Synthesis of Pyrrolo- and Pyrido-[1,2-*a*]benzimidazolequinone Anti-tumor Agents Containing a Fused Cyclopropane Ring

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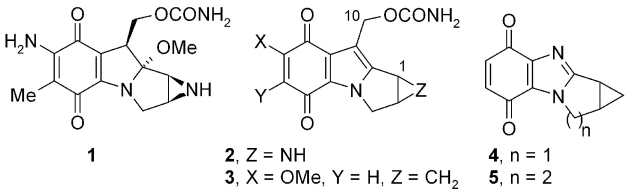
Abstract: A cyclopropane ring has been fused onto tetrahydropyrrolo- and tetrahydropyrido-[1,2-*a*]-benzimidazoles and -benzimidazolequinones via the cycloaddition of diazomethines generated from the thermolysis of *N*-(allyl and but-3-enyl)benzimidazole-2-Eschenmoser hydrazones (aziridinyl imines). At lower temperatures, the 1,3-dipolar [3 + 2] cycloadduct was obtained for only the *N*-allylbenzimidazole-2-Eschenmoser hydrazones.

Key words: benzimidazoles, bioreductive, diazo-compounds, heterocycles, hydrazones

Many quinone derivatives are known to have anti-cancer activity, which is initiated by the reductive activation of the quinone moiety.[1] In the case of mitomycin C (MMC **1**) and aziridinomitosene **2** reductive activation leads to ring-opening of the aziridine ring and elimination of the urethane group to create reactive sites at C-1 and C-10, respectively for alkylation of DNA (Figure 1). Moody and co-workers have prepared analogues of the aziridinomitosene **2** in which the aziridine ring is replaced by a cyclopropane ring, and named these compounds cyclopropamitosene (CPM, **3**).[2–7] The reduced electrophilicity at C-1 in **3** resulted in selective alkylation of nucleophiles at C-10 under chemical reducing conditions.[5] CPM **3** was also shown to undergo single-electron reduction; a process that is selective under bioreductive conditions to hypoxic or O_2-deficient cells present in solid tumours, as it is reversed in the presence of O_2 in healthy cells.[5,6] Under hypoxic conditions, **3** was shown to be 34 and 3 times more toxic than under aerobic conditions and MMC **1** under hypoxic conditions, respectively.[5,6] Bioreduction of **3** to the semiquinone radical anion was speculated to induce radical-ring opening of the cyclopropane ring to give a radical capable of abstracting the 4′-hydrogen from the deoxyribose part of DNA leading to strand cleavage.[5–7] Therefore, the greater selectivity of CPM **3** toward hypoxic conditions, and the different mode of action to **1** and **2**, makes the synthesis of structurally related heterocyclic compounds a worthwhile endeavor. Our interest has been in the preparation of benzimidazoles containing [1,2-*a*] fused alicyclic rings,[8] where literature synthetic methods have been limited to the preparation tricyclic fused systems[9,10] until in a recent preliminary communication, we reported the preparation of new tetracyclic ring systems pyrrolo- and pyrido-[1,2-*a*]benzimidazoles containing a fused cyclopropane ring using benzimidazole-2-Eschenmoser hydrazone synthetic intermediates.[11] The methodology was extended to the preparation of 1,1a,8,8a-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole-3,6-dione (**4**), which is the first prepared diazole analogue of indolequinone **3**.



1

2, Z = NH
3, X = OMe, Y = H, Z = CH_2

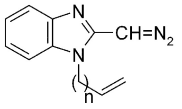
4, n = 1
5, n = 2

Figure 1

Benzimidazolequinone **4** was shown to have a lower reductive potential (–1.052 V, vs. ferrocene, Fc) than indolequinones **1** (–1.421 V, vs. Fc) and **3** (–1.395 V, vs. Fc) under analogous cyclic voltammetry conditions. A reversible one electron reduction was observed at low scan rates in contrast to other reported benzimidazolequinone antitumor agents that show cytotoxic activity via a two-electron reductive activation mediated by DT-diaphorase in an O_2-independent pathway.[10,12] A full account of the synthesis of anti-tumor agent **4** and analogues is given in the present paper, including a first report of the new benzimidazolequinone, 1a,2,3,9b-tetrahydro-1*H*-cyclopropa[3,4]pyrido[1,2-*a*]benzimidazole-5,8-dione (**5**).

The construction of the tetracyclic cyclopropapyrrolo- and cyclopropapyrido-[1,2-*a*]benzimidazole skeleton was accomplished by successful intramolecular cycloaddition of *N*-(allyl and but-3-enyl)benzimidazole-2-diazomethines **6** and **7**, respectively.

Synthetic pathways toward the preparation of benzimidazole-2-hydrazone precursors of **6** and **7** began with the N-alkylation of 1*H*-benzimidazol-2-ylmethanol **8**, rather than 1*H*-benzimidazole-2-carbaldehyde. N-Alkylation of



6, n = 1
7, n = 2

Figure 2

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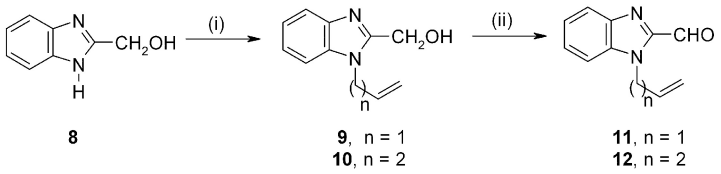
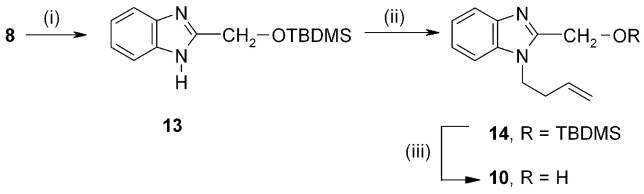


Scheme 1 *Reagents and conditions*: (i) Et_3N, CH_2=CH$(CH_2)_n$Br, THF, reflux, 4 h, 41% for **9** and 30% for **10**; (ii) MnO_2, CH_2Cl_2, reflux, 30 min, 77% for **11** and 55% for **12**.

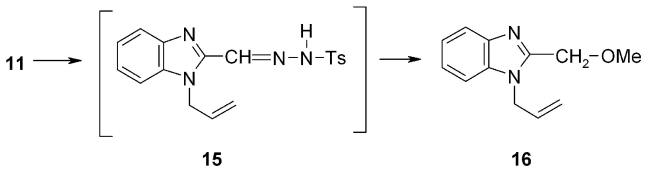
the aldehyde could not be carried out owing to its insolubility in organic solvents, which has been attributed to the formation of the dimeric hemiaminal.[13] *N*-Allyl and (3-butenyl)-1*H*-benzimidazole-2-methanols **9** and **10** were prepared selectively on gram scale, but in only reasonable to poor yields of 41% and 30%, respectively, by treatment of alcohol **8** with a large excess of triethylamine followed by an equal excess of allyl bromide and 4-bromo-1-butene in refluxing THF (Scheme 1). Nevertheless, our alkylations of **8** using triethylamine compared favourably with literature alkylations, which under basic conditions were not selective leading to both N- and O-alkylation.[14]

Improved yields of **10** of 44% overall, were achieved when TBDMS-protection of the 2-hydroxymethyl group of **8** was first carried out to allow alkylation using sodium hydride and 4-bromo-1-butene with subsequent deprotection using TBAF (Scheme 2), as previously reported for other benzimidazole-2-methanol alkylations.[15] Alcohols **9** and **10** were oxidized in half an hour to the required aldehydes **11** and **12** in 77% and 55% yield, respectively, using a large excess of manganese dioxide in refluxing dichloromethane (Scheme 1).



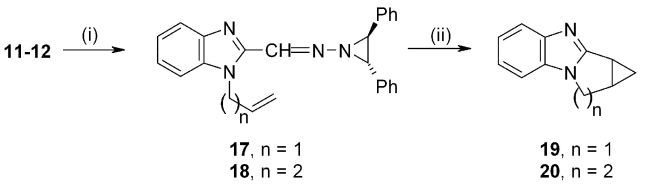
Scheme 2 *Reagents and conditions*: (i) TBDMSCl, pyridine, r.t., 4 h, 100% for **13**; (ii) NaH, CH_2=CH$(CH_2)_2$Br, THF, reflux, 8.5 h, 58% for **14**; (iii) TBAF, THF, r.t., 15 min, 75% for **10**.

The preparation 2-tosylhydrazone **15** as the diazomethine precursor was unsuccessful, and led to the isolation of adduct **16** from the attempted reaction of tosyl hydrazide with benzimidazole-2-carbaldehyde **11** in methanol (Scheme 3). In contrast the literature preparations of *N*-(ω-alkenyl)indole-2-tosylhydrazones were reported to be facile, and efficient intramolecular cycloadditions to form cyclopropapyrrolo[1,2-*a*]indoles,[2] and precursors of CPM **3** and analogues[3,4,7] occurred upon treatment with base. It thus seemed that the 3-*N* basic nitrogen of imidazole was leading to a deprotonation of the 2-tosylhydrazone acidic hydrogen in **15**, probably through a favoured six-membered transition state to generate the 2-diazomethine **6** prematurely, which trapped methanol and lost nitrogen to give **16**.



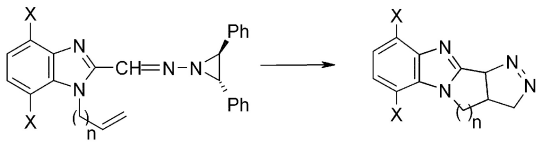
Scheme 3 *Reagents and conditions*: H_2N–NHTs, MeOH, r.t., 18 h, 29% for **16**.

Therefore, alternative precursors for reactive intermediates **6** and **7** were required, and we turned our attention to the preparation of Eschenmoser hydrazones or aziridinyl imines. Jones and Moody reported the thermolysis of *N*-allylindole-2-Eschenmoser hydrazone to cyclopropapyrrolo[1,2-*a*]indole in reasonable yield.[2] Benzimidazole-2-Eschenmoser hydrazones **17** and **18** proved to be effective isolable precursors for **6** and **7**, which were obtained in yields of 77% and 98% from the condensation of aldehydes **11** and **12** with *trans*-1-amino-2,3-diphenylaziridine[16] (Scheme 4). Hydrazones **17** and **18** upon thermolysis in refluxing xylene for 2 hours gave novel tetracyclic systems, cyclopropapyrrolo- and cyclopropapyrido-[1,2-*a*]benzimidazoles **19** and **20** in 85% and 53% yields, respectively.



Scheme 4 *Reagents and conditions*: (i) *E*-1-Amino-2,3-diphenylaziridine, Et_2O, 0 °C, 8 h, 77% for **17** and 98% for **18**; (ii) xylene, reflux, 2 h, 85% for **19** and 53% for **20**.

Thermolysis of hydrazone **17** and 4,7-dimethoxy analogue **21** at lower temperatures (refluxing benzene) for three hours selectively gave the 1,3-dipolar [3+2] cycloadducts **22** and **24** in 56% and 44% yield respectively (Scheme 5), and an X-ray crystal structure of **22** was obtained.[11] Under the latter lower decomposition temperatures, hydrazone **18** also decomposed to cyclopropane **20**, and no evidence of the formation of the 1,3-dipolar [3+2] pyrazoline cycloadduct **23** was obtained. The instability of **23** may be due to steric interactions between the 4,5-hydrogens on the [1,2-*a*]-fused six-membered ring and the fused pyrazoline 1,2-azo nitrogen atoms. 1-Pyrazoline fused onto six membered alicyclic rings in tricyclic sys-



17, X = H, n = 1
18, X = H, n = 2
21, X = OMe, n = 1

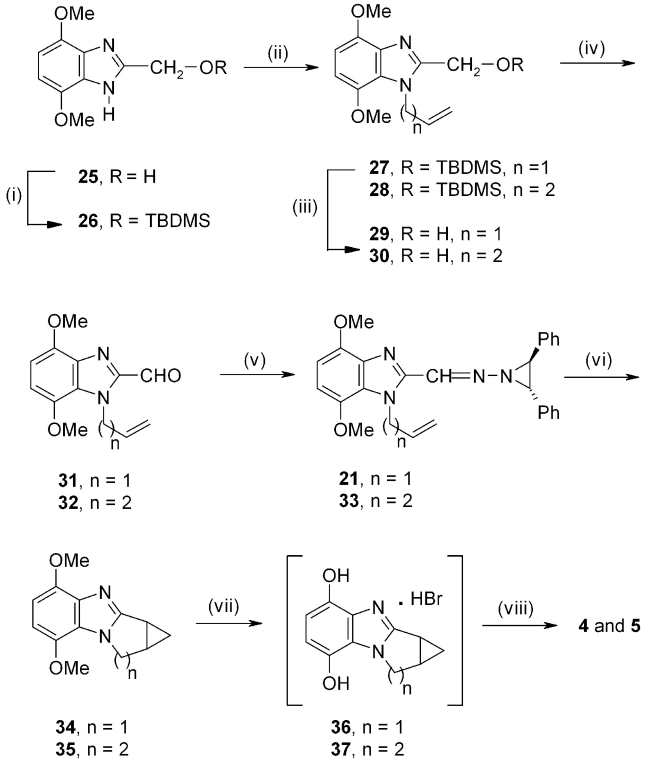
22, X = H, n = 1
23, X = H, n = 2
24, X = OMe, n = 1

Scheme 5 *Reagents and conditions*: PhH, reflux, 3 h, 56%, 0% and 44% for **22**, **23** and **24**, respectively. Adduct **20** isolated in 23% from the reaction using **18**.

tems have been previously isolated, however the aromatic ring was benzene in these cases.[17]

Once the methodology for the incorporation of the fused cyclopropane ring onto pyrrolo- and pyrido[1,2-*a*]benzimidazoles had been established, we turned our attention to functionalising the benzene part in order to form target benzimidazolequinones **4** and **5**. (4,7-Dimethoxybenzimidazol-2-yl)methanol (**25**) was prepared according to the procedure of Weinberger and Day[18] on a multi-gram scale in 46% yield by a modification of the Phillips condensation[19] between 3,6-dimethoxybenzene-1,2-diamine and glycolic acid. We decided to carry out alkylations on benzimidazole by the protection of the 2-hydroxymethyl group of **25** with TBDMS, which allowed us to carry out the N-alkylation using sodium hydride (Scheme 6). N-Alkylation with allyl bromide and 4-bromo-1-butene, TBAF deprotection and manganese dioxide oxidation gave aldehydes **31** and **32** in overall yields of 43% and 39%, respectively, for the four synthetic steps from **25**. Condensation with *trans*-1-amino-2,3-diphenylaziridine gave the 4,7-dimethoxybenzimidazole-2-Eschenmoser hydrazones **21** and **33** in excellent yields of 83% and 86%, and thermolysis in refluxing xylene gave cycloadducts **34** and **35** in yields of 68% and 58%, respectively. Hydrobromic acid induced demethylation of **34** and **35** gave the reactive hydroquinones **36** and **37** in situ, which underwent oxidation almost immediately at room temperature to give novel tetracyclic target benzimidazolequinones **4** and **5** using ferric chloride in identical yields of 64%.

It is interesting to compare our clean synthesis of **5** with the approach by Moody and co-workers to the [1,2-*a*]indolequinone analogue also containing cyclopropane fused onto a six-membered alicyclic ring, in which oxidation of the phenol to the quinone by the free radical, Fremy's salt, resulted in isolation of significant quantities of the by-product due to ring-opening of the cyclopropane ring.[7] This was not observed in our ferric chloride oxidations of hydroquinones **36** and **37** to quinones **4** and **5**, respectively (Scheme 6). Moody suggested the ring-opened product was evidence for one-electron initiated ring-opening of the cyclopropane ring via the phenoxyl radical, albeit under oxidative conditions. This tetrahydrocyclopropapyrido[1,2-*a*]indolequinone showed greater toxicity toward hypoxic conditions than the analogue with a cyclopropane fused onto a five-membered alicyclic ring,[7] however the



25, R = H
26, R = TBDMS

27, R = TBDMS, n =1
28, R = TBDMS, n = 2
29, R = H, n = 1
30, R = H, n = 2

31, n = 1
32, n = 2

21, n = 1
33, n = 2

34, n = 1
35, n = 2

36, n = 1
37, n = 2

4 and **5**

Scheme 6 *Reagents and conditions*: (i) TBDMSCl, pyridine, r.t., 4 h, 90% for **26**; (ii) NaH, CH_2=$CH(CH_2)_n$Br, THF, reflux, 8.5 h, 86% for **27** and 70% for **28**; (iii) TBAF, THF, r.t., 15 min, 85% for **29** and **30**; (iv) MnO_2, CH_2Cl_2, reflux, 30 min, 65% for **31** and 73% for **32**; (v) *E*-1-Amino-2,3-diphenylaziridine, Et_2O, 0 °C, 8 h, 83% for **21** and 86% for **33**; (vi) xylene, reflux, 2 h, 68% for **34** and 58% for **35**; (vii) 48% HBr (aq), reflux, 3 h; (viii) $FeCl_3$ (aq), r.t., 5 min, 64% for **4** and **5** after steps (vii) and (viii).

reductive potential of the former compound was not reported. Cyclic voltammetry carried out on **5** under the same conditions as for **4**[11] gave a similar redox potential of –1.074 vs ferrocene, and showed at low scan rates an analogous reversible single electron transfer process. This indicated a negligable effect on reductive activation of the increase in size by one CH_2 of the fused alicyclic ring. Cytotoxicity and selectivity of **4**, **5** and related [1,2-*a*] fused benzimidazolequinones toward hypoxic conditions will be reported in a subsequent paper.

In conclusion, new tetracyclic diazole ring systems based on pyrrolo- and pyrido-[1,2-*a*]benzimidazoles containing a fused cyclopropane ring were accessible using cycloaddition reactions of diazomethines derived from the thermolysis of benzimidazole-2-Eschenmoser hydrazones or aziridinyl imines in refluxing xylene. At lower temperatures of refluxing benzene, the [3 + 2] pyrazoline cycloadduct was obtained for the *N*-allyl-benzimidazole-2-diazomethines, and not for the *N*-but-3-enyl-benzimidazole-2-diazomethine. The synthesis of bioreductive benzimidazolequinones 1,1a,8,8a-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole-3,6-dione (**4**) and 1a,2,3,9b-tetrahydro-1*H*-cyclopropa[3,4]pyrido[1,2-*a*]benzimidazole-5,8-dione (**5**) is described in full. The

former compound is a diazole analogue of the indolequinone anti-tumor agent, cyclopropamitosene **3**.

Melting points were measured on a Stuart Scientific melting point apparatus SMP3, and are uncorrected. IR spectra were determined using neat samples on a Perkin-Elmer Spectrum 1000 FT-IR with an UATR accessory attached. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ on a Jeol GXFT 400 instrument equipped with a DEC AXP 300 computer work station. Chemical shifts are given in ppm, and *J* values are given in Hz. Electron-impact (EI) and chemical ionization (CI) mass spectra were recorded on a Micro Mass GTC GC-MS spectrometer. EPSRC National Mass Spectrometry Service carried out low resolution EI and CI on a Micromass Quattro II, and high resolution mass spectrometry using peak-matching techniques on the Finnigan MAT 900 XLT in CI mode for compounds **5**, **29** and **30**. TLC was carried out using aluminium-backed plates coated with silica gel (Merck Kiesgel 60 F254) as absorbent or using polyester plates coated with aluminium oxide as absorbent. Column chromatography was carried out using Merck silica gel 60, 234–400 mesh or using Aldrich aluminium oxide, activated neutral, Brockmann grade 3, STD Grade, 150 mesh size. Cyclic voltammetry was performed on an EcoChemie Autolab with PEGSTAT12 potentiostat controlled by GPES software at scan rates 20, 50, 100 and 200 mVs^{-1}. Quinones **4** and **5** were dissolved in DMF, containing 0.1 M tetrabutylammoniumperchlorate as electrolyte and 1 mM ferrocene (Fc) as reference. Cyclic voltammetry was recorded at a platinum disk electrode in a single compartment electrochemical cell (2 mL volume) containing Ag/AgCl reference electrode and a platinum wire counter electrode. All measurements were carried out at r.t. The platinum disc electrode was previously polished on a microcloth pad in 0.05 m alumina slurry, and nitrogen was bubbled through solvents. E_{redox} = –1.052, –1.074 V for **4** and **5** respectively and E_{pc}-$E_{p/2}$ values close to 0.056 V for both quinones allowed us to estimate n = 1.

All anhydrous reactions were carried under an inert atmosphere using distilled and anhydrous solvents. TBAF was a 1 M solution in THF, and used as purchased from Aldrich. Benzimidazole-2-methanols **8**[19] and **25**[18] were prepared in 57% and 46% yield by condensation of 1,2-phenylenediamine and 3,6-dimethoxybenzene-1,2-diamine respectively with glycolic acid in refluxing 4 M hydrochloric acid. *trans*-1-Amino-2,3-diphenylaziridine was prepared according to Eschenmoser's two step procedure[16] in 71% yield starting from *N*-aminophthalimide and *trans*-stilbene and used immediately. We have previously reported the procedure for the conversion of *N*-[(3-Butenyl-1*H*-benzimidazol-2-yl)methylene]-*E*-2,3-diphenylaziridin-1-amine (**18**) to 1a,2,3,9b-tetrahydrocyclopropa[3,4]pyrido[1,2-*a*]benzimidazole (**20**) in 53% yield and the characterization of **18** and 1,1a,8,8a-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole-3,6-dione **4** in a preliminary communication.[11]

Synthesis of *N*-Allyl-1*H*-benzimidazole-2-methanol (9)

Et_3N (23.5 mL, 0.169 mol) and **8** (5.000 g, 33.78 mmol) in THF (100 mL) were refluxed for 1 h. Allyl bromide (14.6 mL, 0.169 mol) was added and the solution refluxed for a further 3 h. Water (30 mL) was added to the cooled reaction mixture which was extracted with Et_2O (3 × 40 mL), dried ($MgSO_4$) and evaporated to dryness. The residue was purified by column chromatography using silica gel as absorbent with CH_2Cl_2 and EtOAc (gradient elution) to yield **9** as a pale yellow solid (2.610 g, 41%); mp 97–98 °C (lit.[14] mp 96 °C).

IR: 3054 (OH) 2833, 2719, 1463, 1410, 1330, 1011, 964, 934, 855 cm^{-1}.

^{1}H NMR: δ = 4.85–4.90 (4 H, m, NCH_2 and CH_2OH), 4.97–5.02 (1 H, d, *J* = 17.1 Hz, 3′-*trans*-H), 5.17–5.19 (1 H, d, *J* = 10.3 Hz, 3′-*cis*-H), 5.90–5.99 (1 H, m, 2′-H), 7.21–7.27 (3 H, m, ArH), 7.66–7.68 (1 H, m, ArH), OH peak not observed.

^{13}C NMR: δ = 45.9 (NCH_2), 56.6 (CH_2OH), 109.0 (ArCH), 117.4 (3′-CH_2), 119.2 (ArCH), 122.3 (ArCH), 122.9 (ArCH), 131.9 (2′-CH), 135.0 (C), 141.4 (C), 153.9 (Im-2-C).

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.21; H, 6.36; N, 14.78.

***N*-(3-Butenyl)-1*H*-benzimidazole-2-methanol (10)**

The same procedure used for the synthesis of **9** yielded **10** as a pale yellow solid (30%); mp 63–64 °C.

IR: 3158 (OH), 1508, 1459, 1418, 1333, 1039, 920 cm^{-1}.

^{1}H NMR: δ = 2.45– 2.49 (2 H, m, 2′-CH_2), 4.15–4.19 (2 H, m, NCH_2), 4.76 (2 H, s, CH_2OH), 4.91–4.95 (2 H, m, 4′-CH_2), 5.63–5.70 (1 H, m, 3′-H), 7.11–7.16 (3 H, m, ArH), 7.54–7.56 (1 H, d, *J* = 8.0 Hz, ArH), OH peak not observed.

^{13}C NMR: δ = 33.9 (2′-CH_2), 43.3 (NCH_2), 56.5 (CH_2OH), 109.7 (ArCH), 118.0 (4′-CH_2), 119.1 (ArCH), 122.1 (ArCH), 122.7 (ArCH), 133.7 (3′-CH), 134.7 (C), 141.4 (C), 153.9 (Im-2-C).

MS (EI): *m*/*z* (%) = 202 (M^+, 9), 161 (50), 131 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}N_2O$, 202.1106; found, 202.1106.

2-{[*tert*-Butyl(dimethyl)silyl]oxymethyl}-1*H*-benzimidazole (13)

TBDMSCl (2.60 g, 17.22 mmol), and **8** (1.50 g, 10.13 mmol) in pyridine (30 mL) were stirred at r.t. for 4 h. The resulting solution was evaporated to dryness, and the residue was dissolved in CH_2Cl_2 (40 mL). The organic layer was washed with sat. $NaHCO_3$ (50 mL), brine (50 mL), dried ($MgSO_4$) and evaporated to dryness. The resultant solid was purified by recrystallisation from hexane–EtOAc to yield **13** as a white solid (2.651 g, 100%); mp 143–144 °C.

IR: 2953, 2857, 1435, 1258, 1103, 829 cm^{-1}.

^{1}H NMR: δ = 0.15 [6 H, s, $Si(CH_3)_2$], 0.96 [9 H, s, $(CH_3)_3$], 5.01 (2 H, s, CH_2O), 7.23–7.56 (4 H, m, ArH), 9.54 (1 H, br s, NH).

^{13}C NMR: δ = –5.5 [$Si(CH_3)_2$], 18.3 (SiC), 25.8 [$C(CH_3)_3$], 60.0 (CH_2O), 111.3 (ArCH), 119.5 (ArCH), 122.3 (ArCH), 122.4 (ArCH), 133.0 (C), 143.4 (C), 153.9 (Im-2-C).

HRMS (CI): *m*/*z* calcd for $C_{14}H_{23}N_2OSi$ [M + H^+], 263.1580; found, 263.1589.

***N*-(3-Butenyl)-2-({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-1*H*-benzimidazole (14)**

TBDMS-protected alcohol **13** (1.000 g, 3.8 mmol) was added to NaH (0.110 g, 4.6 mmol) in THF (100 mL) and refluxed for 30 min. 4-Bromo-1-butene (0.6 mL, 5.7 mmol) was added, and the solution refluxed for a further 8 h. The mixture was cooled and water (100 mL) added, the product was extracted with Et_2O (2 × 75 mL), dried ($MgSO_4$) and evaporated to dryness to yield a pale yellow viscous oil, which was purified by column chromatography using silica gel as absorbent with hexane and EtOAc (gradient elution) to yield **14** as a clear oil (0.697 g, 58%).

IR: 2954, 2929, 2856, 1463, 1414, 1252, 1073 cm^{-1}.

^{1}H NMR: δ = 0.13 [6 H, s, $Si(CH_3)_2$], 0.92 [9 H, s, $(CH_3)_3$], 2.59–2.64 (2 H, m, 2'-CH_2), 4.32–4.35 (2 H, m, NCH_2), 4.98 (2 H, s, CH_2O), 5.08–5.12 (2 H, m, 4′-CH_2), 5.77–5.87 (1 H, m, 3′-H), 7.23–7.29 (2 H, m, ArH), 7.35–7.36 (1 H, m, ArH), 7.75–7.77 (1 H, m, ArH).

^{13}C NMR: δ = –5.5 [$Si(CH_3)_2$], 18.2 (SiC), 25.8 [$C(CH_3)_3$], 33.9 (2′-CH_2), 43.4 (NCH_2), 59.5 (CH_2O), 109.6 (ArCH), 117.7 (4′-CH_2), 120.0 (ArCH), 121.9 (ArCH), 122.6 (ArCH), 134.0 (3′-CH), 135.4 (C), 142.2 (C), 152.2 (Im-2-C).

MS (EI): *m*/*z* (%) = 205 (100), 131 (53), 75 (60), 57 (72).

MS (CI): *m*/*z* (%) = 263 (100), 205 (22), 133 (12).

TBDMS group was found to be labile in attempts to obtain accurate mass.

N-(3-Butenyl)-1*H*-benzimidazole-2-methanol (10); TBDMS-Deprotection of 14

TBDMS-protected alcohol **14** (0.460 g, 1.45 mmol) and TBAF (1.46 mL, 1.46 mmol) in THF (20 mL) were stirred at r.t. for 15 min. The solution was evaporated to dryness to yield a brown residue, which was purified by column chromatography using silica gel as absorbent with hexane and EtOAc (gradient elution) to yield **10** (0.227 g, 75%).

N-Allyl-1*H*-benzimidazole-2-carbaldehyde (11)

Alcohol **9** (40 mg, 0.21 mmol) and activated MnO_2 (0.540 g, 6.21 mmol) were refluxed in CH_2Cl_2 (50 mL) for 30 min. The cooled reaction mixture was filtered through celite, and evaporated to dryness to yield **11**, as a yellow solid (30 mg, 77%); mp 38–39 °C.

IR: 1688 (C=O), 1479, 1463, 1409, 1328, 1240, 1161, 994, 928 cm^{-1}.

^1H NMR: δ = 4.95–4.99 (1 H, d, *J* = 17.1 Hz, 3′-*trans*-H), 5.12–5.15 (1 H, d, *J* = 10.2 Hz, 3′-*cis*-H), 5.19–5.20 (2 H, m, NCH_2), 5.87–5.97 (1 H, m, 2′-H), 7.31–7.40 (3 H, m, ArH), 7.86–7.88 (1 H, m, ArH), 10.04 (1 H, s, CHO).

^{13}C NMR: δ = 46.6 (NCH_2), 111.1 (ArCH), 117.5 (3′-CH_2), 122.2 (ArCH), 124.1 (ArCH), 126.7 (ArCH), 131.8 (2′-CH), 136.1 (C), 142.6 (C), 145.5 (Im-2-C), 184.6 (CHO).

MS (EI): *m*/*z* = 186 (M^+, 93), 157 (100), 130 (57), 77 (47).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}N_2O$, 186.0793; found, 186.0789.

N-(3-Butenyl)-1*H*-benzimidazole-2-carbaldehyde (12)

The same procedure used for the synthesis of **11** yielded **12** as a yellow oil (55%).

IR: 1691 (C=O), 1479, 1468, 1413, 1327, 1240, 913 cm^{-1}.

^1H NMR: δ = 2.44–2.49 (2 H, m, 2′-CH_2), 4.53–4.57 (2 H, m, NCH_2), 4.85–4.90 (2 H, m, 4′-CH_2), 5.62–5.72 (1 H, m, 3′-H), 7.26–7.37 (3 H, m, ArH), 7.80–7.83 (1 H, d, *J* = 8.3 Hz, ArH), 9.99 (1 H, s, CHO).

^{13}C NMR: δ = 34.6 (2′-CH_2), 44.1 (NCH_2), 111.0 (ArCH), 118.1 (4′-CH_2), 122.4 (ArCH), 124.1 (ArCH), 126.8 (ArCH), 133.7 (3′-CH), 136.3 (C), 142.8 (C), 145.9 (Im-2-C), 185.0 (CHO).

MS (CI): *m*/*z* (%) = 201 (M + H^+, 100), 200 (M^+, 9), 172 (3), 159 (39).

HRMS (CI): *m*/*z* calcd for $C_{12}H_{12}N_2O$, 200.0950; found, 200.0962.

N-Allyl-2-(methoxymethyl)-1 *H*-benzimidazole (16)

p-Tosyl hydrazide (0.420 g, 2.25 mmol) and **11** (0.430 g, 2.31 mmol) in MeOH (20 mL) were stirred at r.t. for 18 h. The reaction mixture was evaporated to dryness to give a brown residue, which was purified by column chromatography using silica gel as absorbent with hexane and CH_2Cl_2 (gradient elution) to yield **16** as a clear oil (0.134 g, 29%).

IR: 2823, 1615, 1511, 1462, 1409, 1332, 1157, 1088 cm^{-1}.

^1H NMR: δ = 3.38 (3 H, s, OCH_3), 4.74 (2 H, s, CH_2O), 4.87–4.88 (2 H, m, NCH_2), 5.01–5.05 (1 H, d, *J* = 17.1 Hz, 3′-*trans*-H), 5.19–5.22 (1 H, d, *J* = 10.3, 3′-*cis*-H), 5.91–6.00 (1 H, m, 2′-H), 7.26–7.29 (3 H, m, ArH), 7.77–7.79 (1 H, m, ArH).

^{13}C NMR: δ = 46.1 (NCH_2), 58.2 (OCH_3), 67.1 (CH_2O), 109.7 (ArCH), 117.3 (3′-CH_2), 119.9 (ArCH), 122.2 (ArCH), 123.0 (ArCH), 132.1 (2′-CH), 135.4 (C) 142.7 (C) 150.4 (Im-2-C).

MS (EI): *m*/*z* (%) = 202 (M^+, 60), 172 (86), 157 (75), 131 (90).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}N_2O$, 202.1106; found, 202.1101.

N-[(1-Allyl-1*H*-benzimidazol-2-yl)methylene]-(*E*)-2,3-diphenylaziridin-1-amine (17)

(*E*)-1-Amino-2,3-diphenylaziridine (0.105 g, 0.48 mmol) and **11** (0.370 g, 1.99 mmol) in Et_2O (5 mL) were stirred at 0 °C for 8 h. The solution was evaporated to dryness and the residue was purified by column chromatography using neutral alumina as absorbent with hexane and CH_2Cl_2 (gradient elution) to yield **17** as a yellow oil (0.146 g, 77%).

IR: 3030, 2087, 1602, 1496, 1452, 1408, 1333, 1283, 1161, 1010, 922 cm^{-1}.

^1H NMR: δ = 3.81 (2 H, s, aziridine-H), 4.75–4.80 (1 H, d, *J* = 16.1 Hz, 3′-*trans*-H), 4.85–4.91 (2 H, m, NCH_2), 5.00–5.03 (1 H, d, *J* = 10.5 Hz, 3′-*cis*-H), 5.58–5.66 (1 H, m, 2′-H), 7.22–7.38 (13 H, m, ArH), 7.73–7.76 (1 H, m, ArH), 8.46 (1 H, s, CH=N).

^{13}C NMR: δ = 46.9 (NCH_2 and aziridine-CH), 110.5 (ArCH), 116.5 (3′-CH_2), 120.5 (ArCH), 122.7 (ArCH), 124.2 (ArCH), 127.8 (ArCH), 128.4 (ArCH), 132.5 (2′-CH), 136.2 (C), 142.9 (CH=N), 145.9 (C), 151.3 (Im-2-C).

N-[(3-Butenyl-1*H*-benzimidazol-2-yl)methylene]-(*E*)-2,3-diphenylaziridin-1-amine (18)

The same procedure as for **17** with (*E*)-1-Amino-2,3-diphenylaziridine (70 mg, 0.34 mmol) and **12** (80 mg, 0.43 mmol) in Et_2O (5 mL) yielded **18**,[11] as a yellow oil (0.130 g, 98%).

1,1a,8,8a-Tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole (19)

Aziridinamine **17** (0.112 g, 0.29 mmol) in xylene (20 mL) was refluxed for 2 h. The solution was evaporated to dryness to yield a residue which was purified by column chromatography using neutral alumina as absorbent with hexane and CH_2Cl_2 (gradient elution) to yield **19** as a yellow oil (43 mg, 85%).

IR: 3380, 3055, 2893, 1624, 1538, 1453, 1404, 1268, 1214, 1151, 1032, 931 cm^{-1}.

^1H NMR: δ = 0.76–0.79 (1 H, m, 1-H), 1.36–1.42 (1 H, m, 1-H), 2.48–2.50 (2 H, m, 1a and 8a-H), 4.03–4.13 (2 H, m, 8-CH_2), 7.16–7.18 (3 H, m, ArH), 7.64–7.66 (1 H, m, ArH).

^{13}C NMR: δ = 14.5 (1a-CH), 16.0 (1-CH_2), 20.6 (8a-CH), 45.3 (8-CH_2), 108.8 (ArCH), 119.3 (ArCH), 121.3 (ArCH), 121.7 (ArCH), 132.3 (C), 148.0 (C), 161.9 (Im-1b-C).

MS (EI): *m*/*z* (%) = 170 (M^+, 2), 169 (100), 156 (3).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}N_2$, 170.0844; found, 170.0838.

3,3a,4,10b-Tetrahydropyrazolo[3′,4′:3,4]pyrrolo[1,2-*a*]benzimidazole (22)

Aziridinamine **17** (0.260 g, 0.68 mmol) in benzene (20 mL) was refluxed for 3 h. The solution was evaporated to dryness and the crude residue was purified by column chromatography using neutral alumina as absorbent with hexane and CH_2Cl_2 (gradient elution) to yield **22** as a white solid (76 mg, 56%); mp 189–190 °C.

IR: 1621, 1552, 1517, 1483, 1452, 1416, 1324, 1219, 990 cm^{-1}.

^1H NMR: δ = 3.58–3.64 (1 H, m, 3a-H), 3.72–3.76 (1 H, m, 3-C*H*H), 4.34–4.38 (1 H, m, 3-CH*H*), 4.78–4.92 (2 H, m, NCH_2), 6.13–6.15 (1 H, d, *J* = 8.3 Hz, 10b-H), 7.26–7.28 (3 H, m, ArH), 7.81–7.83 (1 H, d, *J* = 8.1 Hz, ArH).

^{13}C NMR: δ = 36.8 (3a-CH), 48.8 (4-CH_2), 84.3 (3-CH_2), 90.8 (10b-CH), 109.9 (ArCH), 120.9 (ArCH), 122.6 (ArCH), 122.9 (ArCH), 131.9 (C), 149.3 (C), 154.4 (10a-C).

MS (EI): *m*/*z* (%) = 198 (M^+, 10), 169 (100), 156 (6).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}N_4$, 198.0905; found, 198.0910.

6,9-Dimethoxy-3,3a,4,10b-tetrahydropyrazolo[3′,4′:3,4]pyrrolo[1,2-*a*]benzimidazole (24)
The same procedure as for **22** yielded **24** as a white solid (44%); mp 180–181 °C.

IR: 1523, 1257, 1108, 1078 cm^{-1}.

^1H NMR: δ = 3.45–3.51 (1 H, m, 3a-H), 3.75 (3 H, s, OCH_3), 3.79–3.87 (1 H, m, 4-C*H*H), 3.90 (3 H, s, OCH_3), 4.39–4.45 (1 H, m, 4-C*H*H), 4.65–4.79 (2 H, m, 3-CH_2), 5.95–5.97 (1 H, m, 10b-H), 6.44–6.45 (2 H, AB_q, *J* = 8.3 Hz, ArH).

^{13}C NMR: δ = 37.0 (3a-CH), 50.6 (4-CH_2), 55.7 (OCH_3), 56.1 (OCH_3), 84.1 (3-CH_2), 90.3 (10b-CH), 102.5 (ArCH), 102.7 (ArCH), 123.6 (C), 140.8 (C), 141.1 (C), 146.1 (C), 152.8 (10a-C).

MS (CI): *m*/*z* (%) = 259 ($M + H^+$, 2), 231 (100), 230 (13).

HRMS (CI): *m*/*z* calcd for $C_{13}H_{15}N_4O_2$, 259.1195 [$M + H^+$]; found, 215.1192.

2-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-4,7-dimethoxy-1*H*-benzimidazole (26)
The same procedure as for **13** yielded **26** as a white solid (90%); mp 160–161 °C.

IR: 2930, 1519, 1449, 1264, 1253, 1095 cm^{-1}.

^1H NMR: δ = 0.15 [6 H, s, $Si(CH_3)_2$], 0.96 [9 H, s, $(CH_3)_3$], 3.94 (6 H, s, OCH_3), 4.99 (2 H, s, CH_2O), 6.56 (2 H, s, ArH).

^{13}C NMR: δ = –5.3 [$Si(CH_3)_2$], 18.2 (SiC), 25.7 [$C(CH_3)_3$], 55.7 (OCH_3), 59.8 (CH_2O), 102.1 (ArCH), 124.6 (C), 134.7 (C), 140.3 (C), 145.5 (C), 152.1 (Im-2-C).

MS (CI): *m*/*z* (%) = 323 ($M + H^+$, 100), 322 (10), 286 (68).

HRMS (CI): *m*/*z* calcd for $C_{16}H_{26}N_2O_3Si$, 322.1713; found, 322.1715.

1-Allyl-2-({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-4,7-dimethoxy-1*H*-benzimidazole (27)
The same procedure used for the synthesis of **14** yielded **27** as a white solid (86%); mp 40–41 °C.

IR: 2930, 1521, 1453, 1257, 1163, 1075 cm^{-1}.

^1H NMR: δ = 0.15 [6 H, s, $Si(CH_3)_2$], 0.95 [9 H, s, $(CH_3)_3$], 3.89 (3 H, s, OCH_3), 3.99 (3 H, OCH_3), 4.92–4.93 (1 H, m, 3′-C*H*H), 4.97 (2 H, s, CH_2O), 5.13–5.16 (1 H, m, 3′-CH*H*), 5.23–5.24 (2 H, m, NCH_2), 6.03–6.08 (1 H, m, 2′-H), 6.52–6.60 (2 H, AB-q, *J* = 8.8 Hz, ArH).

^{13}C NMR: δ = –5.8 [$Si(CH_3)_2$], 17.9 (SiC), 25.5 [$C(CH_3)_3$], 47.2 (NCH_2), 55.4 (OCH_3), 55.5 (OCH_3), 58.9 (CH_2O), 100.9 (ArCH), 103.2 (ArH), 115.5 (3′-CH_2), 125.9 (C), 133.7 (C), 134.0 (2′-CH), 141.2 (C), 145.8 (C), 151.0 (Im-2-C).

MS (CI): *m*/*z* (%) = 363 (MH^+, 100), 362 (25), 305 (10).

HRMS (CI): *m*/*z* calcd for $C_{19}H_{31}N_2O_3Si$, 363.2026 [$M + H^+$]; found, 363.2039.

1-But-3-en-1-yl-2-({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-4,7-dimethoxy-1*H*-benzimidazole (28)
The same procedure used for the synthesis of **14** yielded **28** as a white solid (70%); mp 48–49 °C.

IR: 2929, 1520, 1265, 1248, 1057 cm^{-1}.

^1H NMR: δ = 0.15 [6 H, s, $Si(CH_3)_2$], 0.95 [9 H, s, $(CH_3)_3$], 2.62–2.68 (2 H, m, 2′-CH_2), 3.96 (3 H, s, OCH_3), 3.99 (3 H, s, OCH_3), 4.53–4.56 (2 H, m, NCH_2), 4.99 (2 H, s, CH_2O), 5.08–5.13 (2 H, m, 4′-CH_2), 5.81–5.90 (1 H, m, 3′-H), 6.53–6.61 (2 H, ABq, *J* = 8.0 Hz, ArH).

^{13}C NMR: δ = –5.5 [$Si(CH_3)_2$], 18.2 (SiC), 25.8 [$C(CH_3)_3$], 35.9 (2′-CH_2), 45.2 (NCH_2), 55.7 (OCH_3), 55.8 (OCH_3), 59.3 (CH_2O), 101.2 (ArCH), 103.1 (ArCH), 117.1 (4′-CH_2), 125.8 (C), 134.1 (C), 134.5 (C), 141.5 (C), 146.0 (C), 151.2 (Im-2-C).

MS (CI): *m*/*z* (%) = 377 ($M + H^+$, 100), 376 (28), 319 (9).

HRMS (CI): *m*/*z* calcd for $C_{20}H_{32}N_2O_3Si$: 376.2182; found: 376.2185.

(1-Allyl-4,7-dimethyloxy-1*H*-benzimidazol-2-yl)methanol (29)
The same procedure used for the deprotection of **14** to **10** yielded **29** as a white solid (85%); mp 154–155 °C.

IR: 3142 (OH), 2936, 1521, 1264, 1231, 1105, 1040 cm^{-1}.

^1H NMR: δ = 3.85 (3 H, s, OCH_3), 3.95 (3 H, s, OCH_3), 4.84–5.17 (6 H, m, CH_2O, 3′-CH_2, NCH_2), 5.97–6.04 (1 H, m, 2′-H), 6.50–6.56 (2 H, m, ArH), OH peak not observed.

^{13}C NMR: δ = 47.3 (NCH_2), 55.9 (OCH_3), 57.2 (CH_2OH), 101.6 (ArCH), 103.6 (ArCH), 116.2 (3′-CH_2), 126.0 (C), 133.8 (2′-CH), 141.5 (C), 145.7 (C), 152.5 (Im-2-C).

MS (CI): *m*/*z* (%) = 249 ($M + H^+$, 100), 233 (28), 219 (7).

HRMS (CI): *m*/*z* calcd for $C_{13}H_{17}N_2O_3$ [$M + H^+$], 249.1234; found, 249.1233.

(1-But-3-en-1-yl-4,7-dimethoxy-1*H*-benzimidazol-2-yl)methanol (30)
The same procedure used for the deprotection of **14** to **10** yielded **30** as a white solid (85%); mp 138–139 °C.

IR: 3168 (OH), 1522, 1464, 1264, 1109, 1081, 1040 cm^{-1}.

^1H NMR: δ = 2.45–2.50 (2 H, m, 2′-CH_2), 3.79 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 4.34–4.37 (2 H, m, NCH_2), 4.79 (2 H, s, CH_2O), 4.90–4.94 (2 H, m, 4′-CH_2), 5.66–5.76 (1 H, m, 3′-H), 6.39–6.46 (2 H, AB_q, *J* = 8.5 Hz, ArH), OH peak not observed.

^{13}C NMR: δ = 35.8 (2′-CH_2), 44.9 (NCH_2), 55.7 (OCH_3), 55.8 (OCH_3), 57.2 (CH_2OH), 101.5 (ArCH), 103.1 (ArCH), 117.5 (4'-CH_2), 125.8 (C), 133.7 (C), 134.2 (3'-CH), 141.4 (C), 145.6 (C), 152.4 (Im-2-C).

MS (CI): *m*/*z* (%) = 263 ($M + H^+$, 100), 249 (50), 233 (79).

HRMS (CI): *m*/*z* calcd for $C_{14}H_{19}N_2O_3$ [$M + H^+$], 263.1392; found, 263.1390.

1-Allyl-4,7-dimethoxy-1*H*-benzimidazole-2-carbaldehyde (31)
The same procedure used for the synthesis of **11** yielded **31** as a yellow solid (65%); mp 98–99 °C.

IR: 1690 (C=O), 1525, 1454, 1264, 1168, 1102 cm^{-1}.

^1H NMR: δ = 3.91 (3 H, s, OCH_3), 4.00 (3 H, s, OCH_3), 4.96–5.00 (1 H, d, *J* = 17.3 Hz, 3′-*trans*-H), 5.10–5.13 (1 H, d, *J* = 10.3 Hz, 3′-*cis*-H), 5.49–5.50 (2 H, m, NCH_2), 5.99–6.08 (1 H, m, 2′-H), 6.56–6.58 (1 H, d, *J* = 8.5 Hz, ArH), 6.72–6.74 (1 H, d, *J* = 8.5 Hz, ArH), 10.07 (1 H, s, CHO).

^{13}C NMR: δ = 48.2 (NCH_2), 55.8 (OCH_3), 56.0 (OCH_3), 102.0 (ArCH), 106.7 (ArH), 116.8 (3′-CH_2), 127.4 (C), 133.8 (2′-CH), 135.5 (C), 141.9 (C), 147.2 (Im-2-C), 184.4 (CHO).

MS (CI): *m*/*z* = 247 (MH^+, 100), 246 (M^+, 8).

HRMS (CI): *m*/*z* calcd for $C_{13}H_{14}N_2O_3$: 246.1004; found: 246.1003.

1-But-3-en-1-yl-4,7-dimethoxy-1*H*-benzimidazole-2-carbaldehyde (32)
The same procedure used for the synthesis of **11** yielded **32** as a yellow solid (73%); mp 72–73 °C.

IR: 2850, 1687 (C=O), 1526, 1464, 1264, 1076 cm^{-1}.

^1H NMR: δ = 2.55–2.57 (2 H, m, 2′-CH_2), 3.93 (3 H, s, OCH_3), 4.00 (3 H, s, OCH_3), 4.91–4.97 (4 H, m, NCH_2 and 4′-CH_2), 5.76–5.80

(1 H, m, 3′-H), 6.55–6.71 (2 H, AB_q, *J* = 8.5 Hz, ArH), 10.07 (1 H, s, CHO).

^{13}C NMR: δ = 36.1 (2′-CH_2), 45.5 (NCH_2), 55.8 (OCH_3), 55.9 (OCH_3), 101.9 (ArCH), 106.4 (ArCH), 117.6 (4′-CH_2), 127.8 (C), 133.9 (3′-CH), 135.6 (C), 141.9 (C), 145.2 (C), 147.1 (Im-2-C), 184.8 (CHO).

MS (EI): *m*/*z* (%) = 260 (M^+, 17), 130 (40), 68 (100).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{16}N_2O_3$, 260.1161; found, 260.1125.

N-(1-Allyl-4,7-dimethoxy-1*H*-benzimidazol-2-yl)methylidene]-(*E*)-2,3-diphenyl-1-aziridinamine (21)

The same procedure used for the synthesis of **17** yielded **21** as a yellow oil (83%).

IR: 2934, 2088, 1523, 1451, 1262 cm^{-1}.

^{1}H NMR: δ = 3.68 (2 H, s, aziridine-H), 3.69 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 4.55–4.59 (1 H, d, *J* = 17.1 Hz, 3′-*trans*-H), 4.81–4.84 (1 H, d, *J* = 9.3 Hz, 3′-*cis*-H), 5.03–5.12 (2 H, m, NCH_2), 5.54–5.64 (1 H, m, 2′-H), 6.34–6.44 (2 H, ABq, *J* = 8.6 Hz, ArH), 7.13–7.40 (10 H, m, ArH), 8.36 (1 H, s, CH=N).

^{13}C NMR: δ = 48.1 (NCH_2 and aziridine-CH), 55.6 (OCH_3), 55.8 (OCH_3), 101.4 (ArCH), 104.7 (ArCH), 115.4 (3′-CH_2), 126.3 (ArCH), 127.4 (ArCH), 127.6 (ArCH), 128.2 (ArCH), 134.3 (2′-CH), 135.2 (C), 137.4 (C), 141.5 (C), 144.9 (CH=N), 146.2 (C), 151.5 (Im-2-C).

N-[(1-But-3-en-1-yl-4,7-dimethoxy-1*H*-benzimidazol-2-yl)methylene]-2,3-diphenylaziridin-1-amine (33)

The same procedure used for the synthesis of **17** yielded **33** as a yellow oil (86%).

IR: 2084, 1521, 1261, 1078 cm^{-1}.

^{1}H NMR: δ = 2.23–2.25 (2 H, m, 2′-CH_2), 3.82 (2 H, s, aziridine-H), 3.84 (3 H, s, OCH_3), 3.92 (3 H, s, OCH_3), 4.53–4.56 (2 H, m, NCH_2), 4.82–4.91 (2 H, m, 4′-CH_2), 5.52–5.56 (1 H, m, 3′-H), 6.45–6.55 (2 H, AB_q, *J* = 8.3 Hz, ArH), 7.28–7.49 (10 H, m, ArH), 8.51 (1 H, s, CH=N).

^{13}C NMR: δ = 35.4 (2′-CH_2), 45.6 (NCH_2 and aziridine-CH), 55.7 (OCH_3), 101.3 (ArCH), 104.4 (ArCH), 116.6 (4′-CH_2), 126.5 (ArCH), 127.1 (ArCH), 127.6 (ArCH), 127.8 (ArCH), 128.4 (ArCH), 128.6 (ArCH), 134.7 (3′-CH), 135.2 (C), 141.5 (CH=N), 144.9 (C), 146.2 (C), 151.8 (Im-2-C).

3,6-Dimethoxy-1,1a,8,8a-tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole (34)

The same procedure used for the synthesis of **19** yielded **34** as a yellow oil 68%.

IR: 1542, 1518, 1387, 1253, 1092 cm^{-1}.

^{1}H NMR: δ = 0.68–0.72 (1 H, m, 1-H), 1.28–1.33 (1 H, m, 1-H), 2.37–2.42 (2 H, m, 1a and 8a-H), 3.79 (3 H, s, OCH_3), 3.90 (3 H, s, OCH_3), 4.25–4.26 (2 H, d, *J* = 4.9 Hz, 8-CH_2), 6.43 (2 H, s, ArH).

^{13}C NMR: δ = 14.1 (1a-CH), 15.5 (1-CH_2), 20.7 (8a-CH), 47.4 (8-CH_2), 55.7 (OCH_3), 56.0 (OCH_3), 101.8 (ArCH), 102.1 (ArCH), 123.7 (C), 139.1 (C), 140.6 (C), 145.4 (C), 160.5 (Im-1b-C).

MS (CI): *m*/*z* (%) = 231 (M + H^+, 100), 230 (20, M^+).

HRMS (CI): *m*/*z* calcd for $C_{13}H_{14}N_2O_2$: 230.1055; found: 230.1059.

5,8-Dimethoxy-1a,2,3,9b-tetrahydro-1*H*-cyclopropa[3,4]pyrido[1,2-*a*]benzimidazole (35)

The same procedure used for the synthesis of **19** yielded **35** as an off-white solid (58%); mp 145–146 °C.

IR: 2927, 1541, 1516, 1401. 1260, 1084 cm^{-1}.

^{1}H NMR: δ = 0.97–1.07 (2 H, m, 1-CH_2), 1.60–1.73 (1 H, m, 1a-H), 2.05–2.16 (2 H, m, 2-CH_2), 2.33–2.39 (1 H, m, 9b-H), 3.60–3.72 (1 H, m, 3-C*H*H), 3.76 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 4.76–4.81 (1 H, m, 3-CH*H*), 6.39 (2 H, s, ArH).

^{13}C NMR: δ = 8.6 (1-CH_2), 11.3 (1a-CH), 13.2 (9b-CH), 20.7 (2-CH_2), 39.6 (3-CH_2), 55.7 (OCH_3), 55.9 (OCH_3), 101.3 (ArCH), 102.3 (ArCH), 124.9 (C), 134.3 (C), 141.3 (C), 145.3 (C), 151.8 (9a-C).

MS (CI): *m*/*z* (%) = 245 (M + H^+, 100), 244 (21, M^+), 215 (2).

HRMS (CI): *m*/*z* calcd for $C_{14}H_{16}N_2O_2$, 244.1212; found, 244.1215.

1,1a,8,8a-Tetrahydrocyclopropa[3,4]pyrrolo[1,2-*a*]benzimidazole-3,6-dione (4)

Cyclopropapyrrolo[1,2-*a*]benzimidazole **34** (40 mg, 0.17 mmol) was refluxed in 48% hydrobromic acid (10 ml) for 3 h. The solution was evaporated to dryness, and 0.7 M $FeCl_3$ solution (10 mL) added. A faint yellow precipitate was observed immediately, and sat. NaOAc solution (10 mL) was added. The solution was extracted with $CHCl_3$ (3 × 15 mL), dried ($MgSO_4$) and evaporated to dryness to yield an orange solid. The crude solid was purified by column chromatography using silica gel as absorbent with hexane and EtOAc (gradient elution) to yield **4**,[11]as a red-orange solid (22 mg, 64%).

1a,2,3,9b-tetrahydro-1 *H*-cyclopropa[3,4]pyrido[1,2-*a*]benzimidazole-5,8-dione (5)

The same procedure used for the synthesis of **4** yielded **5** as a red-orange solid (64%); mp 145 °C (dec.).

IR: 1657 (C=O), 1525, 1285, 1078 cm^{-1}.

^{1}H NMR: δ = 1.11–1.15 (1 H, m, 1-H), 1.23–1.29 (1 H, m, 1-H), 1.85–1.88 (1 H, m, 1a-H), 2.05–2.16 (1 H, m, 2-C*H*H), 2.29–2.34 (1 H, m, 2-C*H*H), 2.42–2.47 (1 H, m, 9b-H), 3.59–3.68 (1 H, 3-C*H*H), 4.81–4.86 (1 H, 3-C*H*H), 6.48–6.62 (2 H, AB_q, *J* = 10.4 Hz, 6 and 7-H).

^{13}C NMR: δ = 9.3 (1-CH_2), 10.9 (9b-CH), 13.7 (1a-CH), 19.7 (2-CH_2), 39.7 (3-CH_2), 129.5 (C), 135.9 (6(7)-CH), 136.9 [6(7)-CH], 141.1 (C), 153.7 (9a-C), 178.2 (C=O), 181.0 (C=O).

MS (CI): *m*/*z* (%) = 215 (13, M + H^+), 213 (7), 198 (54), 188 (100), 139 (53).

HRMS (CI): *m*/*z* calcd for $C_{12}H_9N_2O_2$ [M – H^+], 213.0659; found, 213.0661.

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