0.50 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (40 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **21c** as a white solid (0.10 g, 49%). Mp 168–170 °C. Found: C, 64.01; H, 5.25; N, 6.85%. $C_{22}H_{21}ClN_2O_4$ requires: C, 64.00; H, 5.13; N, 6.79%. ^1H NMR (300 MHz, $CDCl_3$): δ 2.55–2.67 (m, 1H, H10), 2.77–2.88 (m, 1H, H10), 3.76 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.30 (dd, *J*=12.3, 8.2 Hz, 1H, H7), 4.83 (dd, *J*=15.2, 3.0 Hz, 1H, CH_2NO_2), 4.99–5.19 (m, 2H, H11, CH_2NO_2), 5.44 (dd, *J*=15.0, 9.0 Hz, 1H, H7), 5.66–5.76 (m, 2H, H8, H9), 6.26 (s, 1H, H2), 6.81 (s, 1H, H5), 7.29 (d, *J*=8.7 Hz, 2H, ArCH), 7.45 (d, *J*=8.7 Hz, 2H, ArCH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.3, 35.2, 47.1, 55.1, 56.3, 80.6, 89.4, 104.5, 112.6, 115.9, 123.3, 127.5, 128.7, 130.6, 131.4, 133.1, 134.1, 137.8, 153.8, 154.3. IR (KBr): ν_{max} 2936, 2834, 1610, 1587, 1548, 1508, 1488, 1463, 1410, 1378, 1338, 1280, 1201, 1179, 1125, 1089, 1050, 1012, 835, 796 cm^{-1}. UV–vis (MeOH): λ_{max} 297 nm (ε 12,003 cm^{-1} M^{-1}), 228 (22,317). HRMS (ESI^+): found *m/z* 413.1260, $[M+H]^+$; $C_{22}H_{22}{}^{35}ClN_2O_4$ required 413.1268.

*4.1.22. 10,11-Dihydro-1,3-dimethoxy-4-(4-methylphenyl)-11-(nitro methyl)-7H-azocino[3,2,1-hi]indole (**21d**).* This compound was prepared by the same method as compound **21b**, from indole **19d** (0.200 g, 4.76 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (40 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **21d** as a white solid (0.114 g, 61%). Mp 175–177 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H, CH_3), 2.49–2.61 (m, 1H, H10), 2.76–2.83 (m, 1H, H10), 3.70 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 4.25 (dd, *J*=14.9, 8.2 Hz, 1H, H7), 4.76 (dd, *J*=12.9, 3.0 Hz, 1H, CH_2NO_2), 4.94–5.00 (m, 1H, H11), 5.06 (dd, *J*=12.9, 9.4 Hz, 1H, CH_2NO_2), 5.39 (dd, *J*=14.4, 7.7 Hz, 1H, H7), 5.63–5.70 (m, 2H, H8, H9), 6.20 (s, 1H, H2), 6.75 (s, 1H, H5), 7.08 (d, *J*=8.7 Hz, 2H, H3′, H5′), 7.36 (d, *J*=8.7 Hz, 2H, H2′, H6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 35.7, 36.2, 47.6, 55.6, 56.8, 81.3, 89.8, 104.9, 113.4, 117.6, 123.9, 128.6, 129.1, 129.8, 133.2, 133.5, 135.6, 138.2, 154.5, 154.6. IR (KBr): ν_{max} 2920, 1607, 1587, 1549, 1509, 1463, 1375, 1338, 1201, 1176, 1125, 1051, 823, 792 cm^{-1}. UV–vis (MeOH): λ_{max} 292 nm (ε 11,037 cm^{-1} M^{-1}), 233 (23,873). HRMS (ESI^+): found *m/z* 393.1817, $[M+H]^+$; $C_{23}H_{25}N_2O_4$ required 393.1814.

*4.1.23. 4-(4-Bromophenyl)-1,3-dimethoxy-12-(nitromethyl)-7,10,11,12-tetrahydro-7H-azonino[3,2,1-hi]indole (**22b**).* This compound was prepared by the same method as compound **21b**, from indole **20b** (0.313 g, 0.63 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (40 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **22b** as a light tan solid (0.120 g, 40%). Mp 150–152 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 1.80–2.33 (m, 4H, H10, H11), 3.82 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.32–4.41 (m, 1H, H12), 4.62 (dd, *J*=19.3, 8.0 Hz, 1H, H7), 4.79 (dd, *J*=13.2, 4.9 Hz, 1H, CH_2NO_2), 5.11 (dd, *J*=13.2, 8.9 Hz, 1H, CH_2NO_2), 5.29–5.38 (m, 2H, H7, H8), 5.75–5.88 (m, 1H, H9), 6.36 (s, 1H, H2), 6.90 (s, 1H, H5), 7.43 (d, *J*=7.8 Hz, 2H, ArH), 7.49 (d, *J*=7.8 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7, 33.4, 35.7, 49.8, 55.2, 56.0, 80.4, 89.6, 105.5, 112.9, 116.7, 119.6, 124.9, 130.4, 130.4, 131.0, 131.6, 134.6, 138.5, 153.6, 155.0. IR (KBr): ν_{max} 2939, 2837, 1608, 1586, 1547, 1459, 1377, 1203, 1174, 1124, 1070, 1051, 1007, 833, 797 cm^{-1}. UV–vis (MeOH): λ_{max} 299 nm (ε 12,254 cm^{-1} M^{-1}), 232 (21,210). HRMS (ESI^+): found *m/z* 471.0908, $[M+H]^+$; $C_{23}H_{24}{}^{79}BrN_2O_4$ required 471.0919.

*4.1.24. 4-(4-Chlorophenyl)-1,3-dimethoxy-11-(nitromethyl)-7,10,11,12-tetrahydro-7H-azonino[3,2,1-hi]indole (**22c**).* This compound was prepared by the same method as compound **21b**, from indole **20c** (0.263 g, 0.58 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (40 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **22c** as an off white solid (0.10 g, 42%). Mp 166–168 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 1.70–2.19 (m, 4H, H11, H10), 3.70 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.20–4.28 (m, 1H, H12), 4.50 (dd, *J*=18.9, 7.7 Hz, 1H, H7), 4.68 (dd, *J*=13.2, 4.9 Hz, 1H, CH_2NO_2), 5.00 (dd, *J*=13.2, 8.9 Hz, 1H, CH_2NO_2), 5.18–5.27 (m, 2H, H7, H8), 5.72 (dd, *J*=18.9, 9.5 Hz, 1H, H9), 6.25 (s, 1H, H2), 6.78 (s, 1H, H5), 7.23 (d, *J*=8.5 Hz, 2H, ArH), 7.38 (d, *J*=8.5 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.1, 33.9, 36.4, 50.3, 55.5, 56.5, 80.8, 90.2, 105.9, 113.4, 117.2, 125.2, 127.9, 130.9, 131.1, 131.9, 132.3, 134.6, 139.0, 154.1, 155.5. IR (KBr): ν_{max} 2939, 2834, 1615, 1588, 1548, 1463, 1378, 1337, 1203, 1171, 1124, 1089, 1053, 797, 617 cm^{-1}. UV–vis (MeOH): λ_{max} 297 nm (ε 12,457 cm^{-1} M^{-1}), 236 (22,275). HRMS (ESI^+): found *m/z* 427.1425, $[M+H]^+$; $C_{23}H_{24}{}^{35}ClN_2O_4$ required 427.1425.

*4.1.25. 1,3-Dimethoxy-4-(4-methylphenyl)-12-(nitromethyl)-7,10,11,12-tetrahydro-7H-azonino[3,2,1-hi]indole (**22d**).* This compound was prepared by the same method as compound **21b**, from indole **20d** (0.132 g, 3.04 mmol), Grubbs' catalyst (second gen, 5–10 mol %)

and degassed toluene (40 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **22d** as a light tan solid (0.07 g, 54%). Mp 138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.72–1.85 (m, 1H, H11), 1.93–2.05 (m, 1H, H11), 2.08–2.17 (m, 1H, H10), 2.21–2.32 (m, 1H, H10), 2.39 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.27–4.35 (m, 1H, H12), 4.57 (dd, J=19.6, 8.5 Hz, 1H, H7), 4.73 (dd, J=13.2, 4.7 Hz, 1H, CH_2NO_2), 5.09 (dd, J=13.2, 9.0 Hz, 1H, CH_2NO_2), 5.25–5.34 (m, 2H, H7, H8), 5.79 (dd, J=17.9, 9.0 Hz, 1H, H9), 6.32 (s, 1H, H2), 6.85 (s, 1H, H5), 7.16 (d, J=7.8 Hz, 2H, H3′, H5′), 7.44 (d, J=7.8 Hz, 2H, H2′, H6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 25.7, 33.5, 35.9, 49.7, 55.1, 56.1, 80.4, 89.6, 105.5, 113.3, 117.9, 124.8, 128.2, 129.3, 130.3, 131.7, 132.6, 135.2, 138.5, 153.7, 154.8. IR (KBr): ν_{max} 3012, 2920, 2842, 1587, 1548, 1462, 1377, 1338, 1202, 1173, 1124, 1052, 796 cm^{-1}. UV–vis (MeOH): λ_{max} 292 nm (ε 12,239 cm^{-1} M^{-1}), 237 (26,104). HRMS (ESI$^+$): found m/z 407.1963, [M+H]$^+$; $C_{24}H_{27}N_2O_4$ required 407.1971.

*4.1.26. 10,12-Dimethoxy-8,9-diphenyl-3H-[1,5]oxazonino[3,4,5-hi]indol-1-(6H)-one (**23a**).* This compound was prepared by the same method as compound **21b**, from indole **24a** (0.217 g, 4.78 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (20 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **23a** as a white solid (0.077 g, 38%). Mp 189–191 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 5.12 (m, 1H, CH_2), 5.62 (dt, J=10.7, 1.8 Hz, 1H, CH), 6.03 (dt, J=10.7, 4.2 Hz, 1H, CH), 6.29 (s, 1H, H11), 7.12–7.30 (m, 10H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.1, 55.7, 57.7, 61.9, 89.1, 99.4, 113.1, 116.2, 125.9, 127.1, 127.2, 128.4, 128.6, 129.7, 131.6, 131.8, 132.2, 132.6, 132.7, 135.6, 139.8, 156.9, 157.9, 168.3. IR (KBr): ν_{max} 2936, 2844, 1723, 1584, 1457, 1346, 1254, 1201, 1163, 1131, 1099, 1042, 805, 760, 697 cm^{-1}. UV–vis (MeOH): λ_{max} 312 nm (ε 16,168 cm^{-1} M^{-1}), 249 (34,719). HRMS (ESI$^+$): found m/z 426.1705, [M+H]$^+$; $C_{27}H_{24}NO_4$ required 426.1705.

*4.1.27. 9-(4-Bromophenyl)-10,12-dimethoxy-3H-[1,5]oxazonino[3,4,5-hi]indol-1-(6H)-one (**23b**).* This compound was prepared by the same method as compound **21b**, from indole **24b** (0.487 g, 1.07 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (15 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **23b** as an off white solid (0.355g, 78%). Mp 294–296 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.61–4.75 (m, 4H, H3, H6), 5.48 (dt, J=15.5, 5.3 Hz, 1H, CH), 5.89 (dt, J=15.7, 4.3 Hz, 1H, CH), 6.27 (s, 1H, H5), 6.83 (s, 1H, H2), 7.38 (d, J=8.7 Hz, 2H, ArH), 7.46 (d, J=8.7 Hz, 2H, ArH). IR (KBr): ν_{max} 2955, 2929, 2841, 1717, 1609, 1584, 1558, 1543, 1460, 1356, 1261, 1207, 1169, 1140, 1099, 1068, 1007, 795 cm^{-1}. UV–vis (MeOH): λ_{max} 286 nm (ε 6455 cm^{-1} M^{-1}), 239 (12,420). HRMS (ESI$^+$): found m/z 428.0492, [M+H]$^+$; $C_{21}H_{19}{}^{79}BrNO_4$ required 428.0497.

*4.1.28. 9-(4-Chlorophenyl)-10,12-dimethoxy-3H-[1,5]oxazonino[3,4,5-hi]indol-1-(6H)-one (**23c**).* This compound was prepared by the same method as compound **21b**, from indole **24c** (0.255 g, 6.18 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (10 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **23c** as an off white solid (0.035g, 15%). Mp 288–290 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.79 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.62–4.73 (m, 4H, H3, H6), 5.49 (dt, J=15.7, 5.1 Hz, H4), 5.89 (dt, J=15.3, 4.3 Hz, 1H, H5), 6.28 (s, 1H, H11), 6.83 (s, 1H, H8), 7.30 (d, J=8.3 Hz, 2H, ArH), 7.44 (d, J=8.3 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.6, 55.1, 57.4, 65.3, 88.4, 100.4, 111.7, 117.0, 124.5, 126.9, 127.5, 129.8, 130.7, 131.6, 133.9, 139.7, 155.0, 155.7, 167.7. IR (KBr): ν_{max} 2933, 2841, 1719, 1607, 1586, 1563, 1451, 1354, 1262, 1209, 1171, 1141, 1091, 1047, 1012, 962, 832, 800 cm^{-1}. UV–vis (MeOH): λ_{max} 292 nm (ε 4112 cm^{-1} M^{-1}), 239 (6826). HRMS (ESI$^+$): found m/z 384.1006, [M+H]$^+$; $C_{21}H_{19}{}^{35}ClNO_4$ required 384.1003.

*4.1.29. Allyl 1-allyl-4,6-dimethoxy-2,3-diphenyl-1H-indole-7-carboxylate (**24a**).* This compound was prepared by the same method as compound **17a**, from indole **28a** (0.960 g, 2.32 mmol), allyl bromide (1.2 mL, 13.9 mmol), potassium hydroxide (0.542 g, 1.31 mmol) and DMSO (20 mL). The *title compound* **24a** was obtained as a white solid (0.853 g, 81%). Mp 119–121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.73 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.60 (dt, J=4.4, 1.8 Hz, 2H, H1′), 4.68 (dd, J=17.2, 1.2 Hz, 1H, H3′), 4.83 (dt, J=5.7, 1.2 Hz, 2H, H3″), 5.01 (dd, J=10.5, 1.2 Hz, 1H, H3′), 5.28 (dd, J=10.3, 1.2 Hz, 1H, H5″), 5.54 (dd, J=17.2, 1.5 Hz, 1H, H5″), 5.67–5.79 (m, 1H, H2′), 5.98–6.11 (m, 1H, H4″), 6.32 (s, 1H, H5), 7.12–7.27 (m, 10H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.1, 55.2, 57.6, 66.0, 89.1, 101.2, 112.9, 115.8, 115.9, 118.5, 125.3, 126.6, 127.7, 127.8, 131.3, 131.7, 131.9, 133.8, 133.9, 135.5, 137.9, 155.1, 155.8, 167.7. IR (KBr): ν_{max} 3057, 2992, 2936, 2839, 1719, 1587, 1551, 1501, 1448, 1410, 1352, 1261, 1209, 1167, 1130, 1097, 1038, 923, 764, 697 cm^{-1}. UV–vis (MeOH): λ_{max} 300 nm (ε 10,317 cm^{-1} M^{-1}), 240 (25,521). HRMS (ESI$^+$): found m/z 454.2014, [M+H]$^+$; $C_{29}H_{28}NO_4$ required 454.2018.

*4.1.30. Allyl 1-allyl-3-(4-bromophenyl)-4,6-dimethoxy-1H-indole-7-carboxylate (**24b**).* This compound was prepared by the same method as compound **17a**, from indole **28b** (0.583 g, 1.40 mmol), allyl bromide (0.36 mL, 4.16 mmol), potassium hydroxide (0.24 g, 4.28 mmol) and DMSO (20 mL). The *title compound* **24b** was obtained as a white solid (0.587 g, 92%). Mp 122–124 °C. Found: C, 60.55; H, 4.80; N, 3.00%. $C_{23}H_{22}BrNO_4$ requires: C, 60.54; H, 4.86; N, 3.07%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.63 (dt, J=5.4, 1.6 Hz, 2H, H1′), 4.83 (dt, J=5.7, 1.4 Hz, 2H, H3″), 5.03 (dd, J=17.1, 1.2 Hz, 1H, H3′), 6.17 (dd, J=10.3, 1.2 Hz, 1H, H3′), 5.29 (dd, J=10.4, 1.5 Hz, 1H, H5″), 5.44 (dd, J=17.2, 1.5 Hz, 1H, H5″), 5.86–6.10 (m, 2H, H2′, H4″), 6.31 (s, 1H, H5), 6.88 (s, 1H, H2), 7.38 (d, J=8.7 Hz, 2H, ArH), 7.45 (d, J=8.7 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.3, 55.2, 57.6, 66.1, 88.7, 100.7, 112.0, 116.8, 117.6, 118.8, 119.7, 126.7, 130.5, 131.2, 131.9, 133.4, 134.4, 134.6, 155.5, 155.9, 167.5. IR (KBr): ν_{max} 2930, 2841, 1719, 1701, 1604, 1586, 1560, 1460, 1357, 1262, 1242, 1206, 1168, 1141, 1103, 1068, 1021, 923, 791 cm^{-1}. UV–vis (MeOH): λ_{max} 294 nm (ε 17,226 cm^{-1}M^{-}), 239 (33,198). MS (ESI$^+$): m/z 480.02, [M+Na]$^+$.

*4.1.31. Allyl 1-allyl-3-(4-chlorophenyl)-4,6-dimethoxy-1H-indole-7-carboxylate (**24c**).* This compound was prepared by the same method as compound **17a**, from indole **28c** (0.516 g, 1.39 mmol), allyl bromide (0.4 mL, 4.62 mmol), potassium hydroxide (0.202 g, 3.60 mmol) and DMSO (15 mL). The *title compound* **24c** was obtained as a light tan solid (0.355 g, 62%). Mp 116–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.63 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 4.50 (dt, J=5.3, 1.6 Hz, 2H, H1′), 4.69 (dt, J=5.6, 1.5 Hz, 2H, H3″), 4.89 (dd, J=17.2, 1.4 Hz, 1H, H3′), 5.03 (dd, J=10.4, 1.4 Hz, 1H, H3′), 5.16 (dd, J=10.4, 1.5 Hz, 1H, H5″), 5.31 (dd, J=17.2, 1.5 Hz, 1H, H5″), 5.73–5.96 (m, 2H, H2′, H4″), 6.21 (s, 1H, H5), 6.76 (s, 1H, H2), 7.16 (d, J=8.6 Hz, 2H, ArH), 7.31 (d, J=8.6 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.2, 55.1, 57.5, 66.0, 88.6, 100.7, 112.0, 116.7, 117.5, 118.7, 126.7, 127.5, 130.7, 131.5, 131.9, 133.3, 134.1, 134.2, 155.4, 155.8, 167.4. IR (KBr): ν_{max} 3086, 2935, 2841, 1701, 1609, 1590, 1547, 1462, 1452, 1413, 1357, 1264, 1244, 1218, 1184, 1173, 1144, 1102, 1015, 920, 835, 791 cm^{-1}. UV–vis (MeOH): λ_{max} 294 nm (ε 14,673 cm^{-1} M^{-1}), 239 (28,778). HRMS (ESI$^+$): found m/z 412.1312, [M+H]$^+$; $C_{23}H_{23}{}^{35}ClNO_4$ required 412.1316.

*4.1.32. 4,6-Dimethoxy-2,3-diphenyl-7-trichloroacetylindole (**27a**).* Indole **15a** (1.08 g, 3.28 mmol) and trichloroacetyl chloride (1.8 mL, 0.016 mol) were heated at reflux in 1,2-dichloroethane (25 mL) for 3 h. The reaction was quenched with water (80 mL) and extracted with DCM (3×15 mL). The combined organic layers were dried over anhydrous sodium sulfate and reduced in vacuo to give the *title compound* **27a** as a yellow solid (1.00 g, 65%). Mp

176–177 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.19 (s, 1H, H5), 7.22–7.39 (m, 10H, ArH), 10.44 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4, 55.5, 87.7, 98.2, 98.6, 113.4, 115.2, 126.3, 127.3, 127.4, 127.8, 128.4, 131.2, 131.9, 132.9, 135.2, 138.9, 160.2, 161.7, 182.0. IR (KBr): ν_{max} 3052, 2940, 2846, 1632, 1586, 1543, 1463, 1374, 1361, 1239, 1223, 1138, 991, 796, 693 cm^{-1}. UV–vis (MeOH): λ_{max} 310 nm (ε 18,731 cm^{-1} M^{-1}), 270 (22,184), 248 (26,767), 230 (30,919). HRMS (ESI$^+$): found m/z 474.0432, $[M+H]^+$; $C_{24}H_{19}{}^{35}Cl_3NO_3$ required 474.0431.

*4.1.33. 3-(4-Bromophenyl)-4,6-dimethoxy-7-trichloroacetylindole (**27b**).* This compound was prepared by the same method as compound **27a**, from indole **15b** (3.00 g, 9.04 mmol), trichloroacetyl chloride (5.0 mL, 44.8 mmol) and 1,2-dichloroethane (25 mL). Chromatography (SiO_2, 30% DCM/hexane) gave the *title compound* **27b** as a yellow solid (0.613 g, 14%). Mp 187–189 °C. Lit.[33] mp 190–192 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 3.93 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.23 (s, 1H, H5), 7.08 (d, J=2.4 Hz, 1H, H2), 7.40 (d, J=8.6 Hz, 2H, ArH), 7.47 (d, J=8.6 Hz, 2H, ArH), 10.29 (br s, 1H, NH).

*4.1.34. 3-(4-Chlorophenyl)-4,6-dimethoxy-7-trichloroacetylindole (**27c**).* This compound was prepared by the same method as compound **27a**, from indole **15c** (1.08 g, 3.74 mmol), trichloroacetyl chloride (2.0 mL, 17.9 mmol) and 1,2-dichloroethane (10 mL). Chromatography (SiO_2, 50% DCM/hexane) gave the *title compound* **27c** as a yellow solid (0.352 g, 22%). Mp 174–175 °C. Lit.[27] mp 178 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.22 (s, 1H, H5), 7.07 (d, J=2.4 Hz, 1H, H2), 7.34 (d, J=8.7 Hz, 2H, ArH), 7.47 (d, J=8.4 Hz, 2H, ArH), 10.29 (br s, 1H, NH).

*4.1.35. Allyl 4,6-dimethoxy-2,3-diphenyl-1H-indole-7-carboxylate (**28a**).* A mixture of indole **27a** (2.44 g, 5.14 mmol), allyl alcohol (2.1 mL, 30.8 mmol) and potassium hydroxide (0.58 g, 10.4 mmol) in THF (30 mL) was heated at reflux for 2 h. The reaction mixture was quenched with water (80 mL) and the resulting precipitate collected to give the *title compound* **28a** as a white solid (1.84 g, 86%). Mp 137–139 °C. Found: C, 75.37; H, 5.72; N, 3.35%. $C_{26}H_{23}NO_4$ requires: C, 75.53; H, 5.61; N, 3.39%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.92 (dt, J=3.8, 1.4 Hz, 2H, H3′), 5.31 (dd, J=10.5, 1.5 Hz, 1H, H5′), 5.53 (dd, J=17.1, 1.5 Hz, 1H, H5′), 6.01 (m, 1H, H4′), 6.24 (s, 1H, H5), 7.31 (m, 10H, ArH), 10.34 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.2, 57.2, 64.8, 88.9, 94.9, 113.1, 114.4, 117.5, 126.1, 127.0, 127.3, 127.7, 128.4, 131.3, 132.4, 132.6, 132.6, 135.6, 138.5, 159.2, 160.2, 166.9. IR (KBr): ν_{max} 3406, 3059, 2996, 2841, 1661, 1644, 1597, 1550, 1465, 1392, 1359, 1263, 1222, 1180, 1172, 1150, 1106, 990, 799, 752, 698 cm^{-1}. UV–vis (MeOH): λ_{max} 338 nm (ε 17,296 cm^{-1} M^{-1}), 314 (16,910), 248 (26,599). MS (ESI$^+$): m/z 436.12, $[M+Na]^+$.

*4.1.36. Allyl 3-(4-bromophenyl)-4,6-dimethoxy-1H-indole-7-carboxylate (**28b**).* This compound was prepared by the same method as compound **28a**, from indole **27b** (0.848 g, 1.77 mmol), allyl alcohol (0.7 mL, 0.010 mol), potassium hydroxide (0.20 g, 3.56 mmol) and THF (20 mL). The *title compound* **28b** was obtained as a pale yellow solid (0.583 g, 79%). Mp 139–141 °C. Found: C, 57.84; H, 4.39; N, 3.28%. $C_{20}H_{18}BrNO_4$ requires: C, 57.71; H, 4.36; N, 3.36%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.89 (dt, J=5.3, 1.5 Hz, 2H, H3′), 5.30 (dd, J=10.5, 1.5 Hz, 1H, H5′), 5.50 (dd, J=18.8, 1.5 Hz, 1H, H5′), 6.03–6.16 (m, 1H, H4′), 6.28 (s, 1H, H5), 7.09 (d, J=2.3 Hz, 1H, H2), 7.43 (d, J=8.7 Hz, 2H, ArH), 7.48 (d, J=8.7 Hz, 2H, ArH), 10.3 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.1, 57.2, 64.9, 88.8, 89.1, 95.4, 110.3, 117.5, 119.7, 121.4, 130.6, 131.0, 132.5, 134.6, 139.4, 158.8, 160.4, 167.0. IR (KBr): ν_{max} 3415, 2959, 2936, 2841, 1660, 1604, 1588, 1539, 1463, 1389, 1348, 1315, 1262, 1216, 1150, 1083, 1006, 979, 800 cm^{-1}. UV–vis (MeOH): λ_{max} 306 nm (ε 20,889 cm^{-1} M^{-1}), 237 (41,097). MS (ESI$^+$): m/z 439.99, $[M+Na]^+$.

*4.1.37. Allyl 3-(4-chlorophenyl)-4,6-dimethoxy-1H-indole-7-carboxylate (**28c**).* This compound was prepared by the same method as compound **28a**, from indole **27c** (0.853 g, 1.97 mmol), allyl alcohol (0.27 mL, 3.97 mmol), potassium hydroxide (0.222 g, 3.97 mmol) and THF (15 mL). The *title compound* **28c** was obtained as an off white solid (0.613 g, 84%). Mp 145–147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.89–4.91 (m, 2H, H3′), 5.30 (dd, J=10.5, 1.4 Hz, 1H, H5′), 5.50 (dd, J=17.2, 1.5 Hz, 1H, H5′), 6.03–6.16 (m, 1H, H4′), 6.28 (s, 1H, H5), 7.09 (d, J=2.3 Hz, 1H, H2), 7.32 (d, J=8.5 Hz, 2H, ArH), 7.50 (d, J=8.5 Hz, 2H, ArH), 10.3 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.2, 57.2, 64.9, 88.8, 95.4, 101.5, 110.3, 117.5, 121.4, 127.6, 130.6, 131.6, 132.5, 134.1, 139.4, 158.8, 160.4, 155.8. IR (KBr): ν_{max} 3414, 2933, 2839, 1651, 1610, 1590, 1561, 1536, 1463, 1383, 1345, 1314, 1263, 1216, 1147, 1094, 1012, 979, 832, 797 cm^{-1}. UV–vis (MeOH): λ_{max} 307 nm (ε 20,226 cm^{-1} M^{-1}), 283 (18,746), 238 (41,345). HRMS (ESI$^+$): found m/z 394.0810, $[M+Na]^+$; $C_{20}H_{18}{}^{35}ClNNaO_4$ required 394.0822.

*4.1.38. N-Allyl-4,6-dimethoxy-2,3-diphenyl-1H-indole-7-carboxamide (**29**).* Indole **27a** (2.348 g, 4.95 mmol) and allyl amine (2.2 mL, 0.029 mol) were heated at reflux in THF (25 mL) for 3 h. The reaction mixture was quenched with water (80 mL) and the resulting precipitate collected to give the *title compound* **29** as a white solid (1.496 g, 73%). Mp 188–190 °C. Found: C, 75.67; H, 5.99; N, 6.86%. $C_{26}H_{24}N_2O_3$ requires: C, 75.71; H, 5.86; N, 6.79%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.12–4.16 (m, 2H, H3′), 5.18 (dd, J=10.3, 1.5 Hz, 1H, H5′), 5.29 (dd, J=17.2, 1.5 Hz, 1H, H5′), 5.95–6.07 (m, 1H, H4′), 6.23 (s, 1H, H5), 7.19–7.40 (m, 10H, ArH), 8.20 (br s, 1H, NH), 11.32 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 41.9, 55.7, 57.3, 88.1, 97.8, 114.0, 114.3, 115.7, 126.3, 127.4, 127.7, 128.4, 128.6, 131.9, 132.9, 133.7, 135.3, 136.4, 138.9, 156.9, 157.9, 167.9. IR (KBr): ν_{max} 3412, 3358, 3060, 2941, 2842, 1630, 1597, 1530, 1503, 1463, 1449, 1426, 1359, 1335, 1252, 1232, 1187, 1150, 1116, 988, 918, 755, 699 cm^{-1}. UV–vis (MeOH): λ_{max} 332 nm (ε 23,128 cm^{-1} M^{-1}), 317 (23,084), 248 (37,417). MS (ESI$^+$): m/z 435.13, $[M+Na]^+$.

*4.1.39. (1-Allyl-4,6-dimethoxy-2,3-diphenyl-1H-indol-7-yl)(2H-pyrrol-1-yl)methanone (**33**).* This compound was prepared by the same method as compound **21b**, from indole **31** (0.476 g, 0.97 mmol), Grubbs' catalyst (second gen, 5–10 mol %) and degassed toluene (15 mL). Chromatography (SiO_2, DCM) gave the *title compound* **33** as an off white solid (0.367 g, 82%). Mp 198–200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, OCH_3), 3.91–3.97 (m, 1H, H2″), 3.94 (s, 3H, OCH_3), 4.21–4.27 (m, 1H, H2″), 4.39–4.50 (m, 2H, H1′, 5″), 4.58 (dd, J=17.2, 1.0 Hz, 1H, H3′), 4.94 (dd, J=10.6, 1.0 Hz, 1H, H3′), 5.00–5.06 (m, 1H, H5″), 5.67–5.76 (m, 2H, H2′, H3″), 5.90–5.92 (m, 1H, H4″), 6.35 (s, 1H, H5), 7.15–7.27 (m, 10H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.3, 53.1, 54.5, 55.2, 57.1, 88.6, 103.3, 113.2, 113.9, 115.6, 125.2, 125.3, 125.5, 126.5, 127.7, 127.8, 131.2, 131.3, 131.8, 133.4, 135.0, 135.6, 137.9, 152.9, 155.2, 166.7. IR (KBr): ν_{max} 3052, 2958, 2972, 2859, 1634, 1614, 1584, 1449, 1429, 1345, 1258, 1212, 1165, 1118, 1040, 911, 760, 693 cm^{-1}. UV–vis (MeOH): λ_{max} 302 nm (ε 12,646 cm^{-1} M^{-1}), 239 (32,415). HRMS (ESI$^+$): found m/z 465.2175, $[M+H]^+$; $C_{30}H_{29}N_2O_3$ required 465.2178.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.04.019.

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