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Novel applications of hypervalent iodine: PIFA mediated synthesis of benzo[*c*]phenanthiridines and benzo[*c*]phenanthridinones

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Abstract—A short and efficient access to benzo[*c*]phenanthridines and phenanthridinones is achieved by the action of phenyliodine(III)-bis(trifluoroacetate) (PIFA) on properly substituted benzylnaphthylamines and naphthylbenzamides, respectively. This reagent promotes a non-phenolic oxidative biaryl coupling process, the key step of the synthesis. A study of the electronic and steric requirements of the substrates is carried out since, in some cases, dimerization processes prevail over intramolecular cyclization. A mechanistic proposal is also included.

1. Introduction

Benzo[*c*]phenanthridines **1** are among the most biologically active isoquinoline derivatives.[1] However, the high toxicity associated with some of the most active members of this family of alkaloids[2] has encouraged the scientific community to persue the preparation of analogs, along with the search for novel, short and efficient synthetic routes.[3] Towards this end, two main strategies have been commonly employed, as depicted in Fig. 1, both of them featuring the construction of ring C in the final step of the synthesis: (i) reductive amination of 2-aryltetralones **2** and subsequent heterocyclization,[4] and (ii) the intramolecular biaryl coupling of benzylnaphthylamines of type **3** bearing the adequate functional group (FG) in the benzyl ring. In the latter case, radical,[5] photochemical[6] and benzyne-mediated[5c,7] syntheses of the benzophenanthridine skeleton have been reported. Despite of the success of these approaches several steps are needed to prepare such elaborated precursors, and in many cases the overall yields are synthetically unattractive.

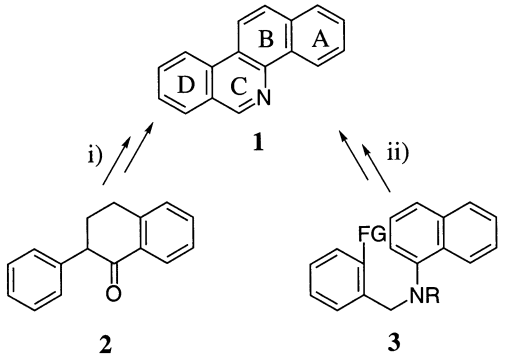

Figure 1.

During the last years, considerable attention has been devoted to the chemistry of hypervalent iodine reagents as a powerful tool for organic synthetic chemists.[8] Among them, easily handling PIFA and PIDA (phenyliodine(III)-diacetate) have been frequently used as radical promoters[8b] to generate alkoxy,[9] aminyl[10] and azidyl[11] radicals starting from the corresponding alcohols, amines and azides, respectively. They have been also used for the generation of arylic radical-cations via a SET mechanism[12] showing the same reactivity than other oxidants as, for example, Tl(III), V(V), Ru(IV) and Fe(III) salts, but with disminished toxicity. Following this strategy a series of nucleophiles (azides,[12,13] acetates,[12] dicarbonyl compounds,[12] thiophenolates[14] and thiocyanates[14b]) has been introduced onto electron-rich benzene rings. In the particular case of using an aryl ring as nucleophile, this methodology would give rise to a new biarylic connection in an elegant and simple way (see Fig. 2).[15] In fact, several reports on hypervalent iodine mediated syntheses of different biologically active compounds containing the biarylic moiety have appeared in the literature,[16] an approach that, to our minds, is far to be deeply extended.

Therefore, in this paper we want to show new applications of the PIFA reagent for the synthesis of the already mentioned heterocycles of type **1** starting from properly substituted benzylamines and benzamides.

Keywords: hypervalent iodine; PIFA; biaryl coupling; benzo[*c*]phenanthridines; benzo[*c*]phenanthridinones.

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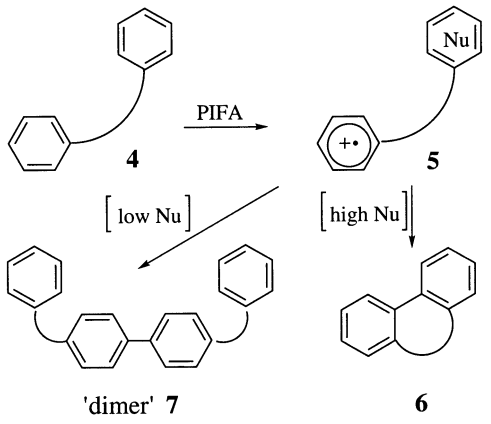


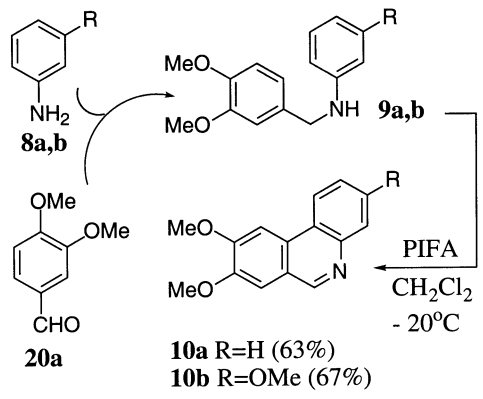
Figure 2.

2. Results and discussion

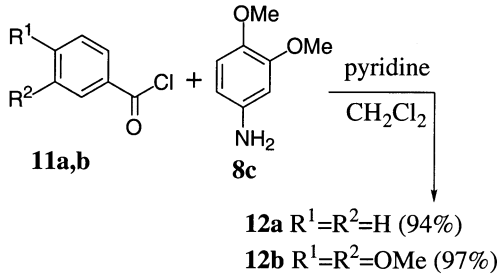
According to the general mechanistic proposal shown in Fig. 2, the success of the synthesis will probably rely on the nucleophilic character of one of the rings involved in the coupling step, and on the ease of formation of the radical cation intermediate located on the other ring. In the absence of such nucleophilic aromatic ring, dimerization processes may result (vide infra). Thus, we first checked this assumption studying the behaviour of amines **9a**,**b** and amides **12a**,**b** under oxidative cyclization conditions in the eventual formation of the corresponding phenanthridines and phenanthridinones.

Amines **9a**,**b** were easily prepared by reductive amination of veratraldehyde using aniline **8a** and *m*-anisidine **8b**, respectively (94, 97% yield). In a typical procedure, treatment of **9a**,**b** with 1.2 equiv. of PIFA, 2.4 equiv. of $BF_3{\cdot}Oet_2$ in CH_2Cl_2 at −20°C produced, after 20 min, a crude material which was purified by column chromatography (SiO_2) giving rise to phenanthridines **10a**,**b**. These results showed, firstly, that a spontaneous aromatization process accompanied the formation of the biaryl bond, as can be deduced by inspection of their ^1H NMR spectra ($\delta_{H\text{-}6}\approx 9.1$ ppm). And, secondly, that the presence of the less activated *N*-aryl ring in substrate **9a** can explain the lower yield obtained in this case with respect to **9b** (63 vs 67%) (Scheme 1).

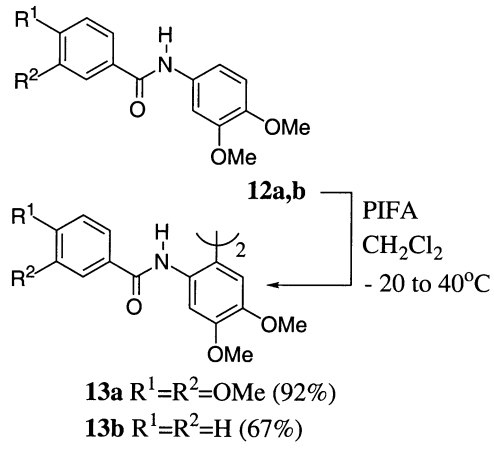
Analogously, amides **12a**,**b** were prepared from the corresponding benzoyl chloride **11a**,**b** and 3,4-dimethoxyaniline



Scheme 1.



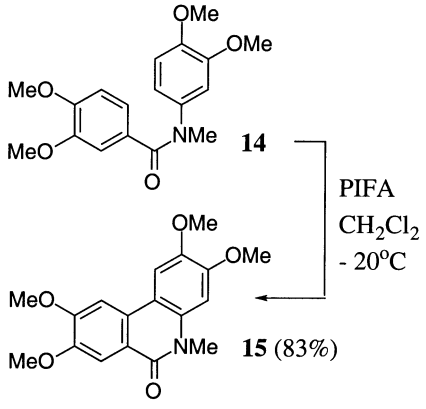
Scheme 2.



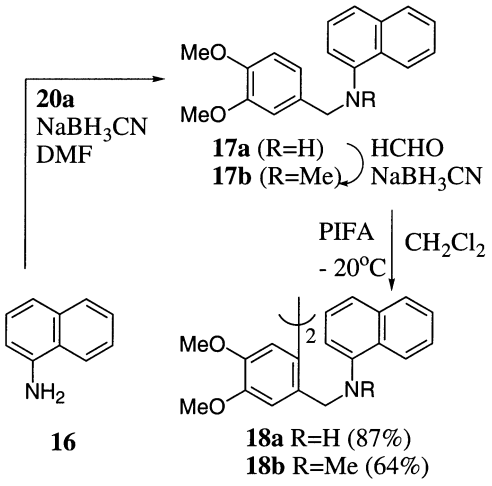
Scheme 3.

8c (which would eventually lead to substrates with a high nucleophilic ring), and submitted to the typical cyclization conditions. However, in this case, dimerization instead of intramolecular biaryl bond formation was the only process observed even under variable temperature conditions (−20 to +40°C). These results can be explained in terms of stabilization of amides **12** in a *trans* conformation which hinders the proximity of both rings needed for the desired intramolecular coupling (Schemes 2 and 3).[17]

In order to circumvent this obstacle, amide **12a** was transformed into the corresponding *N*-methyl derivative **14** (NaH, MeI, THF) to ensure the required conformation. As planned, when oxidative conditions were applied, the expected phenanthridinone **15** was obtained in very good yield (83%) (Scheme 4).



Scheme 4.



Scheme 5.

We next moved to our second objective, namely, the formation of benzo[*c*]phenanthridines, benzo[*c*]phenanthridinones and partially hydrogenated derivatives by using the expressed methodology. Therefore, amine **17a** was prepared as shown in Scheme 5 using naphthylamine **16** and veratraldehyde **20a**, and then *N*-alkylated to render amine **17b**. When both substrates were submitted to our PIFA mediated cyclization conditions, dimers **18a**,**b** were the only products identified (87 and 64% yield, respectively), even when the experiments were run under high dilution conditions. The higher nucleophilicity of the 3,4-dimethoxybenzene ring over the naphthalene system can be argued to explain the more favoured intermolecular dimerization reaction.

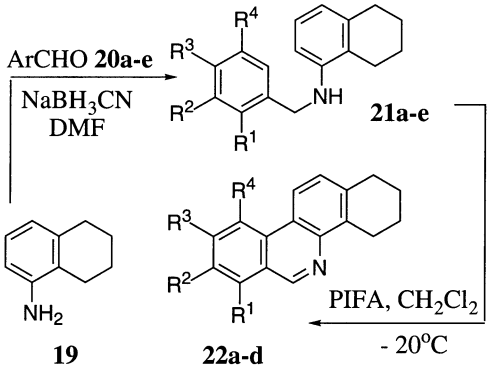
Partially hydrogenated precursors, which eventually would give rise to a more nucleophilic pattern, were prepared using 5,6,7,8-tetrahydronaphthylamine **19** and several aromatic aldehydes **20a**–**e**, and the resulting amines **21a**–**e** were treated with PIFA under the typical conditions. As expected, in all cases under study, the corresponding tetrahydrobenzo[*c*]phenanthridines **22a**–**d** were obtained in very good overall yields (see Table 1) except for **21e**. This is in agreement with previous results from our group indicating that, at least, two methoxy groups are needed for a radical cation to be formed.[18] It should be emphasized that yields are not affected by steric crowding, as could be expected in entry 4 due to the presence of a bulky methoxy group *ortho* to the coupling position (Scheme 6).[19]

In order to accomplish the synthesis of partially hydrogenated benzo[*c*]phenanthridinones of type **24** 5,6,7,8-tetra-

Table 1. Series of benzophenanthridines **22a**–**e** prepared from amines **21a**–**e**

Entry	Substrate	Product	R^1	R^2	R^3	R^4	Yield (%)[a]
1	**21a**	**22a**	H	OMe	OMe	H	77
2	**21b**	**22b**	H	OCH_2O		H	60
3	**21c**	**22c**	OMe	OMe	OMe	H	74
4	**21d**	**22d**	H	OMe	OMe	Ome	73
5	**21e**	**22e**	H	OMe	H	H	<5[b]

[a] Yield for crystallized product (Et_2O).
[b] Not isolated, detected by GC–MS.



Scheme 6.

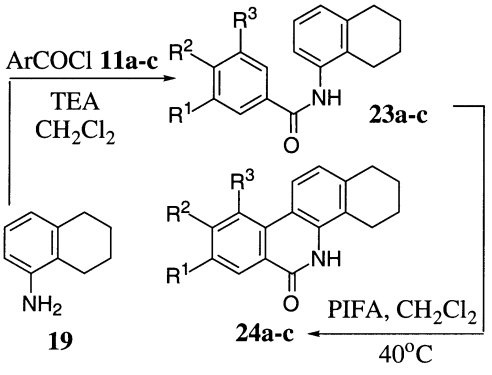
hydronaphthylamine **19** was benzoylated with a series of substituted benzoyl chlorides **11a**–**c**, and the resulting amides **23a**–**c** were submitted to the cyclization conditions affording the results enlisted in Table 2. Amides **23a** and **23c** afforded nicely (69 and 63% yield) the corresponding tetracycle **24a** and **24c**, respectively, provided the reaction temperature was rised to dichloromethane reflux. Otherwise, the starting materials were recovered completely unchanged. These results can be explained considering that, conversely to amides **12**, the energetic barrier between both rotamers in amides **23a** and **23c** can be easily overcome at high temperature (40°C). On the other hand, amide **23b** resulted in a complex mixture of unidentified products. Related reports also show the lability of the methylendioxy group under similar oxidative reaction conditions.[20] To the view of these results, the reason of the successful transformation of the methylendioxy substituted amine **21b** into phenanthridine **22b** is unclear (Schemes 7 and 8).

Finally, amides **25a**,**b** were also tested under the same

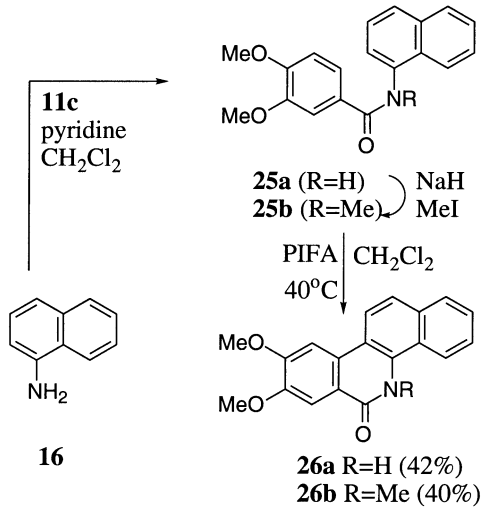
Table 2. Series of benzophenanthridinones **24a**–**c** prepared from amides **23a**–**c**

Entry	Substrate	Product	R^1	R^2	R^3	Yield (%)
1	**23a**	**24a**	OMe	OMe	H	69[a]
2	**23b**	**24b**	OCH_2O		H	–[b]
3	**23c**	**24c**	OMe	OMe	OMe	63[c]

[a] Yield for crystallized product (Et_2O).
[b] Complex mixture of unidentified products.
[c] Yield for crystallized product (hexanes).



Scheme 7.



Scheme 8.

cyclization conditions. Amide **25a** was prepared by benzoylation of 1-naphthylamine, and then *N*-methylated to ensure, if necessary, that the resulting derivative **25b** will adopt the required conformation for the projected intramolecular cyclization. In both cases, when oxidative conditions were applied at solvent reflux temperature, the corresponding benzo[*c*]phenanthridinones **26a**,**b** were obtained in moderate yield (42–40%). Unlike amines **17**, no dimers were detected in this final experiment, which can be explained considering that the carbonyl group in amides **25** deactivates the ring and prevents it from an intermolecular nucleophilic attack, favouring the target heterocyclization.[21]

3. Conclusion

Novel applications of hypervalent iodine chemistry have been described. The formation of the benzo[*c*]phenanthridine skeleton by final closure of ring C has been accomplished in very few steps and with good overall yields. The reaction takes place under mild conditions through the formation of a radical cation intermediate which is trapped by an arylic nucleophile in an internal fashion. Conversely, low nucleophilic aryl rings do not react and dimers are formed.

For the construction of the benzo[*c*]phenanthridinone derivatives higher (rt or solvent reflux) temperatures are required to ensure the proper *cis* conformation of the rotamers in the starting amides. However, for the preparation of simple phenanthridinone, as in **15**, *N*-methylated precursors are required.

4. Experimental[22]

4.1. General procedure for the synthesis of benzylamines 9, 17 and 21

A mixture of the aromatic amine (1.2 mmol) and the corresponding aldehyde (1 mmol) was dissolved in DMF (5 mL) and acetic acid (0.05 mL) was added to the solution. After 1 h, $NaBH_3CN$ (5 mmol) was added at 0°C and the mixture was stirred at rt until complete conversion of the starting material (TLC, 12–18 h). Then, EtOAc (15 mL) was added and the mixture was washed with water (3×15 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was crystallized from diethyl ether yielding the corresponding benzylamines.

4.1.1. *N*-Phenyl-3,4-dimethoxybenzylamine (9a). (94%) Mp 69–71°C (Et_2O); ^1H NMR ($CDCl_3$) 3.88 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.98 (br s, 1H, NH), 4.26 (s, 2H, NCH_2), 6.65 (d, J=8.7 Hz, 1H, H_{arom}), 6.71–6.76 (m, 2H, H_{arom}), 6.82–6.94 (m, 3H, H_{arom}), 7.16–7.23 (m, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 48.2, 55.8, 55.9, 110.6, 111.0, 112.8, 117.5, 119.2, 131.8, 148.1, 149.0; IR (KBr) ν 3366, 2935, 1602, 1515 cm^{-1}; MS (EI) *m/z* (rel. intensity) 243 (M^+, 21), 151 (100); Anal. Calcd for $C_{15}H_{17}NO_2$: C: 74.05, H: 7.04, N: 5.76. Found C: 74.02, H: 7.01, N: 5.79.

4.1.2. *N*-(3-Methoxyphenyl)-3,4-dimethoxybenzylamine (9b). (97%) Mp 78–80°C (Et_2O); ^1H NMR ($CDCl_3$) 3.76 (s, 3H, OCH_3), 3.88 (s, 6H, 2×OCH_3), 3.97 (br s, 1H, NH), 4.24 (s, 2H, NCH_2), 6.21–6.31 (m, 3H, H_{arom}), 6.81–6.90 (m, 3H, H_{arom}), 7.06–7.12 (m, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 48.1, 55.0, 55.7, 55.8, 98.7, 102.5, 105.9, 110.6, 111.0, 119.6, 129.9, 131.6, 148.1, 149.0, 149.5, 160.7 (C_{arom}) IR (KBr) ν 3377, 2936, 1609, 1512 cm^{-1}; MS (EI) *m/z* (rel. intensity) 243 (21), 151 (100); Anal. Calcd for $C_{16}H_{19}NO_3$: C: 70.31, H: 7.01, N: 5.12. Found C: 70.32, H: 6.98, N: 5.14.

4.1.3. *N*-(1-Naphthyl)-3,4-dimethoxybenzylamine (17a). (89%) Mp 124–126°C (Et_2O); ^1H NMR ($CDCl_3$) 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.43 (s, 2H, NCH_2), 4.63 (br s, 1H, NH), 6.65 (d, J=7.5 Hz, 1H, H_{arom}), 6.87 (d, J=8.5 Hz, 1H, H_{arom}), 6.96–7.06 (m, 2H, H_{arom}), 7.28–7.50 (m, 4H, H_{arom}), 7.77–7.84 (m, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 48.4, 55.6, 104.5, 110.3, 110.8, 111.0, 112.8, 117.5, 119.8, 124.6, 125.6, 126.5, 128.6, 131,4, 134.1, 143.2, 148.2, 149.0; IR (KBr) ν 3044, 2932, 1580, 1513, 1463, 1408 cm^{-1}; MS (EI) *m/z* (rel. intensity) 293 (M^+, 21), 152 (11), 151 (100); Anal. Calcd for $C_{19}H_{19}NO_2$: C: 77.79, H: 6.53, N: 4.77. Found C: 77.76, H: 6.54, N: 4.75.

4.1.4. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4-dimethoxybenzylamine (21a). (77%) Mp 93–96°C (Et_2O); ^1H NMR ($CDCl_3$) 1.74–1.90 (m, 4H, 2×CH_2), 2.43 (t, J=5.9 Hz, 2H, CH_2), 2.77 (t, J=5.9 Hz, 2H, CH_2), 3.89 (s, 6H, 2×OCH_3), 4.29 (s, 2H, NCH_2), 6.48–6.56 (m, 2H, H_{arom}), 6.80–7.07 (m, 4H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.6, 23.0, 23.8, 30.0, 48.3, 55.7, 55.8, 107.1, 110.7, 111.0, 118.4, 119.6, 112.1, 121.0, 125.9, 131.9, 137.4, 145.5, 148.0; IR (KBr) ν 3424, 1590, 1512 cm^{-1}; MS (EI) *m/z* (rel. intensity) 297 (M^+, 24), 151 (100); Anal. Calcd for $C_{19}H_{23}NO_2$: C: 76.73, H: 7.80, N: 4.71. Found C: 76.69, H: 7.82, N: 4.70.

4.1.5. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4-methylendioxybenzylamine (21b). (73%) Mp 47–49°C (Et_2O); ^1H NMR ($CDCl_3$) 1.75–1.91 (m, 4H, 2×CH_2), 2.44 (t, J=5.9 Hz, 2H, CH_2), 2.77 (t, J=5.9 Hz, 2H, CH_2), 3.81 (br s, 1H, NH), 4.27 (s, 2H, NCH_2), 5.96 (s, 2H, OCH_2O), 6.46 (d, J=7.8 Hz, 1H, H_{arom}), 6.54 (d, J=7.5 Hz, 1H,

H_{arom}), 6.78–6.90 (m, 3H, H_{arom}), 7.03 (dd, J=7.9, 7.5 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.6, 23.0, 23.8, 30.0, 48.1, 100.9, 107.1, 108.2, 118.4, 120.6, 121.0, 133.4, 137.6, 146.6, 147.8; IR (KBr) ν 3432, 2922, 1590 cm^{-1}; MS (EI) m/z (rel. intensity) 281(M^+, 30), 250 (12), 135 (100); Anal. Calcd for $C_{18}H_{19}NO_2$: C: 76.84, H: 6.81, N: 4.98. Found C: 76.81, H: 6.84, N: 4.97.

4.1.6. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-2,3,4-trimethoxybenzylamine (21c). (71%) Mp 54–56°C (Et_2O); ^1H NMR ($CDCl_3$) 1.77–1.90 (m, 4H, 2×CH_2), 2.45 (dd, J=6.3, 5.9 Hz, 2H, CH_2), 2.79 (dd, J=5.9, 5.5 Hz, 2H, CH_2), 3.88 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 4.33 (s, 2H, NCH_2), 6.55 (d, J=7.9 Hz, 2H, H_{arom}), 6.66 (d, J=8.3 Hz, 1H, H_{arom}), 7.02–7.10 (m, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.3, 22.7, 23.3, 29.7, 42.7, 55.3, 60.2, 60.6, 106.6, 106.8, 117.8, 120.5, 124.7, 125.5, 136.8, 141.7, 154.4, 151.4, 152.6 (C_{arom}); IR (KBr) ν 3466, 2932, 1588, 1507, 1454, 1326 cm^{-1}; MS (EI) m/z (rel. intensity) 327 (M^+, 31), 296 (3), 181 (100), 166 (39); Anal. Calcd for $C_{20}H_{25}NO_3$: C: 73.37, H: 7.70, N: 4.28. Found C: 73.38, H: 7.73, N: 4.30.

4.1.7. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4,5-trimethoxybenzylamine (21d). (67%) Mp 109–111°C (Et_2O); ^1H NMR ($CDCl_3$) 1.76–1.89 (m, 4H, 2×CH_2), 2.44 (dd, J=6.3, 5.9 Hz, 2H, CH_2), 2.76 (t, J=5.9 Hz, 2H, CH_2), 3.85 (s, 3H, OCH_3), 3.86 (s, 6H, OCH_3), 4.27 (s, 2H, NCH_2), 6.48 (d, J=8.3 Hz, 1H, H_{arom}), 6.55 (d, J=7.5 Hz, 1H, H_{arom}), 6.64 (s, 2H, H_{arom}), 7.00–7.04 (m, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.6, 23.0, 23.8, 30.0, 48.9, 55.0, 60.6, 104.3, 107.1, 118.5, 121.0, 126.0, 135.3, 136.8, 137.5, 145.7, 153.3; IR (KBr) ν 3427, 2930, 1589, 1503, 1461, 1419, 1329 cm^{-1}; MS (EI) m/z (rel. intensity) 327 (21), 312 (1), 181 (100); Anal. Calcd for $C_{20}H_{25}NO_3$: C: 73.37, H: 7.70, N: 4.28. Found C: 73.33, H: 7.68, N: 4.25.

4.1.8. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3-methoxybenzylamine (21e). (63%) ^1H NMR ($CDCl_3$) 1.77–1.90 (m, 4H, 2×CH_2), 2.44 (t, J=6.3, 5.9 Hz, 2H, CH_2), 2.76 (t, J=6.3, 5.9 Hz, 2H, CH_2), 3.81 (s, 3H, OCH_3), 4.30 (s, 2H, NCH_2), 6.46 (d, J=7.8 Hz, 1H, H_{arom}), 6.53 (d, J=7.5 Hz, 1H, H_{arom}), 6.84 (dd, J=8.5, 2.0 Hz, 1H, H_{arom}), 6.95–7.04 (m, 3H, H_{arom}), 7.24–7.30 (m, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.6, 23.0, 23.7, 30.0, 48.2, 55.0, 107.1, 112.0, 118.3, 119.6, 120.9, 125.9, 129.5, 137.4, 141.2, 145.6, 159.7; IR (neat) ν 3435, 1588, 1489, 1465, 1314 cm^{-1}; MS (EI) m/z (rel. intensity) 267 (M^+, 100), 252 (5), 236 (22), 146 (73), 121 (84).

4.1.9. *N*-Methyl-*N*-(1-naphthyl)-3,4-dimethoxybenzylamine (17b). HCHO (aq. 37%, 2 mmol) was added to a solution of amine **17a** in MeCN (15 mL) and, after stirring for 30 min, $NaBH_3CN$ (5 mmol) was added at 0°C. Then, the mixture was stirred at rt for 12 h, water (15 mL) was added and extracted with CH_2Cl_2 (3×15 mL). The combined extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed (Hex:EtOAc, 1:1) yielding pure amine **17b** as an oil (78%). ^1H NMR ($CDCl_3$) 2.84 (s, 3H, NCH_3), 3.87 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.29 (s, 2H, NCH_2), 6.86–7.08 (m, 3H, H_{arom}), 7.12 (d, J=7.5 Hz, 1H, H_{arom}), 7.41–7.76 (m, 4H, H_{arom}), 7.88–7.1 (m, 1H, H_{arom}), 8.44–8,47 (m, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 41.3, 55.5, 55.6, 60.7, 110.5, 111.0, 115.5, 120.1, 122.9, 123.5, 125.1, 128.2, 128.9, 130.9, 134.6, 147.7, 148.6, 149.7; IR (neat) ν 2948, 2831, 1576, 1512, 1460, 1395 cm^{-1}; MS (EI) m/z (rel. intensity) 307 (M^+, 17), 151 (100).

4.2. General procedure for the synthesis of benzamides 12, 23 and 25a

Thionyl chloride (20 mmol) was added to a solution of the corresponding aromatic carboxylic acid (10 mmol) in CH_2Cl_2 (20 mL). The mixture was heated at reflux for 4 h. Removal of solvent in vacuo gave the corresponding aroyl chlorides **11** as a residue which, without isolation, was dissolved again in CH_2Cl_2 (20 mL). To this solution, the corresponding amine (10 mmol) and pyridine (5 mL) were added at 0°C and the mixture was stirred at rt until the conversion was complete (TLC, 10–14 h). Then, the solution was washed with saturated $CuSO_4$, the organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by crystallization to yield the following amides.

4.2.1. *N*-(3,4-Dimethoxyphenyl)-3,4-dimethoxybenzamide (12a). (97%) Mp 179–182°C (Et_2O); ^1H NMR ($CDCl_3$) 3.88 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.83–6.97 (m, 3H, H_{arom}), 7.38 (d, J=8.3 Hz, 2H, H_{arom}), 7.51 (d, J=2.3 Hz, 1H, H_{arom}), 7.72 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) 55.8, 55.9, 61.5, 62.0, 104.7, 111.1, 111.6, 115.4, 122.5, 124.6, 124.7, 126.6, 131.9, 145.5, 146.9, 152.4, 162.6; IR (KBr) ν 3325, 2937, 2834, 1663, 1605, 1513, 1473 cm^{-1}; MS (EI) m/z (rel. intensity) 317 (M^+, 31), 165 (100), 122 (14); Anal. Calcd for $C_{17}H_{19}NO_5$: C: 64.34, H: 6.03, N: 4.41. Found C: 64.32, H: 6.07, N: 4.40.

4.2.2. *N*-(3,4-Dimethoxyphenyl)benzamide (12b). (94%) Mp 170–172°C (Et_2O); ^1H NMR ($CDCl_3$) 3.87 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 6.83 (d, J=8.7 Hz, 1H, H_{arom}), 6.99 (dd, J=8.7, 2.3 Hz, 1H, H_{arom}), 7.43–7.54 (m, 3H, H_{arom}), 7.84–7.88 (m, 3H, H_{arom}); ^{13}C NMR ($CDCl_3$) 55.7, 55.9, 105.1, 111.1, 112.2, 126.9, 128.6, 131.5, 131.6, 134.8, 145.8, 148.9, 165.7; IR (KBr) ν 3354, 1649, 1513, 1449 cm^{-1}; MS (EI) m/z (rel. intensity) 257 (M^+, 49), 242 (2), 105 (100); Anal. Calcd for $C_{15}H_{15}NO_3$: C: 70.02, H: 5.88, N: 5.44. Found C: 69.99, H: 5.89, N: 5.47.

4.2.3. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4-dimethoxybenzamide (23a). (91%) Mp 163–165°C (Et_2O); ^1H NMR ($CDCl_3$) 1.80–1.87 (m, 4H, 2×CH_2), 2.68 (t, J=5.8 Hz, 2H, CH_2), 2.81 (t, J=5.8 Hz, 2H, CH_2), 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.90–6.97 (m, 2H, H_{arom}), 7.17 (t, J=7.9 Hz, 1H, H_{arom}), 7.39 (d, J=8.3 Hz, 1H, H_{arom}), 7.52 (s, 1H, H_{arom}), 7.60 (br s, 1H, NH), 7.77 (d, J=7.5, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.4, 22.8, 24.5, 29.7, 55.9, 110.2, 110.7, 119.2, 120.5, 125.8, 126.3, 127.6, 128.5, 135.4, 138.0, 149.1, 151.9, 165.2; IR (KBr) ν 3312, 1561, 1501 cm^{-1}; MS (EI) m/z (rel. intensity) 311 (M^+, 16), 165 (100), 146 (19); Anal. Calcd for $C_{19}H_{21}NO_3$: C: 73.29, H: 6.80, N: 4.50. Found C: 73.33, H: 6.82, N: 4.48.

4.2.4. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4-methylendioxybenzamide (23b). (90%) Mp 182–184°C (Et_2O); ^1H NMR ($CDCl_3$) 1.73–1.86 (m, 4H, 2×CH_2), 2.65 (t,

J=5.9 Hz, 2H, CH_2), 2.80 (t, J=5.9 Hz, 2H, CH_2), 6.05 (s, 2H, OCH_2O), 6.87 (d, J=7.9 Hz, 1H, H_{arom}), 6.93 (d, J=8.0 Hz, 1H, H_{arom}), 7.15 (dd, J=7.5, 7.0 Hz, 1H, H_{arom}), 7.36–7.42 (m, 2H, H_{arom}), 7.54 (br s, 1H, NH), 7.74 (d, J=7.9 Hz, 1H, H_{arom}); ^{13}C NMR (DMSO-d_6) 22.4, 22.7, 24.5, 29.4, 102.0, 107.8, 108.1, 122.8, 124.5, 125.3, 127.1, 128.6, 133.2, 136.3, 137.7, 147.6, 150.1, 164.6; IR (KBr) ν 3268, 1920, 1647, 1481 cm^{-1}; MS (EI) *m/z* (rel. intensity) 295 (M^+, 16), 149 (100), 146 (47), 121 (21); Anal. Calcd for $C_{18}H_{17}NO_3$: C: 73.20, H: 5.80, N: 4.74. Found C: 73.21, H: 5.79, N: 4.73.

4.2.5. *N*-[1-(5,6,7,8-Tetrahydronaphthyl)]-3,4,5-trimethoxybenzamide (23c). (94%) Mp 174–176°C (Et_2O); ^{1}H NMR ($CDCl_3$) 1.73–1.85 (m, 4H, 2×CH_2), 2.65 (t, J=5.9 Hz, 2H, CH_2), 2.79 (t, J=5.9 Hz, 2H, CH_2), 3.90 (s, 9H, 3×OCH_3), 6.95 (d, J= 7.5 Hz, 1H, H_{arom}), 7.08 (s, 2H, H_{arom}), 7.11–7.18 (m, 1H, H_{arom}), 7.63–7.67 (m, 2H, H_{arom}, NH); ^{13}C NMR ($CDCl_3$) 22.4, 22.8, 24.5, 29.7, 56.2, 60.9, 104.4, 120.7, 125.8, 126.5, 128.8, 130.5, 135.2, 138.1, 141.0, 153.2, 165.4; IR (KBr) ν 3272, 1643, 1584 cm^{-1}; MS (EI) *m/z* (rel. intensity) 341 (M^+, 15), 195 (100), 146 (19); Anal. Calcd for $C_{20}H_{23}NO_4$: C: 70.36, H: 6.79, N: 4.10. Found C: 70.40, H: 6.77, N: 4.12.

4.2.6. *N*-(1-Naphthyl)-3,4-dimethoxybenzamide (25a). (89%) Mp 143–146°C (Et_2O); ^{1}H NMR ($CDCl_3$) 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.93 (d, J=8.3 Hz, 1H, H_{arom}), 7.47–7.57 (m, 5H, H_{arom}), 7.73–7.92 (m, 3H, H_{arom}), 7.97 (d, J=7.9 Hz, 1H, H_{arom}), 8.21 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) 56.0, 110.2, 110.8, 119.5, 120.8, 121.3, 125.7, 126.3, 127.3, 127.6, 128.7, 132.5, 134.1, 149.1, 152.0, 165.9; IR (neat) ν 3295, 3053, 2932, 1642, 1597, 1402 cm^{-1}; MS (EI) *m/z* (rel. intensity) 307 (M^+, 20), 165 (100), 137 (10); Anal. Calcd for $C_{19}H_{17}NO_3$: C: 74.25, H: 5.58, N: 4.56. Found C: 74.21, H: 5.55, N: 4.53.

4.3. General procedure for the *N*-methylation of amides

MeI (8 mmol) was added to a solution of the corresponding amide in THF (20 mL). This mixture was added to a cooled (0°C) suspension of NaH (2.5 mmol) in THF (5 mL) and stirred at room temperature during 20 min until total consumption of the starting material (TLC). Then, water (20 mL) was added slowly, the organic phase was separated, and the aqueous phase was extracted with EtOAc (3×25 mL). The combined extracts were dried (Na_2SO_4) and evaporated yielding the corresponding *N*-methylamide.

4.3.1. *N*-(3,4-Dimethoxyphenyl)-*N*-methyl-3,4-dimethoxylbenzamide (14). (77%) ^{1}H NMR ($CDCl_3$) 3.31 (s, 3H, NCH_3), 3.55 (s, 3H, OCH_3), 3.58 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 6.51 (m, 4H, H_{arom}), 6.76 (m, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 38.4, 55.2, 55.3, 55.5, 109.4, 110.1, 110.6, 11.7, 118.5, 122.0, 127.6, 138.1, 147.0, 147.4, 148.7, 149.5, 169.6; IR (neat) ν 2936, 2834, 1642, 1598, 1510 cm^{-1}; MS (EI) *m/z* (rel. intensity) 331 (M^+, 31), 165 (100).

4.3.2. *N*-Methyl-*N*-(1-naphthyl)-3,4-dimethoxybenzamide (25b). (87%) Mp 104–106°C (Et_2O); ^{1}H NMR ($CDCl_3$) 3.15 (s, 3H, NCH_3), 3.42 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 6.34 (d, J=8.3 Hz, 1H, H_{arom}), 6.66 (d, J=1.6 Hz, 1H, H_{arom}), 6.85 (dd, J=8.3, 1.6 Hz, 1H, H_{arom}), 6.97 (d, J=6.7, 1H, H_{arom}), 7.15 (t, J=7.7 Hz, 1H, H_{arom}), 7.37–7.54 (m, 2H, H_{arom}), 7.59 (d, J= 8.3 Hz, 1H, H_{arom}), 7.75 (d, J=7.9 Hz, 1H, H_{arom}), 7.98 (d, J=8.3 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 32.2, 54.7, 55.1, 109.4, 110.8, 121.3, 122.3, 125.4, 125.8, 126.1, 127.0, 127.4, 127.5, 128.3, 129.6, 134.1, 141.4, 147.1, 148.6, 170.8 (C); IR (KBr) ν 3055, 3000, 2933, 2834, 1637, 1581, 1513, 1418, 1355 cm^{-1}; MS (EI) *m/z* (rel. intensity) 321 (M^+, 21), 165 (100); Anal. Calcd for $C_{20}H_{19}NO_3$: C: 74.75, H: 5.96, N: 4.36. Found C: 74.71, H: 5.94, N: 4.39.

4.4. General procedure for the oxidative coupling

A solution of PIFA (1.2 mmol) and $BF_3{\cdot}OEt_2$ (2.4 mmol) in CH_2Cl_2 (10 mL) was added to a solution of the corresponding substrate (1 mmol) in CH_2Cl_2 (15 mL) (at −20°C for amines **9**, **21** and amide **14**, and at solvent reflux for amides **12**, **23** and **25**). After 20 min, at the same temperature, the crude was allowed to rise rt, and the solvent was removed in vacuo. The residue was subjected to flash chromatography yielding the corresponding product.

4.4.1. 8,9-Dimethoxyphenanthridine (10a).[23] (63%) ^{1}H NMR ($CDCl_3$) 4.08 (s, 3H, OCH_3), 4.15 (s, 3H, OCH_3), 7.38 (s, 1H, H_{arom}), 7.65–7.72 (m, 2H, H_{arom}), 7.89 (s, 1H, H_{arom}), 8.17 (d, J=7.4 Hz, 1H, H_{arom}), 8.45 (dd, J=8.9, 7.4 Hz, 1H, H_{arom}), 9.18 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 56.0, 56.1, 101.6, 107.7, 121.5, 121.6, 121.7, 126.6, 127.8, 128.2, 129.7, 149.9, 151.4, 153.0; IR (neat) ν 2923, 1504 cm^{-1}; MS (EI) *m/z* (rel. intensity) 239 (M^+, 100), 224 (17), 196 (39).

4.4.2. 3,8,9-Trimethoxyphenanthridine (10b). (69%) ^{1}H NMR ($CDCl_3$) 3.97 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 7.24–7.30 (m, 2H, H_{arom}), 7.54 (d, J=2.3 Hz, 1H, H_{arom}), 7.75 (s, 1H, H_{arom}), 8.30 (d, J=9.1 Hz, 1H, H_{arom}), 9.09 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 55.5, 56.0, 56.1, 101.2, 107.6, 109.4, 117.9, 122.9, 149.2, 127.3, 128.6, 130.9, 145.3, 151.9, 153.1, 159.4; IR (neat) ν 2924, 1616, 1501 cm^{-1}; MS (EI) *m/z* (rel. intensity) 269 (M^+, 100), 254 (36), 226 (22).

4.4.3. 2,2′-Bis-[4,5-dimethoxy-*N*-(3,4-dimethoxybenzoyl)]-aniline (13a). (92%) Mp 244–246°C (Et_2O); ^{1}H NMR ($CDCl_3$) 3.83 (s, 6H, 2×OCH_3), 3.86 (s, 12H, 4×OCH_3), 4.00 (s, 6H, 2×OCH_3), 6.78 (d, J=8.3 Hz, 2H, H_{arom}), 6.81 (s, 2H, H_{arom}), 7.01 (dd, J=8.3, 1.8 Hz, 2H, H_{arom}), 7.15 (d, J=1.8 Hz, 2H, H_{arom}), 7.78 (s, 2H, 2×NH), 8.23 (s, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 55.7, 55.9, 56.0, 105.3, 109.6, 111.4, 112.7, 118.7, 119.4, 126.5, 129.8, 145.7, 148.9, 152.0, 164.8; Anal. Calcd for $C_{34}H_{36}N_2O_{10}$: C: 64.55, H: 5.74, N: 4.43. Found C: 65.59, H: 5.71, N: 4.39.

4.4.4. 2,2′-Bis-(4,5-dimethoxy-*N*-benzoyl)aniline (13b). (67%) Mp 135–137°C (Et_2O); ^{1}H NMR ($CDCl_3$) 3.82 (s, 6H, 2×OCH_3), 3.96 (s, 6H, 2×OCH_3), 6.78 (s, 2H, H_{arom}), 7.32–7.72 (m, 10H, H_{arom}), 7.91 (br s, 2H, 2×NH), 8.05 (s, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 56.0, 56.1, 106.4, 112.6, 126.7, 128.7, 129.4, 131.8, 134.1, 146.1, 149.1, 165.6; IR (KBr) ν 3311, 2934, 1648, 1517 cm^{-1}. Anal. Calcd for $C_{30}H_{28}N_2O_6$: C: 76.30, H: 5.51, N: 5.47. Found C: 76.28, H: 5.48, N: 5.50.

4.4.5. 5-Methyl-2,3,8,9-tetramethoxyphenanthridin-6-one (15). (83%) Mp 189–191°C (Et_2O); ^1H NMR ($CDCl_3$) 3.77 (s, 3H, NCH_3), 4.01 (s, 9H, 3×OCH_3), 4.07 (s, 3H, OCH_3), 6.78 (s, 1H, H_{arom}), 7.29, (s, 1H, H_{arom}), 7.41 (s, 1H, H_{arom}), 7.83 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 30.1, 56.0, 56.1, 56.5, 98.4, 101.7, 104.9, 108.9, 111.7, 118.5, 128.1, 132.3, 144.9, 148.9, 150.0, 153.0, 161.3; IR (KBr) ν 2916, 1614, 1580, 1505 cm^{-1}; MS (EI) *m/z* (rel. intensity) 329 (M^+, 100), 314 (44), 286 (46); Anal. Calcd for $C_{18}H_{19}NO_5$: C: 65.64, H: 5.81, N: 4.25. Found C: 65.66, H: 5.79, N: 4.22.

4.4.6. 2,2′-Bis-[4,5-dimethoxy-*N*-(1-naphthyl)]benzylamine (18a). (87%) ^1H NMR ($CDCl_3$) 3.92 (s, 12H, 4×OCH_3), 4.49 (s, 4H, 2×NCH_2), 4.71 (br s, 2H, 2×NH), 6.78 (d, *J*=7.5 Hz, 2H, H_{arom}), 6.91 (d, *J*=8.7 Hz, 2H, H_{arom}), 7.05–7.07 (m, 4H, H_{arom}), 7.23–7.49 (m, 8H, H_{arom}), 7.91 (d, *J*=8.3 Hz, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 48.7, 55.9, 56.2, 104.4, 111.0, 111.1, 119.9, 120.0, 123.2, 124.5, 125.6, 127.6, 128.5, 128.9, 131.6, 142.7, 148.3, 149.1; IR (neat) ν 3411, 2931, 1676, 1586, 1512 cm^{-1}; MS (EI) *m/z* (rel. intensity) 584 (M^+, 35), 433 (11), 151 (100).

4.4.7. 2,2′-Bis-[4,5-dimethoxy-*N*-methyl-*N*-(1-naphthyl)]benzylamine (18b). (64%) ^1H NMR ($CDCl_3$) 3.37 (s, 6H, 2×NCH_3), 3.65 (s, 6H, 2×OCH_3), 3.71 (s, 6H, 2×OCH_3), 4.75 (s, 2×NCH_2), 6.55 (d, *J*=8.5 Hz, 2H, H_{arom}), 6.70–6.73 (m, 4H, H_{arom}), 7.37–7.57 (m, 8H, H_{arom}), 7.73–7.82 (m, 2H, H_{arom}), 8.33 (d, *J*=7.5 Hz, 2H, H_{arom}); ^{13}C NMR ($CDCl_3$) 42.3, 55.5, 55.7, 62.6, 110.5, 113.0, 121.4, 122.9, 123.4, 124.7, 126.7, 126.9, 127.7, 128.9, 134.4, 148.5, 149.5; IR (neat) ν 2926, 1593, 1571 cm^{-1}

4.4.8. 8,9-Dimethoxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridine (22a). (77%) Mp 149–151°C (Et_2O); ^1H NMR ($CDCl_3$) 1.90–1.99 (m, 4H, 2×CH_2), 2.97 (t, *J*=5.8 Hz, 2H, CH_2), 3.40 (t, *J*=5.9 Hz, 2H, CH_2), 4.06 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 7.32 (s, 1H, H_{arom}), 7.33 (d, *J*=8.5 Hz, 1H, H_{arom}), 7.84 (s, 1H, H_{arom}), 8.19 (d, *J*=8.5 Hz, 1H, H_{arom}), 9.14 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.9, 23.1, 25.3, 30.1, 55.9, 56.0, 101.5, 107.3, 118.5, 128.3, 121.2, 121.3, 128.5, 135.3, 136.6, 142.3, 149.9, 150.0, 152.6; IR (neat) ν 2930, 1613, 1444 cm^{-1}; MS (EI) *m/z* (rel. intensity) 293 (M^+, 100), 278 (33); Anal. Calcd for $C_{19}H_{19}NO_2$: C: 77.79, H: 6.53, N: 4.77. Found C: 77.82, H: 6.50, N: 4.74.

4.4.9. 8,9-Methylendioxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridine (22b). (60%) Mp 127–129°C (Et_2O); ^1H NMR ($CDCl_3$) 1.91–1.95 (m, 4H, 2×CH_2), 2.97 (t, *J*=5.6 Hz, 2H, CH_2), 3.39 (t, *J*=5.6 Hz, 2H, CH_2), 6.15 (s, 2H, OCH_2O), 7.32 (s, 1H, H_{arom}), 7.36 (d, *J*=8.5 Hz, 1H, H_{arom}), 7.89 (s, 1H, H_{arom}), 8.14 (d, *J*=8.5 Hz, 1H, H_{arom}), 9.10 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.9, 25.4, 29.7, 30.1, 99.8, 101.7, 105.2, 107.1, 108.3, 118.9, 122.5, 128.5, 135.5, 147.7, 150.2, 151.3; IR (neat) ν 2918, 1465, 1438, 1390 cm^{-1}; MS (EI) *m/z* (rel. intensity) 377 (M^+, 100), 262 (47); Anal. Calcd for $C_{18}H_{15}NO_2$: C: 77.96, H: 5.45, N: 5.05. Found C: 77.98, H: 5.41, N: 5.09.

4.4.10. 7,8,9-Trimethoxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridine (22c). (74%) Mp 143–145°C (Et_2O); ^1H NMR ($CDCl_3$) 1.94–1.96 (m, 4H, 2×CH_2), 2.98 (t, *J*=5.5 Hz, 2H, CH_2), 3.41 (t, *J*=5.5 Hz, 2H, CH_2), 4.01 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 7.36 (d, *J*=8.5 Hz, 1H, H_{arom}), 7.66 (s, 1H, H_{arom}), 8.20 (d, *J*=8.5 Hz, 1H, H_{arom}), 9.52 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.9, 23.1, 25.4, 30.1, 56.1, 61.3, 62.1, 97.6, 118.9, 128.3, 116.0, 120.9, 130.7, 135.5, 137.5, 140.7, 146.0, 150.2 156.8; IR (neat) ν 2923, 2849, 1602, 1474, 1369, 1260 cm^{-1}; MS (EI) *m/z* (rel. intensity) 323 (M^+, 100), 208 (19); Anal. Calcd for $C_{20}H_{21}NO_3$: C: 74.28, H: 6.55, N: 4.33. Found C: 74.30, H: 6.56, N: 4.31.

4.4.11. 8,9,10-Trimethoxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridine (22d). (73%) Mp 137–140°C (Et_2O); ^1H NMR ($CDCl_3$) 1.91–1.99 (m, 4H, 2×CH_2), 2.99 (t, *J*=5.9 Hz, 2H, CH_2), 3.40 (t, *J*=5.9 Hz, 2H, CH_2), 4.01 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 7.25 (s, 1H, H_{arom}), 7.40 (d, *J*=8.9 Hz, 1H, H_{arom}), 9.11 (d, *J*=8.9 Hz, 1H, H_{arom}), 9.19 (s, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.9, 23.2, 25.6, 30.0, 56.1, 60.4, 61.3, 105.0, 122.2, 128.9, 121.2, 123.0, 123.5, 134.7, 136.9, 142.0, 146.4, 150.7, 151.2, 152.9; IR (neat) ν 2929, 2852, 1605, 1595, 1482, 1466, 1397 cm^{-1}; MS (EI) *m/z* (rel. intensity) 323 (M^+, 100), 208 (25); Anal. Calcd for $C_{20}H_{21}NO_3$: C: 74.28, H: 6.55, N: 4.33.Found C: 74.32, H: 6.52, N: 4.30.

4.4.12. 8,9-Dimethoxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridin-6-one (24a). (69%) Mp 171–173°C (Et_2O); ^1H NMR ($CDCl_3$) 1.82–2.17 (m, 4H, 2×CH_2), 2.74 (t, *J*=6.0 Hz, 2H, CH_2), 2.88 (t, *J*=6.0 Hz, 2H, CH_2), 4.04 (s, 3H, OCH_3), 4.10 (s, 3H, OCH_3), 7.03 (d, *J*= 8.3 Hz, 1H, H_{arom}), 7.59 (s, 1H, H_{arom}), 7.86 (s, 1H, H_{arom}), 7.88 (d, *J*=8.3 Hz, 1H, H_{arom}), 8.60 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6) 21.9, 22.5, 23.4, 24.6, 55.7, 55.8, 93.6, 109.3, 112.0, 119.7, 121.1, 129.0, 132.8, 148.3, 149.1, 151.3, 153.5, 159.9; IR (KBr) ν 3170, 2918, 1636, 1604 cm^{-1}; MS (EI) *m/z* (rel. intensity) 309 (M^+, 100), 294 (32); Anal. Calcd for $C_{19}H_{19}NO_3$: C: 73.77, H: 6.19, N: 4.53. Found C: 73.70, H: 6.23, N: 4.50.

4.4.13. 8,9,10-Trimethoxy-1,2,3,4-tetrahydrobenzo[*c*]phenanthridin-6-one (24c). (63%) Mp 220–222°C (Hexanes); ^1H NMR ($CDCl_3$) 1.82–1.88 (m, 2H, CH_2), 1.96–2.08 (m, 2H, CH_2), 2.76 (t, *J*=6.1 Hz, 2H, CH_2), 2.88 (t, *J*=6.1 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 7.03 (d, *J*=8.7 Hz, 1H, H_{arom}), 7.86 (s, 1H, H_{arom}), 8.61 (br s, 1H, NH), 8.84 (d, *J*=8.7 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 22.2, 22.7, 23.7, 29.9, 56.1, 60.4, 61.2, 105.3, 107.2, 116.0, 122.1, 122.6, 124.1, 125.2, 138.4, 148.3, 151.5, 153.0, 162.2; IR (neat) ν 2925, 1652, 1598 cm^{-1}; MS (EI) *m/z* (rel. intensity) 339 (M^+, 100), 324 (54), 212 (38); Anal. Calcd for $C_{20}H_{21}NO_4$: C: 70.78, H: 6.24, N: 4.13. Found C: 70.81, H: 6.19, N: 4.52.

4.4.14. 8,9-Dimethoxybenzo[*c*]phenanthridin-6-one (26a). (42%) Mp >300°C (Hexanes) ^1H NMR ($CDCl_3$) 4.00 (s, 3H, OCH_3), 4.09 (s, 3H, OCH_3), 7.04 (d, *J*=8.5 Hz, 1H, H_{arom}), 7.35 (m, 1H, H_{arom}), 7.48 (d, *J*=8.5 Hz, 1H, H_{arom}), 7.65 (m, 1H, H_{arom}), 7.83 (s, 1H, H_{arom}), 7.91 (s, 1H, H_{arom}), 7.97 (dd, *J*=8.3, 2.0 Hz, 1H, H_{arom}), 8.72 (dd, *J*=8.3, 0.6 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 56.0, 56.1, 109.9, 111.0, 112.2, 120.1, 120.9, 122.5, 125.5, 126.3, 126.9, 127.5, 130.9, 135.9, 137.7, 147.3, 149.2, 151.7, 162.8; IR (KBr) ν 2954, 1667, 1496 cm^{-1}; MS (EI) *m/z* (rel. intensity) 305 (M^+, 100), 290 (11), 262 (29), 152 (12), 115 (15). Anal. Calcd for

$C_{19}H_{15}NO_3$: C: 74.74, H: 4.95, N: 4.59. Found C: 74.76, H: 4.92, N: 4.55.

4.4.15. 5-Methyl-9,10-dimethoxybenzo[*c*]phenanthridin-6-one (26b). (40%) Mp >300°C (Hexanes) ^{1}H NMR ($CDCl_3$) 3.99 (s, 3H, NCH_3), 4.07 (s, 3H, OCH_3), 4.18 (s, 3H, OCH_3), 7.26–7.60 (m, 5H, H_{arom}), 8.00 (s, 1H, H_{arom}), 8.23 (s, 1H, H_{arom}), 8.49 (d, J=8.7 Hz, 1H, H_{arom}); ^{13}C NMR ($CDCl_3$) 41.5, 56.3, 102.8, 108.6, 116.6, 119.7, 122.0, 124.7, 125.0, 125.7, 126.5, 127.2, 128.2, 133.6, 134.0, 135.8, 150.0, 153.6, 164.1; IR (KBr) ν 2943, 1629, 1607, 1508 cm^{-1}; Anal. Calcd for $C_{20}H_{17}NO_3$: C: 75.22, H: 5.37, N: 4.39. Found C: 75.19, H: 5.34, N: 4.42.

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