HETEROCYCLES, Vol. 100, No. 9, 2020, pp. 1371 - 1404. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 7th May, 2020, Accepted, 30th June, 2020, Published online, 1st July, 2020
DOI: 10.3987/COM-20-14280

REACTIVITY OF 4,6-DIMETHOXY ACTIVATED BENZIMIDAZOLES

Mahiuddin Alamgir, Glenn C. Condie, Vesna Martinovic, Joanne Wood, Mohan Bhadbhade, Naresh Kumar, and David StC. Black*

School of Chemistry, The University of New South Wales, UNSW Sydney, NSW 2052, Australia. Email: d.black@unsw.edu.au

Abstract – 4,6-Dimethoxy-2-substituted-benzimidazoles undergo formylation, acylation, nitration and bromination at C7. The 7-carbaldehydes can be reduced to the corresponding hydroxymethyl compounds. Benzimidazole-2-carbaldehydes can be prepared by oxidation of 2-methyl- and 2-styryl-benzimidazoles. *N*-Methylation and *N*-allylation have also been investigated and lead to isomeric mixtures of 4,6- and 5,7-dimethoxybenzimidazoles. In general the nucleophilic capacity of the activated benzimidazoles is weaker than that of the related activated indoles, but still provides synthetic routes to a range of new heterocyclic structures.

INTRODUCTION

As part of a programme aimed at expanding the chemical reactivity of certain heterocyclic systems through dimethoxy activation, the investigation of activated benzimidazoles was an early priority. The syntheses of a variety of 4,6-dimethoxy activated benzimidazoles have been reported in a previous paper.[1] Although these new benzimidazoles would be expected to activate the C7 position, the reactivity would be expected to be different from that shown by similarly activated indoles, as a result of the greater basicity of the benzimidazoles. The elucidation of similarities and differences in the behaviour of activated indoles and benzimidazoles was a key part of the investigation. In this context, the benzimidazole C2 position is not nucleophilic enough for electrophilic aromatic substitution. Furthermore the replacement of an indole C3 atom and also any C3-substituent for a simple N3 atom in the related benzimidazole would have steric consequences. We now report a range of fundamental reactions of 4,6-dimethoxybenzimidazoles.

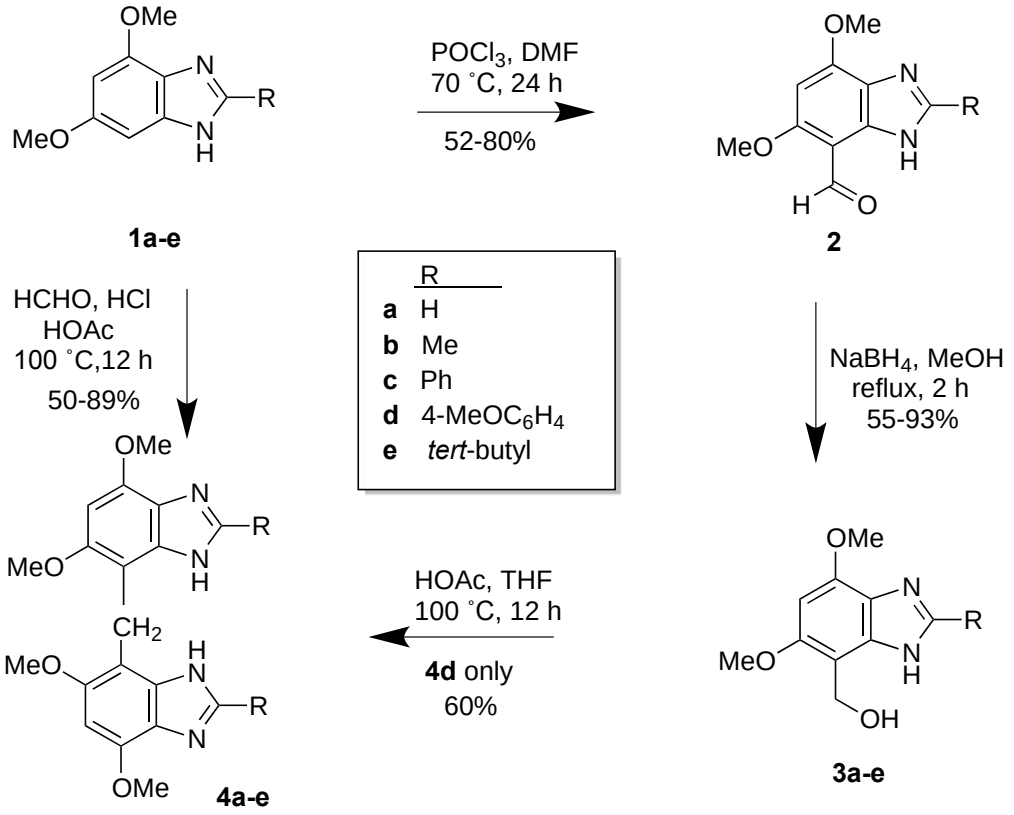
RESULTS AND DISCUSSION

Formylation of 4,6-dimethoxybenzimidazoles and some further reactions of the products

Treatment of the 4,6-dimethoxybenzimidazoles **1a-e** with the Vilsmeier formylating reagent respectively afforded the benzimidazole-7-carbaldehydes **2a-e** (Scheme 1). It was observed that the benzimidazoles required more vigorous reaction conditions compared to those for the related indole examples.[2] Formylation of benzimidazoles with 2-aryl substituents, for example benzimidazoles **1c**,**d**, generally afforded higher yields (75-80%). The lowest yield (52%) is obtained in the case of the 2-methylbenzimidazole **1b**, which can only be formylated using 1.1 equivalents of the formylating reagent, as the presence of two equivalents results in side reactions at the active 2-methyl functional group. Evidence for the formation of benzimidazole-7-carbaldehydes **2a-e** was obtained from their ^{1}H NMR spectra showing the disappearance of the *meta* coupled C5-C7 doublets of the starting benzimidazoles, and the presence of the 7-formyl protons. Tautomerism between 4,6-dimethoxybenzimidazoles and 5,7-dimethoxybenzimidazoles was not observed in the 4,6-dimethoxybenzimidazole-7-carbaldehydes **2a-e**. The reason is presumably that the NH is hydrogen bonded to the formyl oxygen to give a more stable 4,6-dimethoxy tautomer. Oxime derivatives of the aldehydes **2d**,**e** were prepared in a routine manner.

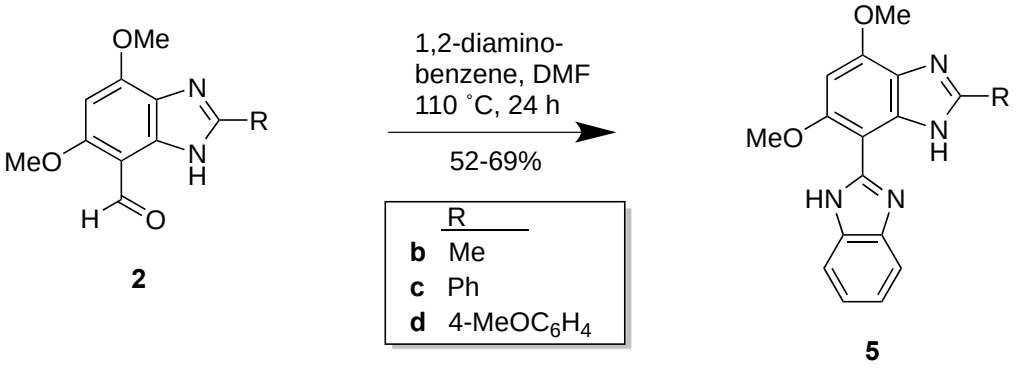
The benzimidazole-7-carbaldehydes **2a-e** when treated with excess sodium borohydride in methanol under reflux for two hours gave the 7-hydroxymethylbenzimidazoles **3a-e** respectively as white solids in high yields (Scheme 1). Again, the NH is probably hydrogen bonded to the hydroxyl oxygen to give a single tautomeric compound.

The 7,7'-dibenzimidazolylmethanes **4a-d** were prepared in moderate to high yields (50-89%) by addition of formaldehyde to hot solutions of the benzimidazoles **1a-d** in glacial acetic acid followed by a few drops of concentrated hydrochloric acid and overnight heating (Scheme 1). However, unlike the activated indoles, the activated benzimidazoles are unable to react effectively with aryl aldehydes. Alternatively, synthesis of the dibenzimidazolylmethane **4d** was also carried out by the reaction of the 7-hydroxymethylbenzimidazole **3d** in tetrahydrofuran with glacial acetic acid at room temperature for 6 h. By comparison, similar reactions of activated indoles to produce the 7,7'-diindolylmethanes require only 3 hours at room temperature.[3] The mechanism involves an *ipso*-substitution with loss of formaldehyde and has been already discussed for the indoles.[4-7]



Scheme 1

Reaction of the benzimidazole-7-carbaldehydes **2b-d** with 1,2-diaminobenzene gave new 2,7'-bisbenzimidazoles **5b-d** by oxidative condensation in *N*,*N*-dimethylformamide **(**Scheme 2**)**. A similar reaction has been observed with related indole-7-carbaldehydes.[8] The X-ray crystal structure of the compound **5c** (Figure 1) showed a planar molecule with hydrogen bonding (d = 2.20 Å) between N1H to the N'3 lone pair of electrons. The N'1H is also hydrogen bonded to a water molecule. The presence of a water molecule was indicated in the elemental analysis. The crystal structure establishes the dominant nature of the 4,6-dimethoxy tautomer over the alternative 5,7-dimethoxy tautomer as a result of the hydrogen bonding. Furthermore, the bisbenzimidazoles **5b-d** have potential as bidentate ligands and divalent metal ions could combine with two bisbenzimidazoles to generate neutral metal complexes.



Scheme 2

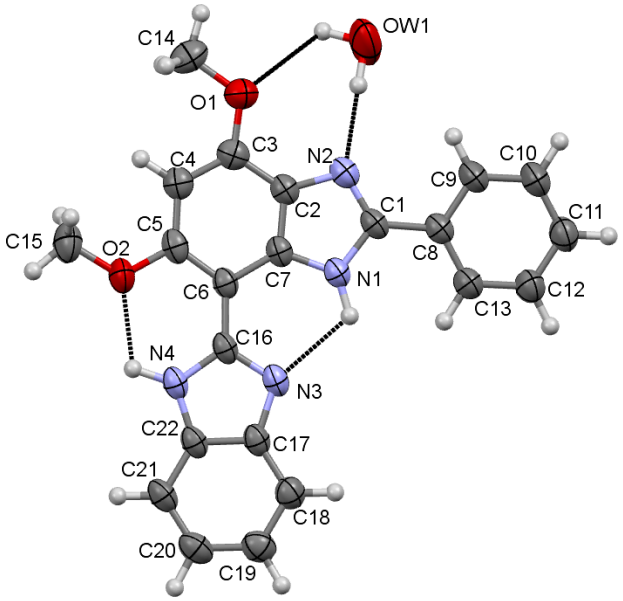
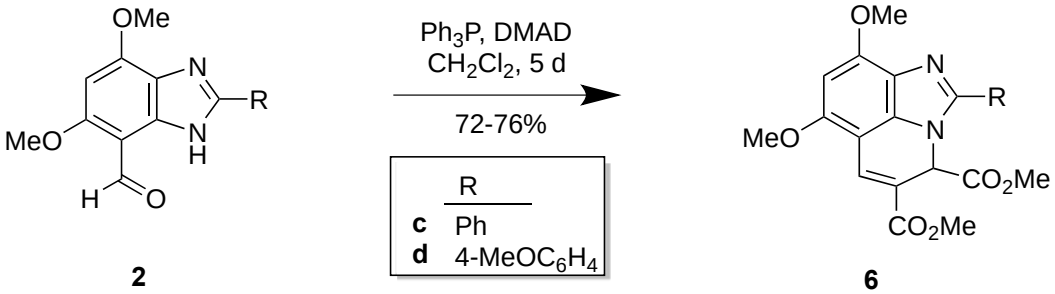


Figure 1. ORTEP diagram of the crystal structure of bisbenzimidazole **5c**

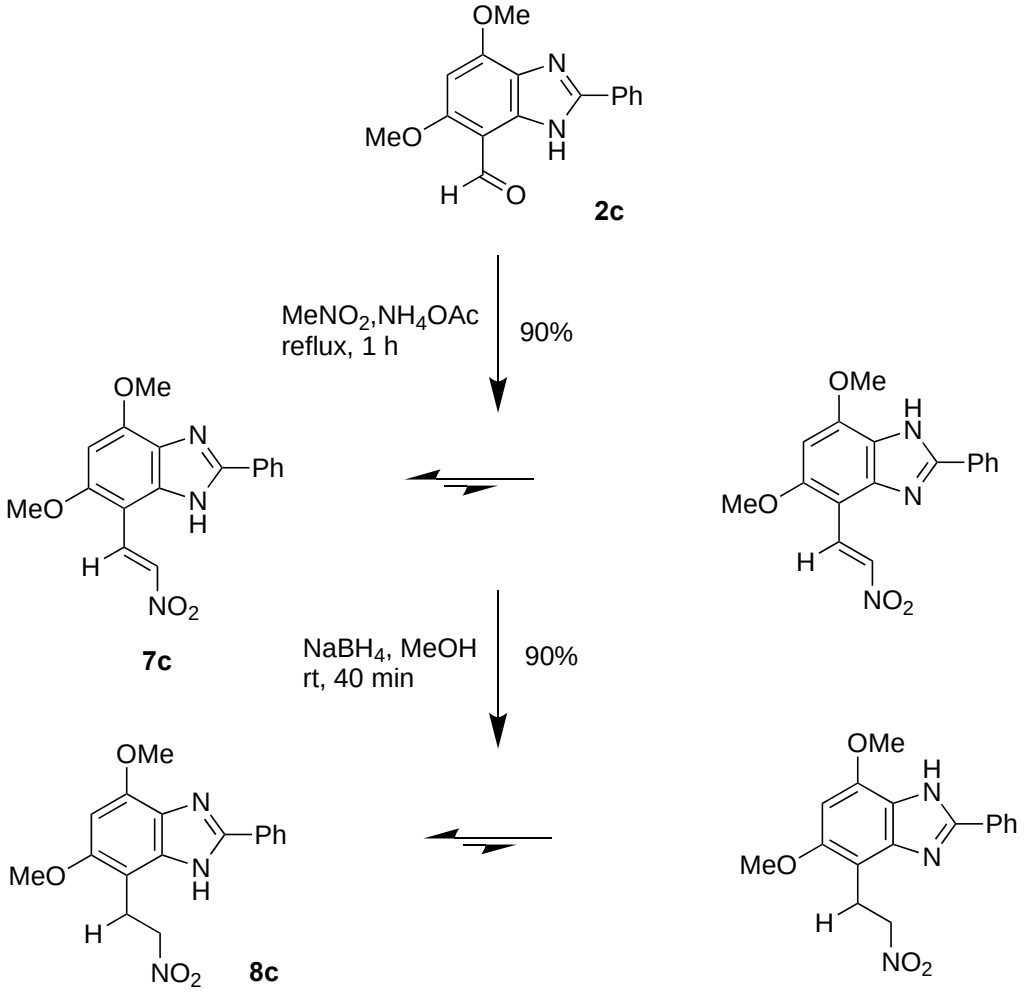
The benzimidazole-7-carbaldehydes **2c-d** were chosen as representative examples and also reacted with dimethyl acetylenedicarboxylate (DMAD) and triphenylphosphine in dry dichloromethane over five days to give the imidazoloquinolines **6c-d** in 72% and 76% yields respectively. The proposed mechanism is assumed to be analogous to that described by Yavari and Ramazani for the preparation of 2*H*-chromenes from salicylaldehyde.[9] The ^{1}H NMR spectra of the imidazoloquinolines **6c-d** showed two additional methoxy groups, the C8 proton was observed at ~6.20 ppm and C4 aliphatic proton at ~6.40 ppm.



Scheme 3

In a single attempt to obtain a 7-substituted-4,6-dimethoxybenzimidazole that would exclude hydrogen bonding from the 7-substituent to the NH, the benzimidazole-7-carbaldehyde **2c** was reacted with nitromethane in the presence of ammonium acetate and gave the 7-nitrovinyl compound **7c** and its tautomer in a 20:1 ratio (Scheme 4). The major tautomer lacks the steric hindrance between the NH and the methoxy group that is present in the minor tautomer. The ^{1}H NMR spectrum identified the major and minor tautomeric structures but did not clearly identify all the components of the minor tautomer.

Consequently, the nitrovinyl compound **7c** was reduced with sodium borohydride in methanol to yield the nitroethyl compound **8c** and its tautomer in a 1.0:1.25 ratio. Both ^{1}H NMR spectra were clearly distinguished in this case.



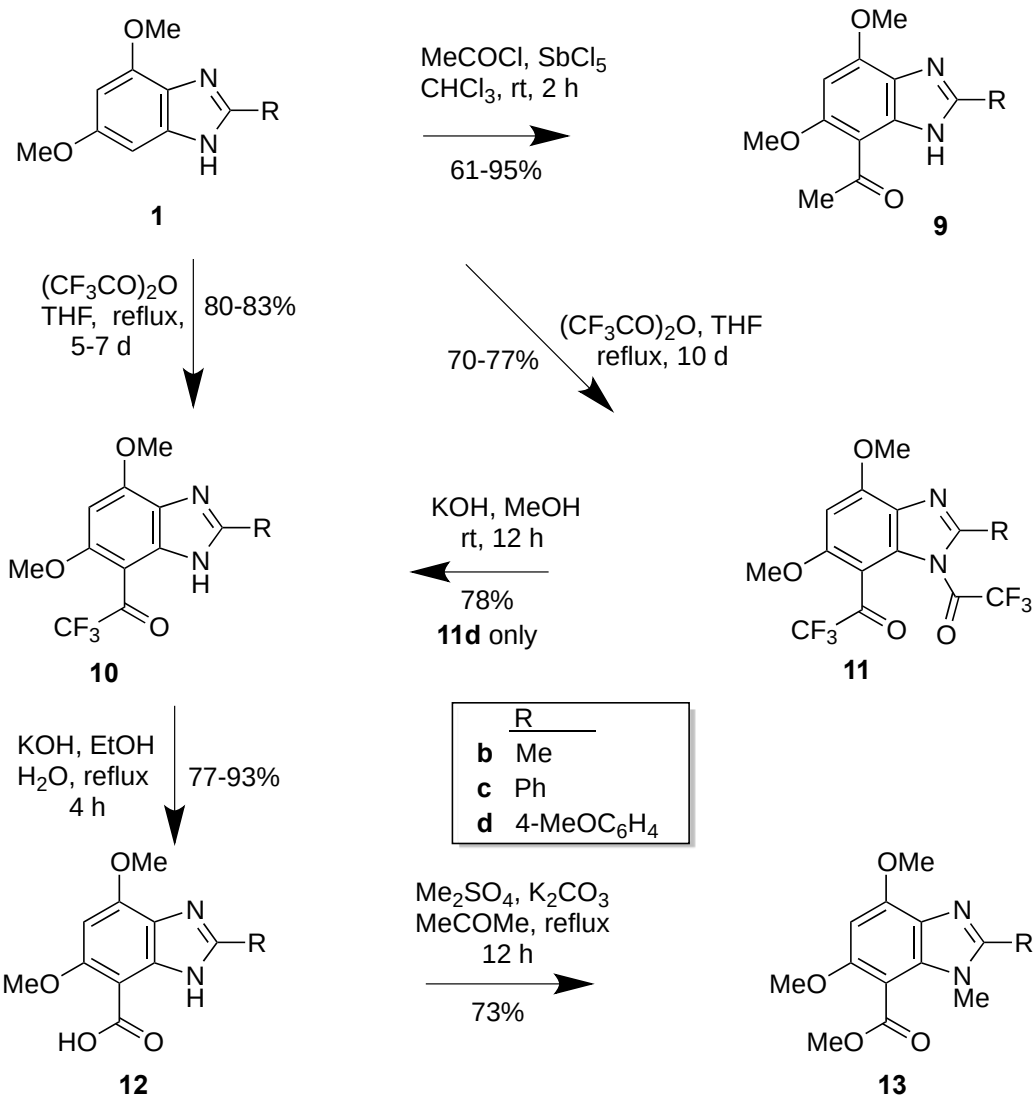
Scheme 4

Acylation of 4,6-dimethoxybenzimidazoles

While the formylation of 4,6-dimethoxyindoles proceeds smoothly, the related acetylation using a modified Vilsmeier reagent of phosphoryl chloride in *N*,*N*-dimethylacetamide is generally a much slower process and gives reduced yields of 7-acetylated products.[10] However, these modified Vilsmeier-Haack reaction conditions were unable to allow acetylation at the C7 position of the benzimidazoles **1b-d**. The failure of this reaction shows again that the C7 position in the activated benzimidazoles is not as nucleophilic as that in the related indoles. Therefore, preparation of the 7-acetylbenzimidazoles **9b-d** required more vigorous Friedel-Crafts acylation of the benzimidazoles **1b-d**. The use of acetyl chloride and antimony pentachloride gave the acetyl compound **9c** in 61% yield after 48 h. When benzimidazole **1c** was reacted with four equivalents of the Friedel-Crafts reagent, a 70% yield of compound **9c** was obtained within two hours. Likewise, the benzimidazoles **1b**,**d** were also acetylated using four equivalents

of Friedel-Crafts reagent in two hours and afforded the 7-acetylbenzimidazoles **9b**,**d** in 95% and 61% yields respectively (Scheme 5). Similar hydrogen bonding between the carbonyl oxygen and nitrogen proton presumably stabilizes the single tautomer observed in the ^{1}H NMR spectrum.

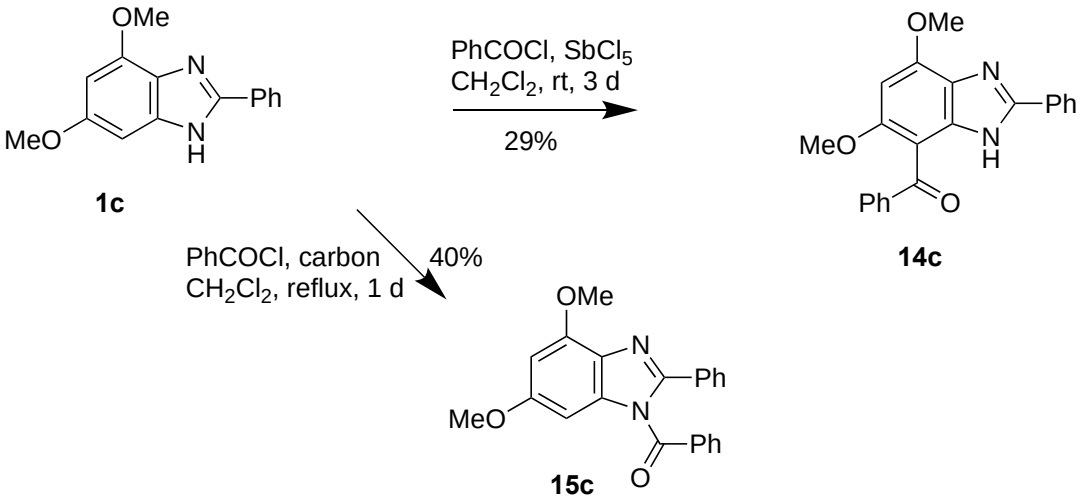
Acylation of benzimidazoles **1c**,**d** with trifluoroacetic anhydride successfully afforded the 7-trifluoroacetylbenzimidazoles **10c**,**d** in 80-83% yield, but only after 5-7 days heating under reflux in tetrahydrofuran (Scheme 5). The corresponding acylation of 4,6-dimethoxyindoles typically occurs over 8 hours at room temperature.[3] This further indicates the relatively low reactivity of the benzimidazoles compared with the indoles. When the benzimidazoles **1c**,**d** were heated with trifluoroacetic anhydride in tetrahydrofuran for 10 days, the major products observed were the disubstituted benzimidazoles **11c**,**d** in 70 and 77 % yield respectively (Scheme 5). The disubstituted compound **11d** was easily *N*-deprotected by methanolic potassium hydroxide at room temperature to give the 7-trifluoroacetylbenzimidazole **10d** in 78% yield.



Scheme 5

The 7-trifluoroacetylbenzimidazoles **10c**,**d** were hydrolyzed to the corresponding benzimidazole-7-carboxylic acids **12c**,**d** respectively in 77% and 80% yields by treatment with ethanolic potassium hydroxide solution (Scheme 5). Treatment of the benzimidazole-7-carboxylic acids **12c**,**d** with excess dimethyl sulfate in acetone gave the methyl *N*-methylbenzimidazole-7-carboxylates **13c**,**d**.

Treatment of the 4,6-dimethoxybenzimidazole **1c** with benzoyl chloride in dry dichloromethane in the presence of antimony pentachloride after 3 days gave the 7-benzoyl product **14c** in only 29% yield (Scheme 6**)**. The compound **14c** was shown to be a single tautomer probably due to the hydrogen bonding of the carbonyl oxygen to the NH. The alternate tautomer would also be unfavourable due to steric hindrance from the methoxy group. On the other hand, reaction of the 4,6-dimethoxybenzimidazole **1c** with benzoyl chloride in dry dichloromethane in the presence of carbon granules[11] for 1 day gave the *N*-benzoylated product **15c** in 40% yield (Scheme 6).



Scheme 6

An X-ray crystal structure of compound **14c** confirmed the single 4,6-dimethoxy tautomer with weak hydrogen bonding between the carbonyl oxygen and the imidazole NH with a distance of 2.43 Å. The crystal structure further revealed the presence of a water molecule strongly attached to the carbonyl oxygen atom and a distance of 1.96 Å from it (Figure 2).

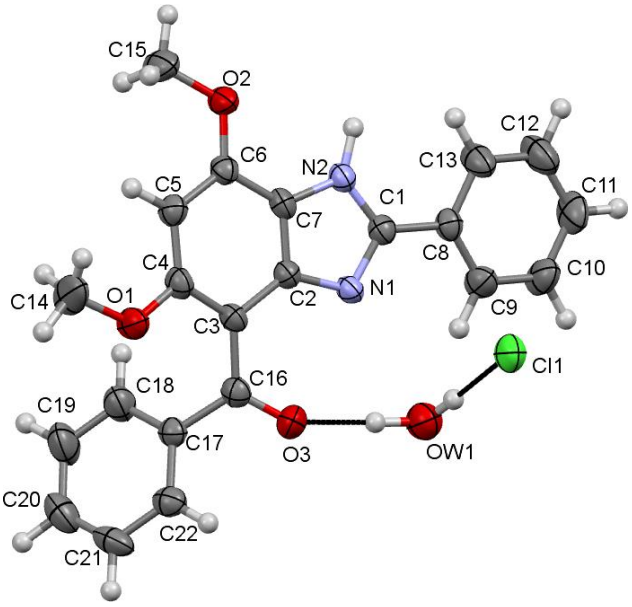
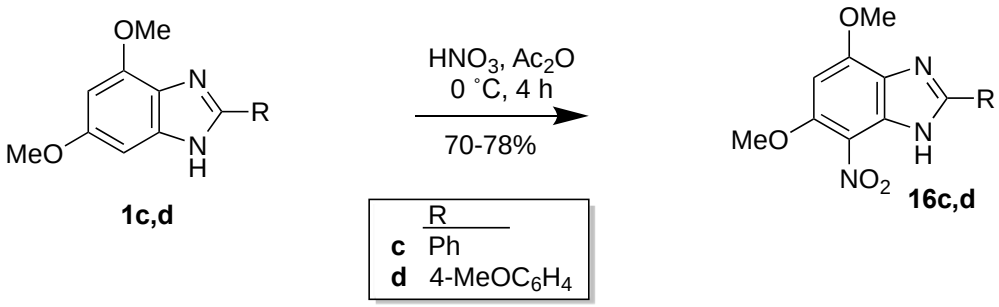


Figure 2. X-Ray crystal structure of the 7-benzoylbenzimidazole **14c** (HCl salt)

Nitration of 4,6-dimethoxybenzimidazoles

Nitration is an important process to introduce additional functionality to an organic molecule, especially as a potential source of amino derivatives. 4,6-Dimethoxybenzimidazoles **1c**,**d** undergo facile nitration using concentrated nitric acid in acetic anhydride to give the 7-nitrobenzimidazoles **16c**,**d** in 70% and 78% yields respectively as yellow crystals (Scheme 7). These observations show a clear difference from the nitration of 4,6-dimethoxyindoles, which only undergo clean reactions if there is an electron withdrawing substituent present.[12,13]

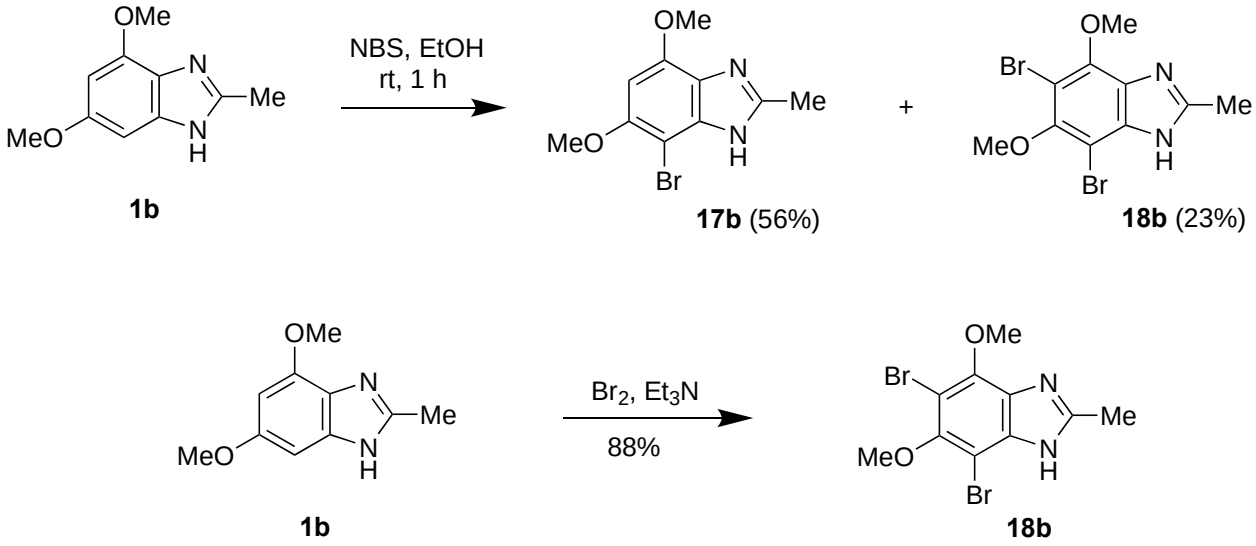


Scheme 7

Bromination of 4,6-dimethoxybenzimidazoles

The 2-methylbenzimidazole **1b** was chosen for a brief investigation of bromination, because of the question of selectivity between the benzene ring and the methyl group. In the event, no bromination was observed on the methyl group under the conditions used. Reaction of 2-methylbenzimidazole **1b** with *N*-bromosuccinimide gave a mixture of 7-bromobenzimidazole **17b** and 5,7-dibromobenzimidazole **18b**

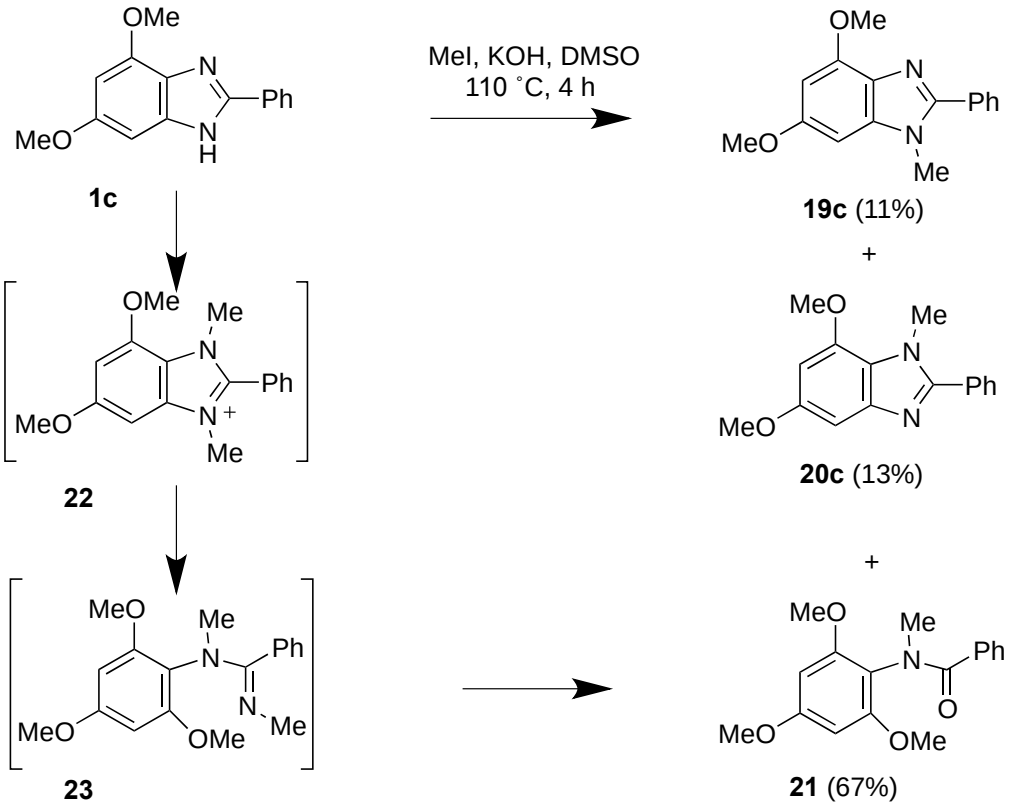
in 56% and 23% yields respectively (Scheme 7). Reaction of benzimidazole **1b** with bromine and triethylamine gave only the dibrominated product **18b** in 88% yield. The disappearance of the H7 proton in the monobrominated compound **17b** and both H5 and H7 protons in the dibromo compound **18b** were significant observations in their ^{1}H NMR spectra. Molecular ions in the mass spectra *m/z* at 272 (M+1), and 351 (M+1) clearly show the respective formation of the mono and dibromo compounds **17b** and **18b**. In contrast to this behaviour, the bromination of related 4,6-dimethoxyindoles leads to complex product mixtures, unless an electron-withdrawing substituent is present.[14,15]



Scheme 8

Alkylation of 4,6-dimethoxybenzimidazoles

N-Alkylation of the 2-phenylbenzimidazole **1c** was tentatively investigated in an attempt to differentiate between reaction at the two different nitrogen atoms, which would lead to two different isomeric compounds. Treatment of the benzimidazole with base would yield an anion that could be delocalized between the nitrogen atoms at N1 and N3 and leave both open to electrophilic attack. However, it was anticipated that *N*-alkylation would favour the N1 position of the 4,6-dimethoxybenzimidazole tautomer rather than the N1 position of the 5,7-dimethoxybenzimidazole tautomer, due to steric hindrance from the neighbouring methoxy group. The 2-phenylbenzimidazole **1c** was reacted with excess methyl iodide in dimethyl sulfoxide in the presence of potassium hydroxide. Purification of the reaction mixture gave three different products, which were identified as the expected *N*-methyl isomers **19c** and **20c** in yields of 11% and 13% respectively, and the unexpected imidazole ring opened trimethoxybenzamide **21** in 67% yield as the major product (Scheme 9).



Scheme 9

The ring-opened compound **21** showed three methoxy signals in the ^{1}H NMR spectrum and protons for the *N*-methyl group. An IR carbonyl group frequency was observed at 1635 cm^{-1}, while the mass spectrum showed a molecular ion *m/z* peak at 301 to match the molecular formula. Final proof of the structure **21** came from an X-ray crystal structure determination (Figure 3).

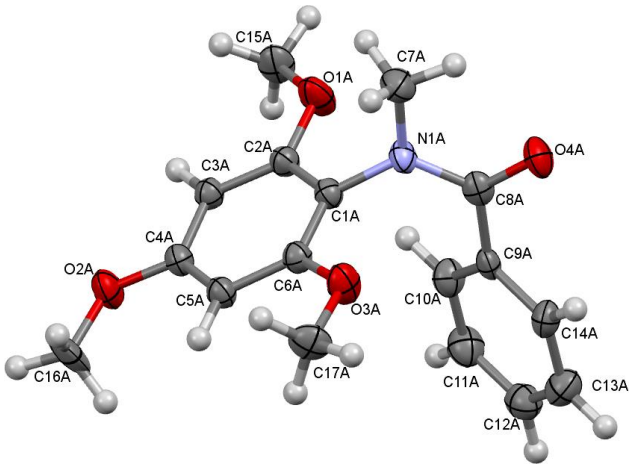
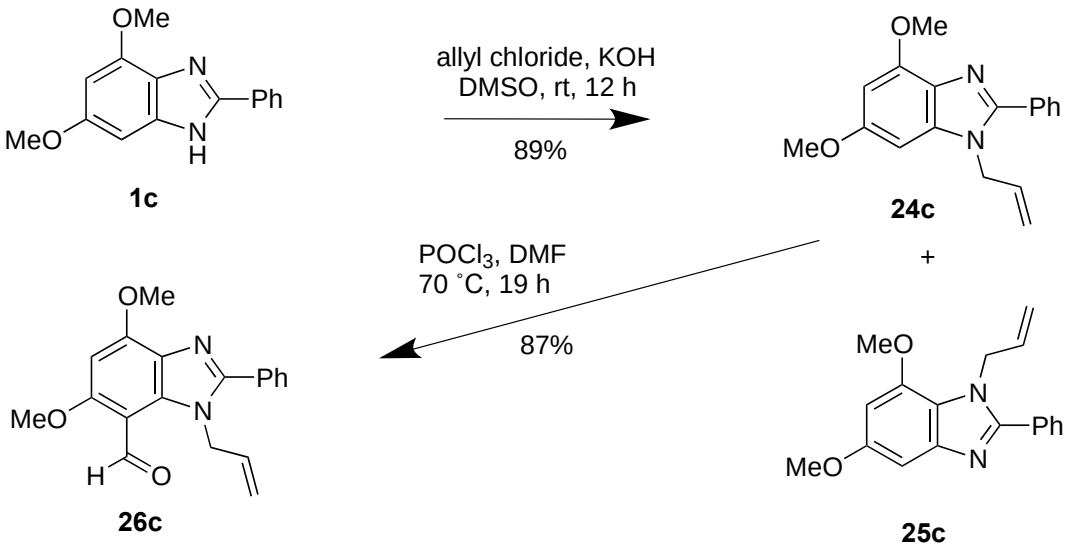


Figure 3. ORTEP drawing of X-ray crystal structure of trimethoxybenzamide **21**

The *N*-methylbenzimidazole isomers **19c** and **20c** could be separated by column chromatography using dichloromethane/ethyl acetate (90:10) as eluent. The isomers were identified by careful analysis of the 2D

NMR spectra. Both the compounds showed direct C-H coupling in the HMQC correlation, while HMBC correlation clearly distinguished between coupling of the *N*-methyl protons to C7a or C3a. The trimethoxy ring-opened product **21** could arise from the attack of methoxide ion at C7a in the presumably sterically strained di-methylated intermediate **22**. This attack is considered to be the most favourable reaction to relieve the steric strain. The methoxide anion could arise in the reaction conditions from the excess methyl iodide and potassium hydroxide. Alternatively, the ring-opening could result from hydroxide ion attack, with subsequent methylation of the phenol group. The intermediate **23** could easily be hydrolyzed to the benzamide **21** during the reaction and aqueous workup. The proposed mechanism is also supported by the reaction with one equivalent of methyl iodide, where only the isomers **19c** and **20c** were isolated, and no ring-opened product was observed.

When the 2-phenylbenzimidazole **1c** was reacted with allyl chloride in dimethyl sulfoxide and potassium hydroxide, an oily mixture of the two possible isomers **24c** and **25c** was obtained in a ratio of 1.6:1.0. (Scheme 10). Attempts to separate and purify the two isomers led to a 9:1 mixture of isomers **24c** and **25c**. In order to obtain a pure derivative, this mixture was formylated using the Vilsmeier reagent, and the 7-carbaldehyde **26c** was isolated in high yield (Scheme 10). This reactivity is comparable with the 7-formylation of *N*-allyl-4,6-dimethoxyindoles.[16]



Scheme 10

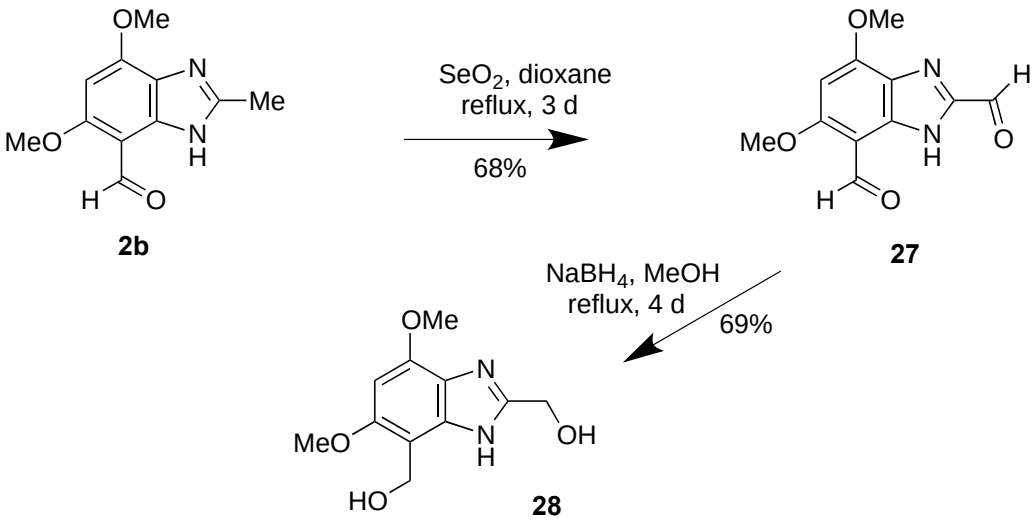
Functionalization at C2: introduction of a 2-formyl group

In the case of 3-substituted-4.6-dimethoxyindoles, functionalization at both C7 and C2 provided a broad scope for reactivity. In particular, formyl groups at both C7 and C2 led to further chemistry including formation of a range of macrocyclic systems.[17] However the benzimidazoles are constructed in such a way that the 2-substituents are predetermined by the reaction of an aldehyde or carboxylic acid with an

aryl 1,2-diamine, or the cyclization of a related amide. It was therefore of interest to investigate the possibility of functional manipulation at C2 to deliver a formyl group in that position.

This was attempted in two ways. The first approach investigated the oxidation of a 2-methyl group and the second sought to generate the aldehyde function by the oxidative cleavage of a 2-styryl group.

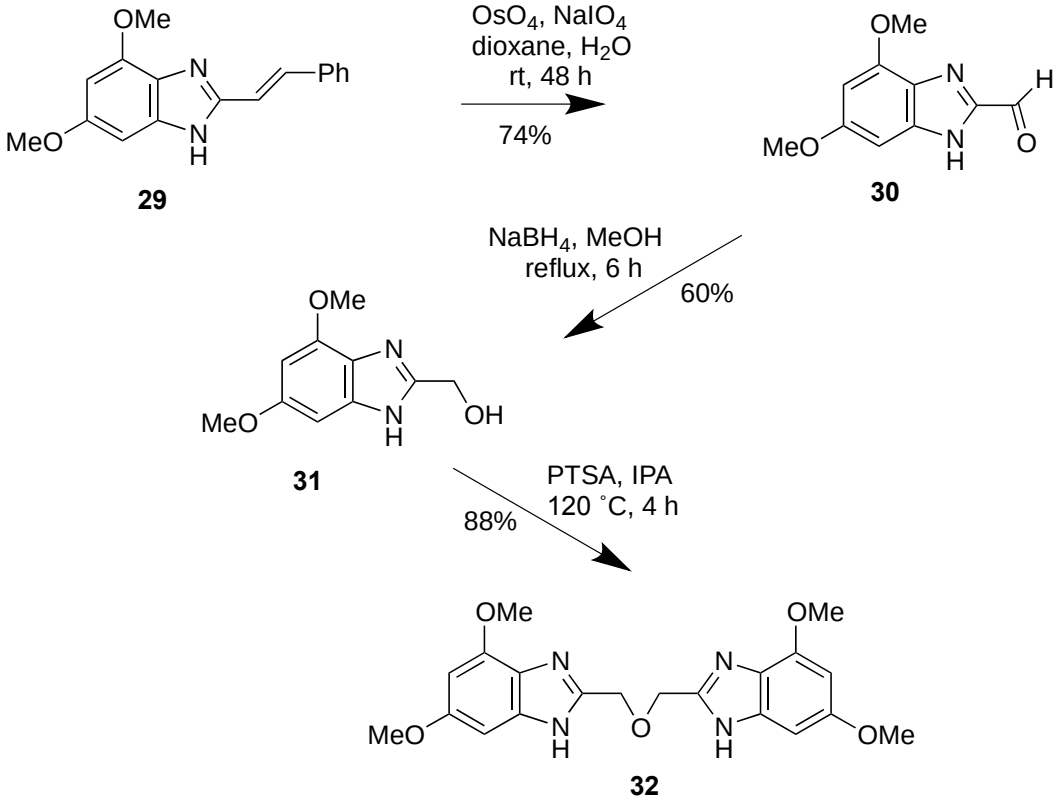
When the benzimidazole **1b** was heated under reflux with selenium dioxide for three days the resulting mixture of compounds showed that reaction occurred at C7 as well as C2 and no pure products could be isolated. In order to block C7 to reactivity, the 2-methylbenzimidazole-7-carbaldehyde **2b** was reacted with selenium dioxide in dry dioxane and produced the benzimidazole-2,7-dicarbaldehyde **27** in 68% yield. The reaction took three days under refluxing conditions to go to completion and is slow compared to related indole oxidations, which required only one day.[18] The characteristic evidence for the formation of the benzimidazole-2,7-dicarbaldehyde **27** was the clear presence of two sharp aldehyde proton peaks and the absence of the starting C2 methyl protons in the ^{1}H NMR spectrum. The benzimidazole-2,7-dicarbaldehyde **27** was reduced to the corresponding 2,7-di(hydroxymethyl)benzimidazole **28** in 69% yield by sodium borohydride in methanol under reflux for four hours (Scheme 11).



Scheme 11

The 2-styrylbenzimidazole **29**[1] underwent osmium tetroxide catalyzed sodium periodate oxidation very slowly (48 h) in aqueous dioxane and following reductive work-up produced the benzimidazole-2-carbaldehyde **30** in 74% yield (Scheme 12). The benzimidazole-2-carbaldehyde **30** was reduced to the corresponding 2-hydroxymethylbenzimidazole **31** by sodium borohydride in refluxing tetrahydrofuran/methanol solution.

It has been reported previously[4,5] that acidic treatment of 4,6-dimethoxyindoles with 2- and or 7-hydroxymethyl groups leads to the formation of calix[3]indoles and calix[4]indoles. Treatment of the di(hydroxymethyl)benzimidazole **28** with a range of protic and Lewis acids yielded only complex product mixtures. However, treatment of the hydroxymethylbenzimidazole **31** with *p*-toluenesulfonic acid in isopropanol gave the ether linked product **32**, which precipitated out from the reaction after cooling (Scheme 12). A molecular ion *m/z* (M+1) at 399 indicated the formation of the dibenzimidazolyl ether **32**. The mechanism of this formation presumably involves the attack of one hydroxymethylbenzimidazole on the carbocation derived from another. No calixbenzimidazoles were observed, presumably because of the comparatively less reactive nature of the C7 position compared to that in the related indoles.



Scheme 12

CONCLUSIONS

4,6-Dimethoxy-2-substituted-benzimidazoles undergo formylation, acylation, nitration and bromination at C7. The 7-carbaldehydes can be reduced to the corresponding hydroxymethyl compounds. Benzimidazole-2-carbaldehydes can be prepared by oxidation of 2-methyl- and 2-styryl-benzimidazoles. *N*-Methylation and *N*-allylation have also been investigated and lead to isomeric mixtures of 4,6- and 5,7-dimethoxy-benzimidazoles. In general the nucleophilic capacity of the activated benzimidazoles is weaker than that of the related activated indoles, but still provides synthetic routes to a range of new heterocyclic structures.

EXPERIMENTAL

General

Melting points were measured using a Mel-Temp melting point apparatus, and are uncorrected. Microanalyses were performed on Carlo Erba Elemental Analyser EA 1108 at the Campbell Microanalytical Laboratory, Univeristy of Otago, New Zealand. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX300 (300 MHz) spectrometer. Mass spectra were recorded on either a Bruker Daltonics Bio Apex II FTICR MS (HRMS-ESI) at School of Chemistry, University of New South Wales, or a Shimadzu LCMS QP 8000 (EI) at the Univeristy of Otago, New Zealand. Infrared spectra were recorded with a Thermo Nicolet 370 FTIR Spectrometer using KBr discs. Ultraviolet-visible spectra were recorded using a Varian Cary 100 Scan Spectrometer. X-ray crystallography was conducted with a suitable single crystal and crystallographic data excluding structure factors have been deposited with the Cambridge Crystallographic Data Centre: Compound **5c** - Deposition Number 1976688, Compound **14c** - Deposition Number 1976693, Compound **21** - Deposition Number 1976687.

Formylation of 4,6-dimethoxybenzimidazoles and associated reactions

General procedure for formylation of 4,6-dimethoxybenzimidazoles

Phosphoryl chloride (2.0 eq.) was added dropwise to ice cooled anhydrous DMF (~5 mL), and this cooled solution of Vilsmeier reagent was added dropwise to a previously ice cooled, stirred solution of benzimidazoles **1** (1.0 eq.) in anhydrous DMF (~5 mL) at 0 °C. The reaction mixture was allowed to come to room temperature, stirred for 2 h and then heated at 70 °C for 18-20 h. The reaction mixture was quenched and made strongly basic by addition of ice water and 2 M NaOH solution and stirred vigorously for 2 h. The resulting precipitate was filtered, thoroughly washed with water and recrystallized from EtOH/H_2O to afford the benzimidazole-7-carbaldehydes **2**.

4,6-Dimethoxybenzimidazole-7-carbaldehyde (2a). This was prepared from benzimidazole **1** (0.50 g, 2.80 mmol) in DMF (3 mL) and phosphoryl chloride (0.50 mL, 5.51 mmol, 2 eq.) in DMF (3 mL). Recrystallization from EtOH afforded the benzimidazole-7-carbaldehyde **2a** as light brown crystals (0.36 g, 63%), mp 238-240 °C; ν_{max} (paraffin): 3120, 1660, 1610, 1520, 1340, 1280, 1220, 1170, 1100, 980, 940, 780, 760, 720 cm^{-1}. λ_{max} (MeOH): 207 nm (ε 16,700 cm^{-1}M^{-1}), 229 (13,100), 302 (14,400). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.99 (3H, s, OMe), 4.19 (3H, s, OMe), 6.31 (1H, s, aryl H5), 7.92 (1H, s, aryl H2), 10.31 (1H, s, CHO), 10.95 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.4, 56.8 (OMe), 89.8, 139.2 (aryl CH), 104.8, 127.7, 134.6, 158.2, 162.5 (aryl C), 187.7 (C=O). Mass Spectrum (+EI): *m/z* (%) 207 (M+1, 14), 206 (M, 97), 205 (M-1, 100), 177 (65), 176 (34), 161 (29), 147 (28), 135 (24), 119 (42). Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.3; H, 4.9; N, 13.6. Found: C, 58.6; H, 5.0; N, 13.3.

4,6-Dimethoxy-2-methylbenzimidazole-7-carbaldehyde (2b). This was prepared from benzimidazole **1b** (0.50 g, 2.60 mmol) in DMF (3 mL) and phosphoryl chloride (0.23 mL, 2.60 mmol, 1 eq.) in DMF (4

mL). Recrystallization from MeOH afforded the benzimidazole-7-carbaldehyde **2b** as yellow crystals (0.30 g, 52%), mp 197-198 °C; ν_{max} (paraffin): 3560, 1636, 1602, 1341, 1272, 1219, 1163, 1117, 1073, 985 cm^{-1}. λ_{max} (MeOH): 207 nm (ε 15,200 $cm^{-1}M^{-1}$), 232 (13,400), 300 (14,000). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.58 (3H, s, Me), 3.96 (3H, s, OMe), 4.12 (3H, s, OMe), 6.25 (1H, s, aryl H5), 10.28 (1H, s, CHO), 10.62 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.7 (Me), 56.4, 56.4 (OMe), 89.1 (aryl CH), 104.6, 127.7, 135.6, 149.8, 157.2, 161.8 (aryl C), 187.8 (C=O). Mass Spectrum (+EI): *m/z* (%) 221 (M+1, 15), 220 (M, 90), 219 (M-1, 100), 205 (20), 191 (50), 190 (30), 175 (25), 161 (21), 149 (22), 133 (28), 69 (40). Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 59.9; H, 5.5; N, 12.7. Found: C, 59.7; H, 5.6; N, 12.5.

4,6-Dimethoxy-2-phenylbenzimidazole-7-carbaldehyde (2c). This was prepared from benzimidazole **1c** (3.0 g, 11.81 mmol) in DMF (20 mL) and phosphoryl chloride (2.26 mL, 23.6 mmol, 2 eq.) in DMF (5 mL). Recrystallization from EtOH/H_2O afforded benzimidazole-7-carbaldehyde **2c** as an off white solid (2.51 g, 75%), mp 210-212 °C; ν_{max} (KBr): 689, 788, 991, 1122, 1171, 1218, 1258, 1278, 1347, 1377, 1449, 1603, 1638, 3315 cm^{-1}. λ_{max} (MeOH): 245 nm (ε 13,700 $cm^{-1}M^{-1}$), 295 (22,800), 309 (21,400, sh), 339 (16,600). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.00 (3H, s, OMe), 4.19 (3H, s, OMe), 6.31 (1H, s, aryl H5), 7.44-7.52 (3H, m, aryl H), 8.06-8.09 (2H, m, aryl H), 10.33 (1H, s, CHO), 11.11 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.4, 56.6 (OMe), 89.5, 126.4, 128.8, 130.0 (aryl CH), 104.8, 128.7, 129.2, 136.1, 150.7, 157.8, 162.3 (aryl C), 187.9 (C=O). Mass Spectrum (+EI): *m/z* (%) 283 (M+1, 32), 282 (M, 100), 281 (M-1, 95), 253 (61), 252 (37), 196 (21), 104 (76), 103 (27). Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 67.9; H, 5.1; N, 10.0. Found: C, 68.1; H, 5.0; N, 9.9.

Benzimidazole-7-carbaldehyde **2c** (0.35 g, 1.24 mmol), crushed KOH (1.40 g) and hydroxylamine hydrochloride (0.86g, 12.4 mmol) heated in EtOH (50 mL) under reflux for 8 h gave the oxime as a white pad (0.25 g, 68%), mp 210-211 °C; ν_{max} (KBr): 3399, 3358, 3161, 1631, 1612, 1452, 1387, 1346, 1252, 1208, 1155, 1118, 998, 793, 687 cm^{-1}. λ_{max} (MeOH): 203 nm (ε 25,600 $cm^{-1}M^{-1}$), 217 (24,800), 251 (22,000), 290 (24,800), 321 (25,700). ^{1}H NMR (300 MHz, Acetone-d_6): δ 3.95 (3H, s, OMe), 4.13 (3H, s, OMe), 6.58 (1H, s, aryl H5), 7.47-7.50 (3H, m, aryl H), 8.07-8.09 (2H, m, aryl H), 8.54 (1H, s, NCH), 10.16 (1H, br s, NH), 10.26 (br s, 1H, OH). ^{13}C NMR (75 MHz, Acetone-d_6): δ 56.1, 56.3 (OMe), 91.6, 126.0, 128.7, 129.4 (aryl CH), 98.0, 128.9, 130.1, 134.2, 149.3, 153.4, 156.0 (aryl C), 144.0 (C=N). Mass Spectrum (+EI): *m/z* (%) 299 (M+2, 21), 298 (M+1, 100), 281 (18), 280 (83). Anal. Calcd for $C_{16}H_{15}N_3O_3$: C, 64.6; H, 5.1; N, 14.1. Found: C 64.9; H, 5.2; N, 14.0.

4,6-Dimethoxy-2-(4'-methoxyphenyl)benzimidazole-7-carbaldehyde (2d). This was prepared from benzimidazole **1d** (0.5 g, 1.76 mmol) in DMF (3 mL) and phosphoryl chloride (0.33 mL, 3.52 mmol, 2 eq.) in DMF (2 mL). Rrecrystallization from EtOH/H_2O afforded the benzimidazole-7-carbaldehyde **2d** as an off white solid (0.44 g, 80%), mp 205 °C; ν_{max} (KBr): 3294, 1631, 1604, 1512, 1489, 1466, 1428,

1397, 1370, 1344, 1312, 1260, 1209, 1176, 1125, 1036, 986, 831, 795, 775 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 21,100 $cm^{-1}M^{-1}$), 296 (23,800), 347 (14,200). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (3H, s, OMe), 4.01 (3H, s, OMe), 4.18 (3H, s, OMe), 6.33 (1H, s, aryl H5), 7.02 (2H, d, *J* 8.6 Hz, aryl H), 8.13 (2H, d, *J* 8.6 Hz, aryl H), 10.31 (1H, s, CHO), 11.04 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.3, 56.4, 56.5 (OMe), 89.3, 114.3, 127.9 (aryl CH), 104.6, 121.8, 128.5, 136.0, 150.8, 157.5, 161.1, 162.0 (aryl C), 187.8 (C=O). Mass Spectrum (+EI): *m/z* (%) 314 (M+2, 19), 313 (M+1, 100). Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.4; H, 5.2; N, 8.9. Found: C, 65.2; H, 5.2; N, 8.8.

Benzimidazole-7-carbaldehyde **2d** (0.10 g, 0.32 mmol), crushed KOH (0.35 g) and hydroxylamine hydrochloride (0.22 g, 3.2 mmol) heated in EtOH (25 mL) under reflux for 8 h gave the oxime as a white solid (87 mg, 83%), mp 242-244 °C; ν_{max} (KBr): 3388, 3150, 1631, 1611, 1483, 1643, 1340, 1272, 1256, 1179, 1153, 995, 829 cm^{-1}. λ_{max} (MeOH): 203 nm (ε 21,100 $cm^{-1}M^{-1}$), 218 (20,300), 262 (17,100), 292 (19,400), 324 (20,500). ^{1}H NMR (300 MHz, Acetone-d_6): δ 3.86 (3H, s, OMe), 3.93 (3H, s, OMe), 4.12 (3H, s, OMe), 6.54 (1H, s, aryl H5), 7.07 (2H, d, *J* 8.6 Hz, aryl H), 8.02 (2H, d, *J* 8.6 Hz, aryl H), 8.52 (1H, s, NCH), 10.91 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.7, 56.4, 57.3 (OMe), 91.7, 114.6, 128.3 (aryl CH), 97.8, 128.9, 130.6, 135.5, 140.1, 152.9, 155.4, 160.8 (aryl C), 143.7 (C=N). Mass Spectrum (+EI): *m/z* (%) 329 (M+2, 14), 328 (M+1, 70), 310 (100). Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.4; H, 5.2; N, 12.8. Found: C, 62.6; H, 5.5; N, 12.5.

2-*tert*-Butyl-4,6-dimethoxybenzimidazole-7-carbaldehyde (2e). This was prepared from benzimidazole **1e** (6.73 g, 28.74 mmol) in DMF (150 mL) and phosphoryl chloride (13.4 mL, 14.4 mmol, 2 eq.) in DMF (30 mL). Recrystallization from EtOH/H_2O afforded the benzimidazole-7-carbaldehyde **2e** as a pale yellow powder (5.21 g, 69%), mp 177-178 °C; ν_{max} (KBr): 3309, 1632, 1610, 1591, 1525, 1466, 1372, 1347, 1276, 1262, 1217, 1174, 1118, 1073, 988, 837, 797, 776 cm^{-1}. λ_{max} (MeOH): 240 nm (ε 15,100 $cm^{-1}M^{-1}$), 305 (18,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (9H, s, CMe_3), 3.95 (3H, s, OMe), 4.09 (3H, s, OMe), 6.23 (1H, s, H5), 10.27 (1H, s, CHO), 10.57 (1H, bs, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.4 C$\underline{Me}_3$), 33.5 $\underline{C}Me_3$), 56.5, 56.4 (OMe), 88.8 (aryl CH), 161.9, 161.5, 157.5, 135.6, 127.7, 104.8 (aryl C), 188.0 (C=O). Mass Spectrum (+EI): *m/z* (%) 263 (M+1, 9), 262 (M, 85), 261 (M-1, 84), 247 (100), 233 (23), 232 (26), 204 (24), 161 (22). Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.1; H, 6.9; N, 10.7. Found: C, 64.0; H, 7.0; N, 10.6.

General procedure for the reduction of 4,6-dimethoxybenzimidazole-7-carbaldehydes

To a solution of benzimidazole-7-carbaldehydes **2** in anhydrous MeOH/dry THF excess $NaBH_4$ was added portionwise and the mixture was heated under reflux for 2 h. The solvent was then concentrated/evaporated in vacuo before water was added followed by optional 2 M NaOH solution. The resulting precipitate was filtered, washed with water and dried to yield the 7-hydroxymethylbenzimidazoles **3**.

4,6-Dimethoxy-7-hydroxymethylbenzimidazole (3a). Benzimidazole-7-carbaldehyde **2a** (100 mg, 0.49 mmol) and $NaBH_4$ (0.10 g) heated under reflux in anhydrous MeOH (10 mL) afforded the 7-hydroxymethylbenzimidazole **3a** as a white solid (63 mg, 62%), mp 240 °C; ν_{max} (paraffin): 3200, 1620, 1530, 1335, 1295, 1230, 1210, 1150, 1110, 1060, 1000, 950, 880, 790 cm^{-1}. λ_{max} (MeOH): 227 nm (ε 18,700 $cm^{-1}M^{-1}$), 262 (7,500). ^1H NMR (300 MHz, DMSO-d_6): δ 3.80 (3H, s, OMe), 3.94 (3H, s, OMe), 4.69 (3H, s, CH_2+OH), 6.48 (1H, s, aryl H5), 7.93 (1H, s, H2), 12.18 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.8 (CH_2), 56.2, 57.4 (OMe), 92.0, 140.7 (aryl CH), 107.2, 126.5, 136.9, 149.6, 153.4 (aryl C). Mass Spectrum (+EI): *m/z* (%) 209 (M+1, 8), 208 (M, 68), 207 (M-1, 42), 191 (50), 179 (100), 164 (46), 161 (99), 160 (48), 150 (30), 133 (31), 117 (43), 115 (33), 105 (27), 91 (85), 77 (45), 65 (30), 52 (32). Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.7; H, 5.8; N, 13.5. Found: C, 57.7; H, 5.9; N, 13.3.

4,6-Dimethoxy-2-methyl-7-hydroxymethylbenzimidazole (3b). Benzimidazole-7-carbaldehyde **2b** (100 mg, 0.45 mmol) and $NaBH_4$ (0.10 g) heated under reflux in anhydrous MeOH (10 mL) afforded the 7-hydroxymethylbenzimidazole **3b** as an off-white solid (63 mg, 63%), mp 212-214 °C; ν_{max} (paraffin): 3489, 1642, 1604, 1342, 1272, 1235, 1170, 1115, 1053, 991 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.59 (3H, s, Me), 3.89 (3H, s, OMe), 3.91 (3H, s, OMe), 4.82 (3H, s, CH_2+OH), 6.58 (1H, s, aryl H5), 11.57 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 16.8 (Me), 56.5, 56.7 (OMe), 58.5 (CH_2), 90.0 (aryl CH), 102.4, 128.5, 131.8, 145.3, 157.4, 160.5 (aryl C). Mass Spectrum (+EI): *m/z* (%) 223 (M+1, 14), 222 (M, 100), 206 (58), 190 (62), 175 (45), 102 (25). The product was not obtained analytically pure but was used directly in formation of compound **4b**.

4,6-Dimethoxy-2-phenyl-7-hydroxymethylbenzimidazole (3c). Benzimidazole-7-carbaldehyde **2c** (50 mg, 0.17 mmol) and $NaBH_4$ (50 mg) heated under reflux in anhydrous MeOH (10 mL) afforded the 7-hydroxymethylbenzimidazole **3c** as a white solid (45 mg, 90%), mp 196-198 °C; ν_{max} (paraffin): 3552, 1630, 1603, 1346, 1308, 1212, 1201, 1153, 1129, 1111, 1007, 974, 890, 796 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 3.81(3H, s, OMe), 3.94 (3H, s, OMe), 4.73 (3H, s, CH_2+OH), 6.50 (1H, s, aryl H5), 7.41-7.50 (3H, m, aryl H), 8.13-8.15 (2H, m, aryl H), 12.27 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.8, 57.0 (OMe), 57.5 (CH_2), 91.0, 126.3, 128.7, 129.6 (aryl CH), 129.6, 129.8, 131.5, 134.6, 138.4, 152.5, 169.5 (aryl C). Mass Spectrum (+EI): *m/z* (%) 285 (M+1, 18), 284 (M, 100), 283 (M-1, 50), 255 (55), 237 (55), 207 (20), 133 (25), 104 (35), 103 (50), 77 (25). Anal. Calcd for $C_{16}H_{16}N_2O_3$ $0.2H_2O$: C, 66.8; H, 5.7; N, 9.7. Found: C, 66.9; H, 5.8; N, 9.5.

4,6-Dimethoxy-2-(4'-methoxyphenyl)-7-hydroxymethylbenzimidazole (3d). Benzimidazole-7-carbaldehyde **2d** (0.20 g, 0.64 and $NaBH_4$ (0.20 g) mmol) heated under reflux in anhydrous MeOH (20 mL) afforded the 7-hydroxymethylbenzimidazole **3d** as a white solid (0.187 g, 93%), mp 116-118 °C; ν_{max} (KBr): 3136, 1612, 1579, 1520, 1489, 1436, 1342, 1309, 1292, 1249, 1211, 1179, 1154, 1128, 1031, 1007, 840, 790, 736 cm^{-1}. λ_{max} (MeOH): 210 nm (ε 35,300 $cm^{-1}M^{-1}$), 257

(24,200), 307 (23,100). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.73 (3H, s, OMe), 3.76 (3H, s, OMe), 3.85 (3H, s, OMe), 5.02 (2H, s, CH_2), 5.76 (1H, br s, OH), 6.21 (1H, s, aryl H5), 6.75 (2H, d, *J* 8.6 Hz, aryl H), 7.86 (2H, d, *J* 8.6 Hz, aryl H), 11.04 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.1, 55.6, 56.8 (OMe), 56.7 (CH_2), 90.7, 113.9, 127.9 (aryl CH), 105.6, 121.9, 126.4, 137.0, 148.9, 150.5, 153.4, 160.7 (aryl C). Mass Spectrum (+EI): *m/z* (%) 316 (M+2, 15), 315 (M+1, 100). Anal. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.9; H, 5.8; N, 8.9. Found: C, 64.3; H, 5.9; N; 8.7.

2-*tert*-Butyl-7-hydroxymethyl-4,6-dimethoxybenzimidazole (3e). Benzimidazole-7-carbaldehyde **2e** (0.50 g, 1.91 mmol) and $NaBH_4$ (0.72 g) stirred in dry THF (25 mL) for 21 h at room temperature afforded a tautomeric mixture of benzimidazole **3e** as a white powder (0.28 g, 55%), mp 156-161 °C; ν_{max} (KBr): 3584, 3522, 3177, 1615, 1536, 1469, 1409, 1335, 1265, 1201, 1146, 1120, 1002, 988, 884, 795 cm^{-1}. λ_{max} (MeOH): 233 nm (ε 6,450 cm^{-1}M^{-1}), 259 (9,070). Mass Spectrum (+EI): *m/z* (%) 265 (M+1, 12), 264 (M, 100), 263 (M-1, 99), 248 (21), 247 (43), 245 (44), 235 (89), 233 (44), 231 (91), 216 (76), 205 (34), 203 (47), 201 (37). Anal. Calcd for $C_{14}H_{20}N_2O_3$: C, 63.6; H, 7.6; N, 10.6. Found: C, 63.4; H, 7.5; N, 10.6.

2-tert-Butyl-7-hydroxymethyl-4,6-dimethoxybenzimidazole (3e). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (9H, s, CMe_3), 2.17 (1H, bs, OH), 3.86 (3H, s, OMe), 3.99 (3H, s, OMe), 5.00 (2H, s, CH_2), 6.34 (1H, s, H5), 9.52 (1H, bs, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 29.6 (C<u>Me</u>$_3$), 33.5 (<u>C</u>Me$_3$), 54.2 (CH_2), 56.0, 57.5 (OMe), 91.4 (aryl CH), 106.0, 127.7, 136.4, 150.3, 153.6, 160.3 (aryl C).

2-tert-Butyl-4-hydroxymethyl-5,7-dimethoxybenzimidazole (**3e** *tautomer*) ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (9H, s, CMe_3), 3.86 (3H, s, OMe), 3.94 (3H, s, OMe), 4.76 (1H, t, OH), 5.11 (2H, d, CH_2), 6.41 (1H, s, H6), 8.90 (1H, bs, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 29.6 (C<u>Me</u>$_3$), 33.6 (<u>C</u>Me$_3$), 55.0 (CH_2), 55.8, 57.8 (OMe), 92.3 (aryl CH), 111.7, 119.6, 143.7, 145.0, 152.9, 162.4 (aryl C).

General procedure for the reaction of 4,6-dimethoxybenzimidazole-7-carbaldehydes (1a-d) with formaldehyde

The benzimidazole in glacial HOAc was treated with HCHO solution, followed by concentrated HCl and the mixture heated at 100 °C overnight and cooled to room temperature before ice water and 20% NaOH solution were added. The resulting precipitate was filtered, washed with water and chromatographed on silica (CH_2Cl_2) or recrystallized from EtOH or MeOH to give the 7,7'-dibenzimidazolylmethane.

Bis(4,6-dimethoxybenzimidazol-7-yl)methane (4a)

Benzimidazole **1a** (0.20 g, mmol) in glacial HOAc (5 mL), HCHO solution (1 mL, 37%) and concentrated HCl (5 drops) gave the 7,7'-dibenzimidazolylmethane **4a** as a white solid (0.18 g, 87%), mp 118-120 °C; ν_{max} (KBr): 3350, 2937, 2837, 1611, 1523, 1497, 1453, 1394, 1336, 1255, 1147, 1116, 991, 804 cm^{-1}. λ_{max} (MeOH): 214 nm (ε 47,400 cm^{-1}M^{-1}), 262 (12,200), 285 (8,100). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.73 (s, 6H, OMe), 3.90 (s, 6H, OMe), 4.24 (s, 2H, CH_2), 6.47 (s, 2H, aryl H5), 8.07 (s, 2H,

aryl H2), 12.64 (br s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): 19.7 (CH_2), δ 56.2, 57.5 (OMe), 92.2, 142.9 (aryl CH), 102.1, 128.1, 139.7, 151.7, 156.3 (aryl C). Mass Spectrum (+EI): *m/z* (%) 370 (M+2, 21), 369 (M+1, 100). Anal. Calcd for $C_{19}H_{20}N_4O_4$ 0.2H_2O: C, 61.4; H, 5.5; N, 15.1. Found: C, 61.3; H, 5.4; N, 14.8.

Bis(4,6-dimethoxy-2-methylbenzimidazol-7-yl)methane (4b). Benzimidazole **1b** (0.10 g, mmol) in glacial HOAc (2 mL), HCHO solution (1 mL, 37%) and concentrated HCl (0.5 mL) gave the 7,7'-dibenzimidazolylmethane **4b** as an off white solid (51 mg, 50%), mp 150-152 °C; ν_{max} (KBr): 3340, 2934, 2836, 1613, 1538, 1517, 1454, 1409, 1340, 1212, 1147, 1120, 998 cm^{-1}. λ_{max} (MeOH): 213 nm (ε 58,200 cm^{-1}M^{-1}), 259 (14,700). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 2.38 (s, 6H, Me), 3.75 (s, 6H, OMe), 3.87 (s, 6H, OMe), 4.11 (s, 2H, CH_2), 6.42 (s, 2H, aryl H5), 12.23 (br s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 14.9 (Me), 19.9 (CH_2), 56.2, 57.6 (OMe), 92.7 (aryl CH), 105.9, 127.0, 136.8, 148.2, 150.9, 153.1 (aryl C). Mass Spectrum (+EI): *m/z* (%) 398 (M+2, 25), 397 (M+1, 100). HRMS (+ESI): $C_{21}H_{25}N_4O_4$ $[M+H]^+$ requires 397.1870, found 397.1876. Anal. Calcd for $C_{21}H_{24}N_4O_4$ 0.3CH_2Cl_2: C, 60.6; H, 5.9; N, 13.3. Found: C, 60.3; H, 5.9; N, 13.1.

Bis(4,6-dimethoxy-2-phenylbenzimidazol-7-yl)methane (4c). Benzimidazole **1c** (0.10 g, mmol) in glacial HOAc (5 mL), HCHO solution (1 mL, 37%) and concentrated HCl (5 drops) gave the 7,7'-dibenzimidazolylmethane **4c** as a white solid (0.09 g, 89%), mp 218-220 °C; ν_{max} (KBr): 3427, 2936, 2838, 1617, 1455, 1399, 1345, 1301, 1210, 1140, 1051, 998, 694 cm^{-1}. λ_{max} (MeOH): 206 nm (ε 83,100 cm^{-1}M^{-1}), 252 (49,200), 303 (41,800). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 3.82 (s, 6H, OMe), 3.89 (s, 6H, OMe), 4.36 (s, 2H, CH_2), 6.54 (s, 2H, aryl H5), 7.64-7.66 (m, 6H, aryl H), 8.32-8.35 (m, 4H, aryl H), 12.24 (br s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 19.3 (CH_2), 55.1, 57.6 (OMe), 110.4, 125.8, 127.0, 128.7 (aryl CH), 128.9, 129.4, 129.9, 132.6, 138.7, 151.4, 159.8 (aryl C). Mass Spectrum (+EI): *m/z* (%) 520 (M, 41), 519 (M-1, 100), 253 (50). HRMS (+ESI): $C_{31}H_{29}N_4O_4$ $[M+H]^+$ requires 521.2183, found 521.2194. Anal. Calcd for $C_{31}H_{28}N_4O_4$ 0.8H_2O: C, 69.6; H, 5.6; N, 10.5. Found: C, 69.7; H, 5.5; N, 10.6.

Bis[4,6-dimethoxy-2-(4'-methoxyphenyl)benzimidazol-7-yl]methane (4d). *Method A:* Benzimidazole **1d** (0.1 g, mmol) in glacial HOAc (2 mL), HCHO solution (1 mL, 37%) and concentrated HCl (0.5 mL) gave the 7,7'-dibenzimidazolylmethane **4d** as a white solid (0.08 g, 60%).

Method B: To a solution of 7-hydroxymethylbenzimidazole **3d** (0.10 g, 0.32 mmol) in dry THF (5 mL), a few drops of glacial HOAc were added and the solution was heated at 100 °C overnight. The mixture was cooled to room temperature, ice water and 10% $NaHCO_3$ solution were added to neutralize the solution. The resulting precipitate was filtered, washed with water, recrystallized from EtOH and dried to give the 7,7'-dibenzimidazolylmethane **4d** as an off white powder (56 mg, 60%), mp 288-290 °C; ν_{max} (KBr): 3406, 2935, 2840, 1636, 1611, 1534, 1507, 1462, 1304, 1265, 1220, 1193, 1130, 1023, 990, 838 cm^{-1}.

λ_{max} (MeOH): 208 nm (ε 71,800 $cm^{-1}M^{-1}$), 259 (47,400), 306 (19,100). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.60 (s, 6H, OMe), 3.88 (s, 6H, OMe), 3.98 (s, 6H, OMe), 4.51 (s, 2H, CH_2), 6.73 (s, 2H, aryl H5), 7.21 (d, *J* 6.1 Hz, 4H, aryl H), 8.30 (d, *J* 6.1 Hz, 4H, aryl H), 14.40 (br s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 27.0 (CH_2), 56.2, 56.7, 57.2 (OMe), 99.2, 116.4, 127.2 (aryl CH), 103.0, 122.8, 130.7, 143.8, 145.9, 149.3, 154.6, 163.3 (aryl C). Mass Spectrum (+EI): *m/z* (%) 582 (M+2, 40), 581 (M+1, 100), 313 (23), 285 (28). HRMS (+ESI): $C_{33}H_{33}N_4O_6$ $[M+H]^+$ requires 581.2394, found 581.2380. Anal. Calcd for $C_{33}H_{32}N_4O_6$ 1.4CH_2Cl_2: C, 59.1; H, 5.0; N, 8.0. Found: C, 59.0; H, 5.0; N, 8.0.

7-(2-Benzimidazolyl)-4,6-dimethoxy-2-methylbenzimidazole (5b). To a solution of benzimidazole-7-carbaldehyde **2b** (0.10 g, 0.45 mmol) in anhydrous DMF (5 mL), 1,2-diaminobenzene (0.05 g, 0.50 mmol) was added and the mixture heated at 110 °C for 24 h. The reaction mixture was allowed to cool to room temperature before ice water was added and the resulting precipitate was filtered and washed with water. The crude solid was recrystallized from EtOH/H_2O to afford the bisbenzimidazole **5b** as a light brown solid (70 g, 52%), mp >350 °C; ν_{max} (KBr): 3395, 2921, 2848, 1644, 1605, 1570, 1452, 1388, 1331, 1213, 1141 cm^{-1}. λ_{max} (MeOH): 222 nm (ε 11,000 $cm^{-1}M^{-1}$), 260 (10,200), 336 (12,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.69 (3H, s, Me), 4.09 (3H, s, OMe), 4.12 (3H, s, OMe), 6.41 (1H, s, aryl H5), 7.26-7.28 (2H, m, aryl H), 7.66-7.69 (2H, m, aryl H), 9.47 (1H, br s, NH). Mass Spectrum (+EI): *m/z* (%) 308 (M+2, 25), 309 (M+1, 100). HRMS (+ESI): $C_{17}H_{17}N_4O_2$ $[M+H]^+$ requires 309.1346, found 309.1349.

7-(2-Benzimidazolyl)-4,6-dimethoxy-2-phenylbenzimidazole (5c)

This compound was prepared as described for the preparation of bisbenzimidazole **5b** from a solution of benzimidazole-7-carbaldehyde **2c** (1.95 g, 6.91 mmol) in anhydrous DMF (5 mL) and 1,2-diaminobenzene (0.82 g, 7.6 mmol) at 110 °C for 48 h to yield the bisbenzimidazole **5c** as a light brown powder (1.76 g, 69%), mp 216-217 °C; ν_{max} (KBr): 3655, 3300, 1620, 1492, 1465, 1450, 1433, 1391, 1335, 1311, 1278, 1237, 1216, 1151, 1102, 994, 791, 742, 692 cm^{-1}. λ_{max} (MeOH): 209 nm (ε 10,200 $cm^{-1}M^{-1}$), 253 (9,000), 323 (11,400). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.13 (3H, s, OMe), 4.14 (3H, s, OMe), 6.45 (1H, s, aryl H5), 7.26-7.29 (2H, m, aryl H), 7.43-7.55 (3H, m, aryl H), 7.67 (2H, s br, aryl H), 7.90 (1H, br s, NH), 8.18-8.21 (2H, m, aryl H), 10.51 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.2, 56.7 (OMe), 89.9, 93.6, 122.4, 126.5, 128.7, 129.7 (aryl CH), 94.5, 117.5, 123.4, 129.8, 136.4, 149.5, 150.6, 152.9, 155.1, 173.1, 174.6 (aryl C). Mass Spectrum (+EI): *m/z* (%) 372 (M+2, 47%), 371 (M+1, 100). Anal. Calcd for $C_{22}H_{18}N_4O_2$ H_2O: C, 68.0; H, 5.2; N, 14.4. Found: C, 68.3; H, 5.3; N, 14.5.

7-(2-Benzimidazolyl)-4,6-dimethoxy-2-(4'-methoxyphenyl)benzimidazole (5d). This compound was prepared as described for the bisbenzimidazole **5b** from a solution of benzimidazole-7-carbaldehyde **2d** (0.20 g, 0.64 mmol) in anhydrous DMF (3 mL) and 1,2-diaminobenzene (76 mg, 0.70 mmol) at 110 °C for 48 h to yield the bisbenzimidazole **5d** as a brown solid (0.14 g, 56%), mp 150-152 °C; ν_{max} (KBr):

3348, 1618, 1488, 1453, 1422, 1384, 1333, 1253, 1213, 1176, 1028, 837, 744 cm^{-1}. λ_{max} (MeOH): 206 nm (ε 51,500 $cm^{-1}M^{-1}$), 258 (31,600), 327 (43,400). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (3H, s, OMe), 3.98 (3H, s, OMe), 4.10 (3H, s, OMe), 6.26 (1H, s, aryl H5), 6.98-7.01 (2H, m, aryl H), 7.28-7.31 (2H, m, aryl H), 7.75 (2H, d, *J* 8.7 Hz, aryl H), 8.15 (2H, d, *J* 8.7 Hz, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.3, 56.7, 57.1 (OMe), 94.1, 114.2, 115.4, 123.6, 128.2 (aryl CH), 102.3, 123.5, 126.8, 138.6, 141.8, 150.1, 153.2, 155.0, 155.8, 1606 (aryl C). Mass Spectrum (+EI): *m/z* (%) 402 (M+2, 26), 401 (M+1, 100). Anal. Calcd for $C_{23}H_{20}N_4O_3$ $0.9H_2O$: C, 66.3; H, 5.3; N, 13.4. Found: C, 66.4; H, 5.2; N, 12.9.

Dimethyl 3,5-dimethoxy-1-phenyl-imidazo[4,5,1-*ij*]quinoline-7,8-dicarboxylate (6c). To a partially dissolved ice cooled solution of benzimidazole **2c** (0.30 g, 1.06 mmol) in dry CH_2Cl_2 (20 mL), Ph_3P (0.31 g, 1.18 mmol) followed by dimethyl acetylenedicarboxylate (0.17 g, 1.20 mmol) in dry CH_2Cl_2 (5 mL) over 10 min. The resulting clear red solution was stirred at room temperature for 5 days under argon and the solvent was evaporated off. The crude product was chromatographed using CH_2Cl_2/EtOAc (90/10) as eluent to yield the imidazoloquinoline compound **6c** as a yellow powder (0.31 g, 72%), mp 187-189 °C; ν_{max} (KBr): 2945, 1748, 1697, 1613, 1523, 1452, 1432, 1261, 1243, 1149, 1067, 775 cm^{-1}. λ_{max} (MeOH): 206 (ε 26,900 $cm^{-1}M^{-1}$), 231 (21,500), 364 (15,600). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.44 (3H, s, OMe), 3.85 (3H, s, OMe), 3.93 (3H, s, OMe), 4.18 (3H, s, OMe), 6.25 (1H, s, aryl H8), 6.46 (1H, s, aryl H4), 7.46-7.48 (3H, m, aryl H), 7.76- 7.80 (2H, m, aryl H), 8.06 (1H, s, aryl H6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.0, 52.8, 56.4, 57.0 (OMe), 56.4 (CH), 91.7, 128.4, 128.7, 129.7, 130.5 (aryl CH), 99.0, 116.0, 125.2, 129.8, 136.6, 152.0, 155.4, 155.5 (aryl C), 165.9, 168.4 (CO). Mass Spectrum (+EI): *m/z* (%) 351 (5), 409 (100) $[M+H]^+$, 410 (26). Anal. Calcd for $C_{22}H_{20}N_2O_6$: C, 64.7; H, 4.9; N, 6.9. Found: C, 64.9; H, 4.8; N, 7.2.

Dimethyl 7,9-dimethoxy-2-(4'-methoxyphenyl)-4*H*-imidazo[3,2,1-*ij*]quinoline-4,5-dicarboxylate (6d). The title compound was prepared from an ice cooled solution of benzimidazole **2d** (0.50 g, 1.60 mmol) in dry CH_2Cl_2 (25 mL), Ph_3P (0.46 g) and dimethyl acetylenedicarboxylate (0.25 g) with stirring under argon for 5 days. The product **6d** was purified by column chromatography using CH_2Cl_2/EtOAc (90/10) as eluent as a yellow powder (0.53 g, 76%), mp 159-160 °C; ν_{max} (KBr): 2951, 2841, 1739, 1706, 1608, 1571, 1520, 1463, 1435, 1298, 1268, 1175, 1145, 1072, 987 cm^{-1}. λ_{max} (MeOH): 203 (ε 40,500 $cm^{-1}M^{-1}$), 233 (31,300), 267 (2,0600), 361 (22800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.45 (3H, s, OMe), 3.79 (3H, s, OMe), 3.85 (3H, s, OMe), 3.91 (3H, s, OMe), 4.16 (3H, s, OMe), 6.23 (1H, s, aryl H8), 6.44 (1H, s, aryl H4), 6.99 (2H, d, *J* 8.28 Hz, aryl H), 7.73 (2H, d, *J* 8.28 Hz, aryl H), 8.03 (1H, s, aryl H6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.0, 52.8, 56.4, 56.5, 56.9 (OMe), 55.3 (CH), 91.5, 114.2, 129.8, 130.6 (aryl CH), 98.9, 115.9, 122.1, 125.0, 136.5, 152.0, 155.2, 155.3, 160.7 (aryl C), 165.9, 168.5 (CO). Mass Spectrum (+EI): *m/z* (%) 439 (100) $[M+H]^+$. Anal. Calcd for $C_{23}H_{22}N_2O_7$ $0.5CH_2Cl_2$: C, 58.7; H, 4.8; N, 5.8. Found: C, 58.8; H, 4.9; N, 5.8.

4,6-Dimethoxy-7-(2-nitroethenyl)-2-phenylbenzimidazole (7c) and its tautomer 5,7-dimethoxy-4-(2-nitroethenyl)-2-phenylbenzimidazole. A mixture of benzimidazole-7-carbaldehyde **2c** (0.50 g, 1.77 mmol) and NH_4OAc (70 mg) in $MeNO_2$ (5.0 mL) was heated under reflux for 1 h and then allowed to cool. EtOAc was added and the mixture was washed twice with water, brine, dried over $MgSO_4$, and the solvent evaporated to give an orange solid that was purified by gravity column chromatography (5% MeOH/CH_2Cl_2) to give compound **7c** and its tautomer, in a 20:1 ratio respectively, as a bright orange powder (0.52 g, 90%), mp 230-235 °C; ν_{max} (KBr): 3267, 1632, 1603, 1588, 1475, 1456, 1291, 1259, 1206, 1165, 1120, 968, 828, 780, 693 cm^{-1}. λ_{max} (MeOH): 231 nm (ε 20,000 $cm^{-1}M^{-1}$), 248 (25,100), 269 (14,800), 292 (11,200), 400 (18,600). Mass Spectrum (+EI): *m/z* (%) 327 (1), 326 (9), 325 (M, 45), 280 (9), 279 (64), 104 (100), 102 (96), 77 (78). Anal. Calcd for $C_{17}H_{15}N_3O_4$: C, 62.8; H, 4.7; N, 12.9. Found: C, 62.9; H, 4.8; N, 12.8.

4,6-Dimethoxy-7-(2-nitroethenyl)-2-phenylbenzimidazole **7c** ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.97 (3H, s, OMe), 4.05 (3H, s, OMe), 6.39 (1H, s, H5), 7.51 (3H, m, aryl H), 8.08 (2H, m, aryl H), 8.72 (1H, d, *J* 13.4 Hz, ethenyl), 8.93 (1H, d, *J* 13.4 Hz, ethenyl), 9.56 (1H, bs, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.55, 57.28 (OMe), 91.53 (C5'), 127.22, 129.20, 130.39 (aryl CH), 131.87, 135.55 (ethenyl CH), 101.45, 120.35, 129.91, 145.00, 151.36, 152.62, 159.09 (aryl C).

5,7-Dimethoxy-4-(2-nitroethenyl)-2-phenylbenzimidazole tautomer ^{1}H NMR unclear.

4,6-Dimethoxy-7-(2-nitroethyl)-2-phenylbenzimidazole (8c) and its tautomer 5,7-dimethoxy-4-(2-nitroethyl)-2-phenylbenzimidazole. $NaBH_4$ (0.15 g, 4.0 mmol) was added portionwise over 20 min to a stirred suspension of the nitroethene **7c** and its tautomer (0.25 g, 0.77 mmol) in MeOH (30 mL) at room temperature. Stirring was continued for 20 min further before the mixture was acidified to pH 6 with glacial HOAc. The solvent was then evaporated and the residue was treated with water and extracted with EtOAc. The organic extract was washed with water, brine, dried over $MgSO_4$, and the solvent was evaporated to give a yellow powder. Purification via gravity column chromatography (5% MeOH/CH_2Cl_2) gave a 1:1.25 tautomeric mixture of compound **8c** and its tautomer as a pale yellow powder (0.23 g, 90%), mp 242-245 °C; ν_{max} (KBr): 3188, 1634, 1619, 1549, 1519, 1456, 1409, 1378, 1341, 1309, 1290, 1221, 1199, 1149, 1128, 1021, 989, 958, 902, 799, 697 cm^{-1}. λ_{max} (MeOH): 254 nm (ε 21,200 $cm^{-1}M^{-1}$), 280 (11,500), 301 (18,200). ^{13}C NMR (75 MHz, DMSO-d_6): δ 29.35 (CH_2), 61.9, 62.2, 63.0, 63.5 (OMe), 80.4, 81.1 (CH_2), 97.9, 98.8 (C5 and C6), 132.6, 133.0, 135.0, 135.6, 135.9 (aryl CH), 104.8, 111.6, 126.1, 136.4, 136.7, 142.6, 150.8, 151.3, 155.9, 156.5, 157.6, 159.5, 160.6 (aryl C). Mass Spectrum (+EI): *m/z* (%) 328 (16, M+1), 327 (M, 100), 326 (16), 281 (67), 280 (85), 267 (21), 265 (66), 251 (31), 237 (30), 223 (25), 193 (22), 105 (22), 104 (93), 103 (47). Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.4; H, 5.2; N, 12.8. Found: C, 62.4; H, 5.4; N, 12.7.

4,6-Dimethoxy-7-(2-nitroethyl)-2-phenylbenzimidazole **8c**

^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 3.61 (2H, t, *J* 7.2 Hz, CH_2), 3.90 (3H, s, OMe), 4.04 (3H, s, OMe), 4.94 (2H, t, *J* 7.2 Hz, CH_2), 6.69 (1H, s, H5), 7.55 (3H, m, aryl H), 8.29 (2H, d, *J* 7.2 Hz, aryl H), 12.86 (1H, bs, NH).

5,7-Dimethoxy-4-(2-nitroethyl)-2-phenylbenzimidazole

^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 3.55 (2H, t, *J* 7.2 Hz, CH_2), 3.90 (3H, s, OMe), 4.04 (3H, s, OMe), 4.75 (2H, t, *J* 7.2 Hz, CH_2), 6.58 (1H, s, H6), 7.55 (3H, m, aryl H), 8.20 (2H, d, *J* 7.2 Hz, aryl H), 12.34 (1H, bs, NH).

Acylation of 4,6-dimethoxybenzimidazoles and associated reactions

7-Acetyl-4,6-dimethoxy-2-methylbenzimidazole (9b). To an ice cooled solution of benzimidazole **1b** (1 g, 5.2 mmol) and acetyl chloride (1.5 mL, 20.8 mmol) in dry $CHCl_3$ (20 mL), $SbCl_5$ (2.5 mL, 20.8 mmol) was added dropwise under argon and the mixture stirred for 2 h at room temperature. The resulting precipitate was filtered, washed with water and recrystallized from EtOH to yield the title 7-acetylbenzimidazole **9b** as a yellow powder (1.15 g, 95%), mp 184-185 °C; ν_{max} (KBr): 3345, 1637, 1562, 1471, 1424, 1273, 1224, 1208, 1177, 1017, 980 cm^{-1}. λ_{max} (MeOH): 206 nm (ε 6,900 cm^{-1}M^{-1}), 230 (5,800), 291 (5,100). ^{1}H NMR (300 MHz, Acetone-*d*$_6$): δ 2.63 (3H, s, Me), 3.01 (3H, s, MeCO), 4.17 (3H, s, OMe), 4.21 (3H, s, OMe), 7.05 (1H, s, aryl H5), 13.37 (1H, br s, NH). ^{13}C NMR (75 MHz, Acetone-*d*$_6$): δ 11.6 (Me), 31.8 (MeCO), 56.6, 56.8 (OMe), 93.8 (aryl CH), 105.5, 116.0, 129.9, 151.6, 161.4, 162.0 (aryl C), 196.3 (CO). Mass Spectrum (+EI): *m/z* (%) 235 (M+2, 18), 235 (M+1, 100). HRMS (+ESI): $C_{12}H_{14}N_2NaO_3$ $[M+Na]^+$ requires 257.0896, found 257.0897.

7-Acetylbenzimidazole **9b** (1.80 g, 7.69 mmol) in EtOH (100 mL), crushed KOH (7.10 g) and hydroxylamine hydrochloride (4.0 g, 57.55 mmol) heating under reflux for 48 h gave the oxime as a white pad (1.21 g, 64%), mp 204-206 °C; ν_{max} (KBr): 3410, 3258, 1613, 1456, 1400, 1336, 1306, 1244, 1211, 1139, 1103, 1023, 991, 899, 786 cm^{-1}. λ_{max} (MeOH): 212 nm (ε 19,400 cm^{-1}M^{-1}), 275 (7,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (3H, s, Me), 2.44 (3H, s, Me), 3.85 (3H, s, OMe), 3.95 (3H, s, OMe), 6.33 (1H, s, aryl H5), 8.88 (2H, br s, NH+OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 14.6 (Me), 55.9, 57.0 (OMe), 91.6 (aryl CH), 102.7, 126.7, 134.4, 149.4, 150.8, 156.1 (aryl C), 155.6 (C=N). Mass Spectrum (+EI): *m/z* (%) 252 (M+2, 16), 250 (M+1, 100). HRMS (+ESI): $C_{12}H_{15}N_3NaO_3$ $[M+Na]^+$ requires 272.1006, found 272.1001. Anal. Calcd for $C_{12}H_{15}N_3O_3$: C, 57.8; H, 6.1; N, 16.9. Found: C, 57.8; H, 6.2; N, 16.8.

7-Acetyl-4,6-dimethoxy-2-phenylbenzimidazole (9c). This was prepared as described for the compound **9b** from benzimidazole **1c** (0.5 g, 1.9 mmol), acetyl chloride (1.5 mL, 7.6 mmol) and $SbCl_5$ (1 mL, 7.6 mmol) in anhydrous $CHCl_3$ (20 mL). The resulting precipitate was collected and purified by column chromatography using CH_2Cl_2/MeOH (95:5) as eluent to afford the 7-acetylbenzimidazole **9c** as a yellow powder (0.39 g, 70%). mp 151-153 °C; ν_{max} (KBr): 3346, 1635, 1566, 1474, 1423, 1382, 1362, 1349,

1284, 1249, 1221, 1179, 1103, 981, 702 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 19,600 $cm^{-1}M^{-1}$), 241 (13,500), 289 (16,500), 330 (14,100). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.68 (3H, s, MeCO), 4.02 (3H, s, OMe), 4.15 (3H, s, OMe), 6.36 (1H, s, aryl H5), 7.43-7.51 (3H, m, aryl H), 8.07-8.10 (2H, m, aryl H), 11.57 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.6 (MeCO), 56.5, 56.5 (OMe), 90.9, 127.2, 129.2, 131.3 (aryl CH), 104.7, 126.4, 136.1, 149.6, 155.3, 161.1, 188.8 (aryl C), 198.1 (CO). Mass Spectrum (+EI): *m/z* (%) 298 (M+2, 22), 297 (M+1, 100). Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.9; H, 5.4; N, 9.4. Found: C, 68.4; H, 5.4; N, 9.3.

7-Acetylbenzimidazole **9c** (0.50 g, 1.69 mmol) in EtOH (50 mL), crushed KOH (2.84 g) and hydroxylamine hydrochloride (2.35 g, 33.78 mmol) heating under reflux for 48 h gave the oxime as a white solid (0.36 g, 69%), mp 128-130 °C; ν_{max} (KBr): 3397, 2937, 1610, 1452, 1376, 1341, 1209, 1146, 1002, 690 cm^{-1}. λ_{max} (MeOH): 204 nm (ε 28,700 $cm^{-1}M^{-1}$), 251 (23,200), 308 (18,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (3H, s, Me), 3.93 (3H, s, OMe), 4.11 (3H, s, OMe), 6.58 (1H, s, aryl H5), 7.45-7.48 (3H, m, aryl H), 8.11-8.13 (2H, m, aryl H), 10.07 (1H, br s, OH), 11.48 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 16.1 (Me), 56.2, 57.4 (OMe), 92.5, 126.9, 129.0, 129.7 (aryl CH), 104.6, 127.5, 128.7, 130.6, 130.7, 135.5, 150.2, 154.6 (aryl C), 151.6 (C=N). Mass Spectrum (+EI): *m/z* (%) 313 (M+2, 20), 312 (M+1, 100), 296 (21), 280 (30). HRMS (+ESI): $C_{17}H_{18}N_3O_3$ $[M+H]^+$ requires 312.1342, found 312.1340. Anal. Calcd for $C_{17}H_{17}N_3O_3$ $0.6H_2O$: C, 63.4; H, 5.7; N, 13.0. Found: C, 63.3; H, 5.6; N, 12.9.

7-Acetyl-4,6-dimethoxy-2-(4'-methoxyphenyl)-benzimidazole (9d). This was prepared as described for the compound **9b** from benzimidazole **1d** (0.25 g, 0.88 mmol), acetyl chloride (0.25 mL, 3.52 mmol) and $SbCl_5$ (0.45 mL, 3.52 mmol) in anhydrous $CHCl_3$ (10 mL). The resulting precipitate was collected and purified by column chromatography using CH_2Cl_2/MeOH (98:02) as eluent to afford the 7-acetylbenzimidazole **9d** as a light brown powder (0.18 g, 61%), mp 126-128 °C; ν_{max} (KBr): 3403, 1625, 1592, 1468, 1429, 1384, 1345, 1288, 1253, 1214, 1177, 1147, 1029, 995, 847 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 15,800 $cm^{-1}M^{-1}$), 292 (16,200), 339 (12,300). ^{1}H NMR (300 MHz, Acetone-*d*$_6$): δ 2.59 (3H, s, MeCO), 3.87 (3H, s, OMe), 4.05 (3H, s, OMe), 4.18 (3H, s, OMe), 6.58 (1H, s, aryl H5), 7.07 (2H, d, 8.4 Hz, aryl H), 8.14 (2H, d, *J* 9.0 Hz, aryl H). ^{13}C NMR (75 MHz, Acetone-*d*$_6$): δ 31.7 (COMe), 54.8, 56.0, 56.3 (OMe), 91.1, 114.9, 128.0 (aryl CH), 104.9, 122.2, 137.6, 150.0, 155.9, 160.1, 161.1 (aryl C), 196.5 (CO). Mass Spectrum (+EI): *m/z* (%) 328 (M+2, 18), 327 (M+1, 100). HRMS (+ESI): $C_{18}H_{18}N_2NaO_4$ $[M+Na]^+$ requires 349.1158, found 349.1167.

4,6-Dimethoxy-2-phenyl-7-trifluoroacetylbenzimidazole (10c). To a solution of benzimidazole **1c** (0.50 g, 1.96 mmol) in THF (20 mL), trifluoroacetic anhydride (2.8 mL) was added and the mixture heated under reflux for 7 days. The solution was allowed to cool to room temperature and ice water was added. The product was extracted with EtOAc, washed with water, dried over $MgSO_4$ and recrystallized from EtOAc to afford 7-trifluoroacetylbenzimidazole **10c** as yellow needles (0.55 g, 80%), mp

200-202 °C; ν_{max} (KBr): 3436, 3058, 1636, 1597, 1470, 1453, 1383, 1355, 1326, 1264, 1239, 1225, 1203, 1155, 1068, 990, 956, 849, 802, 777, 765, 740, 693 cm^{-1}. λ_{max} (MeOH): 207 nm (ε 25,600 $cm^{-1}M^{-1}$), 245 (13,200), 306 (17,600), 358 (7,200). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.00 (3H, s, OMe), 4.21 (3H, s, OMe), 6.31 (1H, s, aryl H5), 7.45-7.51 (3H, m, aryl H), 8.03-8.06 (2H, m, aryl H), 11.16 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.6, 56.8 (OMe), 100.1 (CF_3), 90.3, 126.3, 128.9, 130.2 (aryl CH), 115.1, 118.9, 128.9, 129.0, 138.7, 150.5, 159.1 (aryl C), 161.5 (C=O). Mass Spectrum (+EI): *m/z* (%) 352 (M+2, 20), 351(M+1, 100), 256 (8), 255 (M-$COCF_3$). Anal. Calcd for $C_{17}H_{13}F_3N_2O_3$: C, 58.3; H, 3.7; N, 8.0. Found: C, 58.3 ; H, 3.9; N, 8.0.

4,6-Dimethoxy-2-(4'-methoxyphenyl)-7-trifluoroacetylbenzimidazole (10d). *Method A***:** To a solution of benzimidazole **1d** (0.10 g, 0.35 mmol) in THF (10 mL), trifluoroacetic anhydride (1 mL) was added and the mixture heated under reflux for 5 days. The solution was allowed to cool to room temperature and ice water was added. The resulting precipitate was collected, washed with water and recrystallized from EtOH/H_2O to afford the 7-trifluoroacetylbenzimidazole **10d** as yellow crystals (0.11 g, 83%).

Method B: To a solution of KOH (2.50 g) in MeOH (25 mL), benzimidazole **11d** (1 g, 2.10 mmol) was added and the mixture stirred at room temperature overnight. The solvent was concentrated and water added to give a precipitate, which was collected, washed with water and recrystallized from EtOH/H_2O to give the 7-trifluoroacetylbenzimidazole **10d** as yellow needles (0.62 g, 78%), mp 168-170 °C; ν_{max} (KBr): 3426, 1620, 1594, 1495, 1471, 1432, 1373, 1328, 1260, 1216, 1158, 933 cm^{-1}. λ_{max} (MeOH): 207 nm (ε 30,500 $cm^{-1}M^{-1}$), 302 (21,200), 365 (7,600). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (3H, s, OMe), 4.00 (3H, s, OMe), 4.21 (3H, s, OMe), 6.31 (1H, s, aryl H5), 7.01 (2H, d, *J* 8.7 Hz, aryl H), 8.01 (2H, d, *J* 8.7 Hz, aryl H), 11.09 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4, 56.7, 56.8 (OMe), 90.2, 114.4, 128.1 (aryl CH), 100.0 (CF_3), 117.7, 118.1, 121.0, 128.0, 138.4, 150.6, 158.7, 161.4 (aryl C), 161.5 (C=O). Mass Spectrum (+EI): *m/z* (%) 382 (M+2, 18), 381 (M+1, 100), 285 (35). Anal. Calcd for $C_{18}H_{15}F_3N_2O_4$: C, 56.9; H, 4.0; N, 7.4. Found: C, 57.0; H, 4.0; N, 7.3.

4,6-Dimethoxy-2-phenyl-1,7-ditrifluoroacetylbenzimidazole (11c). To a solution of benzimidazole **1c** (0.50 g, 1.96 mmol) in THF (20 mL), trifluoroacetic anhydride (2.8 mL) was added and the mixture heated under reflux for 10 days. The solvent was concentrated and water added to give a precipitate, which was collected, washed with water and recrystallized from EtOH/H_2O to give the title 1,7-ditrifluoroacetylbenzimidazole **11c** as a white coarse powder (0.61 g, 70%), mp >350 °C; ν_{max} (KBr): 3416, 2925, 1638, 1618, 1505, 1463, 1361, 1303, 1269, 1225, 1190, 1157, 1026 cm^{-1}. λ_{max} (MeOH): 213 nm (ε 1,000 $cm^{-1}M^{-1}$), 247 (900). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.07 (3H, s, OMe), 4.20 (3H, s, OMe), 6.42 (1H, s, aryl H5), 7.47-7.52 (3H, m, aryl H), 8.12-8.14 (2H, m, aryl H). Mass Spectrum (+EI): *m/z* (%) 448 (M+2, 70), 447 (M+1, 100), 445(14), 350(17), 289(12).

4,6-Dimethoxy-2-(4'-methoxyphenyl)-1,7-ditrifluoroacetylbenzimidazole (11d)

To a solution of benzimidazole **1d** (1.0 g, 3.52 mmol) in THF (50 mL), trifluoroacetic anhydride (5 mL) was added and the mixture heated under reflux for 10 days. The solution was allowed to cool to room temperature and ice water was added. The resulting precipitate was collected, washed with water and recrystallized from EtOH/H_2O to afford the 1,7-ditrifluoroacetylbenzimidazole **11d** as an off white powder (1.29 g, 77%), mp 238-240 °C; ν_{max} (KBr): 1689, 1611, 1578, 1509, 1471, 1427, 1352, 1309, 1268, 1186, 1162, 1071, 1017, 841, 714 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 37,200 $cm^{-1}M^{-1}$), 306 (28,900), 358 (9,500). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.91 (3H, s, OMe), 4.08 (3H, s, OMe), 4.20 (3H, s, OMe), 6.45 (1H, s, aryl H5), 7.12 (2H, d, *J* 7.9 Hz, aryl H), 8.31 (2H, d, *J* 7.9 Hz, aryl H). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 55.7, 57.2, 57.6 (OMe), 92.1, 114.5, 129.7 (aryl CH), 100.8 (CF_3), 118.8, 120.4, 125.2, 137.6, 151.6, 156.4, 158.4, 158.9 (aryl C), 160.7, 161.6 (C=O). Mass Spectrum (+EI): *m/z* (%) 477 (M+1, 1), 381 (100), 285 (32). Anal. Calcd for $C_{20}H_{14}F_6N_2O_5$ H_2O: C, 48.6; H, 3.3; N, 5.7. Found: C, 48.7; H, 3.3; N, 5.6.

4,6-Dimethoxy-2-phenylbenzimidazole-7-carboxylic acid (12c). A mixture of benzimidazole **10c** (0.50 g, 1.42 mmol), crushed KOH (1.0 g) in EtOH/H_2O (3 :1) was heated under reflux for 4 h. The reaction was allowed to come to room temperature and concentrated HCl was added to acidify the mixture, which was stirred for half an hour. The insoluble material was filtered off and the filtrate was neutralized with 10% $NaHCO_3$ solution. The resulting precipitate was filtered, washed with water and dried to give the product **12c** as a white solid (0.33 g, 77%), mp 221-222 °C; ν_{max} (KBr): 3611, 3387, 3283, 1701, 1604, 1466, 1455, 1386, 1337, 1255, 1215, 1182, 1149, 990, 800, 699 cm^{-1}. λ_{max} (MeOH): 211 nm (ε 27,600 $cm^{-1}M^{-1}$), 241 (20,200), 262 (15,100), 318 (21,900). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.15 (3H, s, OMe), 4.18 (3H, s, OMe), 6.41 (1H, s, aryl H5), 7.44-7.53 (3H, m, aryl H), 8.09-8.12 (2H, m, aryl H), 11.12 (2H, br s, NH+OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.8, 57.5 (OMe), 90.0, 126.6, 128.9, 130.4 (aryl CH), 94.63, 101.35, 128.68, 137.84, 151.03, 155.90, 157.34 (aryl C), 165.9 (C=O). Mass Spectrum (+EI): *m/z* (%) 299 (M+1, 96), 256 (19), 255 (100). Anal. Calcd for $C_{16}H_{14}N_2O_4$: C, 64.4; H, 4.7; N, 9.4. Found: C, 64.6; H, 4.9; N, 9.3.

4,6-Dimethoxy-2-(4'-methoxyphenyl)benzimidazole-7-carboxylic acid (12d). This was prepared according to the method described for the compound **12c** from benzimidazole **10d** (0.50 g, 1.31 mmol), crushed KOH (1.0 g) in EtOH/H_2O (30 mL, 3 :1) heated under reflux for 4 h to give the product **12d** as a white solid (0.40 g, 93%), mp 260-262 °C; ν_{max} (KBr): 3383, 1700, 1613, 1567, 1479, 1430, 1390, 1321, 1257, 1213, 1176, 1148, 1106, 992, 829 cm^{-1}. λ_{max} (MeOH): 211 nm (ε 23,100 $cm^{-1}M^{-1}$), 260 (15,300), 318 (18,300). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 3.77 (3H, s, OMe), 3.80 (3H, s, OMe), 3.91 (3H, s, OMe), 6.27 (1H, s, aryl H5), 6.90 (2H, d, *J* 9.1 Hz, aryl H), 7.96 (2H, d, *J* 9.1 Hz, aryl H), 13.31 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 55.6, 56.1, 58.0 (OMe), 93.6, 114.5, 127.9 (aryl CH), 123.6, 128.7, 138.1, 149.3, 150.5, 155.3, 156.0, 160.3 (aryl C), 168.5 (C=O). Mass Spectrum (+EI): *m/z* (%) 330

(M+2, 23), 329 (M+1, 100). Anal. Calcd for $C_{17}H_{16}N_2O_5$ 1.1CH_2Cl_2: C, 51.6; H, 4.4; N, 6.6. Found: C, 51.4; H, 4.5; N, 6.7.

Methyl 4,6-dimethoxy-2-phenylbenzimidazole-7-carboxylate (13c). To a solution of benzimidazole **12c** (0.10 g, 0.33 mmol) in MeCOMe (20 mL) containing anhydrous K_2CO_3 (0.05 g), a solution of Me_2SO_4 (9.20 mg, 0.73 mmol) in MeCOMe (2 mL) was added dropwise with stirring. The mixture was heated under reflux overnight and allowed to come to room temperature before water was added and the resulting solid was filtered, washed with water, recrystallized from EtOH and dried to yield the methyl ester **13c** as a white solid (78 mg, 73%), mp 126-128 °C; ν_{max} (KBr): 2957, 1700, 1615, 1471, 1250, 1204, 1121, 1083, 983, 713 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 30,500 $cm^{-1}M^{-1}$), 238 (25,700), 288 (13,000). ^1H NMR (300 MHz, $CDCl_3$): δ 3.94 (3H, s, Me), 3.99 (3H, s, OMe), 4.01 (3H, s, OMe), 4.01 (3H, s, OMe), 6.48 (1H, s, aryl H5), 7.48-7.50 (3H, m, aryl H), 7.71-7.75 (2H, m, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.4 (Me), 52.2, 55.8, 58.1 (OMe), 92.7, 128.5, 129.9, 130.0 (aryl CH), 105.1, 120.9, 128.9, 142.3, 149.4, 154.9, 156.2 (aryl C), 166.0 (C=O). Mass Spectrum (+EI): *m/z* (%) 328 (M+2, 19), 327 (M+1, 100), 269 (22). Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.3; H, 5.6; N, 8.6. Found: C, 66.3; H, 5.8; N, 8.4.

Methyl 4,6-dimethoxy-2-(4'-methoxyphenyl)benzimidazole-7-carboxylate (13d). This compound was prepared according to the method of preparation of the compound **13c** from a solution of benzimidazole **12d** (0.10 g, 0.30 mmol) in MeCOMe (20 mL), anhydrous K_2CO_3 (0.04 g) and a solution of Me_2SO_4 (8.3 mg, 0.66 mmol) in MeCOMe (2 mL) heated under reflux overnight to yield the methyl ester **13d** as an off white solid (78 mg, 73%), mp 124-126 °C; ν_{max} (KBr): 2944, 2843, 1710, 1614, 1468, 1376, 1252, 1211, 1177, 1140, 1097, 1026, 843 cm^{-1}. λ_{max} (MeOH): 211 nm (ε 30,600 $cm^{-1}M^{-1}$), 250 (23,600), 293 (15,500). ^1H NMR (300 MHz, $CDCl_3$): δ 3.86 (3H, s, Me), 3.93 (3H, s, OMe), 4.01 (3H, s, OMe), 4.02 (3H, s, OMe), 6.49 (1H, s, aryl H5), 7.02 (2H, d, *J* 8.6 Hz, aryl H), 7.72 (2H, d, *J* 8.6 Hz, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.3 (Me), 52.1, 55.3, 55.7, 58.0 (OMe), 92.4, 113.9, 131.3 (aryl CH), 105.1, 121.0, 121.5, 142.7, 149.2, 155.1, 156.0, 160.9 (aryl C), 166.2 (C=O). Mass Spectrum (+EI): *m/z* (%) 358 (M+2, 22), 357 (M+1, 100), 299 (36). Anal. Calcd for $C_{19}H_{20}N_2O_5$ 0.2H_2O: C, 63.4; H, 5.7; N, 7.8. Found: C, 63.2; H,5.8; N, 7.7.

7-Benzoyl-4,6-dimethoxy-2-phenylbenzimidazole (14c). To an ice cooled solution of benzimidazole **1c** (0.10 g, 0.39 mmol) in dry CH_2Cl_2 (20 mL), benzoyl chloride (0.14 mL, 1.17 mmol) was added followed by $SbCl_5$ (0.15 mL, 1.17 mmol) and the mixture stirred at room temperature under argon for 3 days. Water was added and the solution was extracted with CH_2Cl_2. The organic extract was washed with water, dried over $MgSO_4$ and the solvent evaporated off. The crude solid was purified by column chromatography using CH_2Cl_2/MeOH (95 :05) as eluent to yield the product **14c** as light yellow crystals (40 mg, 29%), mp 157-158 °C; ν_{max} (KBr): 3406, 1619, 1584, 1401, 1461, 1384, 1298, 1283, 1252, 1213, 1177, 1149, 1120, 931, 774, 744, 691 cm^{-1}. λ_{max} (MeOH): 206 nm (ε 47,800 $cm^{-1}M^{-1}$), 249 (31,100), 307

(25,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.61 (3H, s, OMe), 4.15 (3H, s, OMe), 6.32 (1H, s, aryl H5), 7.36-7.49 (6H, m, aryl H), 7.61-7.65 (2H, m, aryl H), 8.06-8.09 (2H, m, aryl H), 10.93 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.2, 56.3 (OMe), 90.6, 126.4, 127.5, 128.2, 128.8, 129.9, 131.0 (aryl CH), 104.3, 129,1, 129.3, 137.9, 141.3, 150.5, 156.1, 159.2 (aryl C), 195.3 (C=O). Mass Spectrum (+EI): *m/z* (%) 360 (M+2, 24), 359 (M+1, 100). Anal. Calcd for $C_{22}H_{18}N_2O_3$: C, 73.7; H, 5.1; N, 7.8. Found: C, 73.9; H, 5.1; N, 7.9.

1-Benzoyl-4,6-dimethoxy-2-phenylbenzimidazole (15c). To a solution of benzimidazole **1c** (0.10 g, 0.39 mmol) in dry CH_2Cl_2 (20 mL), benzoyl chloride (0.14 mL, 1.17 mmol) was added, followed by activated carbon granules (0.2 g) and the mixture heated under reflux for 1 d under argon. The mixture was allowed to cool to room temperature and the carbon granules were filtered off. The organic solvent was evaporated off and the resulting crude solid was purified by column chromatography using CH_2Cl_2/EtOAc (90/10) to yield the title benzimidazole **15c** as a yellow solid (56 mg, 40%), mp 158-159 °C; ν_{max} (KBr): 3443, 1687, 1613, 1600, 1497, 1447, 1325, 1295, 1285, 1255, 1226, 1178, 1151, 922, 800, 695 cm^{-1}. λ_{max} (MeOH): 205 nm (ε 34,700 cm^{-1}M^{-1}), 237 (20,700), 290 (13,700). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (3H, s, OMe), 4.03 (3H, s, OMe), 6.48 (1H, d, *J* 1.9 Hz, aryl H5), 6.70 (1H, d, *J* 1.9 Hz, aryl H7), 7.17-7.24 (3H, m, aryl H), 7.27-7.29 (2H, m, aryl H), 7.40-7.45 (1H, m, aryl H), 7.54-7.62 (4H, m, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.7, 55.9 (OMe), 88.6, 96.1, 128.0, 128.5, 129.1, 129.2, 130.4, 133.7 (aryl CH), 127.8, 130.5, 133.2, 136.5, 151.2, 151.8, 158.9 (aryl C), 169.5 (C=O). Mass Spectrum (+EI): *m/z* (%) 360 (M+2, 25), 359 (M+1, 100), 256 (8), 255 (48). Anal. Calcd for $C_{22}H_{18}N_2O_3$: C, 73.7; H, 5.1; N, 7.8. Found: C, 73.5; H, 5.2; N, 7.6.

4,6-Dimethoxy-7-nitro-2-phenylbenzimidazole (16c). To an ice cooled solution of benzimidazole **1c** (0.50 g, 1.96 mmol) in Ac_2O (20 mL), a previously cooled solution of HNO_3 (0.15 g, mmol) in Ac_2O (2 mL) was added dropwise over 10 min. The mixture was stirred at 0 °C for a further 2 h before ice water was added and the mixture stirred for another 2 h. The mixture was made neutral by 2 M NaOH solution and the resulting precipitate was filtered, washed with water, recrystallized from EtOH/H_2O and dried to afford the 7-nitrobenzimidazole **16c** as a yellow solid (0.41 g, 70%), mp 207-208 °C; ν_{max} (KBr): 3356, 1621, 1597, 1479, 1448, 1318, 1251, 1118, 980 cm^{-1}. λ_{max} (MeOH): 204 nm (ε 25,300 cm^{-1}M^{-1}), 290 (12,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.09 (3H, s, OMe), 4.22 (3H, s, OMe), 6.40 (1H, s, aryl H5), 7.50-7.52 (3H, m, aryl H), 8.06-8.09 (2H, m, aryl H), 10.88 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.0, 57.3 (OMe), 90.9, 126.5, 128.5, 130.5 (aryl CH), 118.3, 128.7, 129.0, 132.8, 150.7, 156.2, 157.3 (aryl C). Mass Spectrum (+EI): *m/z* (%) 301 (M+2, 18), 300 (M+1, 100). Anal. Calcd for $C_{15}H_{13}N_3O_4$: C, 60.2; H, 4.4; N, 14.0. Found: C, 60.2; H, 4.5; N, 14.1.

4,6-Dimethoxy-2-(4'-methoxyphenyl)-7-nitrobenzimidazole (16d). This compound was prepared as described for the preparation of 7-nitrobenzimidazole **16c** from a solution of benzimidazole **1d** (0.25 g,

0.88 mmol) in Ac_2O (10 mL) and a previously cooled solution of HNO_3 (0.15 g, mmol) in Ac_2O (2 mL) under stirring at 0 °C for 2 h to afford the 7-nitrobenzimidazole **16d** as a yellow solid (0.23 g, 78%), mp 208-209 °C; ν_{max} (KBr): 3454, 1621, 1592, 1477, 1428, 1306, 1250, 1232, 1179, 1024, 982, 567 cm^{-1}. λ_{max} (MeOH): 206 nm (ε 38,800 $cm^{-1}M^{-1}$), 235 (16,700), 293 (24,300). ^1H NMR (300 MHz, $CDCl_3$): δ 3.86 (3H, s, OMe), 4.06 (3H, s, OMe), 4.18 (3H, s, OMe), 6.35 (1H, s, aryl H5), 6.99 (2H, d, *J* 9.0 Hz, aryl H), 7.98 (2H, d, *J* 9.0 Hz, aryl H), 10.74 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.3, 56.8, 57.2 (OMe), 90.7, 114.4, 128.0 (aryl CH), 118.3, 121.2, 128.8, 132.8, 150.8, 155.8, 157.0, 161.4 (aryl C). Mass Spectrum (+EI): *m/z* (%) 331 (M+2, 20), 330 (M+1, 100). Anal. Calcd for $C_{16}H_{15}N_3O_5$: C, 58.4; H, 4.6; N, 12.8. Found: C, 58.7; H, 4.8; N, 12.9.

7-Bromo-4,6-dimethoxy-2-methylbenzimidazole (17b) and 5,7-dibromo-4,6-dimethoxy-2-methylbenzimidazole (18b). To a solution of benzimidazole **1b** (0.10 g, 0.52 mmol) in absolute EtOH (10 mL), *N*-bromosuccinimide (0.18 g, 0.10 mmol) was added and the mixture stirred at room temperature for 1 h. The solvent was concentrated and water added to the mixture, the resulting precipitate was collected, washed with water and dried. The solid was chromatographed by preparative thin layer chromatography using CH_2Cl_2/EtOAc (9:1) as eluent to give two products.

(i) 7-Bromo-4,6-dimethoxy-2-methylbenzimidazole **(17b)** was obtained as an off white powder (79 mg, 56%), mp 234-235 °C; ν_{max} (KBr): 3150, 3081, 1772, 1697, 1635, 1594, 1537, 1456, 1403, 1338, 1295, 1192, 1142, 1095, 1080, 994, 895, 849, 822 cm^{-1}. λ_{max} (MeOH): 216 nm (ε 31,000 $cm^{-1}M^{-1}$), 256 (6,800), 286 (3,200). ^1H NMR (300 MHz, $CDCl_3$): δ 2.59 (3H, s, Me), 3.93 (3H, s, OMe), 3.98 (3H, s, OMe), 6.43 (1H, s, aryl H5), 8.67 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.8 (CH_3), 56.0, 57.7 (OMe), 92.4 (aryl CH), 148.6, 149.5, 152.7, 161.4, 165.1, 174.8 (aryl C). Mass Spectrum (+EI): *m/z* (%) 274 (M+1, ^{81}Br,11), 273 (M, ^{81}Br,100), 272 (M+1, ^{79}Br, 13), 271 (M, ^{79}Br, 88), 215 (10), 194 (15), 193 (98). Anal. Calcd for $C_{10}H_{11}BrN_2O_2$ $0.4CH_2Cl_2$: C, 40.9; H, 3.9; N, 9.2. Found: C, 40.9; H, 3.6; N, 9.0.

(ii) 5,7-Dibromo-4,6-dimethoxy-2-methylbenzimidazole **(18b)** was obtained as an off white powder (43 mg, 23%), mp 177-179 °C; ν_{max} (KBr): 2935, 2837, 1537, 1455, 1391, 1342, 1229, 1115, 1079, 984, 967, 659 cm^{-1}. λ_{max} (MeOH): 216 nm (ε 38,100 $cm^{-1}M^{-1}$), 253 (6,900), 290 (3,100). ^1H NMR (300 MHz, $CDCl_3$): δ 2.65 (3H, s, Me), 3.89 (3H, s, OMe), 4.18 (3H, s, OMe), 6.91 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.7 (Me), 61.1, 61.4 (OMe), 105.1, 129.2, 136.1, 146.0, 148.7, 150.4, 151.0 (aryl C). Mass Spectrum (+EI): *m/z* (%) 354 (M, $^{81/81}Br$, 4), 353 (M+1, $^{79/81}Br$, 41), 351 (M+1, $^{79/79}Br$, 100), 350 (M, $^{79/79}Br$, 3), 349 (51), 273 (15), 271(14), 193 (28), 179 (5). Anal. Calcd for $C_{10}H_{10}Br_2N_2O_2$: C, 34.3; H, 2.9; N, 8.0. Found: C, 34.2; H, 2.8; N, 7.9.

This compound **18b** was also prepared from a solution of benzimidazole **1b** (0.10 g, 0.52 mmol) in CH_2Cl_2 (10 mL), with triethylamine (0.1 mL), followed by slow addition of Br_2 (0.05 mL, 0.97 mmol). The clear yellow solution turned to a fluffy yellow suspension which was stirred for 15 min. Water was

added to the mixture and the organic layer was separated, washed with water, and dried over $MgSO_4$. The solvent was evaporated off and the residue dried as an off white solid to afford the dibromobenzimidazole **18b** (0.16 g, 88%).

Reaction of 2-phenyl-4,6-dimethoxybenzimidazole 1c with excess methyl iodide. To a solution of benzimidazole **1c** (0.50 g, 1.97 mmol) in dry DMSO (10 mL), crushed KOH (0.50 g) was added and the mixture stirred for 1 h. MeI (0.25 mL, 3.94 mmol) was then added and the solution was heated for 3 h at 110 °C. The solution was allowed to cool to room temperature and water was added. The resulting precipitate was filtered, washed with water and dried. The crude product was submitted to column chromatography using CH_2Cl_2/MeOH (95:5) as eluent to yield the following three products.

(i) N-Methyl-N-(2,4,6-trimethoxyphenyl)benzamide (**21**) was obtained as colorless crystals (0.40 g, 67%), mp 186-188 °C; ν_{max} (KBr): 3360, 1635, 1525, 1483, 1451, 1420, 1381, 1350, 1240, 1204, 1188, 1157, 1058, 802, 721, 701 cm^{-1}. λ_{max} (MeOH): 217 nm (ε 40,600 $cm^{-1}M^{-1}$), 291 (3,200). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.89 (3H, s, *N*-Me), 3.16 (3H, s, OMe), 3.55 (3H, s, OMe), 3.71 (3H, s, OMe), 5.62 (1H, d, *J* 2.6 Hz, aryl H4), 5.74 (1H, d, *J* 2.6 Hz, aryl H6), 7.11-7.33 (5H, m, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.2 (Me), 35.0, 55.0, 55.1 (OMe), 86.9, 88.6, 126.6, 127.1, 129.4 (aryl CH), 112.4, 136.2, 146.1, 155.9, 160.7 (aryl C), 174.1 (C=O). Mass Spectrum (+EI): *m/z* (%) 302 (M+1, 12), 301 (M, 58), 283 (10), 270 (18), 269 (100). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.8; H, 6.4; N, 4.7. Found: C, 67.8; H, 6.4; N, 4.6.

(ii) 4,6-Dimethoxy-1-methyl-2-phenylbenzimidazole (**19c**) was obtained as a light brown solid after long standing (60 mg, 11%), mp 73-74 °C; ν_{max} (KBr): 2936, 1615, 1593, 1503, 1470, 1450, 1385, 1353, 1337, 1245, 1207, 1152, 1143, 1071, 818, 781, 707 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 33,500 $cm^{-1}M^{-1}$), 234 (15,500), 295 (13,600). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (3H, s, *N*-Me), 3.85 (3H, s, OMe), 3.97 (3H, s, OMe), 6.37-6.39 (2H, m, aryl H5, H7), 7.42-7.44 (3H, m, aryl H), 7.71-7.74 (2H, m, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.8 (Me), 55.7, 55.8 (OMe), 85.1, 94.1, 128.3, 129.1, 129.3 (aryl CH), 127.9, 130.2, 137.9, 151.4, 151.8, 157.7 (aryl C). Mass Spectrum (+EI): *m/z* (%) 270 (M+2, 18), 269 (M+1, 100). Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.6; H, 6.0; N, 10.4. Found: C, 71.5; H, 6.2; N, 10.3.

(iii) 5,7-Dimethoxy-1-methyl-2-phenylbenzimidazole (**20c**) was obtained as a light brown solid after long standing (66 mg, 13%), mp 73-74 °C; ν_{max} (KBr): 2962, 1625, 1608, 1504, 1470, 1438, 1415, 1304, 1201, 1148, 1113, 1041, 936, 776, 706 cm^{-1}. λ_{max} (MeOH): 208 nm (ε 34,200 $cm^{-1}M^{-1}$), 247 (13,900), 285 (9,300). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (3H, s, OMe), 3.88 (3H, s, OMe), 3.98 (3H, s, *N*-Me), 6.36 (1H, d, *J* 1.9 Hz, aryl H6), 6.84 (1H, d, *J* 1.9 Hz, aryl H4), 7.44-7.47 (3H, m, aryl H), 7.66-7.69 (2H, m, aryl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.1 (Me), 55.5, 55.6 (OMe), 93.5, 95.4, 128.4, 129.3, 129.4 (aryl CH), 120.8, 130.1, 144.7, 147.5, 153.7, 156.7 (aryl C). Mass Spectrum (+EI): *m/z* (%) 270 (M+2, 19), 269 (M+1, 100). Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.6; H, 6.0; N, 10.4. Found: C, 71.6; H, 6.2; N, 10.2.

Reaction of 2-phenyl-4,6-dimethoxybenzimidazole 1c with allyl chloride. A solution of benzimidazole **1c** (1.0 g, 3.93 mmol) in DMSO (10 mL) was stirred at room temperature with KOH (0.39 g, 7 mmol) for 30 min. Allyl chloride (0.30 g, 3.93 mmol) in DMSO (2 mL) and NaI (1.1 g, 7.01 mmol) were added and stirring was continued overnight. The mixture was then diluted with water and extracted with EtOAc. The organic extract was washed with brine, dried over anhydrous $MgSO_4$, and the solvent evaporated to give a clear syrup. Purification via gravity column chromatography (2% MeOH/CH_2Cl_2) gave a 1.6:1.0 tautomeric mixture of the isomeric compounds **23c** and **24c** as a colourless syrup that partially solidified on standing (1.03 g, 89%). R_f (5% MeOH/CH_2Cl_2) 0.60. HRMS (+ESI): $C_{18}H_{18}N_2O_2$ [M^+] requires 294.1368, found 294.1365. ν_{max} (KBr): 1627, 1603, 1508, 1468, 1456, 1397, 1365, 1305, 1224, 1201, 1145, 1121, 1042, 919, 815, 776, 701, 690 cm^{-1}. λ_{max} (MeOH): 251 nm (ε 16,600 $cm^{-1}M^{-1}$), 305 (17,600). Mass spectrum: (+EI) *m/z* (%) 296 (M+2, 2), 295 (M+1, 16), 294 (M, 100), 253 (49), 223 (28), 208 (27), 104 (28).

(i) N-Allyl-4,6-dimethoxy-2-phenylbenzimidazole (**24c**). ^{1}H NMR (300 MHz, $CDCl_3$): δ ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.72 (3H, s, OMe), 3.90 (3H, s, OMe), 4.60 (2H, dd, allyl H1), 4.93 (1H, d, allyl H3), 5.18 (1H, d, allyl H3), 5.85-5.98 (1H, m, allyl H2), 6.26 (1H, d, *J* 2.0 Hz, H5), 6.30 (1H, d, *J* 2.0 Hz, H7), 7.33 (3H, m, phenyl), 7.66 (2H, m, phenyl). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.12 (allyl C1), 55.8 (OMe), 85.8, 94.2 (aryl CH), 117.1 (allyl C3), 128.4, 128.8, 129.1 (phenyl CH), 132.4 (allyl C2), 129.4, 130.3, 137.5, 151.5, 151.9, 157.8 (aryl C).

(ii) N-Allyl-5,7-dimethoxy-2-phenylbenzimidazole (**25c**). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (3H, s, OMe), 3.96 (3H, s, OMe), 4.95 (2H, dd, allyl H1), 5.06 (1H, d, allyl H3), 5.31 (1H, d, allyl H3), 5.85-5.98 (1H, m, allyl H2), 6.39 (1H, d, *J* 2.0 Hz, H6), 6.87 (1H, d, *J* 2.0 Hz, H4), 7.33 (3H, m, phenyl), 7.66 (2H, m, phenyl).

***N*-Allyl-4,6-dimethoxy-2-phenylbenzimidazole-7-carbaldehyde** (**26c**)**:** DMF (5 mL) was cooled in an iced water bath and treated with phosphoryl chloride (0.5 mL, 5.4 mmol) and stirred for 15 min. This solution was then added dropwise to a similarly cooled and stirred solution of a 9:1 mixture of isomers **24** and **25** (0.89 g, 3.01 mmol) in DMF (5 mL). The resulting solution was allowed to warm to room temperature before being heated at 70 °C for 19 h. After cooling to room temperature, chilled water was added and the mixture was basified to high pH with 2M NaOH. The resulting precipitate was filtered, washed with water and dried to give the title compound as an off-white powder (0.85 g, 87%), mp 171-174 °C; ν_{max} (KBr): 1661, 161s, 1590, 1464, 1451, 1399, 1380, 1340, 1327, 1218, 1170, 1160, 1113, 989, 932, 797, 715, 702, 668 cm^{-1}. λ_{max} (MeOH): 246 nm (ε 22,400 $cm^{-1}M^{-1}$), 279 (10,600), 312 (17,800). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98 (3H, s, OMe), 4.01 (3H, s, OMe), 4.87 (1H, d, allyl H3), 4.94 (2H, dd, allyl H1), 5.17 (1H, d, allyl H3), 6.01 (1H, m, allyl H2), 6.39 (1H, s, H5), 7.47 (3H, m, phenyl), 7.73 (2H, m, phenyl), 10.75 (1H, s, CHO). ^{13}C NMR (75 MHz, DMSO-d_6): δ 48.6 (allyl C1), 56.0, 57.1

(OMe), 90.7 (C5), 116.3 (allyl C3), 128.6, 129.7, 130.1 (phenyl CH), 134.5 (allyl C2), 109.6, 120.3, 129.8, 145.8, 152.2, 156.5, 160.7 (aryl C), 188.0 (CHO). Mass spectrum (+EI): *m/z* (%) 323 (M+1, 4), 322 (M, 19), 294 (24), 293 (100), 265 (20), 264 (28), 104 (22). Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.8; H, 5.6; N, 8.7. Found: C, 70.5; H, 5.9; N, 8.5.

4,6-Dimethoxybenzimidazole-2,7-dicarbaldehyde (27). To a solution of 7-formylbenzimidazole **2b** (0.20 g, 0.9 mmol) in dioxane (15 mL), SeO_2 (0.5 g, 4.5 mmol) was added and the mixture was heated under reflux for 3 days. The resulting precipitate was filtered, the filtrate was concentrated and extracted with EtOAc. The extract was washed with water, dried over $MgSO_4$ and concentrated. The residue was chromatographed using CH_2Cl_2/MeOH (95:05) as eluent to yield the 2,7-dialdehyde **27** as a yellow powder (0.143 g, 68%), mp 184-186 °C; ν_{max} (KBr): 3440, 1664, 1649, 1596, 1491, 1458, 1358, 1279, 1220, 1153, 992, 882, 797 cm^{-1}. λ_{max} (MeOH): 207 nm (ε 19,500 $cm^{-1}M^{-1}$), 231 (16,300), 302 (16,400), 327 (11,700). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.04 (3H, s, OMe), 4.20 (3H, s, OMe), 6.39 (1H, s, aryl H5), 9.92 (1H, s, CHO), 10.31 (1H, s, CHO), 11.40 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 56.6, 56. (OMe), 90.6 (aryl CH), 104.6, 129.5, 135.2, 147.3, 159.8, 165.0 (aryl C), 182.1, 187.2 (C=O). Mass Spectrum (+EI): *m/z* (%) 237 (M+3, 12), 236 (M+2, 18), 235 (M+1,100), 221 (4), 207 (22). Anal. Calcd for $C_{11}H_{10}N_2O_4$: C, 56.4; H, 4.3; N, 12.0. Found: C, 56.6; H, 4.2; N, 11.9.

4,6-Dimethoxy-2,7-di(hydroxymethyl)benzimidazole (28). To a solution of 2,7-diformylbenzimidazole **27** (0.10 g, 0.427 mmol) in anhydrous MeOH (20 mL), $NaBH_4$ (0.2 g) was added and the mixture was heated under reflux for 4 h. The reaction mixture was concentrated and cooled before ice water was added. The resulting precipitate was filtered, washed with water, and recrystallized from EtOH to yield the 2,7-dihydroxymethylbenzimidazole **28** (69 mg, 69%), mp 208-210 °C. ν_{max} (KBr): 3249, 2932, 1619, 1451, 1338, 1215, 1154, 1004, 787 cm^{-1}. λ_{max} (MeOH): 216 nm (ε 29,600 $cm^{-1}M^{-1}$), 259 (7,500). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (3H, s, OMe), 3.92 (3H, s, OMe), 4.56 (2H, s, CH_2), 4.57 (1H, s, OH), 4.67 (2H, s, CH_2), 4.75 (1H, s, OH), 6.42 (1H, s, aryl H5), 11.76 (1H, br s, NH). Mass Spectrum (+EI): *m/z* (%) 239 (M+1, 100), 237 (13), 221 (85). HRMS (+ESI): $C_{11}H_{14}N_2NaO_4$ $[M+Na]^+$ requires 261.0845, found 261.0845.

4,6-Dimethoxybenzimidazole-2-carbaldehyde (30). The 2-styrylbenzimidazole **29**[1] (0.42 g, 1.5 mmol) was dissolved in warm dioxane/H_2O (50 mL, 3:1) and cooled in an ice bath. OsO_4 (0.038 g, 0.15 mmol) was added to the mixture which was stirred for 5 min. $NaIO_4$ (1.2 g, 5.61 mmol) was added to this mixture in portions and stirring was continued at room temperature for 48 h. The product was extracted with EtOAc, the extract washed with Na_2SO_3 solution (1M), then water, and dried over $MgSO_4$. The solution was concentrated and the resulting precipitate was collected and dried to yield the benzimidazole-2-carbaldehyde **30** as a light brown solid (0.23 g, 74%), mp 190-192 °C; ν_{max} (KBr): 3484, 3159, 1619, 1521, 1508, 1455, 1437, 1409, 1282, 1234, 1217, 1202, 1159, 1120, 1049, 908, 864, 830, 785

cm^{-1}. λ_{max} (MeOH): 211 nm (ε 21,200 $cm^{-1}M^{-1}$), 252 (6,100), 329 (2,900). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (3H, s, OMe), 3.99 (3H, s, OMe), 6.40 (1H, d, *J* 1.9 Hz, aryl H5), 6.56 (1H, d, *J* 1.9 Hz, aryl H7), 9.89 (1H, s, CHO), 10.53 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.7, 55.8 (OMe), 92.8, 96.3 (aryl CH), 129.7, 136.4, 146.2, 153.5, 161.0 (aryl C), 182.7 (C=O). Mass Spectrum (+EI): *m/z* (%) 205 (M-1, 100), 113 (21). HRMS (+ESI): $C_{10}H_{10}N_2NaO_3$ $[M+Na]^+$ requires 229.0583, found 229.0585. Anal. Calcd for $C_{10}H_{10}N_2O_3$ $0.1H_2O$: C, 57.7; H, 4.9; N, 13.5. Found: C, 57.7; H, 5.0; N, 13.4.

4,6-Dimethoxy-2-hydroxymethylbenzimidazole (31). To a solution of 2-formylbenzimidazole **30** (0.20 g, 0307 mmol) in anhydrous MeOH (20 mL), $NaBH_4$ (0.40 g) was added and the mixture was heated under reflux for 6 h. The reaction mixture was concentrated and cooled before ice water was added. The resulting precipitate was filtered, washed with water, and recrystallized from EtOH to yield the 2-hydroxymethylbenzimidazole **31** as light brown powder (0.121 g, 60%), mp 212-213 °C; ν_{max} (KBr): 3117, 1605, 1454, 1433, 1148, 1130, 1046 cm^{-1}. λ_{max} (MeOH): 205 nm (ε 21,200 $cm^{-1}M^{-1}$), 244 (4,200). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.72 (3H, s, OMe), 3.85 (3H, s, OMe), 4.56 (2H, s, CH_2), 5.50 (1H, br s, OH), 6.27 (1H, s, aryl H5), 6.54 (1H, s, aryl H7), 12.13 (1H, br s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.5, 55.7 (OMe), 57.7 (CH_2), 87.5, 94.7 (aryl CH), 119.1, 136.2, 145.0, 146.4, 156.1, (aryl C). Mass Spectrum (+EI): *m/z* (%) 210 (M+2, 17), 209 (M+1, 100). Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.7; H, 5.8; N, 13.4. Found: C, 57.9; H, 6.1; N, 13.3.

2-[(4,6-Dimethoxybenzimidazol-2-yl)methoxy)methyl]-4,6-methoxybenzimidazole (32). 2-Hydroxymethylbenzimidazole **31** (50 mg, 0.24 mmol) and a few crystals of *p*-toluenesulfonic acid were dissolved in hot *i*PrOH (2 mL). The heating and stirring were continued at 120 °C for 4 h before cooling to room temperature. The resulting precipitate was filtered, washed with cold *i*PrOH and dried to give the benzimidazole **32** as a white solid (42 mg, 88%), mp 212-213 °C; ν_{max} (KBr): 3119, 2833, 2653, 1606, 1504, 1454, 1433, 1299, 1223, 1200, 1148, 1130, 1046, 818 cm^{-1}. λ_{max} (MeOH): 212 nm (ε 37,300 $cm^{-1}M^{-1}$), 253 (8,500). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.76 (6H, s, OMe), 3.90 (6H, s, OMe), 4.68 (4H, s, CH_2), 6.45 (2H, d, *J* 1.9 Hz, aryl H5), 6.60 (2H, d, *J* 1.9 Hz, aryl H), 12.11 (2H, br s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 55.8, 56.0 (OMe), 58.0 (CH_2), 87.2, 94.1 (aryl CH), 128.1, 136.2, 151.2, 152.4, 156.7 (aryl C). Mass Spectrum (+EI): *m/z* (%) 399 (M+1, 17), 281 (24), 223 (17), 209 (100). Anal. Calcd for $C_{20}H_{22}N_4O_5$ H_2O: C, 57.7; H, 5.8; N, 13.4. Found: C, 57.7; H, 5.9; N, 13.3.

ACKNOWLEDGEMENTS

Financial support from the Australian Research Council is gratefully acknowledged. M.A. also acknowledges receipt of an Endeavour International Postgraduate Research Scholarship from the Australian Government.

REFERENCES AND NOTES

1. M. Alamgir, G. C. Condie, V. Martinovic, J. Wood, H. Sholihin, P. K. Bowyer, N. Kumar, and D. StC. Black, *Heterocycles*, DOI: 10.3987/COM-20-14278.
2. D. StC. Black, M. C. Bowyer, A. J. Ivory, K. A. Jolliffe, and N. Kumar, *Tetrahedron*, 1996, **52**, 4687.
3. D. StC. Black, M. C. Bowyer, M. M. Catalano, A. J. Ivory, P. A. Keller, N. Kumar, and S. J. Nugent, *Tetrahedron*, 1994, **50**, 10497.
4. D. StC. Black, M. C. Bowyer, N. Kumar, and P. S. R. Mitchell, *J. Chem. Soc., Chem. Commun.*, 1993, 819.
5. D. StC. Black, D. C. Craig, and N. Kumar, *Tetrahedron Lett.*, 1995, **36**, 8075.
6. R. Chen, K. Somphol, M. Bhadbhade, N. Kumar, and D. StC. Black, *Synlett*, 2013, **24**, 1497.
7. J. C. Dobrowolski, K. Somphol, M. Santoso, H. Duong, C. R. Gardner, N. Kumar, and D. StC. Black, *Aust. J. Chem*., 2017, **70**, 1188.
8. D. StC. Black, N. Kumar, and L. C. H. Wong, *Synthesis*, 1986, 474.
9. I. Yavari and A. Ramazani, *J. Chem. Res. (S)*, 1996, 382.
10. D. StC. Black, R. B. Deb-Das, and N. Kumar, *Aust. J. Chem*., 1992, **45**, 1051.
11. M. Kodomari, Y. Suzuki, and K. Yoshida, *J. Chem. Soc., Chem. Commun*., 1997, 1567.
12. A. W. Jones, B. Purwono, P. K. Bowyer, P. S. R. Mitchell, N. Kumar, S. J. Nugent, K. A. Jolliffe, and D. StC. Black, *Tetrahedron*, 2004, **60**, 10779.
13. T. Keawin, S. Rajviroongit, and D. StC. Black, *Tetrahedron*, 2005, **61**, 853.
14. D. StC. Black, P. A. Keller, and N. Kumar, *Tetrahedron*, 1992, **36**, 7601.
15. P. S. R. Mitchell, I. F. Sengul, H. Kandemir, S. J. Nugent, R. Chen, P. K. Bowyer, N. Kumar, and D. StC. Black, *Tetrahedron*, 2012, **68**, 8163.
16. D. StC. Black, P. A. Keller, and N. Kumar, *Aust. J. Chem*., 1993, **46**, 843.
17. D. StC. Black, N. E. Rothnie, and L. C. H. Wong, *Aust. J. Chem*., 1983, **36**, 2407.
18. A. W. Jones, T. D. Wahyuningsih, K. Pchalek, N. Kumar, and D. StC. Black, *Tetrahedron*, 2005, **61**, 10490.