Iodine-mediated one-pot synthesis of indoles and 3-dimethylaminoindoles *via* annulation of enaminones

Alberto V. Jerezano,[a] Ehecatl M. Labarrios,[a] Fabiola E. Jiménez,[b] María del Carmen Cruz,[b] Diana C. Pazos,[a] Rsuini U. Gutiérrez,[a] Francisco Delgado,[a] and Joaquín Tamariz [a]*

[a] Departamento de Química Orgánica, Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Prol. Carpio y Plan de Ayala S/N, 11 340 México, D.F., Mexico
[b] Centro de Investigación en Biotecnología Aplicada, Instituto Politécnico Nacional, Km 15 Carretera Sta.-Inés Tecuexcomac, Tepetitla, 90 700 Tlaxcala, Mexico
E-mail: jtamariz@woodward.encb.ipn.mx, jtamarizm@gmail.com

Dedicated to Professor Pierre Vogel on the occasion of his 70th birthday

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Abstract
The synthesis of 2-carbonylindoles was achieved via a iodine-mediated cyclization of the corresponding enaminone precursors, which were formed by reaction of the α-arylamino-methylene carbonyl derivatives with *N,N′*-dimethylformamide dimethyl acetal (DMFDMA). An alternative and more efficient procedure consisted of a similar cyclization of the enaminones, but under solvent-free and grinding reaction conditions. In another iodine-promoted procedure, 2-carbonyl-3-dimethylaminoindoles were synthesized via a one-pot cascade reaction between the α-arylaminomethylene carbonyl derivative and DMFDMA.

Keywords: Indoles, 3-dimethylaminoindoles, enaminone, iodine, DMFDMA, grinding reaction, solvent-free

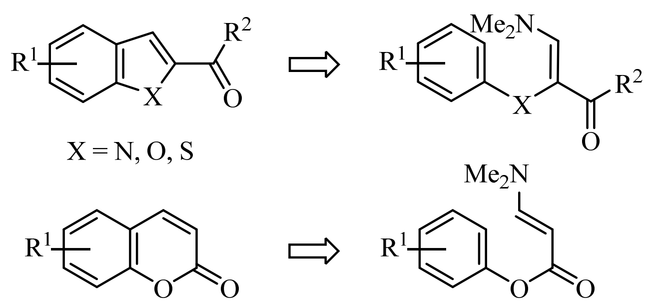
Introduction

For many decades, considerable efforts have been invested in the synthesis[1] and functionalization[2] of the indole core. Even at present, numerous, efficient and elegant approaches are continuously being developed to generate this unique and seminal benzoheterocyclic ring system.[3] This interest arises in view of the fact that the indole is one of the most widely distributed heterocycles in naturally occurring products,[4] as well as in therapeutic and pharmacologically active agents.[5] For instance, tryptophan and serotonin are key molecules in the human diet and in neurotransmitters,[6] respectively, while indomethacin, vincristine, and pindolol are typical clinically used drugs.[7] In particular, 2-carboxyindoles are enzyme inhibitors, such as hyaluronidase,[8] tubuline polymerization,[9] HIV-1 integrase,[10] human cytosolic phospholipase $A_2\alpha$[11] and factor Xa.[12] In the case of 3-aminoindoles and cyclic-fused analogues, they have been found to be effective as anticancer,[13] antiplasmodial and cytotoxic agents.[14]

As a consequence of these relevant activities and applications, a great number of synthetic routes leading to 2-substituted indoles have been described in the literature.[1-3] However, the protocols reported for the synthesis of 3-aminoindole derivatives are limited in scope, and usually require multistep preparation of the starting materials.[13,15] Therefore, the development of straightforward synthetic approaches to 3-dimethylaminoindoles from easily available starting materials is still a pressing task.

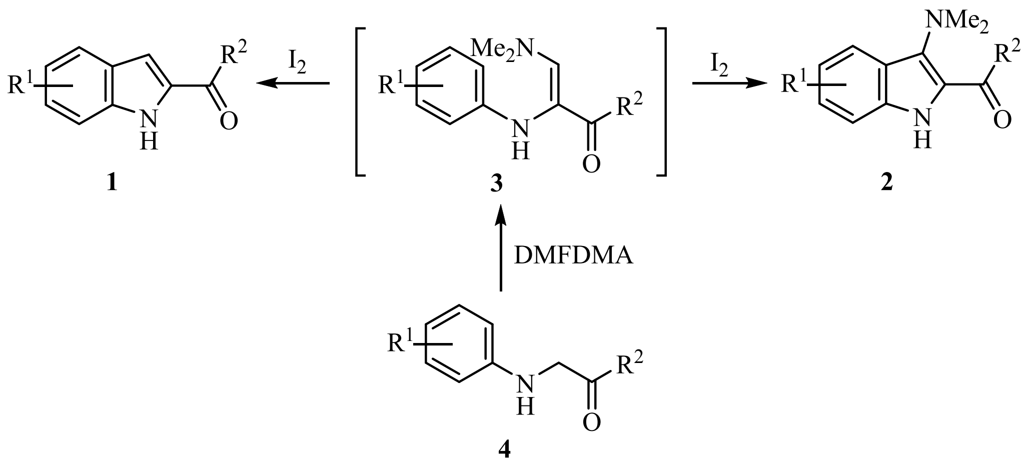
Enaminones[16] play an important role as building blocks for the preparation of many heterocyclic compounds[17] and heterocyclic-fused enaminones.[18] Additionally, they form the basic structure of many alkaloids and their synthetic derivatives, and these exhibit diverse biological activities.[19]

Previously, we designed a new method for the preparation of benzofurans,[20] via a cyclization of functionalized enaminones. This strategy was successfully applied to the synthesis of indoles[21] and coumarins[22] (Scheme 1). In order to optimize this methodology, we found that iodine[23] was an efficient promoter in the annulation of the respective enaminones to obtain benzofurans and benzothiophenes.[24] Iodine-mediated intramolecular reactions are well documented.[25]



Scheme 1. Synthetic strategy for the preparation of five-membered benzoheterocycles and coumarins.

We herein report an extension of this method, starting from a series of 2-anilinoenaminones **3**, to synthesize 2-carbonylated indoles **1**, which was further optimized by grinding a solvent-free mixture of these two components (Scheme 2). Due to the fact that these precursors are prepared by treatment of the 2-anilinocarbonyl derivatives **4** with *N,N'*-dimethylformamide dimethyl acetal (DMFDMA), we also disclose the *in situ* generation of the corresponding enaminones **3**, and their iodine-promoted intramolecular cyclization to provide the unexpected 2,3-substituted indoles **2** (Scheme 2).



Scheme 2. Iodine-mediated synthesis of indoles **1** and 3-dimethylaminoindoles **2** from **4.**

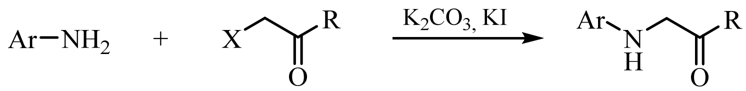
Results and Discussion

Prior reports from this laboratory have shown the efficiency of Lewis acids, particularly $ZnCl_2$ and $AlCl_3$, in promoting the intramolecular cyclization reactions depicted in Scheme 1.[20-22,24] In the absence of a Lewis acid, poor or no reaction is observed even at a high temperature. In the synthetic strategy, for the preparation of indoles **1a**-**p** proposed herein (Scheme 2), the last step of the route involves the iodine-assisted cyclization of the key enaminone precursors **3a**-**p**.

Preparation of α-anilinocarbonyl compounds 4a-p

At first, α–anilinocarbonyl compounds **4a-n** were prepared in good to excellent yields (60-99%) under conditions similar to those previously reported (Table 1, entries 1-14).[21] The mixture of anilines **5a-g**, potassium carbonate and potassium iodide were treated with the corresponding methyl bromoacetate (**6a**) or chloroacetone (**6b**), in dry acetone as the solvent, at 60 ºC for 12 h. However, for analogues **4o-p**, which derive from the 2-bromoacetophenones **6c-d**, this method was only able to provide the desired products in low to moderate yields (30-64%). This result was improved by grinding the solvent-free mixture of aniline **5c** with the respective 2-bromoacetophenones **6c-d** in a mortar, in the presence of potassium carbonate and potassium iodide, at room temperature for 2 h to afford the α-anilinoacetophenones **4o-p** in excellent yields (90-99%) (Table 1, entries 15-16). 2-Bromoacetophenones **6c-d** were prepared by bromination of acetophenones **7a-b** with *N*-bromosuccinimide (NBS) in the presence of *p*-toluenesulfonic acid in good yields (90-95%).[22,24,26]

Table 1. Reagents and yields in the preparation of compounds **4a-p**[a]



5a-g **6a**, X = Br, R = OMe
6b, X = Cl, R = Me
6c, X = Br, R = C_6H_5
6d, X = Br, R = C_6H_4-4-F
4a-p

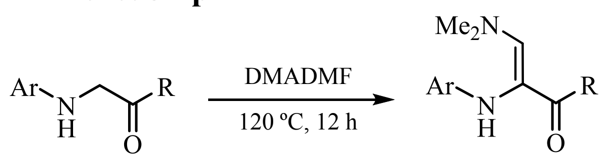
Entry	**5 (Ar)**	**6** (R)	Solvent	T (ºC)	t (h)	**4** (%)[b]
1	**5a** (C_6H_5)	**6a** (OMe)	acetone	60	12	**4a** (87)
2	**5b** (C_6H_4-3-OMe)	**6a** (OMe)	acetone	60	12	**4b** (89)
3	**5c** (C_6H_3-3,5-$(OMe)_2$)	**6a** (OMe)	acetone	60	12	**4c** (92)
4	**5d** (C_6H_4-4-Me)	**6a** (OMe)	acetone	60	12	**4d** (77)
5	**5e** (C_6H_4-4-Cl)	**6a** (OMe)	acetone	60	12	**4e** (96)
6	**5f** (1-naphthyl)	**6a** (OMe)	acetone	60	12	**4f** (78)
7	**5g** (2-naphthyl)	**6a** (OMe)	acetone	60	12	**4g** (77)
8	**5a** (C_6H_5)	**6b** (Me)	acetone	60	12	**4h** (76)
9	**5b** (C_6H_4-3-OMe)	**6b** (Me)	acetone	60	12	**4i** (81)
10	**5c** (C_6H_3-3,5-$(OMe)_2$)	**6b** (Me)	acetone	60	12	**4j** (86)
11	**5d** (C_6H_4-4-Me)	**6b** (Me)	acetone	60	12	**4k** (70)
12	**5e** (C_6H_4-4-Cl)	**6b** (Me)	acetone	60	12	**4l** (60)
13	**5f** (1-naphthyl)	**6b** (Me)	acetone	60	12	**4m** (71)
14	**5g** (2-naphthyl)	**6b** (Me)	acetone	60	12	**4n** (75)
15	**5c** (C_6H_3-3,5-$(OMe)_2$)	**6c** (C_6H_5)[c]	(d)	20	2	**4o** (90)
16	**5c** (C_6H_3-3,5-$(OMe)_2$)	**6d** (C_6H_4-4-F)[c]	(d)	20	2	**4p** (99)

[a] Anilines (**5**) (1.0 mol equiv), K_2CO_3 (1.2 mol equiv), KI (1.1 mol equiv), **6** (1.1 mol equiv), acetone anh. 60 ºC, 12 h. [b] After column chromatography. [c] **6c** and **6d** (1.2 mol equiv). [d] By grinding the solvent-free mixture in a mortar.

Preparation of enaminones 3a-p

We found that increasing the temperature (to 120 ºC from 90 ºC) and the reaction time (to 12 h from 5 h) of the reported method for the treatment of **4a-p** with DMFDMA[21] provided the respective enaminones **3a-p** in higher yields (Table 2). The latter were obtained as a single stereoisomer, whose (*Z*) geometry was established by nuclear Overhauser effect experiments, in which irradiation of the signal assigned to the methyl groups of the dimethylamino group of compound **3e** produced an enhancement of the signals corresponding to the aniline ring. The preference for this configuration is probably due to the greater stability gained by the more efficient resonance effect of the planar π-conjugated enaminone system when the bulky dimethylamino group is located at the opposite side of the carbonyl group. This idea is confirmed by the X-ray structure of compound **3e** (Figure 1), which shows that the enaminone acrylate system adopts a planar *s-cis* conformation, keeping the arylamine group orthogonal to this plane.[21]

Table 2. Preparation of enaminones **3a-p**[a]



4a-p **3a-p**

Entry	**4**	Ar	R	**3a-p** (%)[b]
1	**4a**	C_6H_5	OMe	**3a** (77)
2	**4b**	C_6H_4-3-OMe	OMe	**3b** (88)
3	**4c**	C_6H_3-3,5-$(OMe)_2$	OMe	**3c** (89)
4	**4d**	C_6H_4-4-Me	OMe	**3d** (55)
5	**4e**	C_6H_4-4-Cl	OMe	**3e** (79)
6	**4f**	1-naphthyl	OMe	**3f** (82)
7	**4g**	2-naphthyl	OMe	**3g** (92)
8	**4h**	C_6H_5	Me	**3h** (*c*)
9	**4i**	C_6H_4-3-OMe	Me	**3i** (89)
10	**4j**	C_6H_3-3,5-$(OMe)_2$	Me	**3j** (97)
11	**4k**	C_6H_4-4-Me	Me	**3k** (69)
12	**4l**	C_6H_4-4-Cl	Me	**3l** (73)
13	**4m**	1-naphthyl	Me	**3m** (91)
14	**4n**	2-naphthyl	Me	**3n** (86)
15	**4o**	C_6H_3-3,5-$(OMe)_2$	C_6H_5	**3o** (94)
16	**4p**	C_6H_3-3,5-$(OMe)_2$	C_6H_4-4-F	**3p** (98)

[a] **4a-p** (1.0 mol equiv) and DMFDMA (1.5 mol equiv), 120 ºC, 12 h. [b] After column chromatography. [c] It was used in the next reaction without isolation.

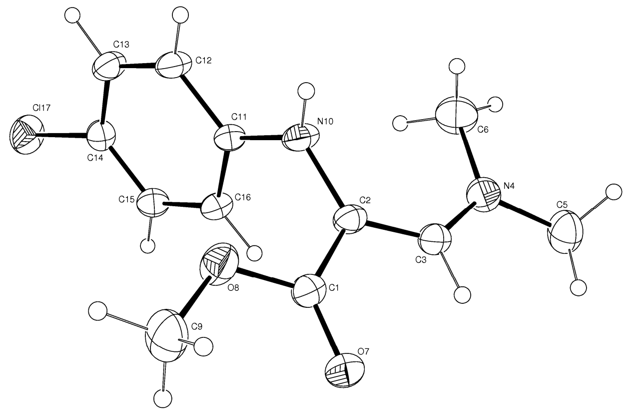


Figure 1. X-Ray structure of enaminone **3e** (ellipsoids with 30% probability).

Preparation of indoles 1a-p

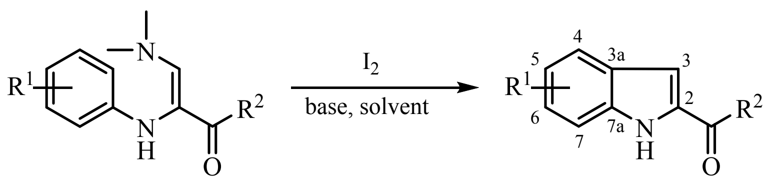
In recent years, molecular iodine has been extensively used as an efficient, inexpensive and non-toxic catalyst for a wide range of reactions under mild conditions.[23,27] In the course of our studies, we have found that molecular iodine (I_2) efficiently promote the intramolecular cyclization of enaminones to afford benzofurans and benzothiophenes.[24] Therefore, we applied it to the cyclization of enaminones **3** to assist their annulation to the desired indoles **1**.

Different solvents (DCM, DMF and MeCN), bases and additives (K_2CO_3, Et_3N, NaI) were evaluated, resulting in no reaction or low to modest yields (Table 3, 1-7). The best results were obtained with base/additive-free conditions and MeCN (ACN) (Table 3, entries 8-13). It was found that the presence of electron-donating groups at the benzene ring of the anilino moiety greatly affect the reactivity of the process, as shown by the contrasting results between unsubstituted enaminone **3a** and methoxy substituted enaminones **3b** and **3c** (Table 3, entries 1, 9 and 11). Moreover, it appears that the carbonylic substituent of the enaminone also plays a role in limiting the efficiency of the cyclization, as evidenced by changing the methoxycarbonyl to the acetyl group (Table 3, entries 9 and 11-13).

Mechanochemistry (grinding reactions) has proved to be an efficient, versatile, and green source of energy to carry out diverse synthetic transformations.[28] Hereby, we have demonstrated that under these conditions compounds **4o**-**p** can be obtained in high yields (Table 1, entries 15-16). Therefore, with the purpose of enhancing the efficiency of the indole synthesis, we investigated the use of solvent-free manual grinding conditions for the conversion of enaminones **3** into indoles **1**. Thus, the iodine-mediated cyclization of enaminone **3b**, carried out by grinding a solvent-free mixture of these components for 6 min, led to indole **1b** in quantitative yield (Table 3, entry 15). The addition of potassium carbonate to the mixture substantially decreased the yield, even after grinding for 3 h (Table 3, entry 16).

Although the grinding method improved the yields of the cyclization of enaminones **3a**-**p** to give the corresponding indoles **1a**-**p**, the best conversion was still observed with the enaminones that possess either electron-donating groups at the appropriate position in the benzene ring of the aniline (Table 4, entries 1-7), or the methoxycarbonyl group. Accordingly, moderate to low yields were observed in the case of enaminones **3i-j** and **3m-n**, and no conversion at all was detected with enaminones **3h** and **3k-l** (Table 4, entries 8-14). In contrast, the cyclization of enaminones **3o-p** resulted in good yields of the corresponding indoles **1o-p** (Table 4, entries 15-16). In spite of some moderate or low yields,[29] the methods summarized in Table 4 are in general more efficient and regioselective than those previously reported with the assistance of Lewis acids.[21] Indeed, the methods with Lewis acids provide even lower yields for the conversion into the 2-acetyl indoles.

Table 3. Synthesis of substituted indoles **1a-c** and **1h-I** [a]

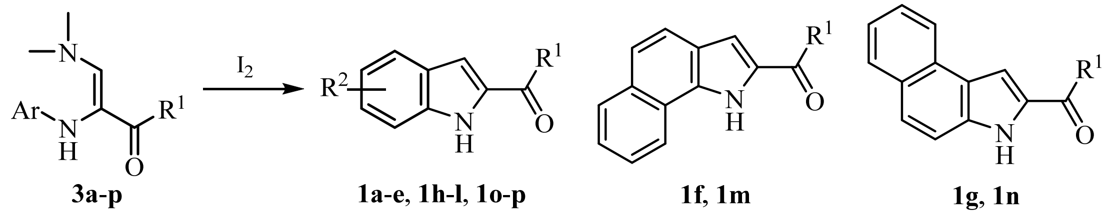


3 **1**

Entry	**3**	R^1	R^2	Base/additive	solvent	t (h)	Yield [(%)][b]
1	**3a**	H	OMe	-	MeCN	12	**1a** (40)
2	**3a**	H	OMe	-	DMF	18	**1a** (38)
3	**3a**	H	OMe	-	DCM	24	(*c*)
4	**3a**	H	OMe	NaI	DMF	15	(*c*)
5	**3b**	3-OMe	OMe	K_2CO_3	MeCN	12	**1b** (12)
6	**3b**	3-OMe	OMe	Et_3N	MeCN	12	(*c*)
7	**3b**	3-OMe	OMe	K_2CO_3/NaI	MeCN	12	(*c*)
8	**3b**	3-OMe	OMe	-	MeCN	5	**1b** (14)
9	**3b**	3-OMe	OMe	-	MeCN	12	**1b** (90)
10	**3b**	3-OMe	OMe	-	DMF	12	**1b** (89)
11	**3c**	3,5-$(OMe)_2$	OMe	-	MeCN	12	**1c** (92)
12	**3b**	3-OMe	Me	-	MeCN	12	**1h** (34)
13	**3c**	3,5-$(OMe)_2$	Me	-	MeCN	12	**1i** (45)
15	**3b**	3-OMe	OMe	-	mortar	0.1	**1b** (99)
16	**3b**	3-OMe	OMe	K_2CO_3	mortar	3	**1b** (45)

[a] Conditions: enaminone **3** (1.0 mol equiv), I_2 (1.1 mol equiv), base (1.2 mol equiv), additive (0.1 mol equiv); solvent (1 mL/0.1 g), at room temperature. [b] After purification by column chromatography. [c] No reaction.

Table 4. Preparation of indoles **1a-p**



Entry	**3**	Ar	R^1	Product	t (h)[a]	**1** (%)[b]	t (min)[c]	**1** (%)[b]
1	**3a**	C_6H_5	OMe	**1a**	12	40	18	50
2	**3b**	C_6H_4-3-OMe	OMe	**1b**	12	90	6	99
3	**3c**	C_6H_3-3,5-$(OMe)_2$	OMe	**1c**	12	92	53	99
4	**3d**	C_6H_4-4-Me	OMe	**1d**	12	37	33	60
5	**3e**	C_6H_4-4-Cl	OMe	**1e**	12	28	60	33
6	**3f**	1-naphthyl	OMe	**1f**	12	41	20	70
7	**3g**	2-naphthyl	OMe	**1g**	12	68	12	95
8	**3h**	C_6H_5	Me	**1h**	24	(*d*)	60-120	(*d*)
9	**3i**	C_6H_4-3-OMe	Me	**1i**	12	34	15	50
10	**3j**	C_6H_3-3,5-$(OMe)_2$	Me	**1j**	12	45	15	60
11	**3k**	C_6H_4-4-Me	Me	**1k**	24	(*d*)	60-120	(*d*)
12	**3l**	C_6H_4-4-Cl	Me	**1l**	24	(*d*)	60-120	(*d*)
13	**3m**	1-naphthyl	Me	**1m**	12	(*d*)	48	25
14	**3n**	2-naphthyl	Me	**1n**	12	(*d*)	20	50
15	**3o**	C_6H_3-3,5-$(OMe)_2$	Ph	**1o**	12	65	20	70
16	**3p**	C_6H_3-3,5-$(OMe)_2$	C_6H_4-4-F	**1p**	12	64	20	75

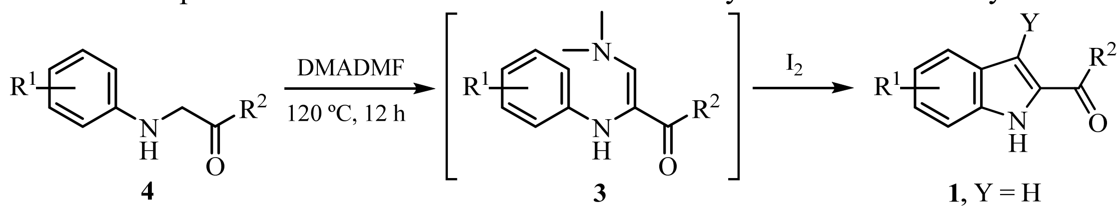
[a] Method A: A mixture of **3** and I_2 (1.1 mol equiv.) in acetonitrile at room temperature. [b] After column chromatography. [c] Method B: A mixture of **3** and I_2 (1.1 mol equiv.) under solvent-free grinding procedure at room temperature. [d] No reaction.

Synthesis of 3-dimethylamino-2-substituted indoles 2a-p

With the aim of optimizing our methodology and shortening the number of steps, the one-pot two-step reaction was investigated.[21] Thus, we started by thermally treating (120 ºC) the α-anilinocarbonyl compound **4a** with DMADMF, then cooling the mixture to room temperature.

Afterwards, iodine (1.1 equiv) was added and stirred for 24 h. Besides the desired indole **1a**, which was obtained in very low yield (5%), the major product was quite unexpected and corresponded to 3-dimethylaminoindole **2a** (Table 5, entry 1). In the case of α-anilinocarbonyl compound **4i**, a slight increment of indole **2i** was observed with the reduction of solvent (Table 5, entries 2-3). Indeed, the lowering or the absence of solvent favored the progress of the reaction enhancing both selectivity and efficiency. The reaction with **4j** was more selective leading to indole **2j** as a single product (Table 5, entry 4), and the solvent-free process starting with **4b** resulted in a high yield of novel compound **2b** (Table 5, entries 5-6).

Table 5. Optimization of reaction conditions for the synthesis of 3-dimethylaminoindoles **2**[a]



1, Y = H
2, Y = NMe_2

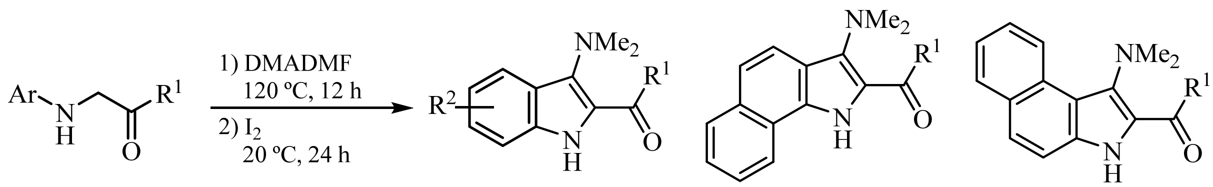
Entry	**4**	R^1	R^2	Solvent (mL)	t (h)[b]	**1** (%)[c]	**2** (%)[c]
1	**4a**	H	OMe	MeCN (0.5)	24	**1a** (5)	**2a** (15)
2	**4i**	3-OMe	Me	MeCN (2.5)	24	**1i** (30)	**2i** (12)
3	**4i**	3-OMe	Me	MeCN (0.5)	24	**1i** (20)	**2i** (25)
4	**4j**	3,5-$(OMe)_2$	Me	MeCN (0.1)	24	Traces	**2j** (30)
5	**4b**	3-OMe	OMe	(d)	12	0	**2b** (88)
6	**4b**	3-OMe	OMe	(d)	24	0	**2b** (90)

[a] Conditions: i) **4** (1.0 equiv), DMADMF (1.5 equiv) at 120 ºC, 12 h; ii) I_2 (1.1 equiv) at 20 ºC. [b] Reaction time of the second step. [c] Yields of isolated products. [d] No solvent.

Table 6 summarizes the structures and yields of the prepared indoles **2a-n**, employing optimized reaction conditions. As expected, the highest yields were obtained for the more activated substrates, **2b-c** (Table 6, entries 2-3). However, even for the non-activated substrates **4k-l**, the respective indoles **2k-l** were obtained, albeit in low yields (Table 6, entries 11-12). Likewise, α-anilinoacetophenones **4o-p** satisfactorily reacted to give indoles **2n-o**, respectively (Table 6, entries 14-15).

Among the series of 3-dimethylaminoindoles, **2d** crystallized and its structure was established by X-ray diffraction crystallography (Figure 2). In contrast with an enaminone structure, such as enaminone **3e** (Figure 1), the conformation of the dimethylamino group is not coplanar to the indolyl ring (C(2)-C(3)-N(4)-C(5) = 144.02(19)) and methoxycarbonyl group conjugated system. The latter is completely coplanar to the heterocycle (torsion angle N(1)-C(2)-C(14)-O(16) = -0.6(2)º). Although the distance (N(1)-O(16) = 2.506Å) and the angles between the atoms involved are not appropriate to form a hydrogen bonding, the oxygen atom of the ester group adopts a conformation that directs it towards the NH moiety. This conformation seems to cause sufficient steric hindrance to twist the dimethylamino group out of the plane of the ring.

Table 6. Preparation of 3-dimethylaminoindoles **2a-o**[a]



Entry	**4**	Ar	R[1]	**2**	Yield (%)[b]
1	**4a**	C_6H_5	OMe	**2a**	40
2	**4b**	C_6H_4-3-OMe	OMe	**2b**	80
3	**4c**	C_6H_3-3,5-$(OMe)_2$	OMe	**2c**	81
4	**4d**	C_6H_4-4-Me	OMe	**2d**	55
5	**4e**	C_6H_4-4-Cl	OMe	**2e**	28
6	**4f**	1-naphthyl	OMe	**2f**	58
7	**4g**	2-naphthyl	OMe	**2g**	79
8	**4h**	C_6H_5	Me	**2h**	36
9	**4i**	C_6H_4-3-OMe	Me	**2i**	64
10	**4j**	C_6H_3-3,5-$(OMe)_2$	Me	**2j**	65
11	**4k**	C_6H_4-4-Me	Me	**2k**	33
12	**4l**	C_6H_4-4-Cl	Me	**2l**	29
13	**4n**	2-naphthyl	Me	**2m**	55
14	**4o**	C_6H_3-3,5-$(OMe)_2$	Ph	**2n**	61
15	**4p**	C_6H_3-3,5-$(OMe)_2$	C_6H_4-4-F	**2o**	68

[a] Conditions: i) **4** (1.0 equiv), DMADMF (1.5 equiv) at 120 ºC, 12 h; ii) I_2 (1.1 equiv) at 20 ºC, 24 h. [b] After column chromatography.

We were also able to obtain crystals in the case of indole **2m**. This was analyzed by X-ray diffraction crystallography (Figure 3). Like indole **2d**, in which the carbonyl group adopts a planar conformation with respect to the plane of the indole ring, in 3-dimethylamino indole **2m** the acetyl group maintains similar coplanarity. The dimethylamino group adopts a conformation out-of-plane to the heterocycle, which is probably due to the steric hindrance generated by both the acetyl group and the naphthyl moiety of the benzoindole skeleton.

Most of the series of enaminones **3a**-**p**, indoles **1a**-**p** and 3-dimethylaminoindoles **2a**-**o** were colored oils or solids, which were fully characterized by spectroscopy. Assignment of the signals of the ^{1}H and ^{13}C NMR spectra was supported by 2D (HMQC and HMBC) experiments.

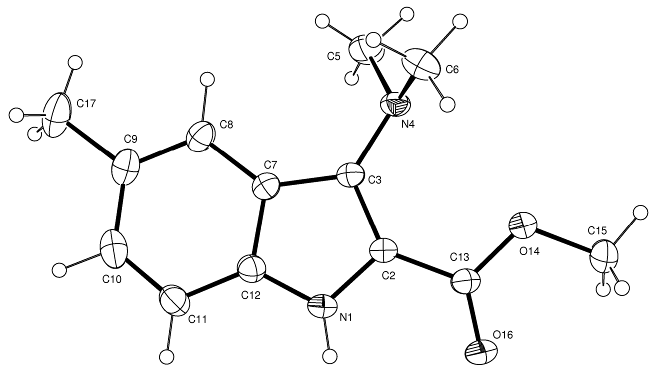


Figure 2. X-Ray structure of indole **2d** (ellipsoids with 30% probability)

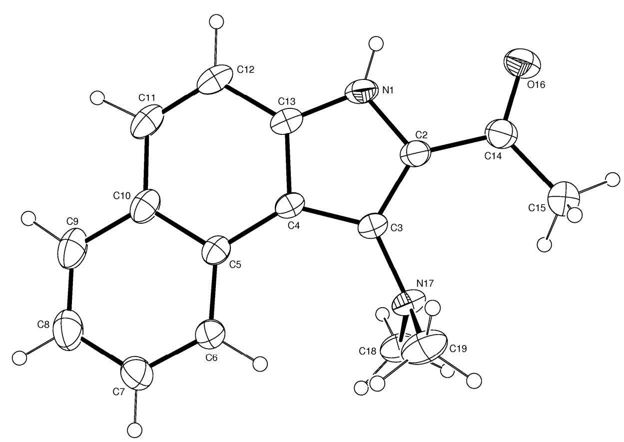
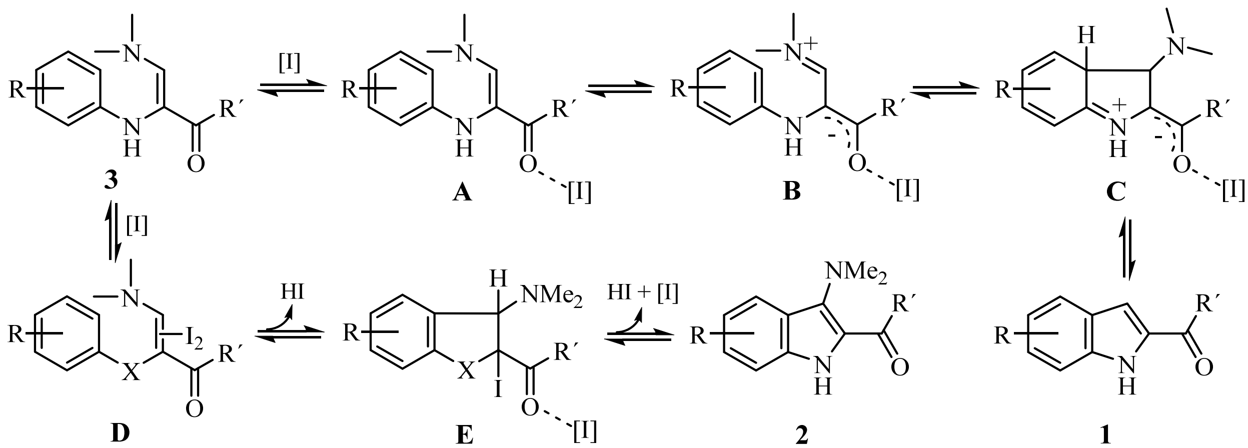


Figure 3. X-Ray structure of 3-dimethylamino indole **2m** (ellipsoids with 30% probability)

Reaction mechanism for the formation of indoles 1a-p and 3-dimethylaminoindoles 2a-o

The effectiveness of iodine as the mediator in the cyclization process for the formation of indoles **1** and **2** appears to be associated with its aptitude to coordinate the oxygen atom at the carbonyl group[27,30] and the conjugated double bond of the enaminone moiety.[31] However, we previously provided evidence that other species derived from iodine, such as structurally unknown HI/I_2 associated species or HI_3,[32] were mainly involved in promoting such cyclization during the syntheses of benzofurans and benzothiophenes.[24] A similar mechanism can be proposed for the formation of indoles **1** and **2** (Scheme 3). These iodine-associated species, [I], can then be coordinated to the carbonyl group (intermediate **A**) of enaminones **3** promoting the polarization of the enaminone system (intermediate **B**) and favoring the attack of the aryl ring to yield the heterocyclic species **C**. Rearomatization of the aryl ring and elimination of the dimethylamino group of the latter, probably as a protonated species (thus forming a more favorable leaving group), will lead to the indole product **1**. In contrast to this pathway, with the one-pot procedure, iodine species can be modified to generate a competitive iodine-π coordination species **D**, which undergoes the annulation process towards the iodinated intermediate **E**. The aromatization of the latter by an HI elimination to furnish the 3-dimethylamino indoles **2** is probably facilitated by the presence of methoxy ions and polar DMF, which are formed in the first step by the decomposition of DMADMF. Although this mechanism is supported by a thorough study on the preparation of benzofurans and benzothiophenes,[24] it cannot be ruled out that there are further [I]-intermediates derived from or stabilized by the coordination with the nitrogen atom of the aniline.



Scheme 3. Proposed mechanism for the formation of indoles **1** and **2.**

Conclusions

We have provided a detailed description for the iodine-mediated preparation of the series of substituted 2-carbonylindoles **1a-g**, **1i-j** and **1m-p** by cyclization of the corresponding enaminones **3a-g**, **3i-j** and **3m-p**. A shorter one-pot two-step procedure starting from the α-anilinocarbonyl compounds **4** afforded the series of novel 3-dimethylaminoindoles **2a-o**. The latter outcome may have resulted from the in situ formation of an iodinated π-intermediate, generated by the intervention of iodine or HI/I_2 species. Interestingly, among the diverse procedures for the optimization of these synthetic approaches, we found that the assistance of a mechanochemical energy source was useful and efficient for the preparation of 2-anilinoacetophenones **4o-p**, and for the solvent-free intramolecular cyclization of enaminones **3** to the indoles **1**.

Experimental Section

General. Melting points were determined with an Electrothermal capillary melting point apparatus. IR spectra were recorded on a Perkin-Elmer (Spectrum 2000) FT-IR spectrometer. ^{1}H (300 or 500 MHz) and ^{13}C (75.4 or 125 MHz) NMR spectra were recorded on Varian Mercury-300 or Varian VNMR System instruments, with TMS as internal standard. Mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained, in electron impact mode (EI) (70 eV), on Thermo-Finnigan Polaris Q and Jeol JSM-GCMateII spectrometers, respectively. The X-ray crystallographic structures were obtained on an Oxford XcaliburS diffractometer. Analytical thin-layer chromatography was carried out by using E. Merck silica gel 60 F_{254} coated 0.25 plates, visualized by long- and short-wavelength UV lamps. Flash column chromatography was performed over silica gel (230-400 mesh) from Natland International Co. (N.C. 27709, USA). All air moisture sensitive reactions were carried out under a nitrogen atmosphere using oven-dried glassware. Acetone was dried by distillation after treatment with potassium permanganate, followed by a second distillation over anhydrous sodium sulfate. Acetonitrile was freshly distilled from molecular sieves (4Å), prior to use. 2-Bromoacetophenones **6c**-**d** were synthesized and their spectroscopic data compared with those previously described.[26]

General Procedure for the synthesis of the arylaminocarbonylic compounds 4a-n

Methyl 2-(phenylamino)acetate (**4a**)**.** To a mixture of aniline (**5a**) (1.000 g, 10.75 mmol), anhydrous K_2CO_3 (1.78 g, 12.9 mmol) and KI (1.96 g, 11.8 mmol), methyl 2-bromoacetate (**6a**) (1.81 g, 11.8 mmol) in dry acetone (5 mL) was added at room temperature and under N_2 atmosphere. The mixture was stirred at 60 °C overnight and then filtered, and the solvent was removed under vacuum. The residue was dissolved with 50 mL of CH_2Cl_2, and washed with a saturated aqueous solution of $NaHCO_3$ (2 × 15 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under vacuum. The residue was purified by column chromatography over silica gel (30 g, hexane/EtOAc, 2:8), to give **4a** (1.54 g, 87%) as a brown solid. R_f 0.60 (hexane/EtOAc, 7:3); mp 47-48 ºC (hexane/EtOAc, 2:8) [Lit.[33] 46 ºC]. IR (film) ν 3395, 3374, 1735, 1609, 1585, 1518, 1441, 1370, 1261, 1229, 1141, 870, 754, 741, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H, CO_2CH_3), 3.91 (s, 2H, CH_2N), 4.22 (br, 1H, NH), 6.61 (dm, *J* = 7.5 Hz, 2H, H-2′), 6.76 (tm, *J* = 7.5 Hz, 1H, H-4′), 7.16-7.23 (m, 2H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 45.7 (CH_2N), 52.2 (CO_2CH_3), 113.0 (C-2′), 118.3 (C-4′), 129.3 (C-3′), 146.9 (C-1′), 171.6 (CO_2Me); MS (70 eV) *m/z* 165 (M^+, 8), 133 (18), 120 (24), 106 (22), 87 (34), 85 (100), 77 (60). HRMS (EI, [M^+]) *m/z* calcd for $C_9H_{11}NO_2$: 165.0790; found: 165.0791.

Methyl 2-(3-methoxyphenylamino)acetate (**4b**).[34] The procedure for **4a** was followed, with **5b** (1.000 g, 8.13 mmol), K_2CO_3 (1.350 g, 9.76 mmol), KI (1.48 g, 8.92 mmol) and **6a** (1.370 g, 8.93 mmol) in dry acetone (5 mL), affording **4b** (1.41 g, 89%) as a brown oil. R_f 0.51 (hexane/EtOAc, 7:3). IR (film) ν 3401, 2953, 1744, 1616, 1515, 1498, 1438, 1362, 1262, 1211, 1165, 1041, 829, 761, 688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 3H, CH_3O), 3.78 (s, 3H, CO_2CH_3), 3.90 (s, 2H, CH_2N), 4.36 (br s, 1H, NH), 6.15 (br t, J = 2.4 Hz, 1H, H-2), 6.22 (ddd, J = 8.1, 2.4, 0.9 Hz, 1H, H-6′), 6.32 (ddd, J = 8.1, 2.4, 0.6 Hz, 1H, H-4′), 7.10 (t, J = 8.1 Hz, 1H, H-5′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.6 (CH_2N), 52.2 (CO_2CH_3), 55.0 (CH_3O), 99.0 (C-2′), 103.3 (C-4′), 105.9 (C-6′), 130.1 (C-5′), 148.3 (C-1′), 160.7 (C-3′), 171.5 (CO_2Me); MS (70 eV) *m/z* 195 (M^+, 40), 179 (99), 131 (100), 128 (34), 118 (64), 104 (74), 101 (34), 93 (34). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_{13}NO_3$: 195.0895; found: 195.0893.

Methyl 2-(3,5-dimethoxyphenylamino)acetate (**4c**). The procedure for **4a** was followed, with **5c** (1.000 g, 6.54 mmol), K_2CO_3 (1.083 g, 7.85 mmol), KI (1.190 g, 7.18 mmol) and **6a** (1.10 g, 7.19 mmol) in dry acetone (5 mL), affording **4c** (1.68 g, 92%) as a yellow oil. R_f 0.40 (hexane/EtOAc, 7:3). IR (film) ν 3389, 1726, 1626, 1598, 1443, 1208, 1156, 1056, 825, 797 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H, CH_3O), 3.79 (s, 3H, CO_2CH_3), 3.89 (br d, J = 4.8 Hz, 2H, CH_2N), 4.26 (br, 1H, NH), 5.79 (d, J = 2.4 Hz, 2H, H-2′, H-6′), 5.92 (t, J = 2.4 Hz, 1H, H-4′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.6 (CH_2N), 52.3 (CO_2CH_3), 55.2 ($2CH_3O$), 90.4 (C-4′), 91.8 (C-2′, C-6′), 148.8 (C-1′), 161.7 (C-3′, C-5′), 171.5 (CO_2Me); MS (70 eV) *m/z* 225 (M^+, 80), 166 (100), 151 (20), 138 (32), 122 (28), 108 (16). HRMS (EI, [M^+]) *m/z* calcd for $C_{11}H_{15}NO_4$: 225.1001; found: 225.1000.

Methyl 2-(4-methylphenylamino)acetate (**4d**).[34] The procedure for **4a** was followed, with **5d** (1.000 g, 9.35 mmol), K_2CO_3 (1.55 g, 11.2 mmol), KI (1.71 g, 10.3 mmol) and **6a** (1.58 g, 10.3 mmol) in dry acetone (5 mL), affording **4d** (1.29 g, 77%) as a yellow solid. R_f 0.62 (hexane/EtOAc, 7:3); m.p 77-78 ºC (hexane/EtOAc, 1:9). IR (film) ν 3376, 1738, 1616, 1525, 1443, 1360, 1319, 1226, 1208, 1180, 1142, 810 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H, CH_3Ar), 3.81 (s, 3H, CO_2CH_3), 3.93 (s, 2H, CH_2N), 4.18 (br s, 1H, NH), 6.58 (d, J = 8.1 Hz, 2H, H-2′), 7.05 (d, J = 8.1 Hz, 2H, H-3′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.2 (CH_3Ar), 45.8 (CH_2N), 52.0 (CO_2CH_3), 112.9 (C-2′), 127.2 (C-4′), 129.6 (C-3′), 144.6 (C-1′), 171.7 (CO_2Me); MS (70 eV) *m/z* 179 (M^+, 92), 120 (100), 91 (60), 77 (24), 65 (40). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_{13}NO_2$: 179.0946; found: 179.0952.

Methyl 2-(4-chlorophenylamino)acetate (**4e**).[21,35] The procedure for **4a** was followed, with **5e** (1.000 g, 7.84 mmol), K_2CO_3 (1.30 g, 9.4 mmol), KI (1.432 g, 8.62 mmol), and **6a** (1.319 g, 8.62 mmol) in dry acetone (5 mL), affording **4e** (1.50 g, 96%) as a white solid. R_f 0.53 (hexane/EtOAc, 7:3); mp 120-122 ºC (hexane/EtOAc, 2:8) [Lit.[35] 116.4-118.8 ºC]. IR (film) ν 3388, 1732, 1601, 1509, 1442, 1370, 1321, 1217, 823 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3H, CO_2CH_3), 3.88 (s, 2H, CH_2N), 4.31 (br s, 1H, NH), 6.48-6.56 (m, 2H, H-2′), 7.10-7.16 (m, 2H, H-3′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.6 (CH_2N), 52.3 (CO_2CH_3), 113.9 (C-2′), 122.7 (C-4′), 129.1 (C-3′), 145.4 (C-1′), 171.3 (CO_2Me); MS (70 eV) *m/z* 201 (M^++2, 25), 199 (M^+, 96), 142 (99), 140 (100), 113 (14), 112 (16), 111 (36), 105 (24), 77 (27), 75 (34). HRMS (EI, [M^+]) *m/z* calcd for $C_9H_{10}ClNO_2$: 199.0400; found: 199.0400.

Methyl 2-(naphthalen-1-ylamino)acetate (**4f**). The procedure for **4a** was followed, with **5f** (1.00 g, 7.0 mmol), K_2CO_3 (1.158 g, 8.38 mmol), KI (1.28 g, 7.7 mmol) and **6a** (1.18 g, 7.7 mmol) in dry acetone (5 mL), affording **4f** (1.17 g, 78%) as a black oil. R_f 0.55 (hexane/EtOAc, 7:3). IR (film) ν 3430, 3064, 1720, 1629, 1595, 1535, 1483, 1408, 1285, 1230, 1142, 1091, 1017, 787, 765 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 3H, CO_2CH_3), 4.00 (s, 2H, CH_2N), 5.10 (br, 1H, NH), 6.42 (br d, J = 7.2 Hz, 1H, H-2′), 7.26 (br d, J = 7.2 Hz, 1H, H-4′), 7.26 (t, J = 7.2 Hz, 1H, H-3′), 7.36-7.52 (m, 2H, H-6′, H-7′), 7.73-7.81 (m, 1H, H-5′), 7.82-7.91 (m, 1H, H-8′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.7 (CH_2N), 52.3 (CO_2CH_3), 104.4 (C-2′), 118.2 (C-4′), 120.0 (C-8′), 123.3 (C-8a′), 124.9 (C-7′), 125.9 (C-6′). 126.3 (C-3′), 128.5 (C-5′), 134.2 (C-4a′), 142.1 (C-1′), 171.5 (CO_2Me); MS (70 eV) *m/z* 215 (M^+, 96), 155 (100), 153 (59), 141 (90), 128 (62), 114 (60), 101 (17), 77 (36). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{13}NO_2$: 215.0946; found: 215.0946.

Methyl 2-(naphthalen-2-ylamino)acetate (**4g**). The procedure for **4a** was followed, with **5g** (1.00 g, 7.0 mmol), K_2CO_3 (1.158 g, 8.38 mmol), KI (1.28 g, 7.7 mmol) and **6a** (1.18 g, 7.7 mmol) in dry acetone (5 mL), affording **4g** (1.16 g, 77%) as a brown solid. R_f 0.64 (hexane/EtOAc, 7:3); mp 68-70 ºC. IR (film) ν 3393, 1734, 1630, 1603, 1523, 1437, 1349, 1214, 827, 746 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H, CO_2CH_3), 4.03 (s, 2H, CH_2N), 4.47 (br, 1H, NH), 6.74 (d, J = 2.4 Hz, 1H, H-1′), 6.94 (dd, J = 8.7, 2.4 Hz, 1H, H-3′), 7.23 (td, J = 6.9, 1.2 Hz, 1H, H-6′), 7.37 (td, J = 6.9, 1.5 Hz, 1H, H-7′), 7.61 (d, J = 8.5 Hz, 1H, H-8′), 7.62 (d, J = 8.5 Hz, 1H, H-4′), 7.66 (d, J = 8.5 Hz, 1H, H-5′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.5 (CH_2N), 52.2 (CO_2CH_3), 104.6 (C-1′), 117.8 (C-3′), 122.3 (C-6′), 126.0 (C-8′), 126.3 (C-7′), 127.6 (C-5′). 127.8 (C-4a′), 129.0 (C-4′), 134.9 (C-8a′), 144.5 (C-2′), 171.4 (CO_2Me); MS (70 eV) *m/z* 215 (M^+, 35), 156 (100), 149 (16), 127 (27), 97 (10), 83 (20), 73 (18), 57 (27). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{13}NO_2$: 215.0946; found: 215.0938.

1-(Phenylamino)propan-2-one (**4h**).[35] The procedure for **4a** was followed, with **5a** (1.000 g, 10.75 mmol), K_2CO_3 (1.78 g, 12.9 mmol), KI (1.964 g, 11.83 mmol) and **6b** (1.094 g, 11.83 mmol) in dry acetone (20 mL), affording **4h** (1.22 g, 76%) as a yellow oil. R_f 0.53 (hexane/EtOAc, 7:3). IR (film) ν 3375, 3053, 1687, 1600, 1550, 1498, 1442, 1380, 1313, 1258, 750, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3H, CH_3CO), 4.00 (s, 2H, CH_2N), 4.51 (br, 1H, NH), 6.56-6.61 (m, 2H, H-2′), 6.73 (tt, J = 7.5, 1.0 Hz, 1H, H-4′), 7.16-7.21 (m, 2H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4 (CH_3CO), 54.2 (CH_2N), 112.8 (C-2′), 117.8 (C-4′), 129.3 (C-3′), 146.8 (C-1′), 204.1 ($COCH_3$); MS (70 eV) *m/z* 149 (M^+, 70), 120 (38), 106 (100), 93 (64), 77 (63). HRMS (EI, [M^+]) *m/z* calcd for $C_9H_{11}NO$: 149.0841; found: 149.0826.

1-(3-Methoxyphenylamino)propan-2-one (**4i**).[21] The procedure for **4a** was followed, with **5b** (1.000 g, 8.13 mmol), K_2CO_3 (1.350 g, 9.76 mmol), KI (1.48 g, 8.92 mmol) and **6b** (0.825 g, 8.92 mmol) in dry acetone (20 mL), affording **4i** (1.17 g, 81%) as a yellow oil. R_f 0.47 (hexane/EtOAc, 7:3). IR (film) ν 3373, 1720, 1616, 1510, 1497, 1454, 1361, 1341, 1214, 1161, 1040, 840, 760, 690 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3CO), 3.77 (s, 3H, CH_3O), 4.00 (br s, 2H, CH_2N), 4.59 (br s, 1H, NH), 6.14 (t, J = 2.5 Hz, 1H, H-2′), 6.21 (ddd, J = 8.3, 2.5, 1.0 Hz, 1H, H-6′), 6.30 (dd, J = 8.5, 2.5 Hz, 1H, H-4′), 7.09 (t, J = 8.3 Hz, 1H, H-5′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4 (CH_3CO), 54.2 (CH_2N), 55.1 (CH_3O), 98.9 (C-2′), 103.0 (C-4′), 105.9 (C-6′), 130.1 (C-5′), 148.2 (C-1′), 160.9 (C-3′), 203.9 ($COCH_3$); MS (70 eV) *m/z* 179

(M^+, 10), 171 (44), 160 (22), 148 (27), 143 (42), 136 (26), 130 (30), 118 (40), 77 (100), 53 (33). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_{13}NO_2$: 179.0946; found: 179.0951.

1-[(3,5-Dimethoxyphenyl)amino]propan-2-one (**4j**).[21] The procedure for **4a** was followed, with **5c** (1.000 g, 6.53 mmol), K_2CO_3 (1.082 g, 7.84 mmol), KI (1.192 g, 7.18 mmol) and **6b** (0.664 g, 7.18 mmol) in dry acetone (20 mL), affording **4j** (1.17 g, 86%) as a yellow oil. R_f 0.36 (hexane/EtOAc, 7:3); [Lit.[36] mp 92-94 °C]. IR (film) ν 3392, 1723, 1612, 1513, 1483, 1457, 1419, 1204, 1171, 1153, 1060, 811, 735, 684 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3CO), 3.75 (s, 6H, CH_3O), 3.98 (br s, 2H, CH_2N), 4.61 (br, 1H, NH), 5.77 (d, *J* = 2.1 Hz, 2H, H-2′, H-6′), 5.90 (t, *J* = 2.1 Hz, 1H, H-4′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4 (CH_3CO), 54.2 (CH_2N), 55.2 (CH_3O), 90.2 (C-4′), 91.7 (C-2′, C-6′), 148.7 (C-1′), 161.8 (C-3′, C-5′), 203.8 ($COCH_3$); MS (70 eV) *m/z* 209 (M^+, 87), 191 (16), 166 (100), 151 (32), 138 (47), 122 (38), 108 (124), 92 (12), 77 (16). HRMS (EI, [M^+]) *m/z* calcd for $C_{11}H_{15}NO_3$: 209.1052; found: 209.1052.

1-[(4-Methylphenyl)amino]propan-2-one (**4k**).[37] The procedure for **4a** was followed, with **5d** (1.000 g, 9.35 mmol), K_2CO_3 (1.55 g, 11.2 mmol), KI (1.707 g, 10.28 mmol) and **6b** (0.95 g, 10.28 mmol) in dry acetone (20 mL), affording **4k** (1.07 g, 70%) as a brown oil. R_f 0.22 (hexane/EtOAc, 7:3). IR (film) ν 3395, 2952, 2919, 1720, 1618, 1531, 1437, 1366, 1255, 821, 805 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3H, COCH_3), 2.23 (s, 3H, ArCH_3), 3.96 (s, 2H, CH_2N), 4.30 (br, 1H, NH), 6.51 (d, *J* = 8.0 Hz, 1H, H-2′), 6.99 (d, *J* = 8.0 Hz, 2H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3 (ArCH_3), 27.3 (CH_3CO), 54.6 (CH_2N), 112.9 (C-2′), 127.0 (C-4′), 129.8 (C-3′), 144.6 (C-1′), 204.4 ($COCH_3$); MS (70 eV) *m/z* 163 (M^+, 12), 162 (23), 134 (39), 132 (34), 120 (22), 118 (34), 106 (37), 91 (100), 69 (28), 65 (27), 55 (20). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_{13}NO$: 163.0997; found: 163.0993.

1-[(4-Chlorophenyl)amino]propan-2-one (**4l**). The procedure for **4a** was followed, with **5e** (1.000 g, 7.84 mmol), K_2CO_3 (1.300 g, 9.41 mmol), KI (1.432 g, 8.62 mmol) and **6b** (0.797 g, 8.62 mmol) in dry acetone (20 mL), affording **4l** (0.86 g, 60%) as colorless crystals. R_f 0.49 (hexane/EtOAc, 7:3); mp 113-115 ºC [Lit.[38] mp 112-113 °C]. IR (film) ν 3387, 1717, 1602, 1514, 1435, 1351, 1187, 821, 801, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3H, CH_3CO), 3.94 (br s, 2H, CH_2N), 4.59 (br s, 1H, NH), 6.48-6.54 (m, 2H, H-2′), 7.10-7.16 (m, 2H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3 (CH_3CO), 54.1 (CH_2N), 113.0 (C-2´), 122.3 (C-4´), 129.1 (C-3´), 145.3 (C-1´), 203.5 ($COCH_3$); MS (70 eV) *m/z* 185 (M^++2, 36), 183 (M^+, 67), 141 (76), 139 (100), 110 (46), 104 (42), 77 (41), 75 (38). HRMS (EI, [M^+]) *m/z* calcd for $C_9H_{10}ClNO$: 183.0451; found: 183.0449.

1-(Naphthalen-1-ylamino)propan-2-one (**4m**). The procedure for **4a** was followed, with **5f** (1.10 g, 7.0 mmol), K_2CO_3 (1.16 g, 8.4 mmol), KI (1.28 g, 7.7 mmol) and **6b** (0.71 g, 7.7 mmol) in dry acetone (20 mL), affording **4m** (0.99 g, 71%) as a black oil. R_f 0.16 (hexane/EtOAc, 7:3). IR (film) ν 3364, 3054, 1688, 1581, 1528, 1481, 1405, 1372 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3CO), 4.05 (d, *J* = 4.2 Hz, 2H, CH_2N), 5.42 (br, 1H, NH), 6.42 (dd, *J* = 7.5, 1.2 Hz, 1H, H-2′), 7.29 (br d, *J* = 7.5 Hz, 1H, H-4′), 7.37 (t, *J* = 7.5 Hz, 1H, H-3′), 7.46-7.54 (m, 2H, H-6′, H-7′), 7.80-7.87 (m, 1H, H-5′), 7.95-8.02 (m, 1H, H-8′); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 27.3 (CH_3CO), 54.0 (CH_2N), 104.2 (C-2′), 117.6 (C-4′), 120.0 (C-8′), 123.1 (C-8a′), 124.8 (C-7′), 125.9 (C-6′), 126.4 (C-3′), 128.4 (C-5′), 134.2 (C-4a′), 141.9 (C-1′), 203.8 (*C*OCH$_3$); MS (70 eV) *m/z* 199 (M$^+$, 28), 170 (62), 155 (78), 141 (100), 129 (38), 127 (64), 115 (58). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0995.

1-(Naphthalen-2-ylamino)propan-2-one (**4n**). The procedure for **4a** was followed, with **5g** (1.00 g, 7.0 mmol), K_2CO_3 (1.16 g, 8.4 mmol), KI (1.28 g, 7.7 mmol) and **6b** (0.71 g, 7.68 mmol) in dry acetone (20 mL), affording **4n** (1.04 g, 75%) as a red solid. R_f 0.43 (hexane/EtOAc, 7:3); mp 124-126 ºC. IR (film) ν 3381, 3051, 1721, 1631, 1602, 1522, 1486, 1398, 1359, 1178, 1133, 827, 746 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.25 (s, 3H, C*H*$_3$CO), 4.06 (s, 2H, C*H*$_2$N), 4.74 (br s, 1H, NH), 6.68 (d, *J* = 2.5 Hz, 1H, H-1′), 6.92 (dd, *J* = 8.5, 2.5 Hz, 1H, H-3′), 7.20 (dd, *J* = 8.0, 7.0 Hz, 1H, H-6′ or H-7′), 7.36 (dd, *J* = 8.5, 7.0 Hz, 1H, H-7′ or H-6′), 7.59-7.65 (m, 2H, H-4′, H-8′), 7.66 (d, *J* = 8.5 Hz, 1H, H-5′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 27.4 (*C*H$_3$CO), 54.1 (*C*H$_2$N), 104.4 (C-2′), 117.8 (C-3′), 122.2 (C-6′), 125.8 (C-8′), 126.4 (C-7′), 127.6 (C-4a′), 127.7 (C-5′), 129.1 (C-4′), 135.1 (C-8a′), 144.5 (C-2′), 203.8 (*C*OCH$_3$); MS (70 eV) *m/z* 199 (M$^+$, 39), 156 (100), 143 (8), 129 (17), 128 (28), 127 (46), 115 (10), 101 (5). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0993.

2-[(3,5-Dimethoxyphenyl)amino]-1-phenylethanone (**4o**)**.** A mixture of **5c** (1.000 g, 6.54 mmol), K_2CO_3 (1.082 g, 7.83 mmol), KI (1.194 g, 7.18 mmol) and **6c (**1.429 g, 7.18 mmol) was ground in a glass mortar at room temperature for 2 h. EtOAc (30 mL) was added to the mixture and then filtered, and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g, hexane/EtOAc, 9:1) to give **4o** (1.59 g, 90%) as a yellow solid. R_f 0.56 (hexane/EtOAc, 7:3); mp 107-109 ºC [Lit.[39] 116-117 °C]. IR (film) ν 3393, 1726, 1701, 1596, 1449, 1278, 1227, 1205, 1176, 1151, 1122, 1070, 959, 808, 753, 711, 687 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.78 (s, 6H, 2(C*H*$_3$O)), 4.60 (br s, 2H, C*H*$_2$N), 4.98 (br s, 1H, NH), 5.87-5.94 (m, 3H, H-2″, H-4″, H-6′), 7.51 (br t, *J* = 7.5 Hz, 2H, H-3′), 7.63 (br t, *J* = 7.5 Hz, 1H, H-4′), 8.01 (br d, *J* = 7.5 Hz, 2H, H-2′); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ 50.2 (*C*H$_2$N), 55.2 (2(*C*H$_3$O)), 90.0 (C-4″), 91.8 (C-2″, C-6″), 127.7 (C-2′), 128.9 (C-3′), 133.9 (C-4′), 134.8 (C-1′), 148.9 (C-1″), 161.8 (C-3″), 194.8 (*C*O); MS (70 eV) *m/z* 271 (M$^+$, 72), 167 (43), 166 (100), 164 (19), 138 (22), 122 (16), 105 (18), 77 (24). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{16}H_{17}NO_3$: 271.1208; found: 271.1209.

2-[(3,5-Dimethoxyphenyl)amino]-1-(4-fluorophenyl)ethanone (**4p**).[40] The procedure for **4o** was followed, with **5c** (1.000 g, 6.54 mmol), K_2CO_3 (1.082 g, 7.83 mmol), KI (1.194 g, 7.18 mmol) and **6d (**1.558 g, 7.18 mmol), affording **4p** (1.87 g, 99%) as a green oil. R_f 0.60 (hexane/EtOAc, 7:3). IR (film) ν 3378, 1691, 1599, 1508, 1455, 1229, 1206, 1156, 838, 811 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.76 (s, 6H, 2(C*H*$_3$O)), 4.54 (s, 2H, C*H*$_2$N), 4.91 (br s, 1H, NH), 5.87 (d, *J* = 2.0 Hz, 2H, H-2″, H-6″), 5.91 (t, *J* = 2.5 Hz, 1H, H-4″), 7.18 (t, *J* = 8.5 Hz, 2H, H-3′), 8.02 (dd, *J* = 8.5, 5.5 Hz, 2H, H-2′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 50.2 (*C*H$_2$N), 55.2 (2(*C*H$_3$O)), 90.1 (C-4″), 91.9 (C-2″, C-6″), 116.0 (d, *J* = 21.8 Hz, C-3′), 130.4 (d, *J* = 9.8 Hz, C-2′), 131.2 (d, *J* = 2.9 Hz, C-1′), 148.9 (C-1″), 161.8 (C-3″, C-5″), 166.0 (d, *J* = 254.9 Hz, C-4′), 193.3 (*C*O); MS (70 eV) *m/z* 289 (M$^+$, 32), 270 (10), 256 (14), 181 (12), 166 (100), 153 (10), 140 (16), 123 (60), 95 (28), 69 (18). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{16}$ FNO_3: 289.1114; found: 289.1111.

(*Z*)-Methyl 3-(dimethylamino)-2-(phenylamino)acrylate (**3a**). A mixture of **4a** (0.100 g, 0.61 mmol) and DMFDMA (0.108 g, 0.91 mmol) placed in a threaded ACE glass pressure tube with a sealed Teflon screw cap, under N_2, was heated to 120 ºC for 12 h. The crude product was purified by column chromatography over silica gel (30 g/g sample, hexane/EtOAc, 7:3) to give **3a** (0.103 g, 77%) as a dark-brown solid. R_f 0.84 (EtOAc); mp 108-109 ºC. IR (film) ν 3361, 2947, 1735, 1684, 1601, 1497, 1432, 1384, 1284, 1216, 1086, 751, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.03 (s, 6H, $(CH_3)_2N$), 3.62 (s, 3H, CO_2CH_3), 4.62 (br s, 1H, NH), 6.61-6.65 (m, 2H, H-2′), 6.70-6.74 (m, 1H, H-4′), 7.13-7.19 (m, 2H, H-3′), 7.39 (s, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.7 (br, $(CH_3)_2N$), 51.1 (CO_2CH_3), 98.9 (C-2), 113.5 (C-2′), 118.1 (C-4′), 129.1 (C-3′), 146.2 (C-3), 149.1 (C-1′), 169.6 (CO_2CH_3); MS (70 eV) *m/z* 218 (M^+-2, 10), 217 (72), 203 (100), 185 (76), 157 (22), 130 (36), 116 (56), 103 (19), 91 (15). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{16}N_2O_2$: 220.1212; found: 220.1210.

(*Z*)-Methyl 2-[(3-methoxyphenyl)amino]-3-(dimethylamino)acrylate (**3b**). The procedure for **3a** was followed, with **4b** (0.100 g, 0.51 mmol) and DMFDMA (0.092 g, 0.77 mmol), affording **3b** (0.113 g, 88%) as a greenish-brown oil. R_f 0.89 (EtOAc). IR (film) ν 3366, 1736, 1642, 1603, 1495, 1463, 1435, 1247, 1158, 1039, 845, 774, 689 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.03 (s, 6H, $(CH_3)_2N$), 3.63 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CH_3O), 4.63 (br s, 1H, NH), 6.18 (t, *J* = 2.5 Hz, 1H, H-2′), 6.26 (ddd, *J* = 8.0, 2.5, 0.5 Hz, 1H, H-6′), 6.29 (ddd, *J* = 8.0, 2.5, 0.5 Hz, 1H, H-4′), 7.07 (t, *J* = 8.0 Hz, 1H, H-5′), 7.38 (s, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.8 (br, $(CH_3)_2N$), 51.2 (CO_2CH_3), 55.0 (CH_3O), 98.7 (C-2), 99.5 (C-2′), 103.2 (C-4′), 106.7 (C-6′), 129.8 (C-5′), 146.3 (C-3), 150.7 (C-1′), 160.8 (C-3´), 169.5 (CO_2CH_3); MS (70 eV) *m/z* 248 (M^+-2, 6), 247 (26), 233 (100), 232 (50), 215 (30), 204 (28), 174 (29), 146 (55). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{18}N_2O_3$: 250.1318; found: 250.1319.

(*Z*)-Methyl 2-[(3,5-dimethoxyphenyl)amino]-3-(dimethylamino)acrylate (**3c**). The procedure for **3a** was followed, with **4c** (0.100 g, 0.44 mmol) and DMFDMA (0.079 g, 0.67 mmol), affording **3c** (0.111 g, 89%) as a dark-red oil. R_f 0.73 (EtOAc). IR (film) ν 3365, 2947, 1743, 1687, 1615, 1457, 1432, 1288, 1203, 1152, 1086, 1066, 816, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.03 (s, 6H, $(CH_3)_2N$), 3.63 (s, 3H, CO_2CH_3), 3.73 (s, 6H, $2(CH_3O)$), 4.66 (br s, 1H, NH), 5.83 (d, *J* = 2.1 Hz, 2H, H-2′, H-6′), 5.90 (t, *J* = 2.1 Hz, 1H, H-4′), 7.38 (s, 1H, H-3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 41.7 (br, $(CH_3)_2N$), 51.1 (CO_2CH_3), 55.0, (2 CH_3O), 90.2 (C-4′), 92.2 (C-2′, C-6′), 98.2 (C-2), 146.3 (C-3), 151.3 (C-1′), 161.5 (C-3′, C-5′), 169.5 (CO_2CH_3); MS (70 eV) *m/z* 280 (M^+, 100), 238 (10), 220 (87), 219 (58), 205 (14), 178 (18), 164 (24), 137 (20), 129 (42), 122 (19), 83 (41). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{20}N_2O_4$: 280.1423; found: 280.1420.

(*Z*)-Methyl 3-(dimethylamino)-2-[(4-methylphenyl)amino]acrylate (**3d**).[21] The procedure for **3a** was followed, with **4d** (0.100 g, 0.56 mmol) and DMFDMA (0.100 g, 0.84 mmol), affording **3d** (0.07 g, 55%) as a blackish-red oil. R_f 0.34 (EtOAc). IR (film) ν 3333, 1737, 1663, 1615, 1515, 1434, 1404, 1281, 1218, 1085, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.23 (s, 3H, C*H*$_3$Ar), 3.03 (s, 6H, (C*H*$_3$)$_2$N), 3.61 (s, 3H, CO$_2$C*H*$_3$), 4.52 (br, 1H, NH), 6.54 (d, *J* = 8.0 Hz, 2H, H-2′), 6.97 (d, *J* = 8.0 Hz, 2H, H-3′), 7.37 (s, 1H, H-3); ^{13}C NMR (125 MHz, CDCl$_3$) δ 20.4 (*C*H$_3$Ar), 41.7 (br, (*C*H$_3$)$_2$N), 51.1 (CO$_2$*C*H$_3$), 99.3 (C-2), 113.5 (C-2′), 127.1 (C-4′), 129.6 (C-3′), 146.1 (C-3), 146.9 (C-1′), 169.7 (*C*O$_2$CH$_3$); MS (70 eV) *m/z* 235 (M$^+$+1, 52), 234 (M$^+$, 100), 203 (6), 187 (12), 174 (78), 73 (76), 159 (18), 144 (16), 130 (16), 118 (46), 105 (18), 91 (38). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{13}H_{18}N_2O_2$: 234.1368; found: 234.1373.

(*Z*)-Methyl 2-[(4-chlorophenyl)amino]-3-(dimethylamino)acrylate (**3e**).[21] The procedure for **3a** was followed, with **4e** (0.10 g, 0.5 mmol) and DMFDMA (0.089 g, 0.75 mmol), affording **3e** (0.101 g, 79%) as colorless crystals. R_f 0.71 (EtOAc); mp 141-142 °C (EtOAc). IR (film) ν 3392, 1678, 1628, 1492, 1432, 1385, 1288, 1216, 1085, 821, 768 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.02 (s, 6H, (C*H*$_3$)$_2$N), 3.62 (s, 3H, CO$_2$C*H*$_3$), 4.68 (br s, 1H, NH), 6.55 (d, *J* = 8.0 Hz, 2H, H-2′), 7.10 (d, *J* = 8.0 Hz, 2H, H-3′), 7.39 (s, 1H, H-3); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ 41.7 (br, (*C*H$_3$)$_2$N), 51.2 (CO$_2$*C*H$_3$), 98.2 (C-2), 114.5 (C-2′), 122.5 (C- 4′), 128.9 (C-3′), 146.5 (C-3), 147.8 (C-1′), 169.3 (*C*O$_2$CH$_3$); MS (70 eV) *m/z* 256 (M$^+$+2, 32), 254 (M$^+$, 88), 194 (100), 192 (38), 179 (13), 138 (42), 127 (22), 111 (36), 83 (39), 75 (28). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{12}H_{15}ClN_2O_2$: 254.0822; found: 254.0814.

(*Z*)-Methyl 3-(dimethylamino)-2-[(naphthalen-1-yl)amino]acrylate (**3f**). The procedure for **3a** was followed, with **4f** (0.100 g, 0.47 mmol) and DMFDMA (0.083 g, 0.70 mmol), affording **3f** (0.103 g, 82%) as a brown solid. R_f 0.66 (EtOAc); mp 193-194 °C. IR (film) ν 3387, 2945, 1685, 1632, 1579, 1523, 1473, 1431, 1402, 1383, 1288, 1217, 1132, 1095, 1082, 789, 771 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.99 (s, 6H, (C*H*$_3$)$_2$N), 3.63 (s, 3H, C*H*$_3$O), 5.36 (br s, 1H, NH), 6.60 (d, *J* = 7.5 Hz, 1H, H-2′), 7.27 (d, *J* = 7.5 Hz, 1H, H-4′), 7.32 (t, *J* = 7.5 Hz, 1H, H-3′), 7.44-7.50 (m, 2H, H-6′, H-7′), 7.48 (s, 1H, H-3), 7.79-7.83 (m, 1H, H-5′), 7.94-7.96 (m, 1H, H-8′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 41.7 (br, (*C*H$_3$)$_2$N), 51.2 (*C*H$_3$O), 98.5 (C-2), 106.9 (C-2′), 118.2 (C-4′), 120.2 (C-8′), 123.7 (C-8a), 124.7 (C-7′), 125.6 (C-6′), 126.6 (C-3′), 128.5 (C-5′), 134.5 (C-4a), 143.9 (C-1′), 145.7 (C-3), 169.4 (*C*O); MS (70 eV) *m/z* 270 (M$^+$, 100), 224 (16), 210 (52), 195 (36), 167 (28), 153 (34), 140 (14), 127 (22). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{16}H_{18}N_2O_2$: 270.1368; found: 270.1368.

(*Z*)-Methyl 3-(dimethylamino)-2-[(naphthalen-2-yl)amino]acrylate (**3g**). The procedure for **3a** was followed, with **4g** (0.100 g, 0.47 mmol) and DMFDMA (0.083 g, 0.70 mmol), affording **3g** (0.116 g, 92%) as an orange solid. R_f 0.80 (EtOAc); mp 179-180 °C. IR (film) ν 3354, 2945, 1682, 1629, 1519, 1472, 1431, 1394, 1289, 1216, 1183, 1132, 1084, 838, 812, 779, 746 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.06 (s, 6H, (C*H*$_3$)$_2$N), 3.66 (s, 3H, C*H*$_3$O), 4.84 (br s, 1H, NH), 6.85 (br d, *J* = 2.1 Hz, 1H, H-1′), 7.00 (dd, *J* = 8.7, 2.1 Hz, 1H, H-3′), 7.21 (ddd, *J* = 8.1, 7.2, 1.2 Hz, 1H, H-6′), 7.37 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H, H-7′), 7.51 (s, 1H, H-3), 7.62 (dd, *J* = 8.1, 0.6 Hz, 1H, H-8′), 7.67 (d, *J* = 8.7 Hz, 1H, H-4′), 7.71 (d, *J* = 8.1 Hz, 1H, H-5′); ^{13}C NMR (75.4 MHz, CDCl$_3$) δ 41.8 (br, (*C*H$_3$)$_2$N), 51.2 (CO$_2$*C*H$_3$), 98.4 (C-2), 106.3 (C-1′), 117.5 (C-3′), 122.0 (C-6′), 126.0 (C-8′), 126.1 (C-7′), 127.6 (C-5′), 128.0 (C-4a′), 128.9 (C-4′), 135.0 (C-8a′), 146.5 (C-3), 146.9 (C-2′), 169.6 (*C*O); MS (70 eV) *m/z* 270 (M$^+$, 100), 210 (73), 167 (13), 154 (28), 141

(14), 127 (34), 105 (10), 83 (18), 57 (32). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{18}N_2O_2$: 270.1368; found: 270.1379.

(*Z*)-4-(Dimethylamino)-3-[(3-methoxyphenyl)amino]but-3-en-2-one (**3i**).[21] The procedure for **3a** was followed, with **4i** (0.100 g, 0.56 mmol) and DMFDMA (0.100 g, 0.84 mmol), affording **3i** (0.116 g, 89%) as a greenish-brown gum. R_f 0.23 (EtOAc). IR (film) ν 3391, 1645, 1601, 1540, 1494, 1456, 1422, 1289, 1262, 1206, 1158, 1044, 853, 776, 689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (br s, 3H, CH_3CO), 3.05 (s, 6H, $(CH_3)_2$N), 3.75 (s, 3H, CH_3O), 4.99 (br, 1H, NH), 6.15 (t, *J* = 2.1 Hz, 1H, H-2′), 6.23 (dd, *J* = 8.2, 1.5 Hz, 1H, H-6′), 6.28 (ddd, *J* = 8.2, 2.4, 0.9 Hz, 1H, H-4′), 7.07 (t, *J* = 8.2 Hz, 1H, H-5′), 7.41 (br, 1H, H-4); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.8 (br, *C*H_3CO), 42.0 (br, (*C*H_3)$_2$N), 55.0 (*C*H_3O), 99.3 (br, C-2′), 102.9 (br, C-4′), 106.3 (br, C-6′), 130.0 (C-5′), 146.9 (br, C-4), 150.0 (C-1′), 160.8 (C-3′), 173.8 (*C*O); MS (70 eV) *m/z* 234 (M^+, 18), 233 (100), 232 (82), 215 (40), 204 (32), 189 (32), 174 (38), 172 (44), 146 (82), 133 (34), 117 (28). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{18}N_2O_2$: 234.1368; found: 234.1368.

(*Z*)-2-[(3,5-Dimethoxyphenyl)amino]-4-(dimethylamino)but-3-en-2-one (**3j**). The procedure for **3a** was followed, with **4j** (0.100 g, 0.48 mmol) and DMFDMA (0.085 g, 0.72 mmol), affording **3j** (0.123 g, 97%) as a greenish-brown gum. R_f 0.37 (EtOAc). IR (film) ν 3364, 2920, 1599, 1457, 1421, 1300, 1203, 1152, 1064, 816 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (br s, 3H, CH_3Ar), 3.06 (s, 6H, $(CH_3)_2$N), 3.74 (s, 6H, 2(CH_3O)), 5.00 (br, 1H, NH), 5.81 (br s, 2H, H-2′, H-6′), 5.89 (t, *J* = 2.1 Hz, 1H, H-4′), 7.41 (br s, 1H, H-4); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.7 (br, *C*H_3CO), 41.9 (br, (*C*H_3)$_2$N), 55.0 (*C*H_3O), 90.0 (br, C-4′), 91.8 (br, C-2′, C-6′), 99.6 (C-2), 146.9 (br, C-4), 150.7 (C-1′), 161.6 (C-3′, C-5′). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{20}N_2O_3$: 264.1474; found: 264.1473.

(*Z*)-4-(Dimethylamino)-3-[(4-methylphenyl)amino]but-3-en-2-one (**3k**). The procedure for **3a** was followed, with **4k** (0.100 g, 0.61 mmol) and DMFDMA (0.109 g, 0.92 mmol), affording **3k** (0.092 g, 69%) as a black oil. R_f 0.34 (EtOAc). IR (film) ν 3334, 2919, 1652, 1614, 1557, 1513, 1426, 1374, 1354, 1299, 1221, 1131, 963, 812 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.11 (br s, 3H, CH_3CO), 2.23 (s, 3H, CH_3Ar), 3.05 (s, 6H, $(CH_3)_2$N), 6.51 (d, *J* = 8.0 Hz, 2H, H-2′), 6.97 (d, *J* = 8.1 Hz, 2H, H-3′), 8.00 (s, 1H, H-4). Signals attributed to a second rotamer: 2.27 (s, CH_3Ar), 2.87 (s, $(CH_3)_2$N), 2.95 (s, $(CH_3)_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.4 (br, *C*H_3Ar), 25.1 (br, *C*H_3CO), 41.8 (br, (*C*H_3)$_2$N), 113.0 (br, C-2′), 115.0 (br, C-3), 127.5 (br, C-4′), 129.6 (C-3′), 146.5 (br, C-1′), 162.3 (C-4′). Signals attributed to a second rotamer: 20.2 (*C*H_3Ar), 31.2 (*C*H_3CO), 36.3 ((*C*H_3)$_2$N), 125.5, 166.9; MS (70 eV) *m/z* 218 (M^+, 17), 185 (13), 162 (87), 147 (41), 129 (36), 120 (64), 106 (48), 91 (92), 83 (51), 73 (84), 69 (71), 57 (100), 55 (90). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{18}N_2O$: 218.1419; found: 218.1411.

(*Z*)-3-[(4-Chlorophenyl)amino]-4-(dimethylamino)but-3-en-2-one (**3l**). The procedure for **3a** was followed, with **4l** (0.100 g, 0.54 mmol) and DMFDMA (0.097 g, 0.82 mmol), affording **3l** (0.095 g, 73%) as a yellow gum. R_f 0.26 (EtOAc). IR (film) ν 3329, 1648, 1596, 1558, 1491, 1423, 1376, 1354, 1307, 1131, 963, 821 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.12 (br s, 3H, CH_3CO), 3.04 (s, 6H, $(CH_3)_2$N), 5.03 (br, 1H, NH), 6.52 (d, *J* = 8.5 Hz, 2H, H-2′), 7.10 (d, *J* = 8.5 Hz, 2H, H-3′), 7.36 (br, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7 (br, *C*H_3CO), 42.0

(br, (CH$_3$)$_2$N), 114.5 (br, C-2′), 122.6 (br, C-4′), 129.1 (C-3′), 146.7 (br, C-4), 147.1 (C-1′); MS (70 eV) *m/z* 240 (M^++2, 32), 238 (M^+, 100), 221 (18), 195 (17), 180 (14), 154 (11), 152 (20), 138 (20), 125 (19), 111 (16). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{15}ClN_2O$: 238.0873; found: 238.0871.

(*Z*)-4-(Dimethylamino)-3-[(naphthalen-1-yl)amino]but-3-en-2-one (**3m**). The procedure for **3a** was followed, with **4m** (0.100 g, 0.50 mmol) and DMFDMA (0.090 g, 0.75 mmol), affording **3m** (0.116 g, 91%) as a black solid. R_f 0.24 (EtOAc); mp 155-157 °C. IR (film) ν 3369, 1652, 1578, 1525, 1474, 1404, 1377, 1354, 1301, 1131, 961, 788, 772 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.17 (br s, 3H, CH_3CO), 3.00 (s, 6H, (CH_3)$_2$N), 5.70 (br, 1H, NH), 6.51 (br d, *J* = 6.5 Hz, 1H, H-2′), 7.26 (d, *J* = 8.0 Hz, 1H, H-4′), 7.30 (t, *J* = 8.0 Hz, 1H, H-3′), 7.44-7.49 (m, 3H, H-6′, H-7′, H-4), 7.78-7.83 (m, 1H, H-5′), 7.94-8.00 (m, 1H, H-8′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 29.3 (br, CH$_3$CO), 42.0 (br, (CH_3)$_2$N), 107.1 (br, C-2′), 118.3 (br, C-4′), 120.2 (br, C-8′), 124.9 (C-6′ or C-7′), 125.7 (C-7′ or C-6′), 126.6 (C-3′), 128.6 (C-5′), 134.5 (C-4a′), 143.1 (C-1′), 145.7 (C-4), 180.1 (CO); MS (70 eV) *m/z* 254 (M^+, 100), 209 (26), 194 (17), 181 (21), 168 (28), 154 (16), 141 (26), 127 (18), 113 (16). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{18}N_2O$: 254.1419; found: 254.1416.

(*Z*)-4-(Dimethylamino)-3-[(naphthalen-2-yl)amino]but-3-en-2-one (**3n**). The procedure for **3a** was followed, with **4n** (0.10 g, 0.5 mmol) and DMFDMA (0.090 g, 0.75 mmol), affording **3n** (0.11 g, 86%) as a brown solid. R_f 0.24 (EtOAc); mp 148-149 °C. IR (film) ν 3312, 1653, 1628, 1601, 1561, 1520, 1424, 1353, 1300, 1220, 1131, 959, 837, 747 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.15 (br s, 3H, CH_3CO), 3.05 (s, 6H, (CH_3)$_2$N), 5.08 (br, 1H, NH), 6.76 (br s, 1H, H-1′), 6.96 (br d, *J* = 7.5 Hz, 1H, H-3′), 7.20 (t, *J* = 7.5 Hz, 1H, H-6′), 7.34 (t, *J* = 7.5 Hz, 1H, H-7′), 7.48 (br, 1H, H-4), 7.57 (d, *J* = 7.5 Hz, 1H, H-8′), 7.65 (d, *J* = 7.5 Hz, 1H, H-4′), 7.67 (d, *J* = 7.5 Hz, 1H, H-5′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 24.8 (br, CH$_3$CO), 42.0 (br, (CH_3)$_2$N), 105.9 (br, C-1′), 117.3 (br, C-3), 122.1 (C-6′), 126.0 (C-8′), 126.3 (C-7′), 127.6 (C-5′), 128.0 (C-4a′), 129.2 (C-4′), 135.1 (C-8a′), 146.2 (C-2′), 146.8 (C-4), 179.5 (CO); MS (70 eV) *m/z* 254 (M^+, 100), 239 (12), 168 (27), 154 (13), 141 (31), 127 (23), 113 (12), 83 (16), 71 (15), 57 (25). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{18}N_2O$: 254.1419; found: 254.1414.

(*Z*)-2-[(3,5-Dimethoxyphenyl)amino]-3-(dimethylamino)-1-phenylprop-2-en-1-one (**3o**). The procedure for **3a** was followed, with **4o** (0.100 g, 0.37 mmol) and DMFDMA (0.066 g, 0.55 mmol), affording **3o** (0.113 g, 94%) as a yellow oil. R_f 0.68 (EtOAc). IR (film) ν 3312, 2934, 1694, 1599, 1556, 1455, 1420, 1320, 1203, 1153, 1064, 818 cm^{-1}; H RMN (500 MHz, CDCl$_3$) δ 3.04 (s, 6H, (CH_3)$_2$N), 3.75 (s, 6H, 2(CH_3O)), 5.33 (br s,1H, NH), 5.90 (d, *J* = 2.5 Hz, 2H, H-2″, H-6″), 5.93 (t, *J* = 2.5 Hz, 1H, H-4″), 7.01 (br s, 1H, H-3), 7.32-7.43 (m, 3H, H-3′, H.4′, H-5″), 7.46-7.52 (m, 2H. H-2′); ^{13}C NMR (125 MHz, CDCl$_3$) δ 42.1 (br, (CH$_3$)$_2$N), 55.1 (2CH$_3$O), 90.8 (C-4″), 93.1 (C-2″, C-6″), 112.8 (br, C-2), 127.9 (C-3′), 128.0 (C-2′), 129.5 (C-4′), 140.6 (C-1′), 150.7 (br, C-3), 150.8 (C-1″), 161.6 (C-3″, C-5″), 193.0 (CO); MS (70 eV) *m/z* 325 (M^+-1, 36), 292 (12), 279 (28), 264 (44), 243 (36), 213 (24), 208 (100), 192 (32), 165 (52), 153 (76), 138 (68), 108 (53), 91 (32), 79 (32), 67 (40). HRMS (EI, [M^+]) *m/z* calcd for $C_{19}H_{22}N_2O_3$: 326.1631; found: 326.1628.

(*Z*)-1-(4-Fluorophenyl)-2-[(3,5-dimethoxyphenyl)amino]-3-(dimethylamino)prop-2-en-1-one (**3p**). The procedure for **3a** was followed, with **4p** (0.100 g, 0.35 mmol) and DMFDMA (0.062 g, 0.53 mmol), affording **3p** (0.117 g, 98%) as a yellow solid. R_f 0.75 (EtOAc); mp. 132-134 ºC. IR (film) ν 3196, 2958, 2926, 1738, 1630, 1599, 1466, 1425, 1285, 1207, 1162, 1020, 865, 849 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.05 (s, 6H, $(CH_3)_2N$), 3.75 (s, 6H, $2(CH_3O)$), 5.23 (br s, 1H, NH), 5.88 (d, J = 2.5 Hz, 2H, H2″, H-6″), 5.93 (t, J = 2.5 Hz, 1H, H-4″), 7.00-7.07 (m, 3H, H-3, H-3′), 7.47-7.53 (m, 2H, H-2′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.1 (br, $(CH_3)_2N$), 55.1 ($2CH_3O$), 90.8 (C-4″), 93.0 (C-2″, C-6″), 112.2 (br, C-2), 114.8 (J = 21.3 Hz, C-3′), 130.3 (J = 8.3 Hz, C-2′), 136.7 (C-1′), 150.5 (br, C-3), 150.6 (C-1″), 161.7 (C-3″, C-5″), 163.6 (J = 242.0 Hz, C-4′), 191.8 (*C*O); MS (70 eV) *m/z* 344 (M^+, 100), 327 (23), 299 (51), 284 (15), 206 (12), 193 (13), 178 (14), 166 (12), 123 (55), 95 (23), 58 (24). HRMS (EI, [M^+]) *m/z* calcd for $C_{19}H_{21}FN_2O_3$: 344.1536; found: 344.1534.

Methyl 1*H*-indole-2-carboxylate (**1a**).[41] **Method A**. In a threaded ACE glass pressure tube with a sealed Teflon screw cap, a mixture of **3a** (0.100 g, 0.45 mmol) and I_2 (0.127 g, 0.50 mmol) in MeCN (3.0 mL) under N_2 was stirred at room temperature for 12 h. The reaction mixture was dissolved in CH_2Cl_2 (20 mL), and then washed with an aqueous saturated solution of $Na_2S_2O_3$ (2 × 20 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under vacuum. The residue was purified by column chromatography over silica gel (20 g, hexane/EtOAc, 9:1), to give **1a** (0.032 g, 40%) as a brown solid. **Method B**. A mixture of **3a** (0.100 g, 0.45 mmol) and I_2 (0.127 g, 0.50 mmol) was ground in a glass mortar at room temperature for 18 min. The mixture was dissolved in CH_2Cl_2 (20 mL), and then washed with an aqueous saturated solution of $Na_2S_2O_3$ (2 × 20 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under vacuum. The residue was purified by column chromatography over silica gel (20 g, hexane/EtOAc, 9:1) to give of **1a** (0.04 g, 50%) as a brown solid. R_f 0.61 (hexane/EtOAc, 7:3); mp 149-150 °C [Lit.[41] 152.5-153 ºC]. IR (film) ν 3315, 1687, 1527, 1439, 1313, 1254, 1210, 823, 773, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, CO_2CH_3), 7.16 (ddd, J = 7.5, 7.0, 1.0 Hz, 1H, H-5), 7.23 (dd, J = 2.0, 1.0 Hz, 1H, H-3), 7.33 (ddd, J = 7.5, 7.0, 1.0 Hz, 1H, H-6), 7.42 (dt, J = 7.5, 1.0 Hz, 1H, H-7), 7.69 (dd, J = 7.0, 1.0 Hz, 1H, H-4), 8.92 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.0 (CO_2CH_3), 108.8 (C-3), 111.8 (C-7), 120.8 (C-5), 122.6 (C-4), 125.4 (C-6), 127.1 (C-2), 127.5 (C-3a), 136.8 (C-7a), 162.4 (CO_2CH_3); MS (70 eV) *m/z* 175 (M^+, 4), 144 (22), 143 (100), 115 (61), 89 (52), 63 (16). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_9NO_2$: 175.0633; found: 175.0633.

Methyl 6-methoxy-1*H*-indole-2-carboxylate (**1b**). Method A was followed as for **1a**, with **3b** (0.10 g, 0.4 mmol) and I_2 (0.112 g, 0.44 mmol), affording **1b** (0.074 g, 90%) as a yellow solid. Method B was followed as for **1a** (except that grinding was for only 6 min), with **3b** (0.10 g, 0.4 mmol) and I_2 (0.112 g, 0.44 mmol), affording **1b** (0.081 g, 99%) as a yellow solid. R_f 0.48 (hexane/EtOAc, 7:3); mp 113-114 °C [Lit.[41] 118.5-119 ºC]. IR (film) ν 3317, 1685, 1626, 1525, 1513, 1254, 1202, 827, 765, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H, CH_3O), 3.92 (s, 3H, CO_2CH_3), 6.82 (dd, J = 8.5, 2.0 Hz, 1H, H-5), 6.83 (br s, 1H, H-7), 7.16 (br d, J = 2.0 Hz, 1H, H-3), 7.54 (d, J = 8.5 Hz, 1H, H-4), 8.90 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ

51.8 (CO_2CH_3), 55.5 (CH_3O), 93.7 (C-7), 109.2 (C-3), 112.3 (C-5), 121.8 (C-3a), 123.4 (C-4), 126.0 (C-2), 138.0 (C-7a), 158.9 (C-6), 162.4 (CO_2CH_3); MS (70 eV) *m/z* 205 (M^+, 100), 176 (28), 150 (60), 143 (28), 127 (20), 118 (28), 117 (19), 110 (40), 90 (22), 77 (7), 69 (8). HRMS (EI, [M^+]) *m/z* calcd for $C_{11}H_{11}NO_3$: 205.0739; found: 205.0742.

Methyl 4,6-dimethoxy-1*H*-indole-2-carboxylate (**1c**). Method A was followed as for **1a**, with **3c** (0.100 g, 0.36 mmol) and I_2 (0.100 g, 0.39 mmol), affording **1c** (0.077 g, 92%) as a white solid. Method B was followed as for **1a** (except that grinding was for only 6 min) with **3c** (0.100 g, 0.36 mmol) and I_2 (0.100 g, 0.39 mmol), affording **1c** (0.083 g, 99%) as a white solid. R_f 0.65 (hexane/EtOAc, 7:3); mp 180-181 ºC [Lit.[42] 178-179 ºC]. IR (film) ν 3328, 3324, 1678, 1621, 1584, 1521, 1444, 1279, 1200, 1139, 814, 770 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3H, CH_3O-C6), 3.90 (s, 3H, CO_2CH_3), 3.91 (s, 3H, CH_3O-C4), 6.19 (d, *J* = 1.5 Hz, 1H, H-5), 6.43 (br s, 1H, H-7), 7.25 (br d, *J* = 2.5 Hz, 1H, H-3), 8.75 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.7 (CO_2CH_3), 55.4 (CH_3O), 55.6 (CH_3O), 86.1 (C-7), 92.7 (C-5), 107.0 (C-3), 113.9 (C-3a), 124.6 (C-2), 138.5 (C-7a), 155.1 (C-4), 160.4 (C-6), 162.3 (CO_2CH_3); MS (70 eV) *m/z* 235 (M^+, 100), 203 (99), 188 (28), 174 (84), 160 (98), 149 (48), 146 (35), 132 (33), 117 (40), 102 (36), 89 (19), 76 (26), 63 (37). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{13}NO_4$: 235.0845; found: 235.0846.

Methyl 5-methyl-1*H*-indole-2-carboxylate (**1d**).[21] Method A was followed as for **1a**, with **3d** (0.100 g, 0.43 mmol) and I_2 (0.119 g, 0.47 mmol), affording **1d** (0.03 g, 37%) as a colorless solid. Method B was followed as for **1a** (except that grinding was for 33 min), with **3d** (0.100 g, 0.43 mmol) and I_2 (0.119 g, 0.47 mmol), affording **1d** (0.049 g, 60%) as a colorless solid. R_f 0.63 (hexane/EtOAc, 7:3); mp 152-153 °C. IR (film) ν 3318, 1697, 1530, 1433, 1330, 1249, 1210, 767, 742, 669 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.43 (s, 3H, CH_3Ar), 3.94 (s, 3H, CO_2CH_3), 7.14 (br s, 1H, H-3), 7.15 (br d, *J* = 8.5 Hz, 1H, H-6), 7.31 (br d, *J* = 8.5 Hz, 1H, H-7), 7.46 (br s, 1H, H-4), 9.00 (br, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4 (CH_3Ar), 51.9 (CO_2CH_3), 108.3 (C-3), 111.5 (C-7), 121.9 (C-4), 127.1 (C-2), 127.4 (C-6), 127.7 (C-3a), 130.1 (C-5), 135.3 (C-7a), 162.5 (CO_2CH_3); MS (70 eV) *m/z* 189 (M^+, 58), 158 (19), 157 (100), 129 (27), 103 (18), 77 (8). HRMS (EI, [M^+]) *m/z* calcd for $C_{11}H_{11}NO_2$: 189.0790; found: 189.0793.

Methyl 5-chloro-1*H*-indole-2-carboxylate (**1e**).[21] Method A was followed as for **1a**, with **3e** (0.100 g, 0.39 mmol) and I_2 (0.110 g, 0.43 mmol), affording **1e** (0.023 g, 28%) as a white solid. Method B was followed as for **1a** (except that grinding was for 60 min), with **3e** (0.100 g, 0.39 mmol) and I_2 (0.110 g, 0.43 mmol), affording **1e** (0.027 g, 33%) as a white solid. R_f 0.63 (hexane/EtOAc, 7:3); mp 215-216 °C [Lit.[43] 214-215 ºC]. IR (film) ν 3324, 1697, 1437, 1375, 1255, 1203, 1058, 866, 793, 763, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, CO_2CH_3), 7.15 (br s, 1H, H-3), 7.28 (ddd, *J* = 8.5, 2.0, 1.0 Hz, 1H, H-6), 7.35 (d, *J* = 8.5 Hz, 1H, H-7), 7.67 (br s, 1H, H-4), 8.95 (br, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.2 (CO_2CH_3), 108.1 (C-3), 113.0 (C-7), 121.8 (C-4), 126.0 (C-6), 126.5 (C-5), 128.4 (C-3a), 135.0 (C-7a), 162.1 (CO_2CH_3); MS (70 eV) *m/z* 211 (M^++2, 18), 209 (M^+, 49), 179 (35), 177 (100), 149 (27), 123 (29), 114 (36), 81 (38), 69 (74), 57 (22), 55 (34). HRMS (EI, [M^+]) *m/z* calcd for $C_{10}H_8ClNO_2$: 209.0244; found: 209.0245.

Methyl 1*H*-benzo[*g*]indole-2-carboxylate (**1f**). Method A was followed as for **1a**, with **3f** (0.100 g, 0.37 mmol) and I_2 (0.270 g, 0.41 mmol), affording **1f** (0.034 g, 41%) as a brown solid. Method B was followed as for **1a** (except that grinding was for 20 min), with **3f** (0.100 g, 0.37 mmol) and I_2 (0.270 g, 0.41 mmol), affording **1f** (0.058 g, 70%) as a brown solid. R_f 0.59 (hexane/EtOAc, 7:3); mp 206-208 °C [Lit.[41] 211-211.5 ºC]. IR (film) ν 3430, 1637, 1506, 1359, 1301, 1270, 829, 745, 683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.00 (s, 3H, CO_2CH_3), 7.34 (d, *J* = 1.8 Hz, 1H, H-3), 7.48-7.61 (m, 3H, H-5, H-7, H-8), 7.68 (d, *J* = 8.7 Hz, 1H, H-4), 7.92 (br d, *J* = 8.1 Hz, 1H, H-6), 8.23 (br d, *J* = 7.8 Hz, 1H, H-9), 10.05 (br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 52.1 (CO_2CH_3), 110.3 (C-3), 120.5 (C-9), 121.3 (C-4), 121.8 (C-9a), 122.1 (C-8), 123.8 (C-3a), 125.4 (C-2), 125.6 (C-5), 125.9 (C-7), 128.9 (C-6), 132.0 (C-5a), 132.9 (C-9b), 161.3 (CO_2CH_3); MS (70 eV) *m/z* 225 (M^+, 96), 193 (100), 165 (70), 139 (30), 97 (16), 83 (8). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{11}NO_2$: 225.0790; found: 225.0787.

Methyl 3*H*-benzo[*e*]indole-2-carboxylate (**1g**). Method A was followed as for **1a**, with **3g** (0.100 g, 0.37 mmol) and I_2 (0.270 g, 0.41 mmol), affording **1g** (0.77 g, 68%) as a white solid. Method B was followed as for **1a** (except that grinding was for only 12 min), with **3g** (0.100 g, 0.37 mmol) and I_2 (0.270 g, 0.41 mmol), affording **1g** (0.043 g, 95%) as a white solid. R_f 0.17 (hexane/EtOAc, 7:3); mp 175-177 °C. IR (KBr) ν 3423, 1712, 1627, 1439, 1250, 1224, 1129, 1100, 1046, 819, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 3H, CO_2CH_3), 7.45 (t, *J* = 7.5 Hz, 1H, H-7), 7.49 (d, *J* = 9.0 Hz, 1H, H-4), 7.58 (t, *J* = 8.0 Hz, 1H, H-8), 7.68 (d, *J* = 9.0 Hz, 1H, H-5), 7.74 (s, 1H, H-1), 7.87 (d, *J* = 7.5 Hz, 1H, H-6), 8.22 (d, *J* = 8.0 Hz, 1H, H-9), 9.40 (br, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.9 (CO_2CH_3), 107.9 (C-1), 113.0 (C-4), 122.8 (C-9), 123.0 (C-9b), 124.2 (C-7), 125.2 (C-2), 126.7 (C-8), 127.0 (C-5), 128.7 (C-9a), 128.8 (C-6), 129.4 (C-5a), 134.3 (C-3a), 162.4 (CO_2CH_3); MS (70 eV) *m/z* 225 (M^+, 14), 207 (15), 179 (100), 152 (53), 127 (54), 97 (29), 73 (32), 69 (46), 57 (50), 55 (42). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{11}NO_2$: 225.0790; found: 225.0790.

1-(6-Methoxy-1*H*-indol-2-yl)ethanone (**1i**).[21] Method A was followed as for **1a**, with **3i** (0.100 g, 0.43 mmol) and I_2 (0.119 g, 0.47 mmol), affording **1i** (0.027 g, 34%) as a white solid. Method B was followed as for **1a** (except that grinding was for 15 min), with **3i** (0.100 g, 0.43 mmol) and I_2 (0.119 g, 0.47 mmol), affording **1i** (0.043 g, 50%) as a white solid. R_f 0.47 (hexane/EtOAc, 7:3); mp 136-138 °C. IR (film) ν 3303, 1644, 1627, 1574, 1512, 1448, 1263, 1235, 1184, 1025, 832 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.56 (s, 3H, $COCH_3$), 3.86 (s, 3H, CH_3O), 6.72-6.92 (m, 2H, H-5′, H-7′), 7.15 (d, *J* = 1.8 Hz, 1H, H-3′), 7.56 (d, *J* = 9.6 Hz, 1H, H-4′), 9.18 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.7 ($COCH_3$), 55.4 (CH_3O), 93.5 (C-7′), 110.6 (C-3′), 112.8 (C-5′), 121.8 (C-3a′), 123.9 (C-4′), 134.7 (C-2′), 138.7 (C-7a′), 159.6 (C-6′), 189.6 ($COCH_3$); MS (70 eV) *m/z* 189 (M^+, 39), 174 (44), 155 (100), 138 (96), 119 (38), 88 (65). HRMS (EI, [M^+]) *m/z* calcd for $C_{11}H_{11}NO_2$: 189.0790; found: 189.0788.

1-(4,6-Dimethoxy-1*H*-indol-2-yl)ethanone (**1j**).[21] Method A was followed as for **1a**, with **3j** (0.100 g, 0.38 mmol) and I_2 (0.106 g, 0.42 mmol), affording **1j** (0.042 g, 45%) as a yellow solid. Method B was followed as for **1a** (except that grinding was for 15 min), with **3j** (0.100 g, 0.38 mmol) and I_2 (0.106 g, 0.42 mmol), affording **1j** (0.056 g, 60%) as a yellow oil. R_f 0.42

(hexane/EtOAc, 7:3). IR (film) ν 3287, 1639, 1614, 1538, 1512, 1461, 1377, 1278, 1219, 1183, 1149, 1134, 982, 809, 716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H, COCH_3), 3.84 (s, 3H, CH_3O), 3.92 (s, 3H, CH_3O), 6.17 (d, *J* = 1.8 Hz, 2H, H-5′), 6.42 (dd, *J* = 1.8, 0.9 Hz, 1H, H-7′), 7.25 (dd, *J* = 2.1, 0.9 Hz, 1H, H-3′), 9.35 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.4 (CO*C*H_3), 55.3 (*C*H_3O), 55.6 (*C*H_3O), 86.0 (C-7′), 92.8 (C-5′), 108.4 (C-3′), 113.9 (C-3a′), 133.5 (C-2′), 139.4 (C-7a′), 155.3 (C-4′), 161.0 (C-6′), 189.4 (*C*OCH_3); MS (70 eV) *m/z* 219 (M^+, 34), 218 (90), 204 (100), 189 (6), 176 (12), 161 (34), 158 (28), 146 (38), 132 (34), 119 (48), 63 (42). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{13}NO_3$: 219.0895; found: 219.0898.

1-(1*H*-Benzo[*g*]indol-2-yl)ethanone (**1m**). Method B was followed as for **1a** (except that grinding was for 48 min), with **3m** (0.100 g, 0.39 mmol) and I_2 (0.270 g, 1.06 mmol), affording **1m** (0.021 g, 25%) as a brown solid. R_f 0.58 (hexane/EtOAc, 7:3); mp 190-191 °C. IR (film) ν 3328, 3290, 1636, 1507, 1448, 1430, 1359, 1301, 1272, 1189, 829, 797, 745, 683 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.66 (s, 3H, COCH_3), 7.31 (d, *J* = 2.1 Hz, 1H, H-3′), 7.44-7.62 (m, 3H, H-5′, H-7′, H-8′), 7.65 (d, *J* = 8.4 Hz, 1H, H-4′), 7. 89 (dd, *J* = 8.2, 1.5 Hz, 1H, H-6′), 8.30 (br d, d, *J* = 7.8 Hz, 1H, H-9′), 10.43 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.8 (CO*C*H_3), 111.6 (C-3′), 121.1 (C-9′), 121.3 (C-4′), 121.9 (C-9a′), 122.3 (C-8′), 123.9 (C-3a′), 126.0 (C-5′ or C-7′), 126.1 (C-7′ or C-5′), 128.8 (C-6′), 132.5 (C-5a′), 133.9 (C-2′), 134.1 (C-9b′), 190.1 (*C*OCH_3). MS (70 eV) *m/z* 209 (M^+, 49), 194 (41), 166 (12), 139 (38), 127 (12), 113 (10), 111 (11), 99 (15), 97 (20), 85 (45), 83 (22), 71 (65), 69 (24), 57 (100), 55 (35). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0848.

1-(3*H*-Benzo[*e*]indol-2-yl)ethanone (**1n**). Method B was followed as for **1a** (except that grinding was for 20 min), with **3n** (0.100 g, 0.39 mmol) and I_2 (0.110 g, 0.43 mmol), affording **1n** (0.041 g, 50%) as a brown solid. R_f 0.36 (hexane/EtOAc, 7:3); mp 204-205 °C. IR (film) ν 3267, 1635, 1618, 1504, 1384, 1246, 1182, 804, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.67 (s, 3H, COCH_3), 7.47 (t, *J* = 8.0 Hz, 1H, H-7′), 7.52 (d, *J* = 9.0 Hz, 1H, H-4′), 7.61 (t, *J* = 8.0 Hz, 1H, H-8′), 7.72 (s, 1H, H-1′), 7.73 (d, *J* = 9.0 Hz, 1H, H-5′), 7.90 (d, *J* = 8.0 Hz, 1H, H-6′), 8.24 (d, *J* = 8.0 Hz, 1H, H-9′), 9.67 (br s, 1H, NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8 (CO*C*H_3), 109.0 (C-1′), 113.2 (C-4′), 122.6 (C-9′), 123.0 (C-9b′), 124.4 (C-7′), 126.9 (C-8′), 128.2 (C-5′), 128.8 (C-9a′), 128.9 (C-6′), 129.4 (C-5a), 133.9 (C-2′), 135.0 (C-3a′), 189.8 (*C*OCH_3); MS (70 eV) *m/z* 209 (M^+, 98), 194 (100), 180 (8), 166 (34), 139 (88). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0840.

1-(4,6-Dimethoxy-1*H*-indol-2-yl)(phenyl)methanone (**1o**). Method A was followed as for **1a**, with **3o** (0.101 g, 0.31 mmol) and I_2 (0.087 g, 0.34 mmol), affording **1o** (0.056 g, 65%) as a yellow solid. Method B was followed as for **1a** (except that grinding was for 20 min), with **3o** (0.101 g, 0.31 mmol) and I_2 (0.087 g, 0.34 mmol), affording **1o** (0.061 g, 70%) as a yellow solid. R_f 0.51 (hexane/EtOAc, 7:3); mp 147-149 ºC. [Lit.[44] 173-175 °C]. IR (film) ν 3307, 1723, 1612, 1585, 1570, 1509, 1463, 1376, 1288, 1220, 1203, 1151, 896, 815 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, CH_3O-C6), 3.91 (s, 3H, CH_3O-C4), 6.20 (d, *J* = 2.0 Hz, 1H, H-5), 6.47 (d, *J* = 0.5 Hz, 1H, H-7), 7.20 (dd, *J* = 2.0, 1.0 Hz, 1H, H-3), 7.48-7.54 (m, 2H, H-3′), 7.56-7.61 (m, 1H, H-4′), 7.93-7.99 (m, 2H, H-2′), 9.21 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4

(*C*H_3O-6), 55.7 (*C*H_3O-4), 86.0 (C-5), 93.0 (C-7), 111.2 (C-3), 114.5 (C-3a), 128.4 (C-3′), 129.0 (C-2′), 131.9 (C-4′), 138.6 (C-2), 138.2 (C-1′), 139.5 (C-7a), 155.7 (C-4), 161.4 (C-6), 186.0 (*C*O); MS (70 eV) *m/z* 281 (M^+, 100), 266 (29), 238 (14), 223 (7), 185 (7), 183 (8), 149 (9), 105 (17), 77 (19). HRMS (EI, [M^+]) *m/z* calcd for $C_{17}H_{15}NO_3$: 281.1052; found: 281.1051.

1-(4,6-Dimethoxy-1*H*-indol-2-yl)(4-fluorophenyl)methanone (**1p**). Method A was followed as for **1a**, with **3p** (0.100 g, 0.29 mmol) and I_2 (0.081 g, 0.32 mmol), affording **1p** (0.056 g, 64%) as a brown oil. Method B was followed as for **1a** (except that grinding was for 20 min) with **3p** (0.100 g, 0.29 mmol) and I_2 (0.081 g, 0.32 mmol), affording **1p** (0.065 g, 75%) as a pale brown solid. R_f 0.53 (hexane/EtOAc, 7:3); mp 150-152 ºC. IR (film) ν 3305, 1618, 1499, 1294, 1226, 1153, 809, 767 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, C*H_3*O-C6), 3.92 (s, 3H, C*H_3*O-C4), 6.20 (d, *J* = 3.0 Hz, 1H, H-5), 6.46 (dd, *J* = 3.0, 1.0 Hz, 1H, H-7), 7.16-7.22 (m, 3H, H-3, H-3′), 7.96-8.03 (m, 2H, H-2′), 9.28 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4 (*C*H_3O-C6), 55.7 (*C*H_3O-C4), 86.0 (C-7), 93.0 (C-5), 111.1 (C-3), 114.5 (3a), 115.5 (*J* = 21.4 Hz, C-3′), 131.4 (*J* = 8.7 Hz, C-2′), 132.3 (C-2), 134.5 (C-1′), 139.6 (C-7a), 155.6 (C-4), 161.5 (C-6), 165.3 (*J* = 225.0 Hz, C-4′), 184.5 (*C*O); MS (70 eV) *m/z* 299 (M^+, 100), 284 (21), 256 (16), 241 (7), 231 (10), 219 (7), 160 (9), 123 (26), 95 (14). HRMS (EI, [M^+]) *m/z* calcd for $C_{17}H_{14}FNO_3$: 299.0958; found: 299.0954.

Methyl 3-(dimethylamino)-1*H*-indole-2-carboxylate (**2a**). In a threaded ACE glass pressure tube with a sealed Teflon screw cap, a mixture of **4a** (0.101 g, 0.61 mmol) and DMADMF (0.109 g, 0.91 mmol) was stirred at 120 °C for 12 h. The mixture was cooled to room temperature and then I_2 (0.170 g, 0.67 mmol) was added and stirred at room temperature for 24 h. The residue was dissolved in CH_2Cl_2 (20 mL) and washed with a saturated aqueous solution of $Na_2S_2O_3$ (2 × 20 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under vacuum. The residue was purified by column chromatography over silica gel (20 g, hexane/EtOAc, 9:1) to give **2a** (0.053 g, 40%) as a green oil. R_f 0.27 (hexane/EtOAc, 7:3). IR (film) ν 3338, 1691, 1542, 1482, 1450, 1338, 1249, 1193, 1086, 743 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.13 (s, 6H, (C*H_3*)$_2$N), 3.91 (s, 3H, CO_2C*H_3*), 7.00-7.07 (m, 1H, H-5), 7.24-7.30 (m, 2H, H-6, H-7), 7.91 (dd, *J* = 8.1, 0.9 Hz, 1H, H-4), 8.55 (br s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.9 ((*C*H_3)$_2$N), 51.4 (CO_2*C*H_3), 112.0 (C-7), 115.2 (C-2), 119.0 (C-5), 122.4 (C-4), 123.2 (C-3a), 125.5 (C-6), 135.2 (C-7a), 138.7 (C-3), 161.3 (*C*O_2CH_3); MS (70 eV) *m/z* 218 (M^+, 4), 217 (23), 185 (80), 172 (32), 157 (50), 144 (44), 130 (100), 116 (24), 100 (20), 89 (28), 72 (21). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{14}N_2O_2$: 218.1055; found: 218.1057.

Methyl 3-(dimethylamino)-6-methoxy-1*H*-indole-2-carboxylate (**2b**). The procedure for **2a** was followed, with **4b** (0.100 g, 0.51 mmol), DMADMF (0.090 g, 0.76 mmol) and I_2 (0.071 g, 0.56 mmol), affording **2b** (0.102 g, 80%) as a yellow solid. R_f 0.8 (hexane/EtOAc, 7:3); mp 124-126 ºC. IR (film) ν 3164, 1694, 1622, 1533, 1456, 1343, 1324, 1262, 1205, 1164, 1079, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.13 (s, 6H, (C*H_3*)$_2$N), 3.83 (s, 3H, C*H_3*O), 3.90 (s, 3H, CO_2C*H_3*), 6.67 (br d, *J* = 2.0 Hz, 1H, H-7), 6.67 (dd, *J* = 8.5, 2.0 Hz, 1H, H-5), 7.78 (d, *J* = 8.5 Hz, 1H, H-4), 8.18 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 45.0 ((*C*H_3)$_2$N), 51.4 (CO_2*C*H_3), 55.4 (*C*H_3O), 93.4 (C-5), 110.7 (C-7), 113.6 (C-2), 117.6 (C-3a), 123.7 (C-4), 136.5

(C-7a), 139.6 (C-3), 159.1 (C-6), 161.0 (*C*O_2CH_3); MS (70 eV) *m/z* 248 (M^+, 4), 247 (16), 215 (100), 187 (52), 172 (94), 160 (50), 146 (52), 119 (35), 117 (24), 91 (10). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{16}N_2O_3$: 248.1161; found: 248.1160.

Methyl 3-(dimethylamino)-4,6-dimethoxy-1*H*-indole-2-carboxylate (**2c**). The procedure for **2a** was followed, with **4c** (0.100 g, 0.44 mmol), DMADMF (0.080 g, 0.67 mmol) and I_2 (0.123 g, 0.48 mmol), affording **2c** (0.10 g, 81%) as a green oil. R_f 0.29 (hexane/EtOAc, 7:3). IR (film) ν 3393, 1743, 1617, 1598, 1521, 1456, 1437, 1204, 1177, 1152, 938 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.96 (s, 6H, (CH_3)$_2$N), 3.82 (s, 3H, CH_3O-C6), 3.89 (s, 3H, CO_2CH_3), 3.92 (s, 3H, CH_3O-C4), 6.11 (d, *J* = 2.0 Hz, 1H, H-5), 6.29 (d, *J* = 2.0 Hz, 1H, H-7), 8.22 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 44.8 ((CH_3)$_2$N), 51.3 (CO_2CH_3), 55.4 (CH_3O-C4), 55.5 (CH_3O-C6), 85.8 (C-7), 92.0 (C-5), 110.1 (C-3a), 115.1 (C-2), 137.6 (C-7a), 139.5 (C-3), 155.5 (C-4), 160.4 (C-6), 161.1 (*C*O_2CH_3); MS (70 eV) *m/z* 278 (M^+, 66), 263 (13), 246 (11), 235 (15), 218 (42), 203 (100), 187 (13), 174 (20), 145 (19), 119 (10), 89 (11), 75 (13). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{18}N_2O_4$: 278.1267; found: 278.1265.

Methyl 3-(dimethylamino)-5-methyl-1*H*-indole-2-carboxylate (**2d**). The procedure for **2a** was followed, with **4d** (0.100 g, 0.56 mmol), DMADMF (0.100 g, 0.84 mmol) and I_2 (0.157 g, 0.62 mmol), affording **2d** (0.071 g, 55%) as yellow crystals. R_f 0.51 (hexane/EtOAc, 7:3); mp 87-88 ºC (hexane/EtOAc, 1:9). IR (film) ν 3345, 1692, 1543, 1437, 1321, 1250, 1194, 1161, 1080, 800, 778 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H, CH_3Ar), 3.10 (s, 6H, (CH_3)$_2$N), 3.87 (s, 3H, CO_2CH_3), 7.07 (d, *J* = 8.3 Hz, 1H, H-6), 7.15 (d, *J* = 8.3 Hz, 1H, H-7), 7.66 (s, 1H, H-4), 8.65 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4 (CH_3Ar), 44.9 ((CH_3)$_2$N), 51.3 (CO_2CH_3), 111.7 (C-7), 115.8 (C-2), 121.5 (C-4), 123.6 (C-3a), 127.6 (C-6), 128.3 (C-5), 133.7 (C-7a), 138.2 (C-3), 161.3 (*C*O_2CH_3); MS (70 eV) *m/z* 232 (M^+, 65), 200 (40), 172 (39), 157 (100), 130 (19), 116 (12), 103 (12), 89 (14). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{16}N_2O_2$: 323.1212; found: 232.1210.

Methyl 5-chloro-3-(dimethylamino)-1*H*-indole-2-carboxylate (**2e**). The procedure for **2a** was followed, with **4e** (0.100 g, 0.50 mmol), DMADMF (0.090 g, 0.75 mmol) and I_2 (0.140 g, 0.55 mmol), affording **2e** (0.035 g, 28%) as a brown-redish solid. R_f 0.58 (hexane/EtOAc, 7:3); mp 153-155 ºC. IR (film) ν 3423, 3149, 1710, 1583, 1552, 1469, 1456, 1436, 1332, 1258, 1206, 1165, 1091, 828, 775 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.42 (s, 6H, (CH_3)$_2$N), 3.99 (s, 3H, CO_2CH_3), 7.41 (dd, *J* = 8.5, 2.0 Hz, 1H, H-6), 7.55 (d, *J* = 8.5 Hz, 1H, H-7), 8.22 (br s, 1H, H-4), 12.71 (br s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 46.6 ((CH_3)$_2$N), 52.8 (CO_2CH_3), 115.2 (C-7), 119.0 (C-4), 119.3 (C-3a), 119.7 (C-2), 123.5 (C-3), 126.1 (C-7a), 126.3 (C-6), 133.0 (C-5), 160.2 (*C*O_2CH_3); MS (70 eV) *m/z* 254 (M^++2, 40), 252 (M^+, 100), 220 (70), 194 (85), 192 (57), 177 (80), 157 (36), 151 (24), 142 (18), 128 (27), 116 (18), 110 (14), 83 (19). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{13}ClN_2O_2$: 252.0666; found: 252.0667.

Methyl 3-(dimethylamino)-1*H*-benzo[*g*]indole-2-carboxylate (**2f**). The procedure for **2a** was followed, with **4f** (0.101 g, 0.47 mmol), DMADMF (0.084 g, 0.71 mmol) and I_2 (0.132 g, 0.52 mmol), affording **2f** (0.072 g, 58%) as a brown solid. R_f 0.49 (hexane/EtOAc, 7:3); mp 117-119 ºC. IR (film) ν 3430, 1656, 1539, 1449, 1308, 1267, 1198, 1124, 804, 773 cm^{-1}; ^{1}H NMR (300

MHz, $CDCl_3$) δ 3.16 (s, 6H, $(CH_3)_2N$), 3.97 (s, 3H, CO_2CH_3), 7.37 (d, *J* = 8.7 Hz, 1H, H-5), 7.41-7.54 (m, 2H, H-7, H-8), 7.80-7.87 (m, 1H, H-6), 7.89 (d, *J* = 8.7 Hz, 1H, H-4), 8.07-8.14 (m, 1H, H-9), 9.38 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 45.1 ($(CH_3)_2N$), 51.6 (CO_2CH_3), 114.2 (C-2), 119.0 (C-3a), 120.2 (C-9), 120.3 (C-5), 121.0 (C-4), 121.5 (C-9a), 125.8 (C-7 or C-8), 125.9 (C-8 or C-9), 128.5 (C-6), 131.2 (C-9b), 132.0 (C-5a), 140.2 (C-3), 161.3 (CO_2CH_3); MS (70 eV) *m/z* 268 (M^+, 98), 236 (100), 207 (78), 192 (92), 178 (26), 166 (20), 152 (12), 139 (14), 118 (16), 96 (10). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{16}N_2O_2$: 268.1212; found: 268.1203.

Methyl 1-(dimethylamino)-3*H*-benzo[*e*]indole-2-carboxylate (**2g**). The procedure for **2a** was followed, with **4g** (0.101 g, 0.47 mmol), DMADMF (0.084 g, 0.71 mmol) and I_2 (0.132 g, 0.52 mmol), affording **2g** (0.099 g, 79%) as a brown solid. R_f 0.64 (hexane/EtOAc, 7:3); mp 167-168 ºC. IR (KBr) ν 3313, 1674, 1476, 1436, 1363, 1275, 1247, 1202, 977, 806, 717 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.00 (s, 6H, $(CH_3)_2N$), 3.97 (s, 3H, CO_2CH_3), 7.36 (d, *J* = 9.0 Hz, 1H, H-4), 7.44 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, H-7), 7.60 (ddd, *J* = 8.0, 6.5, 1.5 Hz, 1H, H-8), 7.64 (d, *J* = 9.0 Hz, 1H, H-5), 7.84 (d, *J* = 8.0 Hz, 1H, H-6), 9.04 (br s, 1H, NH), 9.12 (d, *J* = 8.5 Hz, 1H, H-9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 43.3 ($(CH_3)_2N$), 51.6 (CO_2CH_3), 112.8 (C-4), 118.2 (C-9b), 118.8 (C-2), 123.8 (C-7), 123.9 (C-9), 126.7 (C-8), 127.7 (C-5), 128.5 (C-6), 129.5 (C-9a), 129.6 (C-5a), 132.1 (C-3a), 140.7 (C-1), 161.4 (CO_2CH_3); MS (70 eV) *m/z* 268 (M^+, 100), 253 (9), 236 (49), 207 (67), 193 (95), 181 (18), 178 (23), 166 (20), 152 (16), 139 (20). HRMS (EI, [M^+]) *m/z* calcd for $C_{16}H_{16}N_2O_2$: 268.1212; found: 268.1209.

1-[3-(Dimethylamino)-1*H*-indol-2-yl]ethanone (**2h**). The procedure for **2a** was followed, with **4h** (0.100 g, 0.67 mmol), DMADMF (0.120 g, 0.10 mmol) and I_2 (0.187 g, 0.74 mmol), affording **2h** (0.049 g, 36%) as a yellow solid. R_f 0.67 (hexane/EtOAc, 7:3); mp 139-141 ºC. IR (film) ν 3337, 1691, 1541, 1481, 1450, 1337, 1248, 1193, 1086, 991, 933, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 3H, $COCH_3$), 3.05 (s, 6H, $(CH_3)_2N$), 7.09 (ddd, *J* = 8.1, 6.6, 1.2 Hz, 1H, H-5′), 7.30 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 2H, H-6′), 7.35 (dt, *J* = 8.1, 1.2 Hz, 1H, H-7′), 7.90 (dd, *J* = 8.1, 1.2 Hz, 1H, H-4′), 8.78 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.1 ($COCH_3$), 45.9 ($(CH_3)_2N$), 112.6 (C-7′), 119.6 (C-5′), 123.0 (C-4′), 124.3 (C-3a′), 126.0 (C-6′), 128.7 (C-2′), 135.6 (C-7a′), 137.9 (C-3′), 190.6 (*C*O); MS (70 eV) *m/z* 202 (M^+, 100), 187 (54), 185 (73), 169 (18), 159 (46), 144 (33), 131 (11), 117 (34), 102 (19), 89 (31). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{14}N_2O$: 202.1106; found: 202.1106.

1-[3-(Dimethylamino)-6-methoxy-1*H*-indol-2-yl]ethanone (**2i**). The procedure for **2a** was followed, with **4i** (0.100 g, 0.56 mmol), DMADMF (0.100 g, 0.84 mmol) and I_2 (0.157 g, 0.62 mmol), affording **2i** (0.083 g, 64%) as a green oil. R_f 0.47 (hexane/EtOAc, 7:3). IR (film) ν 3309, 1625, 1570, 1525, 1509, 1447, 1338, 1255, 1154, 1122, 1029, 979, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.69 (s, 3H, $COCH_3$), 3.04 (s, 6H, $(CH_3)_2N$), 3.85 (s, 3H, CH_3O), 6.69-6.76 (m, 2H, H-5′, H-7′), 7.76 (d, *J* = 9.6 Hz, 1H, H-4′), 8.79 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.7 ($COCH_3$), 46.1 ($(CH_3)_2N$), 55.4 (CH_3O), 93.7 (C-7′), 111.4 (C-5′), 118.4 (C-3a′), 124.0 (C-4′), 127.6 (C-2′), 137.1 (C-7a′), 139.1 (C-3), 159.3 (C-6), 189.6 (*C*O); MS (70 eV) *m/z*

232 (M^+, 100), 217 (53), 215 (78), 202 (12), 189 (63), 174 (66), 159 (77), 146 (15), 132 (15), 119 (12), 104, (15). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{16}N_2O_2$: 232.1212; found: 232.1209.

1-[3-(Dimethylamino)-4,6-dimethoxy-1*H*-indol-2-yl]ethanone (**2j**). The procedure for **2a** was followed, with **4j** (0.100 g, 0.48 mmol), DMADMF (0.086 g, 0.72 mmol) and I_2 (0.134 g, 0.53 mmol), affording **2j** (0.082 g, 65%) as a yellow solid. R_f 0.53 (hexane/EtOAc, 7:3); mp 137-139 ºC. IR (film) ν 3319, 1620, 1577, 1524, 1446, 1274, 1215, 1154, 1129, 1046, 972, 812 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.74 (s, 3H, COCH_3), 2.79 (s, 6H, (CH_3)$_2$N), 3.83 (s, 3H, OCH_3-6′), 3.96 (s, 3H, OCH_3-4′), 6.16 (d, *J* = 2.0 Hz, 1H, H-5′), 6.33 (d, *J* = 2.0 Hz, 1H, H-7′), 8.72 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.0 (CO*C*H$_3$), 44.8 ((*C*H$_3$)$_2$N), 55.0 (*C*H$_3$O-C4′), 55.6 (*C*H$_3$O-C6′), 86.1 (C-5′), 92.4 (C-7′), 111.4 (C-3a′), 128.5 (C-2′), 138.2 (C-7a′), 138.4 (C-3′), 155.0 (C-4′), 160.8 (C-6′), 190.7 (*C*OCH$_3$); MS (70 eV) *m/z* 262 (M^+, 91), 247 (70), 245 (100), 232 (24), 219 (63), 204 (40), 189 (22), 176 (15). 161 (28), 146 (15), 103 (19). HRMS (EI, [M^+]) *m/z* calcd for $C_{14}H_{18}N_2O_3$: 262.1318; found: 262.1314.

1-[3-(Dimethylamino)-5-methyl-1*H*-indol-2-yl]ethanone (**2k**)**.** The procedure for **2a** was followed, with **4k** (0.100 g, 0.61 mmol), DMADMF (0.110 g, 0.92 mmol) and I_2 (0.170 g, 0.67 mmol), affording **2k** (0.044 g, 33%) as a brown solid. R_f 0.64 (hexane/EtOAc, 7:3); mp 104-106 ºC. IR (film) ν 3320, 2927, 1627, 1531, 1418, 1333, 1316, 1250, 1224, 977, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.43 (s, 3H, CH_3Ar), 2.74 (s, 3H, COCH_3), 3.04 (s, 6H, (CH_3)$_2$N), 7.11 (d, *J* = 8.5 Hz, 1H, H-6′), 7.25 (d, *J* = 8.5 Hz, 1H, H-7′), 7.66 (s, 1H, H-4′), 9.07 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5 (*C*H$_3$Ar), 27.1 (CO*C*H$_3$), 45.8 ((*C*H$_3$)$_2$N), 112.5 (C-7′), 121.9 (C-4′), 124.3 (C-2′), 128.0 (C-6′), 128.7 (C-5′), 128.8 (C-3a′), 134.2 (C-7a′), 137.2 (C-3′), 190.7 (*C*O); MS (70 eV) *m/z* 216 (M^+, 99), 201 (89), 199 (100), 186 (14), 184 (15), 173 (40), 158 (34), 144 (19), 132 (25), 130 (27), 117 (10), 103 (13), 89 (15), 77 (10). HRMS (EI, [M^+]) *m/z* calcd for $C_{13}H_{16}N_2O$: 216.1263; found: 216.1261.

1-[5-Chloro-3-(dimethylamino)-1*H*-indol-2-yl]ethanone (**2l**). The procedure for **2a** was followed, with **4l** (0.100 g, 0.54 mmol), DMADMF (0.097 g, 0.82 mmol) and I_2 (0.151 g, 0.59 mmol), affording **2l** (0.037 g, 29%) as a yellow solid. R_f 0.62 (hexane/EtOAc, 7:3); mp 147-149 ºC. IR (film) ν 3479, 1592, 1373, 1187, 1176, 1121, 1080, 811, 653 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.76 (s, 3H, COCH_3), 3.02 (s, 6H, (CH_3)$_2$N), 7.23 (dd, *J* = 9.0, 1.8 Hz, 1H, H-6′), 7.33 (d, *J* = 9.0 Hz, 1H, H-7′), 7.86 (d, *J* = 1.8 Hz, 1H, H-4′), 9.33 (br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 27.2 (CO*C*H$_3$), 45.8 ((*C*H$_3$)$_2$N), 114.0 (C-7′), 121.9 (C-4′), 124.8 (C-3a′), 125.0 (C-5′), 126.4 (C-6′), 129.7 (C-2′), 133.9 (C-7a′), 137.2 (C-3′), 190.9 (*C*O); MS (70 eV) *m/z* 238 (M^++2, 56), 236 (M^+, 100), 221 (90), 219 (89), 206 (16), 204 (13), 193 (41), 184 (38), 178 (41), 164 (16), 151 (16), 89 (9). HRMS (EI, [M^+]) *m/z* calcd for $C_{12}H_{13}ClN_2O$: 236.0716; found: 236.0711.

1-[1-(Dimethylamino)-3*H*-benz[*e*]indol-2-yl]ethanone (**2m**). The procedure for **2a** was followed, with **4n** (0.100 g, 0.50 mmol), DMADMF (0.090 g, 0.75 mmol) and I_2 (0.140 g, 0.55 mmol), affording **2m** (0.070 g, 55%) as red crystals. R_f 0.42 (hexane/EtOAc, 7:3); mp 186-187 ºC (CH_2Cl_2/EtOAc, 1:9). IR (film) ν 3295, 1628, 1571, 1519, 1472, 1433, 1392, 1247, 1195, 1012, 972, 810, 748, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.76 (s, 3H, COCH_3), 3.11 (s, 6H, (C*H*$_3$)$_2$N), 7.44 (d, *J* = 9.0 Hz, 1H, H-4′), 7.48 (td, *J* = 8.0, 1.5 Hz, 1H, H-7′), 7.66 (td, *J* = 8.0, 1.0 Hz, 1H, H-8′), 7.71 (d, *J* = 9.0 Hz, 1H, H-5′), 7.90 (br d, *J* = 8.0 Hz, 1H, H-6′), 8.43 (d, *J* = 8.0 Hz, 1H, H-9′), 9.26 (br s, 1H, NH); ^{13}C NMR (125 MHz, CDCl$_3$) δ 27.1 (CO*C*H$_3$), 43.0 ((*C*H$_3$)$_2$N), 113.5 (C-4′), 119.9 (C-9b′), 123.9 (C-7′), 124.6 (C-9′), 126.8 (C-8′), 128.5 (C-5′), 128.7 (C-9a′), 129.1 (C-6′), 129.7 (C-5a′), 129.9 (C-2′), 133.5 (C-3a′), 138.0 (C-1′), 190.1 (*C*O). MS (70 eV) *m/z* 252 (M$^+$, 94), 237 (62), 235 (100), 219 (18), 209 (37), 207 (39), 193 (95), 178 (55), 166 (60), 152 (68), 139 (93), 126 (37), 115 (29), 87 (47). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{16}H_{16}N_2O$: 252.1263; found: 252.1255.

[3-(Dimethylamino)-4,6-dimethoxy-1*H*-indol-2-yl](phenyl)methanone (**2n**). The procedure for **2a** was followed, with **4o** (0.100 g, 0.37 mmol), DMADMF (0.066 g, 0.55 mmol) and I_2 (0.104 g, 0.41 mmol), affording **2n** (0.073 g, 61%) as an orange solid. R_f 0.49 (hexane/EtOAc, 7:3); mp 126-128 ºC. IR (film) ν 3309, 2925, 1624, 1579, 1566, 1537, 1452, 1286, 1220, 1204, 1154, 1140, 981, 809, 733, 697 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.54 ((C*H*$_3$)$_2$N), 3.83 (s, 3H, C*H*$_3$O-C6), 3.91 (s, 3H, C*H*$_3$O-C4), 6.11 (d, *J* = 2.1 Hz, 1H, H-5), 6.33 (d, *J* = 2.1 Hz, 1H, H-7), 7.41-7.54 (m, 3H, H-3′, H-4′), 7.70-7.76 (m, 2H, H-2′), 8.65 (br s, 1H, NH); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 44.6 ((*C*H$_3$)$_2$N), 55.2 (*C*H$_3$O-C4), 55.5 (*C*H$_3$O-C6), 85.9 (C-7), 92.1 (C-5), 110.4 (C-3a), 125.2 (C-2), 127.6 (C-3′), 128.7 (C-2′), 131.0 (C-4′), 139.3 (C-7a), 139.9 (C-1′), 140.2 (C-3), 155.6 (C-4), 161.1 (C-6), 187.1 (*C*O); MS (70 eV) *m/z* 324 (M$^+$, 56), 307 (100), 292 (8), 277 (8), 266 (6), 251 (5), 219 (5), 204 (8), 189 (5), 161 (5), 105 (22), 77 (28). HRMS (EI, [M$^+$]) *m/z* calcd for $C_{19}H_{20}N_2O_3$: 324.1474; found: 324.1476.

[3-(Dimethylamino)-4,6-dimethoxy-1*H*-indol-2-yl](4-fluorophenyl)methanone (**2o**). The procedure for **2a** was followed, with **4p** (0.100 g, 0.35 mmol), DMADMF (0.062 g, 0.52 mmol) and I_2 (0.098 g, 0.39 mmol), affording **2o** (0.081 g, 68%) as a yellow oil. R_f 0.51 (hexane/EtOAc, 7:3). IR (film) ν 3308, 1623, 1600, 1575, 1523, 1454, 1282, 1221, 1204, 1153, 1047, 983, 846, 809, 767 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.54 ((C*H*$_3$)$_2$N), 3.82 (s, 3H, C*H*$_3$O-C6), 3.91 (s, 3H, C*H*$_3$O-C4), 6.12 (d, *J* = 2.0 Hz, 1H, H-5), 6.35 (d, J = 2.0 Hz, 1H, H-7), 7.08-7.15 (m, 2H, H-3′), 7.74-7.79 (m, 2H, H-2′), 8.96 (br s, 1H, NH); ^{13}C NMR (125 MHz, CDCl$_3$) δ 44.6 ((*C*H$_3$)$_2$N), 55.2 (*C*H$_3$O-C4), 55.5 (*C*H$_3$O-C6), 86.1 (C-7), 92.2 (C-5), 110.5 (C-3a), 114.4 (*J* = 21.4 Hz, C-3′), 125.4 (C-2), 131.2 (*J* = 8.8 Hz, C-2′), 136.2 (C-1′), 139.5 (C-7a), 139.7 (C-3), 155.5 (C-4), 161.2 (C-6), 164.5 (*J* = 249.9 Hz, C-4′), 185.9 (*C*O); MS (70 eV) *m/z* 327 (M$^+$, 2), 299 (16), 251 (19), 206 (54), 179 (20), 140 (68), 123 (100), 112 (18), 95 (74). HRMS (EI, [M$^+$]) m/z calcd for $C_{19}H_{19}FN_2O_3$: 342.1380; found: 342.1382.

Single-Crystal X-ray Crystallography

A single-crystal of compound **3e** was obtained by recrystallization from EtOAc, compound **2d** from hexane/EtOAc, 1:9, and compound **2m** from EtOAc/CH_2Cl_2, 9:1. These were mounted on glass fibers. Crystallographic measurements were performed using *Mo K*α radiation (graphite crystal monochromator, λ = 71073 Å) at room temperature. Three standard reflections, which were monitored periodically, they showed no change during data collection. Unit cell parameters were obtained from least-squares refinement of 26 reflections in the range of $2<2\theta<20°$.

Intensities were corrected for Lorentz and polarization effects. No absorption correction was applied. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions and their atomic coordinates refined. Unit weights were used in the refinement. Details of data collection and refinement for these crystals are listed in Table 7 and CIF files, which include bond distances and angles, atomic coordinates, and anisotropic thermal parameters.

Table 7. Crystal and structure refinement data for **2d**, **2m** and **3e**

Structure	**3e**	**2d**	**2m**
Empirical formula	$C_{12}H_{15}ClN_2O_2$	$C_{13}H_{16}N_2O_2$	$C_{16}H_{16}N_2O$
Molecular weight	254.71	232.28	252.31
Temperature	292(2) K	292(2) K	292(2) K
Crystal size	0.50 × 0.48 × 0.36 mm^3	0.53 × 0.18 × 0.18 mm^3	0.62 × 0.48 × 0.35 mm^3
Crystal system	monoclinic	monoclinic	monoclinic
Space group	C1 2/c(1)	P1(21)/c(1)	P1(21)/c(1)
Unit cell parameters	a = 22.1239(8) Å, α = 90º b = 5.7781(2) Å, β = 107.808(4)º c = 21.3240(9) Å, γ = 90º	a = 7.9856(2) Å, α = 90º b = 12.2082(3) Å, β = 97.246(2)º c = 12.8060(3) Å, γ = 90º	a = 15.2873(4) Å, α = 90º b = 10.3222(3) Å, β = 92.290(2)º c = 8.5658(2) Å, γ = 90º
Volume	2595.33(17) Å^3	1238.48(5) Å^3	1350.59(6) Å^3
Z	8	4	4
Density	1.304 mg/m^3	1.246 mg/m^3	1.241 mg/m^3
Absorption coefficient	0.287 mm^{-1}	0.085 mm^{-1}	0.079 mm^{-1}
Theta range	3.66-32.35º	3.07 to 32.45º	2.67 to 32.42°
Reflections collected	14007	8710	9876
Independent reflections	4337	3897	4309
Observed reflections	3304	2635	3126
Final R indices	R_1 = 0.0533; $wR2$ = 0.1329	R_1 = 0.0683; $wR2$ = 0.1539	R_1 = 0.0646; $wR2$ = 0.1781
Goodness-of-fit on F^2	1.049	1.026	1.054

Structures were solved using the SHELXS97[45] programs as implemented in the WinGX suite,[46] and refined using SHELXL97[47] within WinGX, on a personal computer. In all cases ORTEP and packing diagrams were made with PLATON and ORTEP-3.[48,49] They were submitted to Cambridge Crystallographic Data Centre: **3e**, CCDC No. 932772; **2d**, CCDC No. 932773; **2m**, CCDC No. 932774.

Supporting information available

^{1}H and ^{13}C NMR spectra of indoles **1a-g**, **1i-j** and **1m-p**, and of 3-dimethylaminoindoles **2a-o**. Crystallographic information for **2d**, **2m** and **3e** in cif format, including X-ray diffraction data, atomic coordinates, thermal parameters, torsion angles and complete bond distances and angles. This material is available free of charge via the Internet at http://pubs.acs.org and from the Cambridge Crystallographic Data Centre (fax: +44-1223-336-003; e-mail: deposit@ccdc.cam.ac.uk or http//www.ccdc.cam.ac.uk) as supplementary publication numbers.

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