## A Simple General Approach to Phenanthridinones via Palladium-Catalyzed Intramolecular Direct Arene Arylation

Roberta Bernini,<sup>a</sup> Sandro Cacchi,<sup>\*b</sup> Giancarlo Fabrizi,<sup>b</sup> Alessio Sferrazza<sup>a</sup>

- <sup>a</sup> Dipartimento A.B.A.C., Università della Tuscia e Consorzio Universitario 'La Chimica per l'Ambiente', Via S. Camillo De Lellis, 01100 Viterbo, Italy
- <sup>b</sup> Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università degli Studi 'La Sapienza', P.le A. Moro 5, 00185 Rome, Italy

Fax +39(06)49912780; E-mail: sandro.cacchi@uniroma1.it

Received 21 November 2007

**Abstract:** Phenanthridinone derivatives have been prepared in good to high yields via palladium-catalyzed cyclization of readily available *N*-benzyl-*N*-benzoyl-*o*-iodoanilides.

Key words: phenanthridinones, *o*-iodoanilides, cyclization, palladium, arene arylation

Direct arylation of arenes through C–H bond cleavage with arylmetals, usually formed in situ, has recently attracted considerable attention as a mean to achieve clean and economically convenient preparations of polyaryl units.<sup>1</sup> Palladium, rhodium, and ruthenium catalysis have been used in this chemistry,<sup>1a</sup> which has undergone significant advances of late. Palladium-catalyzed C–H activation processes have provided some of the most general arylation methods.<sup>2–4</sup>

In this context, and as part of a program devoted to the conversion of carboxylic acids present in agricultural byproducts<sup>5</sup> into more complex fine chemicals by transitionmetal-catalyzed transformations, we decided to explore a general palladium-catalyzed synthesis of phenanthridinones, a class of compounds which exhibit interesting biological activities,<sup>6</sup> from *o*-iodoanilides **1** through a direct intramolecular arylation at one of the positions ortho to the electron-withdrawing C=O group (Scheme 1).

Known palladium-catalyzed approaches to the construction of the phenanthridinone frame are based on the intramolecular cyclization of *N*-(*o*-halobenzoyl)- or *N*-(*o*triflyloxybenzoyl)anilides,<sup>7</sup> a domino process (including aryl–aryl coupling between two *o*-bromobenzamide units and C–N bond formations concomitant with a deamidation reaction),<sup>8</sup> a one-pot consecutive aryl–aryl and *N*-aryl coupling from iodoarenes bearing ortho electron-releasing substituents and *o*-bromobenzamides,<sup>9</sup> and an Ullmann cross-coupling/reductive cyclization sequence from 1-bromo-2-nitrobenzene and its derivatives with a range of  $\alpha$ -haloenals, -enones or -esters.<sup>10</sup> The palladium-catalyzed cyclization of *N*-(*o*-iodophenyl)benzanilides was also reported. However, the study was limited to investigating the effect of oxygen substituents in the meta posi-

SYNTHESIS 2008, No. 5, pp 0729–0738 Advanced online publication: 08.02.2008 DOI: 10.1055/s-2008-1032169; Art ID: Z27107SS © Georg Thieme Verlag Stuttgart · New York



Scheme 1



Figure 1 By-products obtained in the Pd-catalyzed cyclization of 1a to 2a

tion of the benzoyl fragment on the regiochemistry of the arene arylation.<sup>11</sup> Because of our own current interest in this type of cyclization process, we have explored the scope and limitations of this chemistry and wish now to report the results of this study.

Compounds 1 can be readily prepared from *o*-iodoanilines and activated carboxylic acids in excellent yields. The cyclization of 1a ( $R^1 = R^2 = H$ ) was studied as a model system for optimizing the formation of phenanthridinones. Some of the results of our screening studies are summarized in Table 1.

Using 1 mol%  $Pd_2(dba)_3$  as the Pd(0) source,  $CsOAc^{2e}$  or  $Bu_4OAc$  as bases, and monodentate and bidentate phosphine ligands such as PPh<sub>3</sub>, dppm, dppp, and Xanthphos afforded phenanthridinone **2a** in low yields (Table 1, entries 1–6). One common by-product that we identified, along with variable amounts of the reduction product **5a**,<sup>12,13</sup> was the benzoxazole **6a** (Figure 1), very likely derived from the intramolecular palladium-catalyzed C–O bond-forming reaction involving the amide oxygen and the ortho-iodo fragment.<sup>14</sup>

Using dppe as ligand and CsOAc or  $K_2CO_3$  as base gave **2a** in 50% and 52% yield, but **6a** was still isolated in 22% and 11% yield, respectively (Table 1, entries 7 and 10). Similar results were achieved with the Pd(OAc)<sub>2</sub>/pivalic acid combination in the presence of  $K_2CO_3$  and Davephos

Table 1 Reaction Conditions for the Cyclization of 1a to 2a<sup>a</sup>

Entry	[Pd]	Phosphine ligand <sup>b</sup>	Base	Additive	Solvent	Temp (°C)	Time (h)	Yield of <b>2a</b> (%) <sup>c</sup>	Yield of <b>6a</b> (%) <sup>c</sup>
1	Pd <sub>2</sub> (dba) <sub>3</sub>	PPh <sub>3</sub>	CsOAc	_	DMF	100	48	15	5
2	Pd <sub>2</sub> (dba) <sub>3</sub>	dppm	CsOAc	_	DMF	100	48	10	_
3	Pd <sub>2</sub> (dba) <sub>3</sub>	dppm	Bu <sub>4</sub> OAc	_	DMF	100	24	38	15
4	Pd <sub>2</sub> (dba) <sub>3</sub>	dppp	CsOAc	_	DMF	100	48	19	4
5	Pd <sub>2</sub> (dba) <sub>3</sub>	dppp	CsOAc	_	NMP	100	48	30	12
6	Pd <sub>2</sub> (dba) <sub>3</sub>	Xphos	CsOAc	_	DMF	100	48	11	_
7	Pd <sub>2</sub> (dba) <sub>3</sub>	dppe	CsOAc	_	DMF	100	24	50	22
8	Pd <sub>2</sub> (dba) <sub>3</sub>	dppe	CsOAc	_	NMP	100	48	41	19
9	Pd <sub>2</sub> (dba) <sub>3</sub>	dppe	t-BuONa	_	toluene	100	48	_	_
10	Pd <sub>2</sub> (dba) <sub>3</sub>	dppe	K <sub>2</sub> CO <sub>3</sub>	_	DMF	100	48	52	11
11	$Pd(OAc)_2$	Davephos	Na <sub>2</sub> CO <sub>3</sub> <sup>d</sup>	<i>t</i> -BuCO <sub>2</sub> H	NMP	120	16	51	11
12	$Pd(OAc)_2$	Davephos	$K_2 CO_3^{\ d}$	<i>t</i> -BuCO <sub>2</sub> H	NMP	120	12	46	16
13	$Pd(OAc)_2$	Davephos	$K_2 CO_3^{\ d}$	t-BuCO <sub>2</sub> H	DMA	120	12	48	17
14	$Pd(OAc)_2$	dppe	Li <sub>2</sub> CO <sub>3</sub>	_	DMF	100	24	50	_
15	$Pd(OAc)_2$	dppe	K <sub>2</sub> CO <sub>3</sub>	_	DMF	100	48	44	25
16	$Pd(OAc)_2$	dppe	Cs <sub>2</sub> CO <sub>3</sub>	_	DMF	100	8	_	61
17	$Pd(OAc)_2$	dppe	K <sub>2</sub> CO <sub>3</sub>	LiCl	DMF	100	12	55	_
18	$Pd(OAc)_2$	dppe	$K_2 CO_3^d$	LiCl	DMF	120	7	65	_

<sup>a</sup> Unless otherwise stated, reactions were carried out under argon on a 0.25 mmol scale in 4 mL of solvent using 0.01 equiv  $Pd_2(dba)_3$  or 0.05 equiv of  $Pd(OAc)_2$ , 0.02 equiv of bidentate phosphine ligand with  $Pd_2(dba)_3$  and 0.05 equiv of bidentate phosphine ligand with  $Pd_2(dba)_2$ , 2 equiv of base, 0.3 equiv of pivalic acid (when used), and 2 equiv of LiCl (when used).

<sup>b</sup> PPh<sub>3</sub> (0.04 equiv) was used.

<sup>c</sup> Yields are given for the isolated products.

<sup>d</sup> Base (2.5 equiv) was used.

(Table 1, entries 11–13), reported to have a beneficial effect on the direct arylation of simple arenes.<sup>4</sup> Switching to  $Pd(OAc)_2$  and dppe in the presence of  $Li_2CO_3$  led to a significant increase of the phenanthridinone/benzoxazole selectivity, but the same yield of **2a** was obtained (Table 1, entry 14). The utilization of  $K_2CO_3$  as the base under the same reaction conditions led to the isolation of **2a** in 44% yield combined with a poorer phenanthridinone/benzoxazole ratio (Table 1, entry 15). Somewhat surprisingly, use of  $Cs_2CO_3$  completely reversed the phenanthridinone/benzoxazole selectivity, **6a** being isolated in 61% yield. No phenanthridinone product was formed (Table 1, entry 16).

A slight increase of the yield of **2a** was observed upon addition of LiCl (Table 1, entry 17). Finally, **2a** was isolated in a satisfactory 65% yield subjecting **1a** to  $Pd(OAc)_2$ , dppe, K<sub>2</sub>CO<sub>3</sub>, and LiCl at 120 °C in DMF for seven hours (Table 1, entry 18).

However, when we applied these optimized conditions to other *o*-iodoanilides (**1b**,  $R^1 = p$ -MeO,  $R^2 = H$ ; **1c**,



 $R^1 = m$ -F;  $R^2 = H$ ; 1d,  $R^1 = m$ -MeO;  $R^2 = H$ ), the reaction mixtures were found to contain mostly very polar compounds that we did not investigate further and the corresponding phenanthridinones 2b–d were isolated in low to moderate yields (Figure 2).



Figure 2 Phenanthridinones 2b-d,d'



Figure 3 Palladium coordination to oxygen and nitrogen

Of note is that with 1d, bearing a methoxy substituent meta to the carbonyl group, the new C–C bond was formed regioselectively at the less crowded ortho position of the benzoyl moiety to give 2d. No evidence of the regioisomeric derivative 2d' was attained. This high level of regioselectivity is interesting in view of the known tendency of meta oxygen substituents to direct the formation of the C–C bond to the more crowded ortho position in this type of reaction.<sup>11</sup> Such a behavior was suggested to be due to the oxygen coordination to the palladium atom of the arylpalladium complex formed in situ via oxidative addition. The resultant intermediate 7 (Figure 2) would exert a strong directing effect on the cyclization step.

A possible explanation to account for the result obtained with **1d** is that in the presence of the NH free amide the coordination of nitrogen to palladium to afford **8** (Figure 3) is likely to prevail over oxygen coordination. As a result of the absence of the oxygen directing effect, the usual trend favoring the cyclization at the less crowded ortho position is observed and **2d** is formed regioselectively.

Though the results obtained with *N*-benzoyl-o-iodoanilides **1** might provide some useful applications, we thought that further optimization was needed to develop a generally applicable synthetically effective reaction protocol. As we felt that the free NH group could be at the origin of the unsatisfactory yields obtained with some of the o-iodoanilides that we had investigated, we turned our attention to the utilization of *N*-benzyl derivatives **3** as the starting material.

The benzyl protecting group appeared particularly suited for the purpose: it can be introduced in excellent yield via reaction of benzyl bromide with **1** (DMSO, NaH, room temperature) and can be readily and almost quantitatively removed in the presence of trifluoroacetic acid to give NH free phenanthridinones.<sup>7</sup>

Nevertheless, utilization of *N*-benzyl derivatives **3** poses a selectivity problem between the aromatic rings A and B (Scheme 2). An electrophilic aromatic substitution – a mechanism initially proposed by Miura et al.<sup>15</sup> which, since then, has been usually favored in palladium-cata-lyzed arylations<sup>2c,e,3e,16</sup> – is expected to afford the phenan-thridine derivative **9** because of the higher nucleophilicity of the ring B. A proton abstraction mechanism, as proposed by Echavarren, Maseras et al.<sup>2k,17</sup> for the intramolecular arylation of electron-poor arenes and more recently shown by Fagnou et al.<sup>3k</sup> to be operating in intermolecular palladium-catalyzed arylation of pefluorobenzenes, should give the phenanthridinone product **4**. Arene









arylation might also occur via a Heck-like mechanism involving the carbopalladation of the aromatic ring followed by the anti elimination of HPdX (or isomerization and *syn* elimination of HPdX).<sup>18</sup> However, recent work indicates that this process is rather unlikely.<sup>19</sup>

After some experimentation, we found that the desired **4a** was smoothly formed and isolated in 85% yield by subjecting **3a** ( $R^1 = R^2 = H$ ) to Pd(OAc)<sub>2</sub>, dppe, and K<sub>2</sub>CO<sub>3</sub> in DMF at 100 °C for 20 minutes. No isomeric phenanthridine **9** was observed.

Attempting to gain more insight into the factors influencing the benzoyl-to-benzyl arylation ratio in this cyclization process, we decided to explore the reaction of the N-(*m*-methoxyphenyl)methyl derivative **10**, containing an electron-donating substituent. Notably, treatment of this substrate under the above conditions afforded an approximately 84:16 phenanthridinone/phenanthridine mixture (Scheme 3).

Though only a speculative discussion is possible at this stage, the implication that can be drawn from the outcome of these reactions is that the substitution pattern of the benzyl protecting group may influence the benzoyl/benzyl selectivities through an electronic bias.

With benzyl derivatives **3** the direct intramolecular arene arylation process involves selectively one of the ortho po-

sitions of the electron-poor aryl fragment. This appears to be consistent with a cyclization controlled by the acidity of the C–H bond rather than by the nucleophilicity of the arene and proceeding through a proton abstraction mechanism. When the N-(m-methoxyphenyl)methyl derivative **10** is used as substrate, a competing cyclization at the less crowded ortho position of the electron-rich aromatic ring can take place to give the phenanthridine derivative **12**, the formation of which being compatible with an electrophilic aromatic substitution mechanism. The structure of **12** was assigned by NOESY experiments.

Having established the reaction conditions and the basic substrate requirements for the preparation of phenanthridinones, we next extended the procedure to a variety of anilides **3**. Our preparative results are summarized in Table 2. Phenanthridinones **4**, incorporating a wide range of substituents both in the benzoyl and the aniline moiety, were usually isolated in good to high yields. Some steric hindrance is tolerated (Table 2, entry 10). The presence of electron-donating groups on the benzoyl fragment, which might be expected to weaken the electron-withdrawing effect of the carbonyl group and consequently influence the benzoyl/benzyl selectivity, does not change the general trend favoring the cyclization to phenanthridinones over the formation of phenanthridines, at least with the substrates that we have investigated. For example, the cyclization of **31** which gave **41** in 57% isolated yield along with a mixture of tarry polar material (Table 2, entry 12), did not provide any evidence of a phenanthridine (or dehalogenated) product.

 Table 2
 Palladium-Catalyzed Synthesis of Phenanthridinones 4 from Anilides 3<sup>a</sup>

Entry	Anilide 3		Time (min)	Phenanthridinone 4		Yield (%) <sup>b</sup>
1	N Bn	3a	10	N-Bn	<b>4</b> a	85
2		3b	20	CI N Bn	4b	69
3	F Bn 3	3c	20	F S S S S S S S S S S S S S S S S S S S	4c	82
4	MeO N-Bn	3d	10	MeO N Bn	4d	71
5	Me <sub>2</sub> N Bn	3e	25	Me <sub>2</sub> N Bn	<b>4</b> e	72
6	Ph N Bn	3f	20	Ph Bn	4f	72
7	P P P P P P P P P P P P P P P P P P P	3g	20	F N Bn	4g	83

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Entry	Anilide <b>3</b>		Time (min)	Phenanthridinone 4		Yield (%) <sup>b</sup>
8		3h	300	CI O N-Bn	4h	61
9	MeO OMe	3i	30	MeO OMe OMe	4i	87
10	MeO Me OMe Me Me	3j	30	MeO MeO Me Me Me Me	4j	88
11	F Me Me	3k	30	F Me Me	4k	73
12	MeO Me Me	31	30	MeO Me MeO	41	57
13	Ph N Bn N B	3m	30	Ph N Bn Me	4m	77
14	CI N Bn	3n	20	CI N Bn Me	4n	75
15	F COMe	30	30	F COMe	40	82

 Table 2
 Palladium-Catalyzed Synthesis of Phenanthridinones 4 from Anilides 3<sup>a</sup> (continued)

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 Table 2
 Palladium-Catalyzed Synthesis of Phenanthridinones 4 from Anilides 3<sup>a</sup> (continued)



<sup>a</sup> Reactions were carried out on a 0.25 mmol scale under an argon atmosphere at 100 °C in 3 mL of DMF using 0.05 equiv of Pd(OAc)<sub>2</sub>, 0.05 equiv of dppe and 2 equiv of  $K_2CO_3$ .

<sup>b</sup> Yields are given for isolated products.



#### Scheme 4

NH free phenanthridinones **2** can be readily obtained from the *N*-benzyl derivatives **4** by treatment with trifluoroacetic acid.<sup>7</sup> As an example, **2a** was isolated in 95% yield upon treatment of **4a** with trifluoroacetic acid at 100 °C for 24 hours (Scheme 4).

In conclusion, we have demonstrated that readily available *N*-benzyl derivatives of *N*-benzoyl-*o*-iodoanilides can be converted into the corresponding phenanthridinones usually in good to high yields, providing a simple approach to this class of compounds. The scope of this transformation seems to be rather broad. The benzyl protecting group can be almost quantitatively removed by treatment with trifluoroacetic acid and does not interfere with the desired cyclization to phenanthridinones. Overall, this procedure complements other palladium-based strategies for phenanthridinone formation which require N-(*o*-halobenzoyl)- or N-(*o*-triflyloxybenzoyl)anilides as substrates.

Melting points were determined with a Büchi B-545 apparatus and are uncorrected. All of the reagents, catalysts and solvents are commercially available and were used as purchased, without further purification. Reaction products were purified on axially compressed columns, packed with 25–40  $\mu$ m silica gel (Macherey Nagel), connected to a Gilson solvent delivery system and to a Gilson refractive index detector, and eluting with *n*-hexane–EtOAc mixtures. <sup>1</sup>H NMR spectra (400 MHz) and <sup>13</sup>C NMR spectra (100.6 MHz) were recorded with a Bruker Avance 400 spectrometer. IR spectra were recorded with a Jasco FT/IR-430 spectrometer. Mass spectra were recorded with a Shimadzu GC-MS QP-2010S spectrometer.

# *N*-Benzylphenanthridinone (4a) from *N*-Benzyl-*N*-Benzoyl-*o*-iodoanilide (3a); Typical Procedure

To a solution of **3a** (103 mg, 0.25 mmol) in DMF (3 mL) were added Pd(OAc)<sub>2</sub> (2.8 mg, 0.0125 mmol), dppe (5.1 mg, 0.0125 mmol), and K<sub>2</sub>CO<sub>3</sub> (69 mg, 0.5 mmol) under argon. The mixture was stirred at 100 °C for 30 min. After this time, the mixture was cooled, diluted with Et<sub>2</sub>O (100 mL), and washed with aq 2 N HCl (2 × 10 mL) and brine (10 mL). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure. The residue was purified by chromatography (silica gel, 90:10 *n*-hexane–EtOAc); yield: 61 mg (85%); white solid; mp 112–113 °C.

IR (KBr): 1650, 1489, 752, 723 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 8.66$  (d, J = 7.4 Hz, 1 H), 8.31 (t, J = 7.9 Hz, 2 H), 7.79 (t, J = 8.2 Hz, 1 H), 7.65 (t, J = 8.4 Hz, 1 H), 7.39 (m, 1 H), 7.34–7.25 (m, 7 H), 5.69 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 162.0, 137.4, 136.7, 133.9, 132.8, 129.6, 129.2, 128.9, 128.1, 127.3, 126.6, 125.5, 123.4, 122.6, 121.7, 119.6, 116.1, 46.5.

MS (EI, 70 eV): m/z (%) = 91 (100), 285 (M<sup>+</sup>, 90), 179 (37), 284 (32).

Anal. Calcd for  $C_{20}H_{15}NO$ : C, 84.19; H, 5.30; N, 4.91. Found: C, 83.80; H, 5.69; N, 4.66.

#### 4b

White solid; mp 184-185 °C.

IR (KBr): 1639, 1601, 1439, 1324, 746, 708 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.57 (d, *J* = 8.5 Hz, 1 H), 8.27 (s, 1 H), 8.21 (d, *J* = 8.0 Hz, 1 H), 7.58 (d, *J* = 8.9 Hz, 1 H), 7.43 (m, 1 H), 7.34–7.26 (m, 7 H), 5.66 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 161.3, 139.6, 137.8, 136.4, 123.4, 131.1, 130.3, 128.9, 128.5, 127.4, 126.6, 123.9, 123.5, 122.8, 121.7, 118.5, 116.2, 46.6.

MS (EI, 70 eV): m/z (%) = 91 (100), 319 (M<sup>+</sup>, 30), 213 (18), 65 (17).

Anal. Calcd for C<sub>20</sub>H<sub>14</sub>ClNO: C, 75.12; H, 4.41; N, 4.38. Found: C, 74.88; H, 4.66; N, 4.89.

## 4c

White solid; mp 157–158 °C.

IR (KBr): 1644, 1608, 1443, 1185, 745 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.65 (m, 1 H), 8.15 (d, *J* = 7.6 Hz, 1 H), 7.91 (d, *J* = 8.8 Hz, 1 H), 7.42 (m, 1 H), 7.35–7.26 (m, 8 H), 5.66 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 165.8 (d, *J* = 252.5 Hz), 161.2, 137.9, 136.6, 136.5, 132.5 (d, *J* = 9.8 Hz), 130.4, 128.9, 127.3, 126.6, 123.6, 122.7, 122.1, 118.8, 116.5, 116.2, 107.7 (d, *J* = 23.3 Hz), 46.5.

<sup>19</sup>F NMR (CDCl<sub>3</sub>):  $\delta = -105.9$ .

MS (EI, 70 eV): m/z (%) = 91 (100), 303 (M<sup>+</sup>, 39), 197 (26), 65 (81).

Anal. Calcd for  $C_{20}H_{14}FNO$ : C, 79.19; H, 4.65; N, 4.62. Found: C, 78.80; H, 3.99; N, 4.69.

## 4d

White solid; mp 159-160 °C.

IR (KBr): 1639, 1608, 1452, 1439, 750 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.58 (d, *J* = 8.8 Hz, 1 H), 8.21 (d, *J* = 7.9 Hz, 1 H), 7.67 (s, 1 H), 7.40–7.18 (m, 9 H), 5.66 (br s, 2 H), 4.01 (s, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 163.1, 161.6, 137.8, 136.7, 135.7, 131.3, 129.6, 128.7, 127.1, 126.5, 123.3, 122.3, 119.3, 119.1, 116.0, 115.9, 104.5, 55.5, 46.3.

MS (EI, 70 eV): m/z (%) = 91 (100), 315 (M<sup>+</sup>, 65), 314 (44), 209 (36).

Anal. Calcd for  $C_{21}H_{17}NO_2$ : C, 79.98; H, 5.43; N, 4.44. Found: C, 79.80; H, 5.31; N, 4.69.

## 4e

Pale yellow solid; mp 231-232 °C.

IR (KBr): 1632, 1609, 1354, 1314, 748 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.47 (d, *J* = 8.9 Hz, 1 H), 8.25 (d, *J* = 7.8 Hz, 1 H), 7.37–7.22 (m, 9 H), 7.03 (d, *J* = 8.9 Hz, 1 H), 5.66 (br s, 2 H), 3.20 (s, 6 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 162.1, 153.1, 138.0, 137.3, 135.2, 130.7, 129.2, 128.8, 127.0, 126.6, 123.1, 122.0, 119.9, 116.0, 114.9, 113.5, 102.6, 46.1, 40.4.

MS (EI, 70 eV): m/z (%) = 328 (M<sup>+</sup>, 100), 327 (73), 91 (60), 222 (32).

Anal. Calcd for  $C_{22}H_{20}N_2O;\,C,\,80.46;\,H,\,6.14;\,N,\,8.53.$  Found: C,  $84.11;\,H,\,5.99;\,N,\,8.41.$ 

## 4f

White solid; mp 170–171 °C.

IR (KBr): 1638, 1612, 1440, 751, 700 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.71 (d, *J* = 8.3 Hz, 1 H), 8.51 (s, 1 H), 8.40 (d, *J* = 7.5 Hz, 1 H), 7.87 (d, *J* = 7.9 Hz, 1 H), 7.78 (m, 2 H), 7.58–7.26 (m, 11 H), 5.72 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 161.9, 145.6, 140.5, 137.7, 134.2, 129.9, 129.7, 129.1, 128.9, 128.4, 127.6, 127.3, 127.26, 126.6, 124.4, 123.4, 122.6, 120.3, 119.6, 116.2, 46.5.

MS (EI, 70 eV): m/z (%) = 91 (100), 361 (M<sup>+</sup>, 60), 360 (37), 255 (36).

Anal. Calcd for  $C_{26}H_{19}NO$ : C, 86.40; H, 5.30; N, 3.88. Found: C, 86.11; H, 5.12; N, 3.89.

## 4g

White solid; mp 125–126 °C.

IR (KBr): 1655, 1301, 1232, 752 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.75 (dd, *J* = 2.7, 8.0 Hz, 1 H), 8.52 (d, *J* = 8.8 Hz, 1 H), 7.56 (m, 2 H), 7.42 (m, 2 H), 7.36–7.24 (m, 7 H), 5.69 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 160.9 (d, J = 3.0 Hz), 160.0 (d, J = 253.9 Hz), 137.2, 136.4, 129.7 (d, J = 2.2 Hz), 128.9, 128.3 (d, J = 2.8 Hz), 128.2 (d, J = 17.9 Hz), 127.8 (d, J = 3.3 Hz), 127.3, 126.5, 125.3 (d, J = 3.4 Hz), 123.0, 122.7 (d, J = 8.7 Hz), 120.2 (d, J = 24.4 Hz), 117.3 (d, J = 5.5 Hz), 115.8, 46.9.

<sup>19</sup>F NMR (CDCl<sub>3</sub>):  $\delta = -110.8$ .

MS (EI, 70 eV): m/z (%) = 91 (100), 303 (M<sup>+</sup>, 43), 197 (24), 65 (16).

Anal. Calcd for C<sub>20</sub>H<sub>14</sub>FNO: C, 79.19; H, 4.65; N, 4.62. Found: C, 78.89; H, 4.55; N, 4.51.

## 4h

White solid; mp 170–171 °C.

IR (KBr): 1643, 1597, 1306, 745, 734 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.26 (t, *J* = 7.9 Hz, 2 H), 7.66 (m, 2 H), 7.42 (m, 1 H), 7.32–7.25 (m, 7 H).

 $^{13}\text{C}$  NMR (CDCl<sub>3</sub>):  $\delta$  = 160.9, 138.8, 137.6, 136.2, 136.1, 132.7, 130.9, 130.1, 128.9, 127.7, 125.4, 123.9, 123.7, 121.6, 121.4, 118.8, 117.7, 48.2.

MS (EI, 70 eV): m/z (%) = 91 (100), 319 (M<sup>+</sup>, 43), 213 (35), 318 (15), 321 (15).

Anal. Calcd for C<sub>20</sub>H<sub>14</sub>ClNO: C, 75.12; H, 4.41; N, 4.38. Found: C, 75.01; H, 4.48; N, 4.23.

## 4i

White solid; mp 162–163 °C.

IR (KBr): 1639, 1606, 1589, 1380, 1345, 1063, 747 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 9.21 (d, *J* = 8.4 Hz, 1 H), 7.82 (s, 1 H), 7.33–7.23 (m, 7 H), 6.91 (s, 1 H), 5.70 (br s, 2 H), 4.05 (s, 3 H), 3.99 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 161.5, 159.5, 158.9, 136.6, 135.8, 128.7, 128.4, 127.9, 127.6, 127.1, 126.5, 122.3, 119.6, 117.9, 115.2, 104.7, 101.9, 55.9, 55.6, 47.0.

MS (EI, 70 eV): m/z (%) = 91 (100), 345 (M<sup>+</sup>, 78), 226 (22), 344 (21), 239 (20).

Anal. Calcd for  $C_{22}H_{19}NO_3$ : C, 76.50; H, 5.54; N, 4.06. Found: C, 76.11; H, 5.33; N, 3.99.

## 4j

Pale yellow solid; mp 114–115 °C.

IR (KBr): 1644, 1607, 1376, 1151, 729 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.90 (s, 1 H), 7.69 (s, 1 H), 7.26 (t, *J* = 6.9 Hz, 2 H), 7.18 (m, 1 H), 7.11 (d, *J* = 7.2 Hz, 2 H), 7.03 (s, 1 H), 6.89 (s, 1 H), 5.61 (br s, 2 H), 4.06 (s, 3 H), 3.95 (s, 3 H), 2.50 (s, 3 H), 2.42 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 164.02, 159.38, 158.62, 138.7, 135.4, 133.4, 131.9, 129.0, 128.5, 126.6, 126.1, 125.7, 125.1, 122.0, 118.3, 104.9, 101.9, 56.1, 55.7, 52.6, 23.9, 21.2.

MS (EI, 70 eV): m/z (%) = 282 (100), 91 (71), 267 (22), 344 (M -29.4).

Anal. Calcd for C<sub>24</sub>H<sub>23</sub>NO<sub>3</sub>: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.11; H, 6.33; N, 3.78.

#### 4k

White solid; mp 170-171 °C.

IR (KBr): 1649, 1614, 1323, 858, 733 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.54 (dd, J = 6.2, 8.8 Hz, 1 H), 7.89 (dd, *J* = 2.3, 10.7 Hz, 1 H), 7.85 (s, 1 H), 7.31–7.21 (m, 4 H), 7.13–7.11 (m, 3 H), 5.66 (br s, 2 H), 2.52 (s, 3 H), 2.43 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 163.6 (d, J = 254.1 Hz), 163.5, 136.9, 136.4, 136.1, 133.5 (d, *J* = 8.9 Hz), 131.6, 129.9 (d, *J* = 10.1 Hz), 128.3, 126.9, 124.7, 123.1, 122.0, 117.8, 116.1, 113.0 (d, *J* = 23.3 Hz), 108.1 (d, J = 22.8 Hz), 48.5, 20.1, 24.8.

<sup>19</sup>F NMR (CDCl<sub>3</sub>):  $\delta = -105.8$ .

MS (EI, 70 eV): *m/z* (%) = 91 (100), 240 (53), 331 (M<sup>+</sup>, 33), 225 (24).

Anal. Calcd for C<sub>22</sub>H<sub>18</sub>FNO: C, 79.74; H, 5.47; N, 4.23. Found: C, 79.89; H, 5.55; N, 4.11.

#### 41

White solid; mp 180-181 °C.

IR (KBr): 1636, 1609, 1453, 1237 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.46 (d, J = 8.8 Hz, 1 H), 7.90 (s, 1 H), 7.66 (s, 1 H), 7.28 (t, J = 5.8 Hz, 2 H), 7.21–7.09 (m, 5 H), 5.65 (br s, 2 H), 4.02 (s, 3 H), 2.51 (s, 3 H), 2.43 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 163.9, 163.2, 138.9, 137.3, 136.2, 135.7, 132.0, 131.2, 128.5, 126.5, 125.9, 125.8, 121.8, 121.3, 119.3, 115.7, 104.9, 55.6, 51.3, 23.9, 20.7.

MS (EI, 70 eV): m/z (%) = 252 (100), 91 (87), 343 (M<sup>+</sup>, 52), 237 (33), 253 (18)

Anal. Calcd for C<sub>23</sub>H<sub>21</sub>NO<sub>2</sub>: C, 80.44; H, 6.16; N, 4.08. Found: C, 80.01; H, 6.09; N, 4.21.

#### 4m

White solid; mp 158-159 °C.

IR (KBr): 1650, 1613, 1328, 698 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.70 (d, J = 8.3 Hz, 1 H), 8.48 (s, 1 H), 8.16 (s, 1 H), 7.85 (dd, *J* = 1.4, 7.3 Hz, 1 H), 7.79 (d, *J* = 7.2 Hz, 2 H), 7.57 (t, J = 7.3 Hz, 2 H), 7.49 (m, 2 H), 7.33–7.23 (m, 7 H), 5.68 (br s, 2 H), 2.47 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 161.7, 145.5, 140.5, 136.8, 135.5, 134.2, 132.1, 130.8, 129.9, 129.1, 128.9, 128.4, 127.7, 127.2, 127.1, 126.6, 124.4, 123.5, 120.2, 119.4, 116.1, 46.5, 21.0.

MS (EI, 70 eV): m/z (%) = 91 (100), 375 (M<sup>+</sup>, 68), 270 (33), 212 (19).

Anal. Calcd for C<sub>27</sub>H<sub>21</sub>NO: C, 86.37; H, 5.64; N, 3.73. Found: C, 86.99; H, 5.75; N, 3.66.

## 4n

White solid; mp 159–160 °C.

IR (KBr): 1645, 1602, 1327, 730 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 8.56$  (d, J = 8.0 Hz, 1 H), 8.27 (s, 1 H), 8.00 (s, 1 H), 7.57 (d, J = 7.2 Hz, 1 H), 7.33–7.20 (m, 7 H), 5.65 (br s, 2 H), 2.46 (s, 3 H).

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<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 161.2, 139.4, 136.5, 135.7, 135.2, 132.3, 131.4, 131.1, 128.9, 128.3, 127.3, 126.5, 123.9, 123.6, 121.6, 118.3, 116.1, 46.4, 20.9.

MS (EI, 70 eV): *m/z* (%) = 91 (100), 333 (M<sup>+</sup>, 31), 227 (19), 332 (13).

Anal. Calcd for C<sub>21</sub>H<sub>16</sub>ClNO: C, 75.56; H, 4.83; N, 4.20. Found: C, 75.69; H, 4.75; N, 4.21.

#### 40

White solid; mp 179-180 °C.

IR (KBr): 1679, 1660, 1608, 1247 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.81 (s, 1 H), 8.76 (dd, J = 1.2, 7.6 Hz, 1 H), 7.99 (dd, J = 3.2, 8.8 Hz, 2 H), 7.39–7.25 (m, 7 H), 5.69 (br s, 2 H), 2.68 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 196.4, 167.3 (d, J = 254.3 Hz), 161.3, 141.2, 136.2 (d, J = 9.7 Hz), 135.9, 132,7 (d, J = 10.1 Hz), 131.5, 130.2, 129.0, 127.6, 126.5, 124.2, 122.1, 118.7, 117.0 (d, *J* = 22.8 Hz), 116.2, 108.1 (d, J = 23.6 Hz), 46.7, 26.5.

<sup>19</sup>F NMR (CDCl<sub>3</sub>):  $\delta = -104.2$ .

MS (EI, 70 eV): m/z (%) = 91 (100), 345 (M<sup>+</sup>, 29), 239 (16).

Anal. Calcd for  $C_{22}H_{16}FNO_2$ : C, 76.51; H, 4.67; N, 4.06. Found: C, 76.39; H, 4.55; N, 4.12.

## 4p

Pale yellow solid; mp 195-196 °C.

IR (KBr): 1648, 1610, 1239, 1021 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 8.55$  (d, J = 8.8 Hz, 1 H), 8.14 (s, 1 H), 7.57 (s, 1 H), 7.57–7.20 (m, 8 H), 5.63 (br s, 2 H), 4.03 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 163.3, 161.3, 136.3, 136.28, 134.5, 131.4, 129.4, 128.8, 127.9, 127.3, 126.4, 122.9, 120.7, 119.2, 117.4, 116.7, 104.5, 55.6, 46.3.

MS (EI, 70 eV): m/z (%) = 91 (100), 349 (M<sup>+</sup>, 33), 243 (20), 65 (16).

Anal. Calcd for C<sub>21</sub>H<sub>16</sub>ClNO<sub>2</sub>: C, 72.10; H, 4.61; N, 4.00. Found: C, 72.01; H, 4.39; N, 4.25.

#### 4q

White solid; mp 150-151 °C.

IR (KBr): 1656, 1617, 1589, 1431, 1345, 1327, 747 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 8.64$  (dd, J = 2.3, 7.6 Hz, 1 H), 8.08 (s, 1 H), 7.82 (dd, *J* = 1.1, 7.9 Hz, 1 H), 7.37–7.22 (m, 8 H), 5.63 (br s, 2 H), 4.05 (s, 3 H), 3.99 (s, 3 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 165.9 (d, J = 253.5 Hz), 160.9, 136.4, 136.1, 135.3 (d, J = 9.5 Hz), 132.6 (d, J = 9.6 Hz), 130.2, 129.0, 128.5, 127.5, 126.5, 123.3, 122.3, 120.1, 117.6, 117.0 (d, *J* = 22.8 Hz), 107.9 (d, J = 23.5 Hz), 46.5.

<sup>19</sup>F NMR (CDCl<sub>3</sub>): δ = -104.6.

MS (EI, 70 eV): m/z (%) = 91 (100), 337 (M<sup>+</sup>, 24), 231 (14), 65 (14).

Anal. Calcd for C<sub>20</sub>H<sub>13</sub>ClFNO: C, 71.12; H, 3.88; N, 4.15. Found: C, 71.54; H, 3.75; N, 4.55.

#### 4r

White solid; mp 167-168 °C.

IR (KBr): 1639, 1579, 1310, 713 cm<sup>-1</sup>.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 8.63 (d, J = 7.9 Hz, 1 H), 8.22 (s, 2 H), 7.80 (t, J = 7.5 Hz, 1 H), 7.67 (t, J = 7.3 Hz, 1 H) 7.34–7.22 (m, 7 H), 5.64 (br s, 2 H).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 161.6, 136.2, 135.9, 133.0, 132.7, 129.4, 129.3, 129.0, 128.8, 128.3, 127.4, 126.5, 125.6, 123.1, 121.8, 120.9, 117.5, 46.6.

MS (EI, 70 eV): m/z (%) = 91 (100), 319 (M<sup>+</sup>, 27), 213 (15), 65 (15). Anal. Calcd for C<sub>20</sub>H<sub>14</sub>ClNO: C, 75.12; H, 4.41; N, 4.38. Found: C, 75.25; H, 4.45; N, 4.65.

## Acknowledgment

Work carried out in the framework of FIRB 2003 supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica and by the University 'La Sapienza'.

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