

Reaction of Some 4,6-Dimethoxyindoles with Oxalyl Chloride

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Abstract: 3-(4'-Chlorophenyl)-4,6-dimethoxyindole **1** undergoes reaction with oxalyl chloride to give the corresponding 2- and 7-glyoxyloyl chloride derivatives in differing proportions depending on the solvent and reaction temperature. The glyoxyloyl chlorides **2** and **3** were converted into the related glyoxylic acids, and also a wide range of glyoxylic esters and amides **4** and **5** respectively.

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The reaction of oxalyl chloride and indole was first performed in 1924 by Giua.¹ The product was incorrectly reported to be the indol-2-ylglyoxyloyl chloride but was later confirmed to be the indol-3-ylglyoxyloyl chloride, which has been shown to react readily with alcohols and amines to give the corresponding glyoxylic esters and amides. Oxalyl chloride has more recently been reacted with 4,6-dimethoxy-2,3-diphenylindole to give the 7'-substituted glyoxyloyl chloride and some related glyoxylic esters and amides.² Formylation of a wide range of indoles, and especially 4,6-dimethoxyindoles, has been more extensively studied. As expected, 2,3-disubstituted-4,6-dimethoxyindoles undergo formylation readily at C7, as do various 2- and 3-substituted analogs.³⁻⁶ In particular, when the 3-substituent is aryl, there is very strong selectivity for mono-formylation at C7 in preference to C2, even though the use of excess reagent readily allows the preparation of 2,7-dicarbaldehydes.⁶ In this context it was of interest to investigate the regioselectivity of reaction of oxalyl chloride with 3-aryl-4,6-dimethoxyindoles,⁷ especially as both the 2- and 7-glyoxylic acid derivatives were desired for further synthetic purposes.

Oxalyl chloride was found to react readily with 3-(4'-chlorophenyl)-4,6-dimethoxyindole **1** without a catalyst to yield a mixture of the 2'- and 7'-substituted indolylglyoxyloyl chlorides **2** and **3** respectively. These acid chlorides could be isolated for partial characterisation but need not normally be isolated. Usually they were reacted immediately with water, alcohols or amines to give the corresponding glyoxylic acid or derivatives. The regioselectivity of the reaction of oxalyl chloride with indole **1** could be dramatically altered by varying the solvent. When dichloromethane or tetrachloroethane were used, a 70:30 ratio of 7'-isomer to 2'-isomer was observed. This distribution was reversed when diethyl ether was the solvent and the more polar tetrahydrofuran gave a 55:45 ratio of 7'-isomer to 2'-isomer.

A considerable advantage when diethyl ether was used as the solvent was that the 2'-glyoxyloyl chloride **2** precipitated out of solution as a red solid while the 7'-glyoxyloyl chloride **3** remained in solution, thus avoiding the need for chromatography. Two disadvantages of the use of diethyl ether as the solvent were that the overall yield from indole **1** to a glyoxylic ester for example was only approximately 70%, and the reaction to form the glyoxyloyl chloride was slow, taking 3 hours. Using dichloromethane as the solvent,

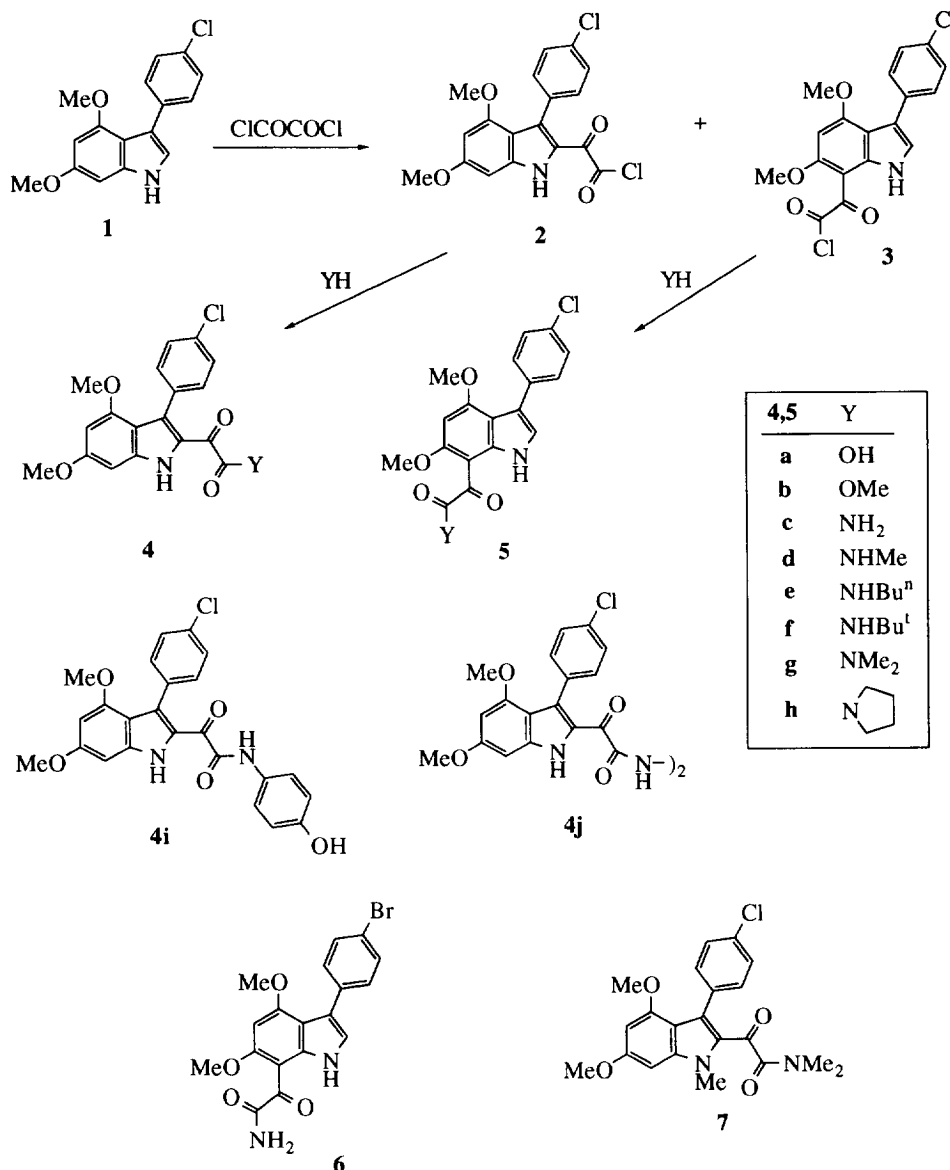
chromatography was required to separate the isomeric products but an 89% yield could be obtained and the reaction was very rapid, taking only 15 minutes at 0°C. The slow rate of the reaction in diethyl ether could be responsible for the lower yield by increasing the possibility of hydrolysis.

An increase in the proportion of 2'-substitution occurred when the reaction of indole **1** with oxalyl chloride in tetrahydrofuran was performed at -5°C compared with room temperature. The 2'-isomer **2** was most favoured when the reaction was performed at room temperature in the non-polar solvent diethyl ether. At the same temperature in the more polar tetrahydrofuran, an increase in the amount of 7'-isomer **3** was observed. However, use of the comparatively polar, non-coordinating solvents dichloromethane and 1,1,2,2-tetrachloroethane gave a significant increase in the amount of 7'-isomer **3**. The amount of 2'-isomer **2** formed in these solvents correlates with reaction time. In diethyl ether the slowest reaction rate was observed and the greatest amount of 2'-isomer **2** was formed. The shortest reaction time occurred when dichloromethane was used as the solvent and gave the most 7'-isomer **3**. The mode of addition of oxalyl chloride also appeared to have an effect on the product distribution. Slow dropwise addition of oxalyl chloride to the indole increased substitution at the 2'-position while rapid addition gave a greater amount of the 7'-substituted product. When an excess of oxalyl chloride was used exclusive 7'-substitution was observed. Significantly only monoacylation was observed presumably due to the significant deactivation caused by the introduction of the first substituent onto the indole ring. It is proposed that the 7'-isomer **3** is the product of thermodynamic control because it is favoured at high temperatures and faster reaction rates and that the 2'-isomer **2** in these solvents is the kinetic product, being favoured at lower temperatures and slower reaction rates. It appears that the energies of activation for the two reaction paths are similar, because small changes in conditions have a pronounced effect on the outcome of the reaction.

The indolyglyoxyloyl chlorides **2** and **3** can be converted directly into glyoxylic acids **4a** and **5a**, glyoxylic esters **4b** and **5b**, and glyoxylamides **4c-h** and **5c-h** effectively in quantitative yield. In addition, the amide **4i** and the hydrazide **4j** were derived from the acid chloride **2**, and the amide **6** was obtained from 3-(4'-bromophenyl)-4,6-dimethoxyindole. If the 2'-substituted product was required, the reaction between indole **1** and oxalyl chloride was performed in diethyl ether for 3 hours at room temperature and the 2'-glyoxyloyl chloride **2** was filtered off as a red solid (Method A). The acid chloride **2** was then partially redissolved in diethyl ether and treated with water, methanol or the amine, to give the desired product in approximately 50% yield. The filtrate from this reaction contained the 7'-glyoxyloyl chloride **3** which could similarly be converted to the desired acid, ester or amide in approximately 25% yield. If the 7'-isomer was required, the reaction of indole **1** and oxalyl chloride was carried out in dichloromethane for 15 minutes at 0°C (Method B). The resulting solution contained a mixture of the 2'-acid chloride **2** and the 7'-acid chloride **3**, to which water, methanol or the desired amine was added. Chromatography was then performed on the resulting crude mixture to obtain the 7'-glyoxylic acid **5a**, the 7'-methyl glyoxylate **5b**, or the 7'-glyoxylamides **5c-h** in approximately 50% yield. The corresponding 2'-glyoxylic acid **4a** and its various derivatives were obtained in approximately 25% yield.

The spectroscopic data of these compounds showed some interesting patterns and variations. When comparing the indole NH chemical shift in the ¹H NMR spectra of the various derivatives, it was evident that the greatest degree of hydrogen bonding occurred in the 2'-substituted primary and secondary amides **4c-f**, where values ranged from 11.31 to 11.61. The 2'-substituted tertiary amides **4g,h** and the 2'-substituted ester **4b** showed NH chemical shifts in the range 9.40-9.47. All the 7'-substituted amides **5c-h** and ester **5b** showed

similar NH chemical shifts from 10.46-10.75. The major contrast is between the strongly hydrogen bonded 2'-substituted amides **4c-f** and the weakly hydrogen bonded ester analog **4b**, implying a different conformation.



There are a number of possible hydrogen bonded structures for both the 2'- and 7'-glyoxylamides **4** and **5** brought about by the presence of two carbonyl groups. The four basic intramolecular hydrogen bonded ring systems possible are shown in Figure 1. The 2'-glyoxylamides **4** can in principle contain two systems, S(5) or S(6) while the 7'-glyoxylamides **5** can contain either an S(6) or an S(7) system.^{8,9}

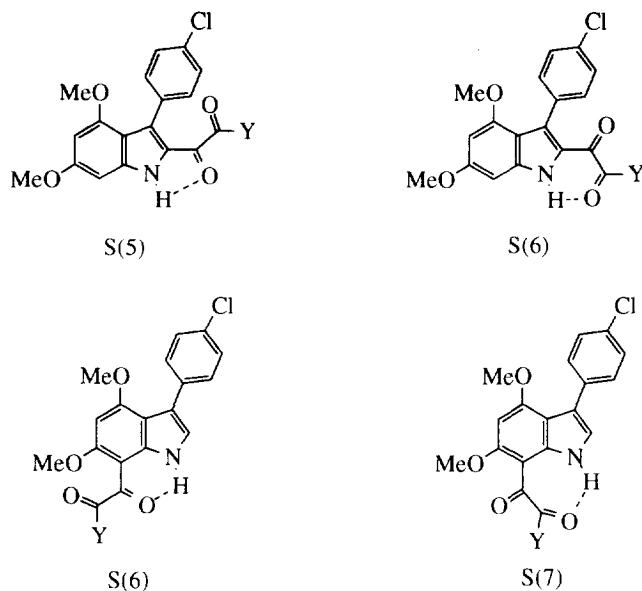


Figure 1: Four possible intramolecular hydrogen bonded rings

The 7'-glyoxylamides **5** represent the simpler of the two systems as there is less variation in the spectroscopic data. It is instructive to consider the ^1H NMR NH chemical shifts of some related 7-carbonyl-substituted 3-aryl-4,6-dimethoxyindoles, which can only give rise to S(6) systems due to the absence of a second carbonyl group. The chemical shift value for the parent indole **1** occurs at 8.06⁷ and represents the situation where no hydrogen bonding occurs. Corresponding values for the related 7-formyl, 7-acetyl and 7-(4'-chlorobenzoyl)-compounds are 10.49, 11.12 and 10.30 respectively¹⁰, reflecting the electronic effect of substituents on the strength of hydrogen bonding. The observed chemical shift values for the 7'-glyoxylamides **5** are all within the proposed range for an S(6) system and there is no evidence for an S(7) system.

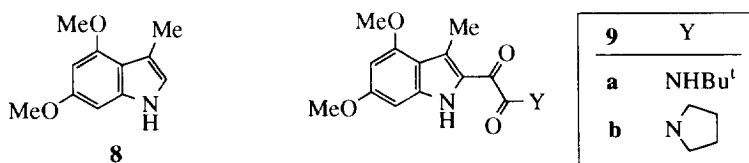
The chemical shifts of the keto carbons of the glyoxylamides **5** all occur at 191 ppm: the amide carbonyls occur between 167.8 and 170.0 ppm. The spectra of glyoxylamide **5f** were obtained in both d_6 -DMSO and CDCl_3 to investigate the effect of solvent on the ^{13}C NMR chemical shift of the carbonyl carbons. The amide carbonyl chemical shift remained the same while the keto carbonyl was shifted upfield by 1.4 ppm when the spectrum was obtained in d_6 -DMSO. The keto carbonyl infrared stretching frequencies for the 7'-glyoxylamides **5** are in the range 1700-1635 cm^{-1} and decrease as the indole NH chemical shift increases, thus providing further evidence for an S(6) system. The corresponding amide carbonyl stretching frequencies occur from 1615-1575 cm^{-1} and presumably reflect changes in the degree of intermolecular hydrogen bonding.

The structure of the 2'-glyoxylamides **4** are somewhat more complicated because the ^1H NMR resonances of the indole NHs vary greatly depending on the type of amide. Primary and secondary amides give rise to highly deshielded indole NHs when compared with the parent indole, while tertiary amides are much less deshielded. The ^1H NMR resonance of the indole NH for the primary 2'-glyoxylamide **4c** occurs at

11.31 ppm, suggesting a stronger degree of hydrogen bonding than the S(6) system present in the 7'-substituted case **5c** or than similar S(5) systems, which show indole NH resonances at 9.2 ppm¹⁰. The hydrogen bond must therefore be occurring between the amide carbonyl and the indole NH to form an S(6) system. This situation is predictable as not only are S(6) systems favoured over S(5), but also amide carbonyls are better donors than keto carbonyls. The more alkyl substituents on the amide nitrogen the greater the donation capacity of the amide carbonyl, so the order of hydrogen bond strength should be tertiary>secondary>primary. This is indeed the case for all the secondary 2'-glyoxylamides **4d-f** where there is an approximate 0.3 ppm shift downfield from the primary 2'-glyoxylamide **4c**. However the tertiary glyoxylamides **4g,h** show the weakest hydrogen bonding of all the 2'-glyoxylamides and their indole NH resonances are consistent with the values previously seen for S(5) systems. The reason for the change from an S(6) system to an S(5) system in the tertiary 2'-glyoxylamides **4g,h** could be either due to increased steric hindrance of the amide or the absence of an amide NH. The ¹³C NMR chemical shifts of the keto group of the 2'-glyoxylamides **4** show considerably more shielding than the 7'-glyoxylamides **5**, occurring in the range 173.5-182.8 ppm: the amide carbonyl chemical shifts can be seen from 162.9-166.8 ppm.

The amide carbonyl stretch for the primary glyoxylamide **4c** is at a higher frequency than those for the secondary glyoxylamides **4d-f**, which supports the existence of a stronger hydrogen bond in the secondary case. However, the tertiary glyoxylamides **4g,h** display comparable amide carbonyl stretching frequencies to those of the secondary glyoxylamides and this does not correspond to the weaker hydrogen bond observed by ¹H NMR spectroscopy. The carbonyl stretching frequency of the tertiary 2'-glyoxylamides could be caused by intermolecular hydrogen bonding. The *N*-methyl derivative **7**, which cannot hydrogen bond, was prepared by methylation of compound **4g** for spectroscopic comparison.

In several isolated experiments, the 3-methylindole **8**, prepared in a new way by reduction of ethyl 3-hydroxy-4,6-dimethoxyindolin-2-one-3-carboxylate¹¹, underwent regiospecific acylation with oxalyl chloride at C2, leading to the amides **9a,b**. Presumably the decreased steric hindrance of the 3-methyl group is significant in activating C2 at the expense of C7.



EXPERIMENTAL

General Information

¹H and ¹³C NMR spectrum were recorded at 300 MHz on a Bruker AC300F spectrometer and at 500 MHz on a Bruker AM500 spectrometer. Chemical shifts were measured on the δ scale internally referenced to the solvent peaks: CDCl₃ (7.30 ppm, 77.7 ppm) and d₆-DMSO (2.30 ppm, 39.0 ppm). EI mass spectral analyses were performed on a VG Quattro mass spectrometer at 70eV ionisation voltage and 200°C ion source temperature. Microanalyses were performed by Dr. H.P. Pham of the UNSW Microanalytical Unit.

Infrared spectra were obtained on a Perkin Elmer 298 IR spectrometer and a Mattson Sirius FTIR using KBr discs while ultraviolet spectra were carried out on a Hitachi U-3200 and Carey 5 spectrophotometers.

2-(3'-(4''-Chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxyloyl chloride 2 and

2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxyloyl chloride 3

Indole 1 (0.50 g, 1.74 mmol) was partially dissolved in anhydrous diethyl ether (50 ml), oxalyl chloride (0.45 ml, 4.6 mmol) was added and the mixture was stirred for 3h. at room temperature. The resulting red precipitate was filtered off to yield the 2'-glyoxyloyl chloride 2 (0.33 g, 50%) as red needles, m.p. 200-201°C. ¹H NMR (CDCl₃): δ 3.69, 3.93, 2s, OMe; 6.17, 6.45, 2d, *J* 1.9 Hz, H5', H7'; 7.38-7.40, m, aryl; 9.18, br, NH. ¹³C NMR (d₆-DMSO): δ 55.7, 56.0, OMe; 86.8, C5'; 93.9, C7'; 127.3, 133.1, aryl CH; 112.8, 127.1, 127.2, 132.6, 132.9, 140.5, 156.7, 161.7, aryl C; 166.4, 180.1, CO.

The filtrate yielded as a minor product the 7'-glyoxyloyl chloride 3 (0.13g, 20%) as a red solid. ¹H NMR (CDCl₃): δ 3.99, 4.04, 2s, OMe; 6.24, s, H5'; 7.15, d, *J* 2.4 Hz, H2'; 7.38, 7.51, 2d, *J* 8.6 Hz, aryl; 10.40, br, NH.

2-(3'-(4''-Chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylic acid 4a and

2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylic acid 5a

Indole 1 (1.00 g, 3.48 mmol) was partially dissolved in anhydrous diethyl ether (40 ml), oxalyl chloride (0.41 ml, 4.61 mmol) was added and the mixture stirred at room temperature for 3h. The resulting red precipitate was filtered off and dissolved in wet tetrahydrofuran and stirred overnight. The resulting solid was filtered off and dried to yield the 2'-glyoxylic acid 4a (0.64 g, 51%) as a red solid, m.p. 208°C. ν_{\max} 3368, 1765, 1620, 1134 cm⁻¹. λ_{\max} 259 (ε15,900), 339nm (10,000). ¹H NMR (CDCl₃): δ 3.70, 3.93, 2s, OMe; 6.14, 6.46, 2d, *J* 1.5 Hz, H5', H7'; 7.39-7.43, m, aryl, OH; 10.81, br, NH. ¹³C NMR (d₆-DMSO): δ 55.2, 55.4, OMe; 86.2, C5'; 93.4, C7'; 126.8, 132.7, aryl CH; 112.3, 126.3, 127.6, 130.7, 132.3, 140.0, 156.2, 161.0, aryl C; 165.9, 179.7, CO. *m/z* 361 (M³⁷Cl, 25%), 359 (M³⁵Cl, 75%), 331 (30), 316 (30), 314 (50), 287 (50), 280 (70), 279 (100).

Wet tetrahydrofuran was added to the filtrate and the solution was stirred overnight. The resulting solid was filtered off and dried to yield the 7'-glyoxylic acid 5a (0.28 g, 22%) as an orange solid, m.p. 251°C (Found: C, 60.0; H, 3.9; N, 3.8. C₁₈H₁₄ClNO₅ requires C, 60.0; H, 3.9; N, 3.9%). ν_{\max} 3372, 1591, 1217, 1105 cm⁻¹. λ_{\max} 242 (ε23,000), 269 (13,100), 312nm (9,200). ¹H NMR (d₆-DMSO): δ 3.94, 3.94, s, OMe; 6.50, s, H5'; 7.21, d, *J* 2.2 Hz, H2'; 7.40, 7.54, 2d, *J* 8.5 Hz, aryl; 11.53, br, NH; 13.50, br, OH. ¹³C NMR (d₆-DMSO): δ 55.9, 57.2, OMe; 88.7, C5'; 123.9, C2'; 127.6, 130.7, aryl CH; 100.7, 110.5, 116.4, 130.4, 134.2, 136.8, 161.3, 161.7, aryl C; 167.7, 186.0, carbonyl C. *m/z* 361 (M³⁷Cl, 20%), 359 (M³⁵Cl, 50%), 316 (100), 314 (85).

Methyl 2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylate 4b and

methyl 2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylate 5b

Indole 1 (3.00g, 10.43 mmol) was partially dissolved in anhydrous diethyl ether (100ml), oxalyl chloride (1.22ml, 13.83 mmol) was added and the mixture stirred at room temperature for 3h. The resulting red precipitate was filtered off and added to methanol (50ml) and stirred for 1h. The resulting yellow precipitate was filtered off to yield the 2'-glyoxylic ester 4b (1.98g, 51%) as yellow rhombs, m.p. 219°C (from ethyl acetate/light petroleum). (Found: C, 61.0; H, 4.5; N, 3.5. C₁₉H₁₆ClNO₅ requires C, 61.1; H, 4.3; N, 3.8%). ν_{\max} 3331, 1742, 1601, 1134 cm⁻¹. λ_{\max} 260 (ε10,200), 349nm (8,600). ¹H NMR (CDCl₃): δ 3.43, s, CO₂Me; 3.68, 3.91, 2s, OMe; 6.15, 6.44, 2d, *J* 1.7 Hz, H5', H7'; 7.38, s, aryl; 9.41, br, NH. ¹³C NMR (d₆-

DMSO): δ 51.9, 55.3, 55.4, OMe; 86.1, C5'; 93.6, C7'; 126.9, 132.5, aryl CH; 112.4, 127.2, 132.1, 132.4, 132.5, 140.3, 156.3, 161.5, aryl C; 164.2, 177.4, CO. m/z 375 (M ^{37}Cl , 40%), 373 (M ^{35}Cl , 90%), 316 (35), 314 (80), 279 (100).

Methanol (10 ml) was added slowly to the filtrate and allowed to stir for 1h. Water was then added and extracted with dichloromethane. The organic layer was then washed with water, dried (MgSO_4) and the solvent was removed under reduced pressure to yield the 7'-glyoxylic ester **5b** (0.95g, 24%) as yellow needles, m.p. 166-167°C (from ethyl acetate/light petroleum). (Found: C, 61.2; H, 4.5; N, 3.6. $\text{C}_{19}\text{H}_{16}\text{ClNO}_5$ requires C, 61.1; H, 4.3; N, 3.8%). ν_{max} 3420, 1736, 1588, 1468, 1221 cm^{-1} . λ_{max} 228 (ϵ 12,700), 255 (16,200), 265 (15,200) 340nm (6,400). ^1H NMR (CDCl_3): δ 3.94, 3.97, 3.97, 3s, OMe; 6.19, s, H5'; 7.10, d, J 2.6 Hz, H2'; 7.36, 7.50, 2d, J 8.2 Hz, aryl; 10.58, br, NH. ^{13}C NMR (CDCl_3): δ 52.8, 56.1, 57.8, OMe; 88.1, C5'; 122.7, C2'; 128.4, 131.3, aryl CH; 101.4, 111.2, 118.7, 132.6, 134.3, 139.0, 162.8, 162.8, aryl C; 167.1, 185.3, CO. m/z 375 (M ^{37}Cl , 15%), 373 (M ^{35}Cl , 45%), 316 (30), 314 (100).

2-(3'-(4''-Chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylamide 4c and

2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylamide 5c

Method A. Indole **1** (1.00 g, 3.48 mmol) was partially dissolved in anhydrous diethyl ether (40 ml), oxalyl chloride (0.51 ml, 5.22 mmol) was added and the mixture stirred for 3h. at room temperature. The resulting red precipitate was filtered off and added to excess ammonia and stirred for 1 h. The resulting precipitate was filtered off, washed with water and dried (MgSO_4) to yield the 2'-glyoxylamide **4c** (0.58 g, 47%) as orange plates, m.p. 217-218°C (from chloroform/light petroleum). (Found: C, 60.1; H, 4.3; N, 7.6. $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_4$ requires C, 60.3; H, 4.2; N, 7.8%). ν_{max} 3441, 3383, 1692, 1642, 1622, 1520, 1246, 1211, 816 cm^{-1} . λ_{max} 262 (ϵ 27,300), 351nm (15,100). ^1H NMR (CDCl_3): δ 3.65, 3.88, 2s, OMe; 5.64, br, NH_2 ; 6.10, 6.42, 2d, J 2.0 Hz, H5', H7'; 7.34-7.42, m, aryl; 11.31, br, NH. ^{13}C NMR (d_6 -DMSO): δ 55.1, 55.3, OMe; 86.6, C5'; 93.2, C7'; 126.5, 132.6, aryl CH; 112.2, 125.6, 126.9, 131.6, 133.2, 139.5, 156.0, 160.5, aryl C; 166.8, 180.5, CO. m/z 360 (M ^{37}Cl , 20%), 358 (M ^{35}Cl , 65%), 316 (25), 314 (80), 279 (100), 264 (30).

The reaction also yielded the 7'-glyoxylamide **5c** (0.31 g, 25%) as yellow needles, m.p. 282-283°C (from chloroform/light petroleum). (Found: C, 60.1; H, 4.3; N, 7.6. $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_4$ requires C, 60.3; H, 4.2; N, 7.8%). ν_{max} 3414, 3364, 3327, 1676, 1109, 802 cm^{-1} . λ_{max} 224 (ϵ 17,700), 254 (17,700), 265, (14,700), 337nm (8,600). ^1H NMR (CDCl_3): δ 3.97, 4.01, 2s, OMe; 5.50, br, NH_2 ; 6.26, s, H5'; 7.13, d, J 2.0 Hz, H2'; 7.37, 7.52, 2d, J 8.7 Hz, aryl; 10.46, br, NH. ^{13}C NMR (d_6 -DMSO): δ 55.7, 57.2, OMe; 89.0, C5'; 123.7, C2'; 127.5, 130.7, aryl CH; 101.3, 110.0, 116.1, 130.3, 134.3, 137.1, 160.4, 161.4, aryl C; 170.0, 189.9, carbonyl C. m/z 360 (M ^{37}Cl , 10%), 358 (M ^{35}Cl , 35%), 316 (30), 314 (100).

N-Methyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylamide 4d and

N-methyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylamide 5d

Using method A, indole **1** (3.03 g, 10.53 mmol), oxalyl chloride (1.10 ml, 12.64 mmol), anhydrous diethyl ether (100 ml) and methylamine (20 ml, 40% aqueous solution) gave the 2'-glyoxylamide **4d** (1.82 g, 46%) as yellow prisms, m.p. 245-246°C (from ethyl acetate/light petroleum). (Found: C, 61.5; H, 4.8; N, 7.2. $\text{C}_{19}\text{H}_{17}\text{ClN}_2\text{O}_4$ requires C, 61.2; H, 4.6; N, 7.5%). ν_{max} 3368, 3291, 1618s 1208, cm^{-1} . λ_{max} 262 (ϵ 16,100), 351nm (14,500). ^1H NMR (CDCl_3): δ 2.96, d, J 5.1 Hz, NMe; 3.68, 3.92, 2s, OMe; 6.13, 6.45, 2d, J 2.1 Hz, H5', H7'; 7.39, 7.44, 2d, J 8.7 Hz, aryl; 7.55, br, CONH; 11.59, br, NH. ^{13}C NMR (CDCl_3): δ 26.6, NMe; 55.8, 56.3, OMe; 86.4, C5'; 94.4, C7'; 127.8, 132.5, aryl CH; 114.0, 127.5, 130.4, 133.7, 133.8, 140.4, 157.4,

162.8, aryl C; 164.9, 173.3, CO. m/z 374 (M ^{37}Cl , 20%), 372 (M ^{35}Cl , 60%), 316 (30), 314 (80), 279 (100), 264 (24).

The filtrate yielded the 7'-glyoxylamide **5d** (0.87 g, 22%) as yellow needles, m.p. 235-237°C (from ethyl acetate/light petroleum). (Found: C, 61.5; H, 4.9; N, 7.2. $\text{C}_{19}\text{H}_{17}\text{ClN}_2\text{O}_4$ requires C, 61.2; H, 4.6; N, 7.5%). ν_{max} 3401, 3326, 1674, 1585, 525 cm^{-1} . λ_{max} 228 (ϵ 17,600), 255 (17,900), 267 (15,200), 341 (10,400), 364nm (9,000). ^1H NMR (CDCl_3): δ 3.04, d, J 4.9 Hz, NMe; 3.94, 3.97, 2s, OMe; 5.97, q, J 4.7 Hz, CONH; 6.21, s, H5'; 7.09, d, J 2.2 Hz, H2'; 7.36, 7.50, 2d, J 13.3 Hz, aryl; 10.46, br, NH. ^{13}C NMR (d_6 -DMSO): δ 25.1, NMe; 55.7, 57.5, OMe; 88.9, C5'; 123.7, C2'; 127.5, 130.7, aryl CH; 101.5, 110.0, 116.2, 130.3, 134.3, 137.1, 160.5, 161.5, aryl C; 168.7, 189.7, CO. m/z 374 (M ^{37}Cl , 10%), 372 (M ^{35}Cl , 30%), 316 (30), 314 (100), 256 (15), 178 (15).

Method B. Indole **1** (3.07 g, 10.67 mmol) was dissolved in anhydrous dichloromethane (80 ml) and the solution cooled to 0°C with an ice bath. Oxalyl chloride (1.10 ml, 12.64 mmol) was then added rapidly and the solution was allowed to stir for 15min. at this temperature. The solution was then warmed to room temperature and excess methylamine (25% aqueous solution) was added and stirred for a further 1h. Water was then added and extracted with dichloromethane once and ethyl acetate twice. The organic phases were combined and washed with water until neutral, then dried (MgSO_4). The solvent was removed under reduced pressure to yield a crude mixture of the 2'-glyoxylamide **4d** and the 7'-glyoxylamide **5d**. The crude solid was partially dissolved with heating in a small volume of dichloromethane and the resulting light yellow precipitate was filtered off to yield the 7'-glyoxylamide **5d** (0.60 g). The dichloromethane solution was then loaded onto a plug of silica gel and eluted with dichloromethane to obtain the 2'-glyoxylamide **4d** (1.12 g, 28%). The column was then eluted with chloroform to obtain the 7'-glyoxylamide **5d** (1.81 g) to give a total yield of the 7'-glyoxylamide **5d** (2.41 g, 61%).

***N-n*-Butyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylamide 4e** and
***N-n*-butyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylamide 5e**

Using method A, indole **1** (0.80 g, 2.78 mmol), anhydrous diethyl ether (40 ml), oxalyl chloride (0.41 ml, 4.18 mmol) and excess *n*-butylamine yielded the 2'-glyoxylamide **4e** (0.46 g, 40%) as orange plates, m.p. 146-147°C (from ethyl acetate/light petroleum). (Found: C, 63.9; H, 5.8; N, 6.7. $\text{C}_{22}\text{H}_{23}\text{ClN}_2\text{O}_4$ requires C, 63.7; H, 5.6; N, 6.8). ν_{max} 3330, 1630, 1620, 1580, 1510, 1210, 815 cm^{-1} . ^1H NMR (CDCl_3): δ 0.97, t, J 7.2 Hz, Me; 1.35-1.47, m, CH_2 ; 1.53-1.62, m, CH_2 ; 3.38, q, J 6.5 Hz, CH_2 ; 3.68, 3.91, 2s, OMe; 6.13, 6.44, 2d, J 1.8 Hz, H5', H7'; 7.39, 7.44, 2d, J 8.7 Hz, aryl; 7.56, t, J 4.9 Hz, NH; 11.61, br, NH ppm. ^{13}C NMR (CDCl_3): δ 14.3, Me; 20.6, 31.8, 39.7, CH_2 ; 55.8, 56.3, OMe; 86.3, C5'; 94.4, C7'; 127.8, 132.6, aryl CH; 114.0, 127.8, 130.4, 133.7, 133.9, 140.4, 157.4, 162.8, aryl C; 164.2, 173.5, CO. m/z 416 (M ^{37}Cl , 15%), 414 (M ^{35}Cl , 40%), 316 (30), 314 (100), 279 (100).

The reaction also yielded the 7'-glyoxylamide **5e** (0.23 g, 20%) as thin yellow threads, m.p. 231-232°C (from ethyl acetate/light petroleum). ν_{max} 3380, 1700, 1585, 790 cm^{-1} . ^1H NMR (CDCl_3): δ 1.00, t, J 7.7 Hz, Me; 1.43-1.55, m, CH_2 ; 1.62-1.72, m, CH_2 ; 3.47, q, J 6.7 Hz, CH_2 ; 3.94, 3.97, 2s, OMe; 5.96, t, J 5.6 Hz, CONH; 6.22, s, H5'; 7.09, d, J 2.0 Hz, H2'; 7.36, 7.50, 2d, J 8.2 Hz, aryl; 10.46, br, NH ppm. ^{13}C NMR (CDCl_3): δ 14.4, Me; 20.7, 32.2, 39.7, CH_2 ; 56.0, 57.7, OMe; 88.6, C5'; 122.4, C2'; 128.4, 131.3, aryl CH; 102.0, 111.2, 118.5, 132.5, 134.4, 139.3, 162.2, 162.9, aryl C; 168.6, 190.8, carbonyl C. m/z 416 (M ^{37}Cl , 10%), 414 (M ^{35}Cl , 20%), 316 (30), 314 (100).

**N-*t*-Butyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylamide 4f and
N-*t*-butyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylamide 5f**

Using method A, indole **1** (1.00 g, 3.48 mmol), anhydrous diethyl ether (40 ml), oxalyl chloride (0.40 ml, 4.10 mmol) and excess *t*-butylamine yielded the 2'-glyoxylamide **4f** (0.68 g, 47%) as orange needles, m.p. 170–171°C (from ethanol). (Found: C, 63.9; H, 5.8; N, 6.6. C₂₂H₂₃ClN₂O₄ requires C, 63.7; H, 5.6; N, 6.8%). ν_{\max} 3370, 3330, 1635, 1615 cm⁻¹. λ_{\max} 261 (ϵ 7,600), 349nm (8,000). ¹H NMR (CDCl₃): 1.41, s, CMe₃; 3.64, 3.86, 2s, OMe; 6.09, 6.39, 2d, *J* 1.8 Hz, H5', H7'; 7.34, 7.39, 2d, *J* 8.9 Hz, aryl; 7.45, br, CONH; 11.61, br, NH ppm. ¹³C NMR (CDCl₃): δ 28.9, CMe₃; 52.1, CMe₃; 55.8, 51.2, OMe; 86.4, C5'; 94.4, C7'; 127.8, 132.5, aryl CH; 113.9, 127.8, 130.4, 133.7, 134.1, 140.3, 157.4, 162.8, aryl C; 163.8, 174.2, CO. *m/z* 416 (M ³⁷Cl, 20%), 414 (M ³⁵Cl, 55%), 316 (30), 314 (100), 279 (80).

The reaction also yielded the 7'-glyoxylamide **5f** (0.36 g, 25%) as thin yellow threads, m.p. 244°C (from ethyl acetate/light petroleum). (Found: C, 64.0; H, 6.0; N, 6.5. C₂₂H₂₃ClN₂O₄ requires C, 63.7; H, 5.6; N, 6.8%). ν_{\max} 3410, 3360, 1665, 1615, 1575, 1225 cm⁻¹. λ_{\max} 225 (ϵ 23,900), 256 (22,700), 269 (22,500), 331 (9,600), 369nm (7,000). ¹H NMR (CDCl₃): δ 1.50, s, CMe₃; 3.96, 3.99, 2s, OMe; 5.63, br, CONH, 6.25, s, H5', 7.13, d, *J* 2.0 Hz, H2'; 7.37, 7.52, 2d, *J* 8.2 Hz, aryl; 10.48, br, NH. ¹³C NMR (CDCl₃): δ 29.4, CMe₃; 52.4, CMe₃; 56.1, 57.5, OMe; 88.6, C5'; 122.4, C2'; 128.4, 131.3, aryl CH; 101.8, 111.2, 118.6, 132.5, 134.5, 139.5, 162.1, 162.8, aryl C; 167.8, 190.9, carbonyl C. ¹³C NMR (d₆-DMSO): 28.8, CMe₃; 50.5, CMe₃; 55.9, 57.0, OMe; 88.9, C5'; 123.8, C2'; 127.8, 130.9, aryl C; 101.4, 110.1, 116.3, 130.5, 134.6, 137.7, 160.5, 161.4, aryl C; 167.8, 189.5, CO. *m/z* 416 (M ³⁷Cl, 5%), 414 (M ³⁵Cl, 20%), 316 (35), 314 (100).

**N,N-Dimethyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxylamide 4g and
N,N-dimethyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxylamide 5g**

Using method A, indole **1** (1.00 g, 3.48 mmol), anhydrous diethyl ether (40 ml), oxalyl chloride (0.40 ml, 4.10 mmol) and excess dimethylamine (40% aqueous solution) yielded the 2'-glyoxylamide **4g** (0.67 g, 50%) as light yellow needles, m.p. 217–218°C (from ethyl acetate/light petroleum). (Found: C, 62.2; H, 5.1; N, 7.0. C₂₀H₁₉ClN₂O₄ requires C, 62.1; H, 5.0; N, 7.2%). ν_{\max} 3250, 1620 cm⁻¹. λ_{\max} 259 (ϵ 11,700), 348nm (12,800). ¹H NMR (CDCl₃): δ 2.50, 2.75, 2s, NMe; 3.65, 3.91, 2s, OMe; 6.14, 6.48, 2d, *J* 1.9 Hz, H5', H7'; 7.38, s, aryl; 9.40, br, NH. ¹³C NMR (d₆-DMSO): δ 32.5, 36.3, NMe; 55.2, 55.4, OMe; 86.2, C5'; 93.3, C7'; 126.4, 132.3, aryl CH; 112.5, 125.6, 127.8, 132.0, 132.1, 139.8, 156.2, 161.0, aryl C; 165.6, 182.8, CO. *m/z* 288 (M ³⁷Cl, 10%), 386 (M ³⁵Cl, 40%), 316 (30), 314 (100), 279 (50), 256 (10), 228 (10).

The reaction also yielded the 7'-glyoxylamide **5g** (0.31 g, 23%) as light yellow cubes, m.p. 203°C (from ethyl acetate/light petroleum). (Found: C, 62.4; H, 5.2; N, 7.0. C₂₀H₁₉ClN₂O₄ requires C, 62.1; H, 5.0; N, 7.2%). ν_{\max} 3381, 1651, 1348, 1289, 1221 cm⁻¹. λ_{\max} 227 (ϵ 17,200), 255 (18,900), 266 (16,100), 339nm (8,500). ¹H NMR (CDCl₃): δ 3.01, 3.12, 2s, NMe; 3.96, 4.00, 2s, OMe; 6.23, s, H5'; 7.14, d, *J* 2.2 Hz, H2'; 7.37, 7.52, 2d, *J* 8.5 Hz, aryl; 10.75, br, NH. ¹³C NMR (CDCl₃): δ 34.4, 37.3, NMe; 56.1, 58.0, OMe; 88.3, C5'; 122.6, C2'; 128.4, 131.3, aryl CH; 102.5, 111.3, 118.5, 132.5, 134.5, 139.2, 162.3, 162.6, aryl C; 169.8, 190.8, CO. *m/z* 388 (M ³⁷Cl, 10%), 386 (M ³⁵Cl, 30%), 316 (30), 314 (100), 256 (20).

**2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxyl-1-pyrrolidide 4h and
2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxyl-1-pyrrolidide 5h**

Using method A, indole **1** (1.00 g, 3.48 mmol), anhydrous diethyl ether (40 ml), oxalyl chloride (0.40 ml, 4.10 mmol) and excess pyrrolidine yielded the 2'-glyoxylamide **4h** (0.71 g, 50%) as yellow rods, m.p. 233–234°C (from ethanol). (Found: C, 64.2; H, 5.3; N, 6.7. C₂₂H₂₁ClN₂O₄ requires C, 64.0; H, 5.1; N, 6.8%). ν_{\max}

3340, 1630, 1585, 1520, 1260, 1205, 810 cm^{-1} . λ_{max} 261 (ϵ 15,100), 349nm (16,300). ^1H NMR (CDCl_3): δ 1.70-1.81, m, CH_2 ; 3.11, 3.30, 2t, J 6.6 Hz, CH_2 ; 3.67, 3.91, 2s, OMe; 6.15, 6.45, 2d, J 1.8 Hz, H $5'$, H $7'$; 7.36, 7.41, 2d, J 8.7 Hz, aryl, 9.47, br, NH ppm. ^{13}C NMR (CDCl_3): δ 24.4, 26.4, CH_2 ; 45.7, 47.1, NCH_2 ; 55.8, 56.3, OMe; 86.5, C $5'$; 94.3, C $7'$; 127.5, 133.0, aryl CH; 114.0, 127.9, 128.1, 132.4, 134.1, 140.4, 157.5, 162.7, aryl C; 165.1, 182.7, CO. m/z 414 (M ^{37}Cl , 15%), 412 (M ^{35}Cl , 40%), 316 (35), 314 (100), 279 (75).

The reaction also yielded the 7'-glyoxyamide **5h** (0.37 g, 26%) as light yellow needles, m.p. 208-209°C (from ethanol). (Found: C, 64.3; H, 5.4; N, 6.7. $\text{C}_{22}\text{H}_{21}\text{ClN}_2\text{O}_4$ requires C, 64.0; H, 5.1; N, 6.8%). ν_{max} 3340, 1635, 1575, 1260, 1215, 795 cm^{-1} . λ_{max} 225 (ϵ 19,800), 255 (19,600), 268 (16,600), 338 (12,000), 368nm (10,000). ^1H NMR (CDCl_3): δ 1.95-2.03, m, CH_2 ; 3.43, 3.66, 2t, J 6.5 Hz, CH_2 ; 3.96, 3.98, 2s, OMe, 6.23, s, H $5'$; 7.14, d, J 2.2 Hz, H $2'$; 7.37, 7.51, 2d, J 8.6 Hz, aryl; 10.74, br, NH ppm. ^{13}C NMR (CDCl_3): δ 25.0, 26.5, CH_2 ; 45.5, 46.9, NCH_2 ; 56.1, 58.0, OMe; 84.7, C $5'$; 122.6, C $2'$; 128.4, 131.3, aryl CH; 102.0, 111.3, 118.5, 132.5, 134.5, 139.3, 162.3, 162.6 aryl C; 168.2, 190.8, CO. m/z 414 (M ^{37}Cl , 5%), 412 (M ^{35}Cl , 20%), 316 (30), 314 (100).

N-(4''-Hydroxyphenyl)-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxyamide 4i

Glyoxyloyl chloride **2** (100 mg, 0.26 mmol) was dissolved in anhydrous tetrahydrofuran and an excess of *p*-aminophenol was added and allowed to stir overnight. Water was then added and extracted with ethyl acetate. The organic phase was washed with water, saturated brine solution and dried (MgSO_4). The solvent was removed under reduced pressure and the crude solid was purified using a plug of silica with chloroform/methanol (97.5:2.5) eluant to yield the desired glyoxyamide **4i** (70 mg, 60%) as red rods, m.p. 161-163°C (from ethyl acetate). (Found: C, 63.8; H, 4.4; N, 6.1. $\text{C}_{24}\text{H}_{19}\text{ClN}_2\text{O}_4$ requires C, 63.9; H, 4.3; N, 6.2%). ν_{max} 3380, 3350, 1630, 1595, 1260, 810 cm^{-1} . λ_{max} 261 (ϵ 24,500), 352nm (17,700). ^1H NMR (d_6 -DMSO): δ 3.68, 3.91, 2s, OMe; 6.26, 6.69, J 1.8Hz, H $5'$, H $7'$; 6.75, 7.22, 2d, J 8.8 Hz, aryl; 7.27, 7.41, 2d, J 8.4 Hz, aryl; 9.37, br, CONH; 10.41, s, OH; 12.06, br, NH. ^{13}C NMR (d_6 -DMSO): δ 55.4, 55.6, OMe; 86.6, C $5'$; 93.5, C $7'$; 115.1, 121.6, 126.7, 132.6, aryl CH; 112.5, 126.4, 127.5, 129.4, 131.9, 133.0, 140.0, 154.1, 156.3, 161.0, aryl C; 162.9, 180.9, CO. m/z 452 (M ^{37}Cl , 5%), 450 (M ^{35}Cl , 15%), 316 (15), 314 (40), 279 (50), 108 (100).

1,2-Di-(2-(3'-(4''-chlorophenyl)-4',6'-dimethoxyindol-2'-yl)glyoxyloyl)hydrazide 4j

The 2'-glyoxyloyl chloride **2** (0.35 g, 0.93 mmol) was dissolved in anhydrous tetrahydrofuran and stirred at room temperature. Hydrazine hydrate (0.025 ml, 0.52 mmol) was added and the solution allowed to stir overnight. The solvent was removed and hot ethyl acetate was added. The resulting solid was filtered and washed with hot ethyl acetate to yield the hydrazide **4j** (0.18 g, 54%) as a red solid, m.p. >285°C. ^1H NMR (d_6 -DMSO): δ 3.69, 3.90, 2s, OMe; 6.25, 6.76, 2d, J 1.8 Hz, H $5'$, H $7'$; 7.43, s, aryl; 10.94, br, NH; 11.93, s, NH. ^{13}C NMR (d_6 -DMSO): δ 55.2, 55.4, OMe; 86.7, C $5'$; 93.5, C $7'$; 126.7, 132.4, aryl CH; 112.3, 126.4, 126.8, 131.7, 133.0, 139.9, 156.0, 160.9, aryl C; 162.0, 177.6, CO. m/z 716 (M ^{37}Cl , 5%), 714 (M ^{35}Cl , 10%), 316 (35), 314 (95), 279 (100).

2-(3'-(4''-Bromophenyl)-4',6'-dimethoxyindol-7'-yl)glyoxyamide 6

3-(4'-Bromophenyl)-4,6-dimethoxyindole (1.04 g, 3.13 mmol) was dissolved in anhydrous tetrahydrofuran (40 ml), oxalyl chloride (1.07 ml, 10.96 mmol) was added rapidly and the solution stirred at room temperature for 1.5h. Concentrated ammonia (10 ml) was added slowly and allowed to stir for a further 1h. Water was then added and extracted with ethyl acetate to yield the 7'-glyoxyamide **6** (0.93 g, 74%) as yellow needles, m.p. 285-287°C (from ethyl acetate/light petroleum). (Found: C, 53.5; H, 3.7; N, 6.7. $\text{C}_{18}\text{H}_{15}\text{BrN}_2\text{O}_4$

requires C, 53.6; H, 3.8; N, 7.0%). ν_{\max} 3362, 3327, 1678, 1588, 1345 cm^{-1} . λ_{\max} 231 (ϵ 18,400), 254 (18,300), 267 (15,500), 336nm (9,000). $^1\text{H NMR}$ (CDCl_3): δ 3.97, 4.01, 2s, OMe; 5.60, br, NH_2 ; 6.26, s, H5'; 7.14, d, J 2.1 Hz, H2'; 7.46, 7.53, 2d, J 8.7 Hz, aryl; 10.45, br, NH. m/z 404 (M ^{81}Br , 40%), 402 (M ^{79}Br , 40%), 360 (100), 358 (100), 206 (27); 193 (30), 178 (45).

N,N-Dimethyl-2-(3'-(4''-chlorophenyl)-4',6'-dimethoxy-1'-methylindol-2'-yl)glyoxylamide 7

The 2'-glyoxylamide **4g** (0.50g, 1.34 mmol) was dissolved in dimethylsulfoxide (20 ml) and excess crushed potassium hydroxide was added until a strong red colour was evident. Iodomethane (0.20 ml, 2.96 mmol) was added and stirred for 1h. Water was then added and the resulting precipitate filtered, washed with water and dried under reduced pressure to yield the glyoxylamide **7** (0.40g, 75%), as a yellow solid, m.p. 193°C. $^1\text{H NMR}$ (CDCl_3): δ 2.43, 2.75, 2s, CONMe; 3.60, s, NMe; 3.95, 4.10, 2s, OMe; 6.13, 6.37, 2d, J 1.8 Hz, H5', H7'; 7.34, s, aryl. $^{13}\text{C NMR}$ (d_6 -DMSO): δ 32.1, 32.2, CONMe; 36.0, NMe; 54.8, 55.1, OMe; 84.3, C5'; 93.0, C7'; 125.7, 132.0, aryl CH; 110.8, 126.8, 127.1, 131.6, 131.6, 141.1, 155.7, 160.8, aryl C; 164.9, 183.2, CO. m/z 402 (M ^{37}Cl , 5%), 400 (M ^{35}Cl , 20%), 330 (10), 328 (40), 293 (60).

4,6-Dimethoxy-3-methylindole 8¹²

Sodium borohydride (4.05 g, 107.1 mmol) was partially dissolved in anhydrous dioxan (40 ml) and cooled with an ice bath and a reflux condenser was attached. Acetic acid (6.13 ml, 107.1 mmol) was added very cautiously to the sodium borohydride/dioxan mixture. Ethyl 3-hydroxy-4,6-dimethoxyindolin-2-one-3-carboxylate¹¹ (1.95 g, 5.85 mmol) (from 3,5-dimethoxyaniline and diethyl oxomalonate) was then added rapidly as a solid and the solution allowed to warm to room temperature. The solution was allowed to stir at room temperature for 30min. The solution was then warmed to 60°C with an oil bath and allowed to stir at this temperature for 3.5h. Water was added cautiously until hydrogen evolution ceased and was then extracted with ethyl acetate. The organic layer was washed with water, saturated brine solution and dried (MgSO_4). The resulting crude oil was purified using a plug of silica and elution with dichloromethane to yield 3-methylindole **8** (0.65 g, 58%) as a light brown oil and ethyl 4,6-dimethoxyindole-3-carboxylate (0.15 g, 10%). $^1\text{H NMR}$ (CDCl_3): δ 1.40, t, J 7.2 Hz, Me; 3.72, 3.89, 2s, OMe; 4.37, q, J 7.2 Hz, CH_2 ; 6.34, 6.41, 2d, J 2.0 Hz, H5, H7; 7.73, d, J 2.6 Hz, H2; 9.59, br, NH. $^{13}\text{C NMR}$ (CDCl_3): δ 15.1, Me; 56.0, 56.2, OMe; 60.5, CH_2 ; 87.9, C5; 94.7, C7; 131.0, C2; 109.3, 110.4, 139.4, 155.0, 158.6, aryl C; 165.7, CO.

N-*t*-Butyl-2-(4',6'-dimethoxy-3'-methylindol-2'-yl)glyoxylamide 9a

4,6-Dimethoxy-3-methylindole **8** (0.55 g, 2.88 mmol), anhydrous tetrahydrofuran (30 ml), oxalyl chloride (0.35 ml, 4.02 mmol) and excess *t*-butylamine yielded glyoxylamide **9a** (0.63 g, 69%) as orange needles, m.p. 161°C (from dichloromethane/light petroleum). (Found: C, 64.5; H, 7.3; N, 8.6. $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_4$ requires C, 64.2; H, 7.0; N, 8.8%). ν_{\max} 3340, 1665, 1630 cm^{-1} . λ_{\max} 252 (ϵ 4,800), 340nm (3,000). $^1\text{H NMR}$ (CDCl_3): δ 1.49, s, CMe_3 ; 2.87, s, Me; 3.86, 3.92, 2s, OMe; 6.09, 6.32, 2d, J 2.0 Hz, H5', H7'; 7.61, br, CONH; 11.23, br, NH. $^{13}\text{C NMR}$ (CDCl_3): δ 14.0, Me; 29.0, CMe_3 ; 52.0, CMe_3 ; 55.9, 56.2, OMe; 86.3, C5'; 93.4, C7'; 114.7, 128.6, 131.2, 140.6, 158.8, 162.7, aryl C; 164.0, 174.8, CO. m/z 318 (M, 10%), 219 (15), 218 (100), 160 (20), 145 (25), 57 (35).

2-(4',6'-Dimethoxy-3'-methylindol-2'-yl)glyoxyl-1-pyrrolidide 9b

This compound was similarly obtained as an oily red solid. $^1\text{H NMR}$ (CDCl_3): δ 1.96-2.00, m, CH_2 ; 3.53-3.68, m, CH_2 ; 3.87, 3.91, 2s, OMe; 6.12, 6.33, 2d, J 1.9 Hz, H5', H7'; 9.60, br, NH. m/z 316 (M, 10%), 219 (10), 218 (35), 98 (95), 70 (100), 56 (40), 55 (60).

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